Navigate references by clicking on the desired chart.

Use the "Table of Contents" bookmark to return.

MUSCULOSKELETAL & CONNECTIVE TISSUE

NEUROLOGY

OBSTETRICS & GYNECOLOGY

OVER THE COUNTER (OTC) & HERBAL MEDICATIONS

PSYCHIATRY

RESPIRATORY

SMOKING CESSATION

MISCELLANEOUS

INDICES

Other Online EBM Resources/Links:

EBM Portal Links (SK): http://web.mac.com/malees/Primary_Care_Portal/EBM.html; Evidence Updates service: http://plus.mcmaster.ca/EvidenceUpdates/Default.aspx

General: U of T: http://www.cebm.utoronto.ca/; Oxford: http://www.cebm.net/?o=1011; McMasters: How to teach evidence based clinical practice – Links: http://hsl.mcmaster.ca/ebcp/. Dynamed: *www.ebscohost.com/dynamed/*

User's Guide: UofA, Centre for Health Evidence: http://www.cche.net/usersguides/main.asp; UBC: http://www.ti.ubc.ca/; Grey Literature Searching: http://www.cadth.ca/index.php/en/cadth/products/grey-matters

ScHARR Intro to Evidence Based Practice (Sheffield, UK) http://www.shef.ac.uk/scharr/ir/netting/; BMJ – Clinical Evidence Links: http://clinicalevidence.bmj.com/ceweb/resources/useful_links.jsp; NNTs http://www.thennt.com/

Clinical significance CALCULATORS: UBC: http://spph.ubc.ca/sites/healthcare/files/calc/clinsig.html; Wisconsin: http://intsmain.is.mcw.edu/clincalc/bayes.html. Essential Evidence Plus: http://www.essentialevidenceplus.com/

Dalhousie Katie Clinical Significance Calculator: http://ktcalc.cme.dal.ca/site/login.php

RxFiles – Select Trial Summaries (more available online at www.RxFiles.ca)

Diabetes: Landmark Trials Summary: Glucose: http://www.rxfiles.ca/rxfiles/uploads/documents/CHT-Diabetes-Landmark-Trials-Links.pdf

Landmark Trials Summary: NON-Glucose: http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-DIABETES-Landmark-Trials-Non-Glucose.pdf

ACCORD-ADVANCE Comparison: http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-A1C-ACCORD-vs-ADVANCE-COMPARISON.pdf

ACCORD-BP & LIPID: http://www.rxfiles.ca/rxfiles/uploads/documents/ACCORD-BP-Lipid-Trial-Overview.pdf

ACCORD: Glucose http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-Targets-ACCORD-A1C.pdf

ADVANCE: http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-ADVANCE-trial.pdf

AVANDIA & CV risk – Meta-analysis: http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-Avandia-CV-Meta-Comments.pdf

DREAM: http://www.rxfiles.ca/rxfiles/uploads/documents/Dream-QandA.pdf

RECORD:http://www.rxfiles.ca/rxfiles/uploads/documents/Diabetes-RECORD-Trial-Summary.pdf

Hypertension: Summary Table: http://www.rxfiles.ca/rxfiles/uploads/documents/HTNLandmarkHypertensionTrials.pdf

ACCOMPLISH: http://www.rxfiles.ca/rxfiles/uploads/documents/HTN-QandA-Accomplish.pdf

ALLHAT: http://www.rxfiles.ca/rxfiles/uploads/documents/HTN-Update-2003-Final.pdf

ANBP2: http://www.rxfiles.ca/rxfiles/uploads/documents/HTN-QandA-ANBP2.pdf

ASCOT-BPLA: http://www.rxfiles.ca/rxfiles/uploads/documents/HTN-QandA-ASCOT.pdf

Trial Summary table - abridged: http://www.rxfiles.ca/rxfiles/uploads/documents/members/cht-HTN-trial-summary.pdf

HF: CHARM: http://www.rxfiles.ca/rxfiles/uploads/documents/CHARM-Comments.pdf

Hirsutism: http://www.rxfiles.ca/rxfiles/uploads/documents/members/Hirsutism%20Trial%20Summary.pdf

HRT: WHI: http://www.rxfiles.ca/rxfiles/uploads/documents/HRT Post-WHI-2002-Header.pdf

WHI & Age: http://www.rxfiles.ca/rxfiles/uploads/documents/HRT-Age-and-the-WHI.pdf ;

WHI & Extras/Perspectives on NNTs, NNHs: http://www.rxfiles.ca/rxfiles/uploads/documents/HRT-WHI-Extras-Perspectives.pdf

Lipid: Summary Table: http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-lipid agents-major trials.pdf

& Q&A 2004: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-QandA-Update-Oct04.pdf

AIM-HIGH: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-AIM-HIGH-nicotinic-acid-Niaspan-trial.pdf

ASCOT-LLA: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-QandA-ASCOT.pdf

CARDS: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-QandA-CARDS.pdf

ENHANCE: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-ENHANCE trial overview.pdf

IDEAL: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-QandA-IDEAL.pdf

JUPITER: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-Jupiter-trial-overview.pdf

PROVE-IT: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-QandA-Prove-It.pdf

SHARP: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-Sharp-CKD-trial.pdf

SPARCL: http://www.rxfiles.ca/rxfiles/uploads/documents/Lipid-QandA-SPARCL.pdf

Thrombotic (antithrombotics: ASA, clopidogrel, anticoagulants: warfarin) :

ACTIVE-A & ACTIVE-W trials http://www.rxfiles.ca/rxfiles/uploads/documents/ACTIVE-A-Trial-Summary.pdf

Antithrombotics Summary Chart:: http://www.rxfiles.ca/rxfiles/uploads/documents/members/cht-AntiThrombotics.pdf

CHARISMA: http://www.rxfiles.ca/rxfiles/uploads/documents/Charisma-Q&A.pdf

Clopidogrel-PPI drug interaction: http://www.rxfiles.ca/rxfiles/uploads/documents/Clopidogrel-PPI-interaction-QandA.pdf

RE-LY: Dabigatran vs warfarin in Atrial Fibrillation http://www.rxfiles.ca/rxfiles/uploads/documents/RE-LY-Trial-Dabigatran.pdf

ROCKET-AF: Rivaroxaban vs warfarin in A Fib: http://www.rxfiles.ca/rxfiles/uploads/documents/ROCKET-AF-Rivaroxaban.pdf

ARISTOTLE: Apixaban vs warfarin in A Fib: http://www.rxfiles.ca/rxfiles/uploads/documents/ARISTOTLE-AF-Apixaban.pdf

MISC.:

Catie-AD: Atypical Antipsychotics in Patients with Alzheimer's http://www.rxfiles.ca/rxfiles/uploads/documents/Psych-CATIE-AD-trial-summary.pdf

Meloxicam: SELECT, MELISSA; *celecoxib* CLASS, *rofecoxib* VIGOR,: http://www.rxfiles.ca/rxfiles/uploads/documents/QandA-Meloxicam-2.pdf

OAB: Darifenacin-Oxybutynin Memory Trial : http://www.rxfiles.ca/rxfiles/uploads/documents/UI-Darifenacin-Kay-Trial-QandA.pdf

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2009 Canadian -10yr risk of Cardiovascular (CVD) disease (based on Framingham Heart Study).

RISK*	MEN									
AGE	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75+
Age points	0	2	5	7	8	10	11	12 or 13	14	15
TOTAL CHOL										
<4.1 mmol/l						0				
4.1-5.2						1				
5.2-6.2						2				
6.2-7.2						3				
≥ 7.2						4				
HDL mmol/l	<0.9		0.9-1.2		1.2-1.3	1.3-1.6		≥1.6		
	+2		+1		0	-1		-2		
	Not Treated					Treated				
SYSTOLIC BP	<120	-2				<120	0			
	120-129	0				120-129	2			
	130-139	1				130-139	3			
mmHg	140-159	2				140-159	4			
	≥160	3				≥160	5			
SMOKER										
No						0				
Yes						4				
Diabetic										
No						0				
Yes						3				
TOTAL POINTS										

Guidelines use "13" but this appears to be an error; should be "12" .based on reference.

POINTS	MEN: actual 10yr CVD risk %												
<3	-2-1	2-3	4-5	6	7	8	9	10	11	12	13-14	15-16	>17
<1% (10yr % Risk→)	1	2	3	4	5	6	7	9	11	13	15-18	21-25	>29

WOMEN										
30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75+
0	2	4	5	7	8	9	10	11	12
				0					
				1					
				3					
				4					
				5					
<0.9		0.9-1.2		1.2-1.3		1.3-1.6		≥1.6	
+2		+1		0		-1		-2	
	Not Treated					Treated			
<120	-3					<120	-1		
120-129	0					120-129	2		
130-139	1					130-139	3		
140-149	2					140-149	5		
150-159	4					150-159	6		
>160	5					>160	7		
				0					
				3					
				0					
				4					

POINTS	WOMEN actual 10yr CVD risk %												
<-2	-1-2	3-5	6-7	8-9	10	11	12	13	14-15	16-17	18-20	≥21
<1% (10yr % Risk→)	1	2	3	4-5	6	7	8	10	11-13	15-18	21-27	≥30

Key: Low risk <10% Moderate risk 10-19% High risk ≥ 20%

*Risk assessments based on Framingham data; other risk factors such as **family history** of CAD (2x CAD 10yr risk %=actual risk %), physical inactivity, obesity & left ventricular hypertrophy should also be considered.

Patients with **High risk→ ALL pts with CAD,CVD,PAD; most with DIABETES** age >40 or >30 with 15yr hx DM **& chronic renal dx** GFR <30ml/min regardless of risk score.

Cardiac Risk Tools: 1) www.statcoder.com 2) www.nhlbi.nih.gov/guidelines **3) http://www.framinghamheartstudy.org/**

4) Reynold Risk Score (also incorporates family cardiac history & CRP results, but is based on non-diabetic individuals) **http://www.reynoldsriskscore.org/**

5) Cardiovascular Life Expectancy Model Risk Score (also incorporates family cardiac history) **http://www.chiprehab.com/**

6) Cardiovascular Disease Risk Calculator: **http://bestsciencemedicine.com/chd/calc2.html**

7) AHA'13 CV Risk Calculator **http://my.americanheart.org/professional/StatementsGuidelines/PreventionGuidelines/Prevention-Guidelines_UCM_457698_SubHomePage.jsp**

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9) Systemic Cerebrovascular and Coronary Risk Evaluation (SCORE) risk calculator: http://www.score-canada.ca/

10) Patient friendly risk calculator: http://www.myhealthcheckup.com

For suggested lipid targets, see bottom of page 15 on the RxFiles Lipid chart.

Comparative 10yr CAD % risks by AGE		30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74yr
Males	**Low** risk % →	2%	3	4	4	6	7	9	11	14
	Average risk % →	3%	5	7	11	14	16	21	25	30
Females	**Low** risk % →	<1%	<1	2	3	5	7	8	8	8
	Average risk % →	<1%	<1	2	5	8	12	12	13	14

Risk	TC /HDL
High	<4
Mod	>5
Low	>6

Previous TC/HDL ratio thresholds used in previous risk assessments.

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FDA June/10 June 14, 2010 (Washington, DC) — The FDA is conducting a safety review of the angiotensin receptor blocker **olmesartan** (Benicar, Daiichi Sankyo) after determining that diabetic patients taking the drug in two completed phase 3 trials may have had an excess risk of **cardiovascular death**, the regulatory body has announced [1].The safety announcement says that the FDA's review is "ongoing, and the agency has not concluded that Benicar increases the risk of death. FDA currently believes that the benefits of Benicar in patients with high blood pressure continue to outweigh its potential risks." The agency also notes that "other controlled clinical trials evaluating Benicar and other ARBs have not suggested an increased risk of cardiovascular-related death."The primary end points of the two trials were dominated by measures of renal function.In the Randomized Olmesartan and Diabetes Microalbuminuria Prevention (ROADMAP) study, conducted in Europe, 4447 patients with diabetes and at least one additional cardiovascular risk factor, but no evidence of renal dysfunction, were randomized to receive either olmesartan at 40 mg/day (n=2232) or placebo (n=2215). The trial, sponsored by Sankyo Pharma, ended in July 2009 [2]. In the Olmesartan Reducing Incidence of End Stage Renal Disease in Diabetic Nephropathy Trial (ORIENT), conduced in Japan and Hong Kong, 566 patients with diabetes and renal dysfunction were randomized to receive olmesartan at 10 mg/day to 40 mg/day (n=282) or placebo (n=284).

FDA June/11 Food and Drug Administration drug safety: **No increase in risk of cancer** with certain blood pressure drugs—**angiotensin receptor blockers (ARBs).** June 2, 2011.

http://www.fda.gov/Drugs/DrugSafety/ucm257516.htm
FDA Apr/12 notified healthcare professionals of possible risks when using blood pressure medicines containing aliskiren with other drugs called angiotensin converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) in patients with diabetes or kidney (renal) impairment. (Altitude study)
FDA July/13 is warning that the blood pressure drug **Olmesartan** Medoxomil (marketed as Benicar, Benicar HCTZ, Azor, Tribenzor, and generics) can cause intestinal problems known as sprue-like enteropathy. Symptoms of **sprue-like enteropathy** include severe, chronic diarrhea with substantial weight loss. FDA has approved changes to the labels of these drugs to include this concern. Sprue-like enteropathy has not been detected with ARB drugs other than olmesartan.
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Health Canada Feb/14 wishes to inform healthcare professionals and patients of the risks associated with **combining more than one of the following blood pressure medicines**: aliskiren (renin inhibitor), angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs).
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Thiazide Like Diuretics and Miscellaneous Antihypertensives

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Antihypertensives: Landmark & Recent Trials – Summary

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What is bridging? What does it attempt to do?

"Bridging anticoagulation refers to giving a short-acting anticoagulant, typically low-molecular-weight heparin (LMWH), before and after surgery to minimize the time that patients are not anticoagulated, and thereby minimize the risk for thromboembolism."[2]

Sub Q or SC or SQ? Loren? Preference for RxFiles? – Thrombosis Canada uses SC LMWH

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ç=scored tab ☎=EDS in SK ✘ =Non formulary in SK ✆=prior approval for NIHB ⊗=not covered by NIHB ▼ =covered by NIHB **#**=facture **1º**=primary **2º**=secondary ♂=male ♀=female **ACEI**=angiotensin converting enzyme inhibitor **AF**=atrial fibrillation **ASA**=acetylsalicylic acid **ACS**=acute coronary syndrome **AVR**=atrial valve repair **ASx**=asymptomatic **BMS**=bare metal stent **BP**=blood pressure **CABG**=coronary artery bypass graft **CAD**=coronary artery dx **CBC**=complete blood count **CBZ**=carbamazepine **CVD**=cardiovascular dx **D/C**=discontinue **DES**=drug eluting stent **Dx**=disease **DVT**=deep vein thrombosis **EC**=enteric coated **EF**=ejection fraction **fx**=function **GI**=gastrointestinal **HA**=headache **HF**=heart failure **HIT**=heparin-induced thrombocytopenia **HR**=heart rate **HTN**=hypertension **Hx**=history **ICH**=intracranial hemorrhage **LDUH**=low dose unfractionated heparin **LFT**=liver function test **LMWH**=low molecular weight heparin **LV**=left ventricular **LVH**=left ventricular hypertrophy **MHV**=mechanical heart valve **MI**=myocardial infarction **MOA**=mechanism of action **MVP**=mitral valve prolapse **MVR**=mital valve repair **MVS**=mitral valve strands **NNH/T**=number needed to harm/treat **NS**=non-significant **NSR**=normal sinus rhythm **OAC**=oral anticoagulant **OTC**=over the counter **PAD**=peripheral artery disease **PCI**=percutaneous coronary intervention **PE**=pulmonary embolism **PFO**=patent foramen ovale **P-gp**=P-glycoprotein **PK**=pharmacokinetics **Pts**=patients **RR**=relative risk **sx**=surgery **TIA**=transient ischaemic attack **THA**=total hip arthroplasty **TKA**=total knee arthroplasty **TTP**=Thrombotic thrombocytopenic purpura **tx**=treatment **VTE**=venous thromboembolism **WBC**=white blood cell **wt**=weight **wks**=weeks

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EAFT (European Atrial Fibrillation Trial) Study Group. Secondary prevention in non-rheumatic atrial fi brillation after transient ischaemic attack or minor stroke. Lancet 1993; 342: 1255–62.
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a bad cardiovascular outcome (relative risk = 1.22; 95% CI, 1.0 - 1.5). (LOE = 1b))
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136. Effects of Fondaparinux on Mortality and Reinfarction in Patients With Acute ST-Segment Elevation Myocardial Infarction: The **OASIS-6** Randomized Trial. JAMA. 2006 Mar 14; [Epub ahead of print] CONCLUSION: In patients with STEMI, particularly those not undergoing primary percutaneous coronary intervention, **fondaparinux** significantly reduces mortality & reinfarction without increasing bleeding and strokes. (InfoPOEMs: Fondaparinux (Arixtra) reduces the risk of mortality and reinfarction without increasing the risk of severe bleeding events in patients with acute ST-segment elevation myocardial infarction. Patients undergoing primary percutaneous coronary intervention (PCI) received no additional benefit from fondaparinux compared with unfractionated heparin (UFH). (LOE = 1b-)) Mehta SR, et al.; ASPIRE Investigators. Randomized, blinded trial comparing fondaparinux with unfractionated heparin in patients undergoing contemporary percutaneous coronary intervention: Arixtra Study in Percutaneous Coronary Intervention: a Randomized Evaluation (ASPIRE) Pilot Trial. Circulation. 2005 Mar 22;111(11):1390-7.
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Furie Karen L., Kasner Scott E., Adams Robert J., et al., and on behalf of the American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council on Clinical Cardiology, and Interdisciplinary Council on Quality of Care and Outcomes Research. Guidelines for the **Prevention of Stroke in Patients With Stroke or Transient Ischemic Attack**. (Secondary Prevention) A Guideline for Healthcare Professionals From the American Heart Association (AHA)/American Stroke Association (ASA). Stroke published October 21, 2010, doi:10.1161/STR.0b013e3181f7d043. http://stroke.ahajournals.org/cgi/reprint/STR.0b013e3181f7d043v1
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Chandra D, Parisini E, and Mozaffarian D. **Travel** and risk for venous thromboembolism. Ann Intern Med 2009.
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http://www.cadth.ca/media/pdf/OP0508_warfarin_rec-report_e.pdf
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Brain Natriuretic Peptide (BNP) has diagnostic value for both types of HF and is recommended where available, when diagnosis in unclear. The use of BNP in non-acute HF and community outpatient practice remains to be clarified.[3]

Table: Brain natriuretic peptide (BNP mainly secreted by ventricular myocardium**) & prohormone of BNP (NT-proBNP** longer half life, affected by renal fx**) assay cut-off points for the diagnosis of HF** [3]

	Age	HF unlikely	HF possible but consider alternative diagnoses	HF very likely
BNP (pg/mL)	**All**	**<100**	**100-500**	**>500**
NT-proBNP (pg/mL)	**<50**	**<300**	**300-450**	**>450**
	50-75	**<300**	**300-900**	**>900**
	>75	**<300**	**300-1800**	**>1800**

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syndromes (2.1 years of follow-up) and 3 evaluated 30,953 patients with stable coronary artery disease (5.8 years of follow-up). After 1 year of treatment, the LDL cholesterol levels decreased by an average 0.51 mmol/L (20 mg/dL). The annual rate of major vascular events cardiovascular death, nonfatal myocardial infarction, revascularization, or stroke) was 4.5% in the intensive therapy group and 5.3% in the less intense therapy group (number needed to treat [NNT] = 200 per year). Of the 14 trials comparing statin therapy with control (128,596 patients with 4.8 years of follow-up), 6 appear to be primary prevention studies and the remainder were for secondary prevention. In these 14 studies, after 1 year of treatment the LDL cholesterol levels decreased by 1.07 mmol/L (41 mg/dL). The annual rate of major vascular events was 2.8% in the patients taking statins compared with 3.6% in patients taking a control agent (NNT = 125 per year). Although they don't report the annual rate of death from any cause for each treatment group, the authors report the total death rate for the intensively treated patients plus the statin-treated patients (2.1%) compared with the rate of the less intensively treated patients plus control patients (2.3%). This works out to a number needed to treat of 500 per year. The authors also try to correlate the outcomes data with the LDL levels achieved by the various interventions. However, since none of the trials actually randomized patients to specific lipid targets, this information should be interpreted cautiously and is best used to generate hypotheses. If you subscribe to the lipid theory of atherogenesis, you will love this part of the study. If you subscribe to alternate theories (eg, inflammation, plaque stability, and so forth) or are a methodologic purist, you will be annoyed by the authors' extrapolations.

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FDA June/11: Food and Drug Administration drug safety communication: New restrictions, contraindications, and dose limitations for Zocor (simvastatin) to reduce the risk of muscle injury. June 8, 2011. Limit using the 80-mg dose unless the patient has already been taking the drug for 12 months and there is no evidence of myopathy.
FDA Nov/11 notified healthcare professionals the cholesterol-lowering medicine Trilipix (fenofibric acid) may not lower a patient's risk of having a heart attack or stroke.
FDA Feb/12 has approved important safety label changes for the class of cholesterol-lowering drugs known as statins. The changes include removal of routine monitoring of liver enzymes from drug labels. Information about the potential for generally non-serious and reversible cognitive side effects and reports of increased blood sugar and glycosylated hemoglobin (HbA1c) levels has been added to the statin labels. The lovastatin label has been extensively updated with new contraindications and dose limitations when it is taken with certain medicines that can increase the risk for muscle injury.
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Health Canada Nov/12: Merck Canada Inc., in consultation with Health Canada, would like to inform you of important safety recommendations on dosage related to the increased risk of myopathy/rhabdomyolysis, particularly with the 80 mg dose of ZOCOR® (simvastatin; also marketed as generics). An increased risk of myopathy/rhabdomyolysis within the recommended dose range for ZOCOR® (simvastatin) can also be seen with concomitant administration of certain medications.
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QT PROLONGATION and TORSADES DE POINTES: DRUGS and SUDDEN DEATH

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FDA Feb/10 notified healthcare professionals and patients that it is reviewing clinical trial data about a potentially serious effect on the heart from the use of Invirase (saquinavir) in combination with Norvir (ritonavir), antiviral medications given together to treat HIV infection. The data suggest that together the two drugs may affect the electrical activity of the heart, known as prolonged QT or PR intervals.

FDA Nov/10 is requesting that manufacturers of the painkiller **propoxyphene** pull the drug from the market because of concerns over cardiotoxicity. (Propoxyphene is marketed alone as Darvon & combined with acetaminophen as Darvocet.) The agency's request is based on data showing that, even when taken at therapeutic doses, the drug can lead to potentially dangerous changes in the heart's electrical activity, including prolonged PR & QT intervals & widened QRS complex. FDA advises clinicians to stop prescribing propoxyphene and to ask current users to discontinue the drug. FDA's MedWatch alert

FDA Dec/10 The injectable form of dolasetron mesylate (Anzemet) should not be used to prevent nausea or vomiting related to chemotherapy because the drug increases the risk for torsade de pointes, the FDA announced on Friday. The FDA recommends against using Anzemet injections in patients with congenital long-QT syndrome. The warning does not apply to Anzemet tablets because the risks for developing an abnormal heart rhythm are not as high as with the injections. FDA MedWatch alert (Free)

FDA July/11 FDA has added a warning to the label of the atypical antipsychotic quetiapine (Seroquel) cautioning about potential increases in the QT interval. Postmarketing cases of QT prolongation have been reported in some 17 patients, according to the *New York Times.* These patients had overdosed on quetiapine, had other illnesses, or were taking other medications that can cause electrolyte imbalance or QT prolongation.

FDA Aug/11 The antidepressant citalopram (marketed as Celexa) should not be prescribed at doses above 40 mg/day because higher dosages can cause arrhythmias, the FDA has warned.

FDA Sep/11 The U.S. Food and Drug Administration (FDA) is informing the public of an ongoing safety review of the anti-nausea drug Zofran (ondansetron, ondansetron hydrochloride and their generics). Ondansetron may increase the risk of developing abnormal changes(QT prolongation & torsades) in the electrical activity of the heart.

FDA July/12 Alerting clinicians that a single 32-mg intravenous dose of ondansetron (Zofran and generics) may lead to QT interval prolongation, which in turn may put patients at risk for torsades de pointes.

FDA Dec/12 is working with the manufacturers of all **32 mg dose Ondansetron** Injectable Products (brand and generic) to voluntarily recall them from the market due to QT serious cardiac toxicity.

FDA Mar/13 is warning the public that **azithromycin (Zithromax or Zmax)** can cause abnormal changes in the electrical activity of the heart that may lead to a potentially fatal irregular heart rhythm. Patients at particular risk for developing this condition include those with known risk factors such as existing **QT interval prolongation**, low blood levels of potassium or magnesium, a slower than normal heart rate, or use of certain drugs used to treat abnormal heart rhythms, or arrhythmias.

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Health Canada Aug/10 **Droperidol** Injection USP is associated with severe arrhythmia (eg. QT) and the Canadian Monograph of this product has been updated to reflect this risk.

Health Canada Nov/10 **Darvon-N (dextropropoxyphene) - Recall and Withdrawal in Canada** - Paladin Labs Inc. Paladin Labs Inc. in collaboration with Health Canada would like to inform healthcare professionals of the voluntary recall and withdrawal of the opioid analgesic Darvon-N (dextropropoxyphene) in Canada. (widen the QRS complex, prolong the QT interval and therefore increase the risk of serious abnormal heart rhythms.)

Health Canada Feb/12 has recently approved vandetanib (CAPRELSA) to treat medullary thyroid cancer in adult patients where either the tumour cannot be removed by surgery or it has spread from the thyroid gland to other parts of the body. CAPRELSA can cause serious QT heart rhythm changes which may result in sudden death, if left untreated.

Health Canada Mar/12: **Domperidone** should be used at the lowest possible dose. The risk of serious ventricular arrhythmias and sudden cardiac death may be higher in patients taking daily doses greater than 30 mg, and in patients over 60 years old.

Health Canada Oct/12: Ondansetron can cause a dose-dependent prolongation of the electrocardiographic-corrected QT interval (QTc), which can lead to Torsade de Pointes, a potentially life-threatening heart rhythm abnormality. The new maximum recommended single intravenous (IV) dose of ZOFRAN ® is 16 mg infused over 15 minutes.

Health Canada Oct/13 has completed a safety review of the drug Sensipar (**cinacalcet**) that identified a possible link between the drug and abnormal heart rhythm (QT) associated with low blood calcium.

Health Canada Feb/14: **TELZIR** (fosamprenavir) should not be used with the antiarrhythmic drugs amiodarone, lidocaine (systemic), or quinidine, as this may cause serious and/or life-threatening reactions such as abnormal heart rhythm (arrhythmias). In addition, Telzir should not be used with delavirdine, another antiviral drug to treat HIV, because it may reduce the effectiveness of delavirdine.

Health Canada Mar/14: REMERON / REMERON RD (**mirtazapine**) – Abnormal Heart Rhythm - Merck Canada Inc. Cases of abnormal heart rhythm (eg. QT prolongation) have been reported with the antidepressant REMERON / REMERON RD (mirtazapine) mainly with drug overdose or when taking other drugs known to cause heart rhythm problems. The product information has been updated.

Health Canada Jun/14 Zofran (ondansetron) – Dosage and Administration of Intravenous Ondansetron in Geriatrics (>65 years of age) –

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GlaxoSmithKline Inc. Zofran (ondansetron) is associated with a risk of QT interval prolongation, which is expected to be greater with faster rate of infusion and larger doses for the intravenous administration. New dosing restrictions are recommended to mitigate this risk in elderly patients. The dosing restrictions for geriatrics are summarized below: In patients ≥75 years of age, the initial IV dose must not exceed 8 mg. In patients <75 years of age, the initial IV dose must not exceed 16 mg. Subsequent IV doses must not exceed 8 mg and may be given 4 and 8 hours after the initial dose. All IV doses must be diluted in 50–100 mL of saline or other compatible fluid. All IV doses must be infused over no less than 15 minutes.

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Recommendation 1 (Disclosure): Clinicians should inform patients of arrhythmia risk when they prescribe methadone. Recommendation 2 (Clinical History): Clinicians should ask patients about any history of structural heart disease, arrhythmia, and syncope. Recommendation 3 (Screening): Obtain a pretreatment electrocardiogram for all patients to measure the QTc interval and a follow-up electrocardiogram within 30 days and annually. Additional electrocardiography is recommended if the methadone dosage exceeds 100 mg/d or if patients have unexplained syncope or seizures. Recommendation 4 (Risk Stratification): If the QTc interval is greater than ms but less than 500 ms, discuss the potential risks and benefits with patients and monitor them more frequently. If the QTc interval exceeds 500 ms, consider discontinuing or reducing the methadone dose; eliminating contributing factors, such as drugs that promote hypokalemia; or using an alternative therapy. Recommendation 5 (Drug Interactions): Clinicians should be aware of interactions between methadone and other drugs that possess QT interval-prolonging properties or slow the elimination of methadone.

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Other acne drugs

	Salicylic Acid = SA▼x Oxy, Clearasil, Neutrogena, others Gels, lotions, toners, cleansers, sticks, pads, washes & astringents 0.5, 1, 2 & 3.5%	Common: less irritating than BPO, burning, stinging, pruritius & erythema Serious: rare systemic salicylate toxicity: nausea, vomiting, diarrhea, dizziness, loss of hearing, lethargy, psychic disturbances & hyperpnea ?protect from sun 8-12 weeks for noted improvement	√Used with topical retinoids to treat mild comedonal acne or 2nd line monotherapy agent[3] (also for seborrhea & psoriasis) ☒Not commonly recommended (less potent than equal strength BPO) DI: ↑ skin irritation or drying effect: Abrasive or medicated soaps or cleansers; Acne preps (e.g., BPO, Resorcinol, Sulfur, Tretinoin); alcohol-containing topicals (After-shave lotions, perfumed toiletries, cosmetics/soaps with a strong drying effect); Isotretinoin DAILY or BID, 3-6% is keratolytic , OTC: $10-15

Tetracycline Lactation Ratings: a more conservative approach was used for acne (i.e. safe/likely safe changed to caution) as lactation data is only available for short-term courses versus the 8-12 weeks of therapy for acne.

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November 8, 2006 -- QLT Inc. announced positive results of a Phase IV clinical trial of Aczone(TM) dapsone in more than 50 patients with G6PD deficiency that was performed to meet a post-approval commitment requested by the FDA. Mar/08 FDA removes G6PD screening & labeling requirements from the label. June 6/08 /CNW/ - QLT Inc. (NASDAQ: QLTI; TSX: QLT) announced today that Health Canada has completed its review of QLT USA, Inc.'s labeling supplement (SNDS) for Aczone(R) and has removed the glucose-6-phosphate dehydrogenase (G6PD) screening and blood monitoring requirements.

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For more information, topics and products see: **www.RxFiles.ca**

Web sites:
American Academy of Dermatology www.skincarephysicians.com/acnenet/FAQ.html www.aad.org/public/publications/pamphlets/common_acne.html?media=print
Medline Plus www.nlm.nih.gov/medlineplus/tutorials/acne/htm/index.htm
National Institute of Arthritis and Musculoskeletal and Skin Diseases www.niams.nih.gov/Health_Info/Acne/default.asp

EXTRAS:

Eczema in Children – NICE guideline approach http://www.nice.org.uk/guidance/index.jsp?action=byID&o=11636

Tx Escalator ⇑			
			Systemic treatment
			Phototherapy
		Bandages	Bandages
		Topical calcineurin inhibitors	Topical calcineurin inhibitors
	Mild potency corticosteroids	Mild potency corticosteroids	Mild potency corticosteroids
	emolliants	emolliants	emolliants
	Mild	**Moderate**	**Severe**
	Atopic ezema severity		

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Relative Absorption

Forearm	***1.0***
Sole	***0.14***
Back	***1.7***
Scalp	***3.5***
Forehead	***6.0***
Cheek	***13.0***
Scrotum	***42.0***

Cushing Syndrome (pituitary-adrenal axis suppression)**:**
- 50g of 0.05% clobetasol/wk or
- 500g of 1% hydrocortisone/wk
- in infants: a little as 1g/day x several days may ↓ HPA

Topical Corticosteroids: Comparison Chart

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Useful tables from Canadian Glaucoma Guidelines 2009:

Table 19—Staging each eye for glaucoma damage

Suspect	One or two of the following: IOP >21 mm Hg; suspicious disc or cup to disc (C/D) asymmetry of >0.2; suspicious 24-2 (or similar) VF defect
Early	Early glaucomatous disc features (e.g. C/D* <0.65) and (or) mild VF defect not within 10° of fixation (e.g. MD better than –6 dB on HVF 24-2)
Moderate	Moderate glaucomatous disc features (e.g. vertical C/D* 0.7–0.85) and (or) moderate VF defect not within 10° of fixation (e.g. MD from –6 to –12 dB on HVF 24-2)
Advanced	Advanced glaucomatous disc features (e.g. C/D* >0.9) and (or) VF defect within 10° of fixation† (e.g. MD worse than –12 dB on HVF 24-2)

Adapted from Damji et al.[160]

Please refer to text in order to decide whether a nerve exhibits characteristics of glaucomatous damage.
*Refers to vertical C/D ratio in an average size nerve. If the nerve is small, then a smaller C/D ratio may still be significant; conversely, a large
nerve may have a large vertical C/D ratio and still be within normal limits.
†Also consider baseline 10-2 VF (or similar)
Note: MD, mean deviation; HVF, Humphrey Visual Field Analyzer.

Table 20—Suggested upper limit of initial target IOP for each eye

Stage	Suggested upper limit of target IOP. Modify based on longevity, QOL and risk factors for progression	Evidence
Suspect in whom a clinical decision is made to treat	24 mm Hg with at least 20% reduction from baseline	OHTS,[47] EGPS[325]
Early	20 mm Hg with at least 25% reduction from baseline	EMGTS,[48] CIGTS[326]
Moderate	17 mm Hg with at least 30% reduction from baseline	CNTGS,[12] AGIS[11]
Advanced	14 mm Hg with at least 30% reduction from baseline	AGIS,[11] Odberg[327]

Adapted from Damji et al.[160]

Note: Target IOP may need to be adjusted during the course of follow-up. Extremes of CCT may be helpful in the setting of target IOP. For example, if the cornea is very thin, this may encourage a more aggressive approach with more frequent follow-up.[161]

Table 21—Advantages and disadvantages of single and combined cataract and glaucoma procedures

Procedure	Advantages	Disadvantages
Phacoemulsification alone	Quick procedure with more rapid visual recovery	Postoperative IOP spike is a potential risk, particularly in patients with advanced VF loss
	Improved vision, which benefits QOL	Not regarded as a consistent or powerful means of lowering IOP
	May lower IOP a small amount in some patients	IOP should be watched closely in both the early postoperative period and later
Trabeculectomy alone	Quicker than combined procedure	Will not improve vision
	May achieve superior long-term IOP lowering than combined procedure or cataract alone	May cause or worsen cataract
Combined procedure	Minimizes anesthetic risk by combining 2 procedures in 1	May not be as effective at long-term IOP control as trabeculectomy alone
	Convenience to patient with 1 trip to operating room rather than 2	Increased risk of complications with 2 procedures rather than 1
	Cost savings	Slower visual recovery than doing cataract alone
	May blunt potentially damaging postoperative IOP spikes in patients with advanced VF loss	
	Opportunity to improve IOP control and improve vision at the same time with enhanced QOL	

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Other drugs for Glaucoma:

- Osmotic Agents (used for acute rises in IOP)
    - Glycerol – onset 10 min; max effect in 1-2 hours
    - Mannitol – Onset 10-30min; max effect in 1 hour

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Bodybuilding.com and FDA Nov/09 notified healthcare professionals and patients of a nationwide and international recall of all lots and expiration dates of 65 dietary supplement products that were sold through the Company's website, www.bodybuilding.com. FDA believes that the recalled products contain the following ingredients that are currently classified, or the FDA believes should be classified, as steroids: **"Superdrol," "Madol," "Tren," "Androstenedione," and/or "Turinabol."** Acute liver injury is known to be a possible harmful effect of using steroid-containing products. In addition, steroids may cause other serious long-term adverse health consequences in men, women, and children. These include shrinkage of the testes and male infertility, masculinization of women, breast enlargement in males, short stature in children, a higher predilection to misuse other drugs and alcohol, adverse effects on blood lipid levels, and increased risk of heart attack, stroke, and death.

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FDA May/09 notified healthcare professionals that it will require two prescription topical testosterone gel products, AndroGel 1% and Testim 1%, to include a boxed warning on the products' labels after receiving reports of adverse effects in **children** who were **inadvertently exposed** to testosterone through contact with another person being treated with these products. Of the fully reviewed cases, adverse events reported in these **children** included inappropriate enlargement of the genitalia (penis or clitoris), premature development of pubic hair, advanced bone age, increased libido and aggressive behavior.

FDA Aug/09 not to use body-building products marketed as containing **steroids or steroid-like substances** such as TREN-Xtreme, MASS Xtreme, ESTRO Xtreme, AH-89-Xtreme, HMG Xtreme, MMA-3 Xtreme, VNS-9 Xtreme, and TT-40-Xtreme..

FDA Nov/09 & IDS Sports notified consumers that five of the IDS's dietary supplement products (**Bromodrol, Dual Action Grow Tabs, Grow Tabs, Mass Tabs, and Ripped Tabs TR**) contain the following undeclared substances, which FDA considers to be steroids: "Madol," "Turinabol," "Superdrol," &/or "Androstenedione."

FDA Dec/09 for **S-DROL**: a voluntary recall by the manufacturer of one lot (lot# 810481, expiry date 01/2012) of S-DROL after FDA testing found it to contain undeclared desoxymethyltestosterone.

FDA Dec/09 warned consumers to stop using bodybuilding products manufactured by American Cellular Labs after they were found to contain unauthorized synthetic steroids in **TREN-Xtreme, MASS Xtreme, ESTRO Xtreme, AH-89-Xtreme, HMG Xtreme, MMA-3 Xtreme, VNS-9 Xtreme, TT-40-Xtreme.**

FDA Jan/10 & **MuscleMaster(dot)com**, Inc. notified consumers and healthcare professionals of the voluntary nationwide recall of all lots and expiration dates of the seventeen dietary supplements listed in the firm press release, sold between June 1, 2009 and November 17, 2009. FDA informed MuscleMaster(dot)com that it believes that the recalled products contain ingredients that are **steroids**.

FDA Oct/11 notified the manufacturer that lab analyses found that the product; **Uprizing 2.0** , sold as a testosterone booster, contains **superdrol**, a synthetic steroid, making it an unapproved new drug.

FDA Aug/13 Purity First Health Products is recalling two lots of **Healthy Life Chemistry B-50** (100 capsules), one lot of **Healthy Life Chemistry Multi-Mineral** (200 capsules) and all lot numbers for **Healthy Life Chemistry Vitamin C** (200 capsules). The B-50 capsules were found on testing by FDA to contain Methasterone (a schedule III controlled substance) and Dimethazine. Testing of the Multi-Mineral and Vitamin C capsules appear to indicate the presence of Dimethyltestosterone.

FDA Dec/13 is advising consumers to immediately stop using a product called **Mass Destruction**, marketed as a dietary supplement for muscle growth. The product is labeled to contain at least one synthetic anabolic steroid and has been linked to at least one reported serious illness.

FDA Feb/14 is investigating the **risk of stroke, heart attack, and death in men taking FDA-approved testosterone products**. We have been monitoring this risk and decided to reassess this safety issue based on the recent publication of two separate studies that each suggested an increased risk of cardiovascular events among groups of men prescribed testosterone therapy.

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Health Canada July/07 is warning Canadians not to use the dietary supplement **MdMt**, or any other supplements containing the synthetic steroids methyl-1-testosterone or methyldienolone that are obtained without a prescription, due to potentially serious health risks including reduced fertility and liver disorders.
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Postmenopausal women with decreased sexual desire associated with personal distress and with no other identifiable cause may be candidates for testosterone therapy. Testosterone treatment without concomitant estrogen therapy cannot be recommended because of a lack of evidence. When evaluating awoman for testosterone therapy, recommendations are to rule out causes not related to testosterone levels (eg, physical and psychosocial factors, medications) and to ensure that there is a physiologic cause for reduced testosterone levels (eg, bilateral oophorectomy). Laboratory testing of testosterone levels should be used only to monitor for supraphysiologic levels before and during therapy, not to diagnose testosterone insufficiency. Monitoring should also include subjective assessments of sexual response, desire, and satisfaction as well as evaluation for potential adverse effects. Transdermal patches and topical gels or creams are preferred over oral products because of first-pass hepatic effects documented with oral formulations. Custom-compounded products should be used with caution because the dosing may be more inconsistent than it is with government-approved products. Testosterone products formulated specifically for men have a risk of excessive dosing, although some clinicians use lower doses of these products in women. Testosterone therapy is contraindicated in women with breast or uterine cancer or in those with cardiovascular or liver disease. It should be administered at the lowest dose for the shortest time that meets treatment goals. Counseling regarding the potential risks and benefits should be provided before initiating therapy.
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Extras – RxFiles.ca – Oral Hypoglycemics

Hypoglycemics & Sulfa Allergy

Articles: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1783707/?tool=pubmed
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Summary & Overview:

⇨Warnings don't always correspond with available evidence; there is little information to suggest cross-sensitivity among the different sulfa chemical classes, however, those who have experienced a previous allergic reaction (to any drug) are more likely to experience a subsequent allergic reaction (to a related or unrelated drug)

⇨ Specific drugs

- *Chlorpropamide (Diabinese) (Apo-Chlorpropamide - Canada) - no warning*
- *Gliclazide (Diamicron) – Warning- (Contraindicated-Health Canada)*
- *Glimepiride (Amaryl)- Warning- (Contraindicated-Health Canada)*
- *Glipizide (Glucotrol)- no warning*
- *Glyburide (DiaBeta, others) - Warning (Contraindicated-Health Canada)*
- *Tolbutamide (Orinase) (Apo-Tolbutamide - Canada) - Warning*

⇨One case report of contact dermatitis with tolbutamide in a patient with sensitivity to sulfanilamide vaginal cream. After discontinuation of tolbutamide, therapy was changed to chlorpropamide, which was tolerated without difficulty.

⇨Another case report describes an allergic reaction to glyburide in a patient with a known allergy to sulfamethoxazole.

DC'd

Glimepiride/rosiglitazone AVANDARYL ✗ ⊗
(1,2,4/4mg tabs) daily with a meal ($325) D/C 2011

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FDA Aug/09 Patients with diabetes who take therapeutic products containing nonglucose sugars (e.g., **peritoneal dialysis solution and some immunoglobulins**) can have falsely elevated readings from blood glucose test strips that use glucose dehydrogenase pyrroloquinoline quinone (**GDH-PQQ**) technology, according to an FDA public health notification. The strips are in wide use, and we have provided a link to a listing of the affected products. The FDA cites 13 deaths associated with hypoglycemia not detected by the test strips, which cannot distinguish between lucose and other sugars such as maltose and xylose. Ten patients were receiving icodextrin peritoneal dialysis solution. The FDA advises physicians to avoid using GDH-PQQ test strips in health care facilities and to rely, instead, on laboratory assays of glucose — especially in patients taking the therapeutic products listed in the alert. Interfering products containing nonglucose sugars include icodextrin peritoneal dialysis solution, certain immunoglobulins, abatacept (Orencia, Bristol-Myers Squibb), tositumomab (Bexxar, GlaxoSmithKline), and any product containing or metabolized into maltose, galactose, or xylose. Several test strips and associated monitors use GDH-PQQ methodology: ACCU-CHEK (Roche), FreeStyle (Abbott Diabetes Care), TRUEtest (Home Diagnostics), CoZmonitor blood glucose module (for use with the Deltec Cozmo insulin pump, Smiths Medical MD), and OmniPod insulin management system (Insulet).

FDA Sep/10 & Takeda, conducted a planned analysis of the study data at the five-year mark, and submitted their results to FDA. Overall, there was no statistically significant association between **Actos exposure and bladder cancer risk**. However, further analyses were also performed looking at how long patients were on Actos and the total amount of the drug they received during that time. An increased risk of bladder cancer was observed among patients with the longest exposure to Actos, as well as in those exposed to the highest cumulative dose of Actos. FDA notified healthcare professionals and patients that the Agency is reviewing data from an ongoing, ten-year epidemiological study designed to evaluate whether Actos (pioglitazone) is associated with an increased risk of bladder cancer.

FDA May/11 Updated risk evaluation and mitigation strategy **(REMS) to restrict access to rosiglitazone**-containing medicines including Avandia, Avandamet, and Avandaryl. May 18, 2011. http://www.fda.gov/Drugs/DrugSafety/ucm255005.htm

FDA June/11 **Victoza** (liraglutide [rDNA origin]) Injection: REMS - Risk of **Thyroid C-cell Tumors, Acute Pancreatitis**. http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm258826.htm

FDA June/11 drug safety communication: Update to ongoing safety review of **Actos (pioglitazone) and increased risk of bladder cancer**- use for more than 12 months linked to an increased risk of bladder cancer. http://www.fda.gov/Drugs/DrugSafety/ucm259150.htm

FDA Mar/13 is evaluating unpublished new findings by a group of academic researchers that suggest an increased risk of **pancreatitis and pre-cancerous cellular** changes called pancreatic duct metaplasia in patients with type 2 diabetes treated with a class of drugs called incretin mimetics **(glucagonlike peptide-1 (GLP-1) agonists and the DPP-4 inhibitors, or "gliptins**). These findings were based on examination of a small number of pancreatic tissue specimens taken from patients after they died from unspecified causes.

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Health Canada Jan/06 & July/07 Association of **AVANDIA** & 6 reports of parotid gland enlargement http://www.hc-sc.gc.ca/dhp-mps/medeff/bulletin/carn-bcei_v16n1_e.html#2
Health Canada Apr/07 is warning consumers from The Hong Kong Department of Health found **Lanmei Keili Ji to be adulterated with gliclazide**, a hypoglycaemic agent (lowers blood sugar).
Health Canada May/07 is advising consumers not to use **Xiaokeshuping Jiangtangning Jiaonang** capsules in Hong Kong to contain the undeclared pharmaceutical drugs phenformin, rosiglitazone, and glibenclamide, which may be used in diabetes to lower blood sugar.
Health Canada May& June/07 is advising consumers & health professionals about heart risks with **Avandia** http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/public/2007/avandia_pc-cp_3_e.html
Health Canada Sept/07 is advising consumers not to use foreign health products due to concerns about possible side-effects: **Jacaranda**, **Queenmer Fat Loss**, **Li Da Dai Dai Hua Jiao Nang, J-minus** and **Jelimel Slimming Capsules**. These products are promoted for weight loss and have been found to be adulterated with the prescription drug sibutramine. Sibutramine is used for treating obesity and should only be taken under the supervision of a health professional. **Junyu Jiaonanyihao** has been found to contain the undeclared prescription drugs sibutramine and dexamethasone, as well as phenolphthalein, which is currently prohibited in Canada.. **Heng Tong Jiangtangning Jiaonang** was found to contain the prohibited drug phenformin, and the prescription drug glibenclamide (glyburide) which should only be taken under the supervision of a health professional.
Health Canada Nov/07 Rosiglitazone (**AVANDIA®**) is no longer approved as monotherapy for type 2 diabetes, except when metformin use is contraindicated or not tolerated. Rosiglitazone is no longer approved for use in combination with a sulfonylurea, except when metformin is contraindicated or not tolerated. Treatment with all rosiglitazone products is now contraindicated in patients with any stage of heart failure (i.e., NYHA Class I, II, III or IV).
Health Canada April/08 warns that Singapore's Health Sciences Authority (HSA) advised the public not to use the product **Power 1 Walnut**, because it was found to contain the prescription drugs sildenafil and glibenclamide.
Health Canada April/08 is advising consumers not to use The Hong Kong Department of Health advised the public not to use the product **Tian Sheng Yi Bao** because it was found to contain two pharmaceutical products, glibenclamide and phenformin.
Health Canada June/08 **Nangen Zengzhangsu** (may also be known as Nangen or Nangeng), Sanbianwan, Jiu Bian Wang, Tian Huang Gu Shen Dan, Zui Xian Dan Gong Shi Zi, and Power Up. The Hong Kong Department of Health has warned consumers not to use these herbal/proprietary Chinese medicine products promoted for erectile dysfunction because they have been found to contain sildenafil and/or glibenclamide.
Health Canada June/08 **Zhong Hua Niu Bian**. Zhong Hua Niu Bian is an herbal/proprietary Chinese medicine product promoted for erectile dysfunction. Singapore's Health Sciences Authority has warned against the use of this product because it has been found to contain sildenafil, glibenclamide, tadalafil and sibutramine
Health Canada Nov/08 is advising consumers not to use foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned consumers not to buy or use **Lu Quan** because it contains undeclared glibenclamide and sildenafil.
Health Canada Nov/10 AVANDIA®/AVANDAMET®/AVANDARYL® is now indicated only in patients with type 2 diabetes mellitus for whom all other oral antidiabetic agents, in monotherapy or in combination, do not result in adequate glycemic control or are inappropriate due to contraindications or intolerance. Prior to starting or renewing a prescription for **AVANDIA®/AVANDAMET®/ AVANDARYL®,** physicians should consider whether a rosiglitazone-containing product is an appropriate therapeutic choice, and if so: Document the eligibility of patients to meet the above criteria; Counsel each patient on the risks and benefits of AVANDIA®/AVANDAMET®/ AVANDARYL®, including the cardiovascular risks; and Obtain the patient's written informed consent to take the drug.
Health Canada Nov/11 **Pancre-Plus** The Hong Kong Department of Health warned that this counterfeit Chinese medicine contains an unauthorized drug (phenformin) and a prescription drug (glyburide). **Tian Ma Tu Chung Seven Leave Ginseng, Vall-Boon Tongkat Al, and Pao Ni Kang** The Singapore Health Sciences Authority warned that these traditional herbal products contain prescription and over-the-counter drugs (dexamethasone, ketoconazole, repaglinide, pheniramine, and chlorpheniramine).
Health Canada Apr/12 has recently completed a safety assessment of the available data for **rosiglitazone-ACTOS**, an oral anti-diabetic drug, and the label was updated to reflect the potential risk of **bladder cancer** in treated patients.

Health Canada May/12 1. **Jin Yu Tang Tai Han Kang Pai Pu Ling Jiao Nang; TangBaoKouFuYiDaoSuJiaoNang; Tangren 365 Kangxunpai sangge huoyisu jiaonang; Tong Ren Xiu Fu Kou Fu Yi Dao Su.** The Hong Kong Department of Health warned that these products contain a combination of prescription drugs (metformin, glibenclamide [also known as glyburide], rosiglitazone, glimepiride, hydrochlorothiazide) and unauthorized drugs (phenolphthalein, phenformin).

Health Canada Jan/13: informing Canadians of a labelling update for all cholesterol-lowering drugs (also known as **statins**) regarding the risk of increased blood sugar levels and a small increased **risk of diabetes** among patients already at risk for the disease.

Health Canada Apr/14: **San Xiao Ping Tang Jin Qi Jiao Nang**: The Hong Kong Department of Health warned consumers not to use this product after it was found to contain phenformin, pioglitazoneand glibenclamide**.**

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Important Advice for Managing Your Patients

In Canada, Avandia® is NOT approved for use:
- with insulin therapy
- with the combination of metformin AND a sulfonylurea
- in patients with pre-diabetes.

Avandia® is contraindicated in patients with NYHA Class III and IV cardiac status.
Avandia® should be used with caution in any patient with NYHA Class I and II cardiac status.
All patients should be monitored for signs and symptoms of fluid retention, edema, and rapid weight gain.

The dose of Avandia® used in combination with a sulfonylurea should not exceed 4mg daily.

More links, information and a RxFiles Q&A Summary available at: http://www.rxfiles.ca/Rosiglitazone-CV-Controversy.htm

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FDA Aug/10 and CDC have noted a progressive increase in the reports of bloodborne infection transmission over the past 10 to 15 years (primarily hepatitis B virus), resulting from shared use of fingerstick and point-of-care [POC] blood testing devices.

FDA Aug/13 Nova Diabetes Care initiated a voluntary recall of 21 lots of the Nova Max Glucose Test Strips distributed both in the USA and outside the continental USA.

FDA Jan/14 Nipro Diagnostics initiated a voluntary recall and replacement of a limited number of TRUEbalance and TRUEtrack Blood Glucose Meters distributed both in the United States and outside the United States. The company determined that certain isolated TRUEbalance and TRUEtrack Blood Glucose Meters have an incorrect factory-set unit of measure that displays the glucose result in mmoi/L rather than mg/dl. If a consumer were not to notice the incorrect unit of measure, it is possible that the meter result could be read as a lower than expected blood glucose result. BACKGROUND: There are 501 affected TRUEbalance meters and 105 affected TRUEtrack meters that were distributed in the United States from September 2008 to May 2013. The company is sending notifications to pharmacies, durable medical equipment providers, mail order companies and distributors where the TRUEbalance and TRUEtrack meters are recommended or sold in the United States.

FDA Mar/14 Abbott is conducting a recall for the FreeStyle Blood Glucose Meter and the FreeStyle Flash Blood Glucose Meter. When used with the Abbott FreeStyle test strips, the FreeStyle Blood Glucose Meter and the FreeStyle Flash Blood Glucose Meter may produce mistakenly low blood glucose results.

FDA Apr/14 is advising people with diabetes and health care professionals to stop using GenStrip Blood Glucose Test Strips because the strips may report incorrect blood glucose levels.

FDA Jun/14 Diabetic Supply of Suncoast, Inc. initiated a nationwide voluntary recall of all BMB-BA006A Advocate Redi-Code+ blood glucose test strip lots manufactured by BroadMaster Bio-Tech Corp due to a labeling error which could result in confusion about which meter models the Redi-Code+ BMB-BA006A blood glucose test strips are designed to be used with. In the incorrect labeling, the test strips model (BMB-BA006A) was omitted.

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Ontario Aug 2013: introducing limitations in funding for diabetes test strips. And these new r estrictions are okay with the Canadian Diabetes Association, which worked with the government to ensure that new self-management of diabetes reflects the best evidence and clinical experience available. According to a notice posted on the Ontario Public Drug Programs (OPDP) website, research indicates that Blood Glucose Test Strips (BGTS) have a limited clinical benefit for many patients who don't take insulin. Based on this evidence, Ontario will restrict the number of BGTS allowed in a 365-day period, while ensuring continued access to those who need test strips to manage their blood sugar. The province's Health Network System (HNS) will track and determine the reimbursement level based on each patient's diabetes treatment. Under the new rules, patients managing diabetes with insulin will be allowed 3,000 BGTS a year, while patients managing diabetes with anti-diabetes medication with high risk of causing hypoglycemia will get 400 BGTS. Patients managing diabetes using anti-diabetes medication with low risk of causing hypoglycemia and those who are managing diabetes through diet/lifestyle therapy only will be allowed 200 BGTS.
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Extras

Recently Discontinued Insulin Devices (within last 3 years): HumaPen Ergo (discontinued 2007) & Novolin-Pen 3

AutoPen 24 (3ml penfill) A) green – up to 21 units 1-21 units in 1 unit increments B) blue – up to 42 units 2-42 units in 2 unit increments		**LANTUS** (glargine) ◆ free with Lantus insulin	◆ has side-mounted injection button ◆ small white numbers on a dark background; does not have number window (e.g. number not magnified.) ◆ does NOT have dial back capabilities, dose must be wasted if overdialed ◆ if insufficient insulin in cartridge, number remaining on dial will show remaining dose to be given
Novolin-Pen Junior (3ml penfill) 1-35 units in ½ unit increments {Blue with green or yellow with green}		As per NovoPen 4 [Novo-Pen Junior being replaced by NovoPen Echo]	◆ small increments useful: children & insulin sensitive pts ◆ does NOT have dial back capability; barrel and cartridge holder should be pulled apart & button reset to correct dose ◆ small white numbers on a black background ◆ if insufficient insulin in cartridge, number remaining on dial will show remaining dose to be given
HumaPen Luxura (3ml cartridge) 1-60 units in 1 unit increments {Champagne or Burgundy with hard case}		**HUMULIN** (R, N, 30/70) **HUMALOG** (lispro) **HUMALOG** Mix25 (lispro+lispro protamine) **HUMALOG** Mix50 (lispro+lispro protamine) [HumanPen Luxura being replaced by HumaPen Savvio]	◆ has dial back capability, decreases wastage ◆ audible click on dialing doses ◆ dark numbers on a white background ◆ if insufficient insulin in cartridge, number remaining on dial will show remaining dose to be given ◆ Luxura last up to 6 years

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Temporary Extras:

◆{Pen devices: ↑'d portability, convenience & ease of use; but ↑ potential for contamination, needle sticks, malfunction & cost}

◆T1DM: A1C difference between SAIA and HI is less than 1/10th of the difference between intensive and conventional tx groups in the DCCT; based on this, expected NNT for 1 less retinopathy = 650 / year

◆Epidural Corticosteroids: expect ↑BG levels for a few days Even JL, Crosby CG, Song Y, McGirt MJ, Devin CJ. Effects of epidural steroid injections on blood glucose levels in patients with diabetes mellitus. Spine 2012;37(1):E46-50.

◆Insulin Pump (CSII): may allow for ↓A1C by 0.3-0.6%; ↓ insulin dose by 10-20%; potentially useful if ↑ A1C despite best attempt with MDI &/or who have continued disabling hypoglycemia. Also of use in 1st trimester of pregnancy, or before, if A1C <6.1% not achieved.

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FDA Aug/09 Patients with diabetes who take therapeutic products containing nonglucose sugars (e.g., peritoneal dialysis solution and some immunoglobulins) can have falsely elevated readings from blood glucose test strips that use glucose dehydrogenase pyrroloquinoline quinone (GDH-PQQ) technology, according to an FDA public health notification. The strips are in wide use, and we have provided a link to a listing of the affected products. The FDA cites 13 deaths associated with hypoglycemia not detected by the test strips, which cannot distinguish between lucose and other sugars such as maltose and xylose. Ten patients were receiving icodextrin peritoneal dialysis solution. The FDA advises physicians to avoid using GDH-PQQ test strips in health care facilities and to rely, instead, on laboratory assays of glucose — especially in patients taking the therapeutic products listed in the alert. Interfering products containing nonglucose sugars include icodextrin peritoneal dialysis solution, certain immunoglobulins, abatacept (Orencia, Bristol-Myers Squibb), tositumomab (Bexxar, GlaxoSmithKline), and any product containing or metabolized into maltose, galactose, or xylose. Several test strips and associated monitors use GDH-PQQ methodology: *ACCU-CHEK* (Roche), *FreeStyle* (Abbott Diabetes Care), *TRUEtest* (Home Diagnostics), *CoZmonitor* blood glucose module (for use with the *Deltec Cozmo* insulin pump, Smiths Medical MD), and *OmniPod* insulin management system (Insulet).
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Related links: http://www.medscape.com/viewarticle/705198?src=mp&spon=34&uac=93517FV ; http://www.nationalpost.com/life/health/story.html?id=4578946f-1f50-426e-b92a-bc0f7dd86eed ; http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_2009/2009_115-eng.php ;
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Multfactorial intervention - blood pressure, lipids, possibly ASA, lifestyle – in addition to glucose control, is essential in reducing macrovascular endpoints!

See also RxFiles Landmark Trials Chart: Summary of Lipid, BP & ASA diabetes related trials: http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-DIABETES-Landmark-Trials-Non-Glucose.pdf

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the United Kingdom Prospective Diabetes Study (UKPDS) trial were maintained and to some extent extended during a 10-year nonrandomized follow-up period, even though all patients quickly had similar glycohemoglobin levels. The benefit was most pronounced with metformin. Note that patients in the "intensive therapy" group had a mean glycohemoglobin of approximately 8% at the end of the randomized portion of the study, and the recent ACCORD study found that more aggressive control offered no benefit and may be harmful (N Engl J Med 2008;358:2545-59, POEM #100825). (LOE = 2b)"}

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Extras

- ASCEND (A Study of Cardiovascular Events iN Diabetes) and ACCEPT-D (Aspirin and Simvastatin Combination for Cardiovascular Events Prevention Trial in Diabetes). These are large, ongoing studies that will enrol up to 15,000 participants with anticipated completion dates of 2011 and 2013, respectively.

ETDRS 5 yrs, n=3,711	T1DM & T2DM plus diabetic retinopathy; ~50% of pts with hx of CV disease <10% hx of MI or stroke	aspirin 2 x 325mg/day vs placebo	◆ 1°: all-cause mortality, 12.1 vs 14.9, RR 0.91 [99% CI, 0.75 to 1.11, p=0.24] ◆ 2°: cardiovascular mortality, 9.3 vs 11.2, RR 0.87 [99% CI, 0.7 to 1.1, p=0.12] ◆ 2°: fatal or non-fatal MI, 9.1 vs 12.3, RR 0.83 [99% CI, 0.66 to 1.04] ◆ 2°: fatal or non-fatal stroke, 4.5 vs 3.8, RR 1.17 [99% CI, 0.79 to 1.28] -no evidence of harmful effects of aspirin

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- From CCS 2011: For the predetermined secondary endpoint of fatal or nonfatal MI, the difference was significant at 5 years (RR 0.72, 99% CI 0.55-0.95) but not at 7 years (RR 0.83, 99% CI 0.66-1.04).

Extras

NNTs in T2DM - (Standardized for 5 yrs)

- ↓ Mortality: Metformin 2550mg/d in obese NNT=$7_{/5yrs}$ UKPDS-34
- ↑ Mortality: intensive blood glucose control $_{(A1C\ target=6)}$; NNH=$66_{/5yrs}$ ACCORD
- Blood pressure control: ?HOT trial??
- Major CHD Event: Atorvastatin 10mg daily; NNT=$26_{/5yrs}$ CARDS

Type 2 Diabetes Mellitus (T2DM): An Approach to Drug Treatment & Overview

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FDA approves **Orlistat for OTC**, Pharmacist's Letter Mar 2007.

FDA Nov/08 Fashion Sanctuary announced a recall of **Zhen De Shou Fat Loss** Capsules because FDA analysis found the product to contain undeclared sibutramine, an FDA approved drug used as an appetite suppressant for weight loss.

FDA Jan/09 notified consumers not to take Venom **HYPERDRIVE 3.0**, a product sold as a dietary supplement but containing sibutramine.

FDA Mar/09 Herbal **Xenicol** (found to contain cetilistat, an obesity drug not approved in the U.S.) along with **Slimbionic** and **Xsvelten** (both containing sibutramine, a prescription-only weight loss drug) have been added to the list of tainted dietary supplements. There are now **72 products** on the list. http://www.fda.gov/bbs/topics/NEWS/2009/NEW01977.html

FDA Apr/09: **ABC Beauty Supply** & FDA notified consumers and healthcare professionals of a recall of 34 dietary supplement products. FDA lab analyses identified undeclared **sibutramine**, an FDA- approved drug, used as an appetite suppressant for weight loss. http://www.fda.gov/oc/po/firmrecalls/universalabc04_09.html **(34 products listed)**

FDA July/09 notified healthcare professionals that four weight loss dietary supplements sold and marketed by the firm (**Slimbionic, One Weight Loss Pill, SlimDemand Capsules, Botanical Weight Loss**) contain sibutramine.

FDA Aug/09 notified healthcare professionals and patients that it is reviewing new safety information regarding reports of liver-related adverse events in patients taking orlistat. **Orlistat** is marketed in the United States as a prescription product, Xenical, and as an over-the-counter (OTC) product, Alli. Between 1999 and October 2008, 32 reports of serious liver injury, including **6 cases of liver failure**, in patients using orlistat were submitted to FDA's Adverse Event Reporting System. The most commonly reported adverse events described in the 32 reports of serious liver injury were jaundice, weakness, and abdominal pain.

FDA Nov/09 & GMP Herbal Products notified consumers and healthcare professionals of a recall of **Pai You Guo**, a weight loss dietary supplement, due to the presence sibutramine & phenolphthalein **.**

FDA Jan/10 notified consumers and healthcare professionals about a counterfeit and potentially harmful version of **Alli 60 mg capsules** (120 count refill kit). The **counterfeit** version contained the controlled substance sibutramine and did not contain orlistat, the active ingredient.

FDA July/10 analysis of **Que She** found that it contains: fenfluramine – a stimulant drug withdrawn from the U.S. market in 1997 after studies demonstrated that it caused serious heart valve damage, propranolol – a prescription beta blocker drug that can pose a risk to people with bronchial asthma and certain heart conditions, sibutramine – a controlled substance and prescription weight loss drug, sibutramine was the subject of a recent study whose preliminary findings showed an association between sibutramine use and increased risk of heart attack and stroke in patients who have a history of heart disease, & ephedrine – a stimulant drug that is legally marketed over-the-counter for temporary relief of asthma but can pose a risk to people with certain cardiovascular conditions.

FDA Aug/10 lab analysis of **Solo Slim** was found to contain the undeclared drug ingredient Didesmethyl Sibutramine.

FDA July/10 lab analysis of **Slim-30** Herb Supplement distributed by the company was found to contain undeclared N-Desmethyl Sibutramine and traces of Sibutramine.

FDA July/10 lab analysis of this herb supplement, **Joyful Slim** Herb Supplement, was found to contain the undeclared drug, desmethyl sibutramine.

FDA Oct/10 notified consumers that **Slimming Beauty Bitter Orange Slimming Capsules** contain the active pharmaceutical ingredient sibutramine, a prescription-only drug which is a stimulant.

FDA Oct/10 Abbott Laboratories notified healthcare professionals and patients about the **voluntary withdrawal of Meridia (sibutramine)**, from the U.S. market because of clinical trial data indicating an increased risk of heart attack and stroke.

FDA Dec/10 has received multiple reports of adverse events associated with the use of **Fruta Planta**, including several cardiac events and one death. FDA laboratory analysis confirmed that Fruta Planta contains sibutramine.

FDA Jan/11 laboratory analysis confirmed that **Celerite Slimming Capsules** contain sibutramine

FDA Mar/11 lab analysis of **Svelte 30** orange & gray capsules determined that the product contains Sibutramine.

FDA Mar/11 notified Biotab Nutraceuticals, Inc. that two lots of counterfeit product purporting to be **Extenze** contain undeclared drug ingredients. Specifically, lot 0709241 contains tadalafil and sildenafil, and lot 0509075 contains tadalafil and sibutramine.

FDA Mar/11 laboratory analyses of **Celerite Slimming Tea**: Recall - were found to contain undeclared Sibutramine.

FDA May/11 laboratory analysis confirmed that "**Slim Xtreme Herbal Slimming Capsule**" contains sibutramine.

FDA July/11 is advising consumers not to purchase or use "**Slim Forte Slimming Capsules**," "**Slim Forte Slimming Coffee**," and "**Botanical Slimming Soft Gel & Slim Forte Double Power Slimming Capsules**. FDA laboratory analysis confirmed that these products contain sibutramine.

FDA Dec/11 took joint action against several companies selling over-the-counter **hCG products** that falsely and illegally claim to promote weight loss. Labeled "homeopathic" by the seven companies who received the letters, the products contain human chorionic gonadotropin (hCG), a hormone produced during pregnancy by cells that form the placenta. 1. HCG Diet Direct LLC- HCG Diet Homeopathic Drops, 2. The hCG Drops LLC- Homeopathic HCG, 3. HCG Platinum LLC; RightWay Nutrition- HCG Platinum, HCG Platinum X-30, HCG Platinum X-14, 4. Nutri Fusion Systems LLC- HCG Fusion 30, HCG Fusion 43, 5. www.resetthebody.com; www.theoriginalhcgdrops.com-Homeopathic Original HCG, Homeopathic HCG, 6. Hcg-miracleweightloss.com- HCG Extra Weight Loss Homeopathic Drops, 7. Natural Medical Supply- Alcohol Free hCG Weight Loss Formula.

FDA Feb/12 **Healthy People Co.** notified the public of a recall of the company's dietary supplements sold under the brand names Healthy People Co. FDA lab analysis confirmed the presence of Sibutramine and Tadalafil, making these products unapproved new drugs. (**Mince Belle Dietary Supplement, PERFECT Men Dietary Supplement , EVERLAX Dietary Supplement, EVER Slim Dietary Supplement, Herbal Drink Acai-man Mangosteen Dietary Supplement, EVER SLIM Shake Mix Dietary Supplement**)

FDA Feb/12 is advising consumers not to purchase or use "**Japan Weight Loss Blue**," a product for weight loss sold on various websites, laboratory analysis confirmed that "Japan Weight Loss Blue" contains sibutramine, analogs of sibutramine, and ephedrine alkaloids.

FDA Apr/12 laboratory analysis confirmed that "**Japan Rapid Weight Loss Diet Pills Yellow**" contains sibutramine and phenolphthalein.

FDA Oct/12 is advising consumers not to purchase or use "**Ultimate Formula Bee Pollen Capsules (Ultimate Formula)**," or "**Zi Xiu Tang Bee Pollen Capsules**," also referred to as "**Zi Xiu Tang Beauty, Face & Figure Capsule**," products promoted and sold for weight loss because they contain sibutramine.

FDA Dec/12 is advising consumers not to purchase or use "**SLIMDIA Revolution**," a product promoted and sold for weight loss on various websites, including www.pinkfatty.com, and in some retail stores since it contains Sibutramine.

FDA Jan/13 is advising consumers not to purchase or use "**MAXILOSS** Weight Advanced," a product promoted and sold for weight loss on various websites, includingwww.dreamlifeweightloss.com, and in some retail stores since it contains sibutramine.

FDA Feb/13 Olaax Corp announced a nationwide recall of the company's dietary supplement sold under the brand name **Maxiloss Weight Advanced Softgels** to the user level, because FDA testing found the Maxiloss Weight Advanced product to contain Sibutramine.

FDA Jun/13 FDA laboratory analysis confirmed that **"Bethel 30", & "XIYOUJI QINGZHI CAPSULE**" & **JaDera** contains sibutramine. .

FDA Jun/13 A sample of **Extreme Body Slim, Fat Zero, Fruit & Plant Slimming, & Paiyouji Plus** all contains silbutramine.

FDA Jun/13 Beta Labs has recalled certain lots of **Oxyphen, Phentalene, Phen FX, and Red Vipers** because they contain 1,3 dimethylamylamine (DMAA), the FDA announced over the weekend. The products are used as pre-workout stimulants and for weight loss, but the agency has previously warned that DMAA can be dangerous: it can elevate blood pressure and lead to cardiovascular complications. One distributor, GNC, faces FDA seizure of over 3000 cases of two other DMAA-containing products, **Jack3d and OxyElitePro**. Although the manufacturer of those supplements has ceased production, GNC continues to sell its remaining stocks, according to the *New York Times*.

FDA July/13 **Meizi Revolution, Strawberry Balance** contains silbutramine.

FDA Aug/13 Herbal Give Care LLC issued a voluntarily recall of all lots of **Esbelin silouttete** and **Esbelin silouttе Herbal Blend with L-Carnitine** (30 Capsules), to the consumer level. The products have been found to contain undeclared Sibutramine, N-Desmethylsibutramine, and N-di-Desmethylsibutramine.

FDA Aug/13 Bethel Nutritional Consulting, Inc., New York, NY, is voluntarily recalling **Quick Thin and Bethel Advance** to the consumer level. These products have been found to contain Sibutramine and Phenolphthalein, and may pose a threat to consumers.
FDA Aug/13 CTV Best Group announced that it is conducting a voluntary nationwide recall of all lots of a dietary supplement products distributed by the company under the names **BEST SLIM 40 Pills** to the consumer level. Testing by FDA revealed the presence of Sibutramine in Best Slim.
FDA Aig/13 Herbal Give Care LLC is voluntarily recalling all lots of **Esbelder man (30 capsules), Esbelder fem (30 capsules) and Esbelder siloutte** (30 capsules) to the consumer level. The products have been found to contain undeclared Sibutramine, N-Desmethylsibutramine, and N-di-Desmethylsibutramine.
FDA Sep/13 laboratory analysis confirmed that **Shou Fu Ti Tun Guo Xiang Xing Jian Fei Jiao Nang** contains sibutramine.
FDA Oct/13: B@B Trade, Inc., Florida is voluntarily recalling all lots of **Slim Fortune, Lidiy, and Slim Expert** to the consumer level. The FDA laboratory analysis of these dietary supplements found to contain undeclared Sibutramine.
FDA Oct/13 is advising consumers not to purchase or use **Perfect Body Solutions or Burn 7**. FDA laboratory analyses confirmed that Perfect Body Solutions and Burn 7 contain sibutramine.
FDA Oct/13 is advising consumers not to purchase or use **Dr. Mao Slimming Capsules**. FDA laboratory analysis confirmed that Dr. Mao Slimming Capsules contain sibutramine.
FDA Oct/13 is advising consumers not to purchase or use **Bella Vi Insane Amp'd or Bella Vi Amp'd Up.** FDA laboratory analyses confirmed that Bella Vi Insane Amp'd and Bella Vi Amp'd Up contain sibutramine.
FDA Nov/13 **SlimExtra Herbal** capsules contain silbutramine.
FDA Dec/13 laboratory analysis found the **Burn 7 Capsules** to contain undeclared Sibutramine.
FDA Jan/14 is advising consumers not to purchase or use **Magic Slim or Dream Body Slimming Capsule**, products promoted and sold for weight loss and sold on various websites and in some stores, since FDA lab analysis confirmed they contains sibutramine.
FDA Jan/14 **Citrus Fit Gold, Hot Detox & Thinogenics** contains sibutramine. **Tonic Life BP** contains phenolphthalein.
FDA Feb/14: MyNicKnaxs, LLC notified the public it is recalling all lots of "**Reduce Weight Fruta Planta**". FDA lab analysis of the product found Reduce Weight Fruta Planta to contain 10.2 mg of Phenolphthalein.
FDA Mar/14 is advising consumers not to purchase or use **Vitaccino Coffee**, a product promoted and sold for weight loss. FDA laboratory analysis confirmed that Vitaccino Coffee contains sibutramine.
FDA Mar/14: New Life Nutritional Center is recalling all lots of "**Super Fat Burner capsules, Maxi Gold capsules and Esmeralda softgels**" to the user level after FDA analysis revealed the products contain undeclared active pharmaceutical ingredients: sibutramine, phenolphthalein or a combination of both sibutramine and phenolphthalein.
FDA Mar/14: **Bella Vi Insane Bee Pollen Capsules, Bella Vi BTrim Ultimate Boost, Bella Vi BTrim Max, Bella Vi Extreme Accelerator, Bella Vi Insane Amp'd, and Bella Vi Amp'd U**, contain silbutramine with or without phenolphthalein.
FDA Mar/14: GlaxoSmithKline (GSK) Consumer Healthcare is **voluntarily recalling** all alli weight loss products from U.S. and Puerto Rico retailers as the company believes that some packages of the product were tampered with and may contain product that is not authentic **Alli**.
FDA Apr/14: FDA analysis on **New You** contains silbutramine.
FDA Apr/14 has tested multiple **Zi Xiu Tang Bee Pollen** products from various distributors in the United States (US). All products that have been tested, including those that claim to be "genuine" and "anti-counterfeit," have been found to contain one or both of the undeclared drug ingredients sibutramine and Phenolphthalein.
FDA Apr/14 laboratory analysis confirmed that **Infinity & Lite Fit** USA contains sibutramine.
FDA Apr/14: Nature's Universe notified the public it is recalling all lots of **Thinogenics** product sold prior to February 6, 2014 to the user level after FDA analysis revealed that the affected product contained undeclared sibutramine.
FDA May/14 laboratory analysis confirmed that **Slim Trim U & Natural Body Solution** contains sibutramine.
FDA May/14 is advising consumers not to purchase or use **Asset Bee Pollen**, a product promoted and sold for weight loss because it contains sibutramine.
FDA May/14 is advising consumers not to purchase or use **Asset Bold**, a product promoted and sold for weight loss. FDA laboratory analysis confirmed that Asset Bold contains sibutramine.
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FDA Jun/14 laboratory analysis confirmed that **Sliming Diet** contains sibutramine.
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Health Canada Apr/07 is warning consumers about **Bitter orange** & cardiovascular reactions in the Canadian Adverse Reactions April 2007 Newsletter.

Health Canada Apr/07 is warning consumers from the Hong Kong Department of Health found **Lexscl Fat Rapid Loss capsules to be adulterated with sibutramine** and thyroid hormones.

Health Canada via July/07 Medsafe also advised the public not to use the product **Dai Dai Hua Jiao Nang** because it was found to contain sibutramine.

Health Canada Aug/07 is advising Canadians of a recall in the United States of one lot of **Metaboslim Apple Cider Vinegar**, which is marketed as a dietary supplement, because it has been found to contain sibutramine, a prescription medication that should only be taken under medical supervision.

Health Canada Sept/07 is advising consumers not to use foreign health products due to concerns about possible side-effects: **Jacaranda**, **Queenmer Fat Loss**, **Li Da Dai Dai Hua Jiao Nang**, **J-minus** and **Jelimel Slimming Capsules**. These products are promoted for weight loss and have been found to be adulterated with the prescription drug sibutramine. Sibutramine is used for treating obesity and should only be taken under the supervision of a health professional. **Junyu Jiaonanyihao** has been found to contain the undeclared prescription drugs sibutramine and dexamethasone, as well as phenolphthalein, which is currently prohibited in Canada.. **Heng Tong Jiangtangning Jiaonang** was found to contain the prohibited drug phenformin, and the prescription drug glibenclamide (glyburide) which should only be taken under the supervision of a health professional.

Health Canada Jan/08 is warning Canadians not to use the unauthorized product **Physio Care Lida Dai Dai Hua Jiao Nang Slimming Capsules** (batch number 28012007 / expiration date: Jan 2009). This product is promoted for weight loss and has been found to contain a derivative of the prescription drug sibutramine.

Health Canada April/08 is advising consumers not to use **Xian Zhi Wei II** was found to contain sibutramine and phenolphthalein, which are not meant for self-care and may cause serious side effects.

Health Canada Aug/08 is advising consumers not to use 9 foreign health products due to concerns about possible side-effects: **Dan Bai Shou Shen Su** was found to contain undeclared thyroid hormones and sibutramine. **Karntien and Karntien Easy to Slim** were adulterated with sibutramine and a compound that is similar in structure to sibutramine (N-desmethylsibutramine). **More Slim** was found to contain the undeclared pharmaceutical ingredient sibutramine. **Soloslim** was found to contain an undeclared substance similar in structure to the prescription drug sibutramine. It also contains the prescription drug L-carnitine, as well as synephrine, which is not authorized for sale in weight loss products in Canada.

Health Canada Aug/08 is advising consumers not to use 8 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned against the use of Natural (Xin Yi Dai) and Lasmi because Natural (Xin Yi Dai) was found to contain sibutramine and phenolphthalein, and Lasmi was found to contain sibutramine and spironolactone. The Hong Kong Department of Health warned against the use of AA Qu Feng Shu Jin Wan because it was found to contain the undeclared pharmaceutical ingredient dexamethasone. Apisate contained fenfluramine and Energy ll contained sibutramine. Obat Asam Urat and Asam Urat both contained dexamethasone, phenylbutazone and piroxicam. The Hong Kong Department of Health warned against the use of Slim 3in1 (Xiao Nan zhi Bao) because it was found to contain the undeclared pharmaceutical ingredients sibutramine and phenolphthalein.

Health Canada Sep/08 is advising consumers not to use 2 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned against the use of **Hanguo shoushen yihao** (meiti xing) because it was found to contain the undeclared pharmaceutical ingredient sibutramine. The Hong Kong Department of Health warned against the use of **ARMA - Sin Gang San** and New ARMA - Sin Gang San because they were found to contain the undeclared pharmaceutical ingredients sibutramine and fenfluramine.

Health Canada Nov/08 is advising that the Hong Kong Department of Health warned consumers not to buy or use **Fat Killer, Carbohydrate Cut and Sugar-Carbohydrate Cut** because they contain sibutramine and an unauthorised substance similar in structure to sibutramine.

Health Canada Jan 2009 is advising consumers not to use 4 foreign products: **Zhuang Tjar Gere** because it contains the undeclared prescription drugs sildenafil & tadalafil, **Zhixhue** Capsules manufactured by Vital Pharmaceutical Holdings Ltd. due to concerns of serious side- effects including liver dysfunction, **Tonik Warisan Banjar** because it contains undeclared dexamethasone & **Healthily Slim** because it contains sibutramine.

Health Canada Mar/09 Foreign Product: **68 Weight Loss Products**; Best-life Fat Burning Capsules; Bevidan;Huiji Yin Chiao Chieh Tu Pien & Relacore. Plus Lami, Linglongquxian, Menergy M-Essence, Nyal Day & Night Cold & Flu Fighter (AUST L 146264), Nyal Cold & Flu Fighter (AUST L 146263), 999 Radix Notoginseng, Batch no. 0807021, Slim Pure, Carbohydrate, Kalomee, K Carbohydrate, K Tighten Slim, & K Slimming Pills. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_fpa-ape_2009/index-eng.php

Health Canada June/09 Foreign Product Alerts: **Jia Yi Jian** (undeclared sibutramine & tadalafil); **Shan Dian Qiang Xiao Shou** (undeclared sibutramine & phenolphthalein).

Health Canada June/09 is warning consumers not to use the unauthorized product **Slim Magic Herbal**, which is promoted as a weight-loss product, as it was found to contain an undeclared pharmaceutical ingredient similar to the prescription drug sibutramine.

Health Canada is warning consumers not to use the unauthorized product **Nutural Slim**, which is promoted as a weight-loss product, as it was found to contain the undeclared pharmaceutical ingredient sibutramine and also an undeclared pharmaceutical ingredient similar to sibutramine.

Health Canada June/09 warns of foreign Product Alerts: ***Herbal Xenicol*** because it contains undeclared cetilistat. ***BioEmagrecim***, which the FDA had previously warned contained sibutramine, was also found to contain fluoxetine, furosemide and fenproporex. Products: ***Slimbionic***, ***Xsvelten***, ***999 Fitness Essence***, ***24" ince***, ***Light Some***, ***Paiyouji***, ***Pearl White Slimming***, & ***Reducing Weight Easily*** contain undeclared pharmaceutical ingredients (sibutramine and/or phenolphthalein) and/or excessive levels of lead, and may cause serious health effects..

Health Canada Aug/09 is advising via Singapore Health Sciences Authority (HSA) that **Delima Raja Urat** contains undeclared dexamethasone, chlorpheniramine, pheniramine and sibutramine.

Health Canada Dec/09 is advising Canadians not to use certain Acai Berry products after a large number of shipments of adulterated products were stopped at the border. The product names include: **Anti-Aging Acai Berry, Guarana Blast, Brazillian Pure, Anti-aging Vital Rez V, Weight Loss VitalAcai, Dietary Supplement Acai Power Blast and Muscle Mass**. These products for anti-aging and weight loss were found to contain undeclared sildenafil.

Health Canada Dec/09 is warning consumers not to use "**RevolutionDS Weight Loss**", an unauthorized health product promoted for weight loss, because it contains benzylpiperazine (BZP), and may pose serious health risks.

Health Canada Jan/10 informs that U.S. FDA: **Pai You Guo** contains sibutramine and phenolphthalein. Hong Kong Department of Health: **Ku Xiu Ba Xiang Jian Fei Wan** contains sibutramine and an unauthorized substance similar to sibutramine; **Super Slim (Yani)** contains sibutramine and phenolphthalein; **SHoufsy** contains sibutramine & **MIGAC (sic) FAT BURMING (sic) FACTOR** contains sibutramine.

Health Canada Jan/10 is warning consumers not to use the unauthorized product "**The Slimming Coffee**," which was previously sold as "**Lose Weight Coffee**," because it was found to contain sibutramine.

Health Canada Mar/10 is warning Canadians that an unauthorized health product, "**Herbal Diet Natural**" has been found on the Canadian market and contains an undeclared pharmaceutical ingredient similar to the prescription drug sibutramine.

Health Canada is warning Canadians that an unauthorized health product, "**West Pharm Therma Lean Fat Burner Energizer**" was found on the Canadian market. West Pharm Therma Lean Fat Burner Energizer contains Ephedrine and caffeine, which combined together, may cause serious and possibly fatal adverse effects.

Health Canada Apr/10 is warning Canadians that an unauthorized health product, "Slim-30" distributed in Ontario and Quebec by Duxx Enterprises Inc., contains an undeclared pharmaceutical ingredient similar to the prescription drug, sibutramine.

Health Canada May/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **Ba Bao Xiao Ke Dan** The Hong Kong Department of Health warned consumers not to buy or use Ba Bao Xiao Ke Dan after it was found to contain undeclared glibenclamide. 2. **Seven Slim 7 Seshou** (Qingchun Shaonüxing, Jieshixing, Guifurenxing, Songchixing), Shoushen Jiaoguan-Tinei Yundong Wan (Jian Xiabanshen, Jian Quanshen Feipang) The Hong Kong Department of Health warned consumers not to buy or use the six products listed above after they were found to contain undeclared sibutramine and phenolphthalein.

Health Canada May/10 is advising consumers not to use 1. **Botanical Slimming 100% Natural Soft Gel, also sold as Meizitang** The Australian Therapeutic Goods Administration warned consumers not to buy or use this product after it was found to contain undeclared sibutramine. 2. **Marsha Slim Plus** The Hong Kong Department of Health warned consumers not to buy or use Marsha Slim Plus after it was found to contain undeclared sibutramine, an unauthorized substance similar to sibutramine and phenolphthalein. 3**. S&S Super Slender** The Hong Kong Department of Health warned consumers not to buy or use S&S Super Slender after two samples were found to contain agent similar to sibutramine. One of the tested samples also contained undeclared sibutramine and phenolphthalein.

Health Canada June/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **COMECOO, ZHONGCAOYAO-JIANKANGJIANFEI** The Hong Kong Department of Health warned consumers not to buy or consume these two products after they were found to contain undeclared phenolphthalein, sibutramine and two unauthorized substances similar to sibutramine. 2. **Qingzhi Santian Shou** The Hong Kong Department of Health warned consumers not to buy or consume Qingzhi Santian Shou after it was found to contain undeclared sibutramine and an unauthorized substance similar to sibutramine.

Health Canada July/10 is advising consumers not to use the following foreign health product(s) 1.. **Po Chai Pills** (capsule form) The Hong Kong Department of Health warned consumers not to buy or use this product after it was found to contain undeclared sibutramine and phenolphthalein. Sibutramine is a prescription drug and should only be used under the supervision of a health care practitioner while phenolphthalein is no longer authorized for sale in Canada because it may cause

cancer. Po Chai Pills (capsule form) has been recalled by the manufacturer. 2. **LiPO-8 Cap and Glucomi 600 Cap** Hong Kong Department of Health warned consumers not to buy or use these products because they contain undeclared sibutramine.

Health Canada July/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1 Body Beautiful** The Hong Kong Department of Health warned consumers not to buy or consume *1 Body Beautiful* after it was found to contain undeclared phenolphthalein and sibutramine. 2. **USA Yaku Cell Slimming Capsules, Dong Gua Pai You Su, Qing Gua Pai You Su, and Mu Gua Pai You Su** The Hong Kong Department of Health warned consumers not to buy or consume these four products after they were found to contain undeclared phenolphthalein, sibutramine and an unauthorized substance similar to sibutramine.

Health Canada Aug/10 is advising consumers not to use the following foreign health product(s): **Que She** The U.S. FDA warned consumers not to buy or use Que She after it was found to contain undeclared fenfluramine, propranolol, sibutramine and ephedrine. **Sheng Yuan Fang** The Hong Kong Department of Health (HKDH) warned consumers not to buy or use Sheng Yuan Fang after it was found to contain undeclared phenolphthalein and sibutramine.

Health Canada Sep/10 is advising consumers not to use : **Joyful Slim Herb** Supplement The U.S. FDA informed consumers of a recall of one lot (#101408) of Joyful Slim Herb Supplement after FDA tests found it to contain undeclared desmethyl sibutramine. The lot is being voluntarily recalled nationwide in the U.S. by the company J & H Besta Corp.

Health Canada Oct/10 is informing healthcare practitioners and Canadians that Abbott Laboratories is **voluntarily withdrawing the prescription weight-loss drug sibutramine**, which is marketed as Meridia®, from the Canadian market.

Health Canada Nov/10 **Amana Care Seven Slim Herbal Capsules**: The Israel Ministry of Health informed consumers that it found the product Amana Care Seven Slim Herbal Capsules to contain undeclared sibutramine and residue of sildenafil.

Health Canada Nov/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Goya–Bitter Melon - Miyura Fit'x Capsules** contained undeclared phenolphthalein and sibutramine **2. Solo Slim Extra Strength - Revivexxx Extra Strength** contained undeclared didesmethyl sibutramine.

Health Canada Nov/10 "**Fat Burner No. 1**" (labelled in Chinese characters translated as "**Qian Mei Yin Zi**", an unauthorized Chinese herbal weight loss medicine, is being voluntarily recalled by Ying Tai TCM Supplying Ltd. after Health Canada lab tests revealed the product contains two pharmaceutical ingredients: a chemical similar to sibutramine (N,N- didesmethylsibutramine), and sildenafil.

Health Canada Dec/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **Slimming Beauty Bitter Orange Slimming Capsule (Slimming Beauty)** The U.S. Food and Drug Administration warned consumers not to buy or use Slimming Beauty after FDA lab tests revealed that this product contains undeclared sibutramine.

Health Canada Jan/11 The product **Synerate**, manufactured for Strive and distributed by Upper 49th, is being voluntarily recalled from the Canadian market because of the risk of serious, potentially fatal adverse effects from the combination of the ingredients in the product. Synerate, a product used for weight loss or body building, contains caffeine and synephrine, which is similar to ephedrine.

Health Canada Feb/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Fruta Planta, Reduce Weight Fruta Planta** The U.S. FDA warned consumers not to buy or use Fruta Planta and Reduce Weight Fruta Planta after FDA lab tests revealed that this product contains undeclared sibutramine. **2. Slimming Factor** The Australian TGA warned consumers not to buy or use Slimming Factor after TGA lab tests confirmed the presence of the undeclared substances sibutramine, fenfluramine and phenolphthalein. According to the TGA release, the product is sold over the Internet.

Health Canada Mar/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **Celerite Slimming Capsules**: The U.S. FDA informed consumers of a company recall of CeleriteTM Slimming Capsules after it was found to contain undeclared sibutramine. 2. **Herbal Flos Lonicerae** (Herbal Xenicol) Natural Weight Loss Formula: The product was found to contain undeclared sibutramine at more than twice the dose that was normally prescribed before sibutramine was removed from the UK market in 2010.

Health Canada May/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Dr. Health Series CM Factor** The Hong Kong Department of Health warned consumers not to buy or use this product after it was found to contain an unauthorized substance similar to sibutramine that may pose similar health risks.

Health Canada July/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Slim Xtreme Herbal Slimming Capsules** The U.S. Food and Drug Administration informed consumers of a voluntary recall after *Slim Xtreme Herbal Slimming Capsules* was found to contain undeclared sibutramine.

Health Canada Aug/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Celerite Slimming Tea** The U.S. FDA informed consumers of a company recall of Celerite Slimming Tea after it was found to contain undeclared sibutramine. **2. Pink Lady for Women Capsules, St Nirvana Herbal Slimming Capsules** The Australian TGA warned consumers not to use these products after Pink Lady for Women Capsules was found to contain undeclared tadalafil while St Nirvana Herbal Slimming Capsules was found to contain undeclared sibutramine and phenolphthalein. According to the TGA advisories, these products are sold over the Internet. **3. Fifteen products promoted for weight loss** The Hong Kong Department of Health (HKDH) warned consumers not to buy or use these 15 products after they were found to contain at least one of the following undeclared substances: phenolphthalein, sibutramine, and/or an unauthorized substance similar to sibutramine.

Health Canada Oct/11 is advising Canadians not to use these foreign health products as they may pose a health risk. **Slim Forte Slimming Capsules**, **Slim Forte Double Power Slimming Capsules**, **Slim Forte Slimming Coffee** and **Meizitang Botanical Slimming Soft Gel**-The U.S. Food and Drug Administration warned that these weight loss products contain an unauthorized drug (sibutramine). **OxyELITE Pro capsules and Pure Fat Three Days Reduce Weight capsules-** The Australian Therapeutic Goods Administration warned that these weight loss products contain an unauthorized drug (sibutramine), or a prescription drug (yohimbine).

Health Canada Nov/11 is advising Canadians not to use these foreign health products as they may pose a health risk. 1. **Metabolic Advantage** The Singapore Health Sciences Authority warned that this weight-loss product contains prescription drugs (thyroid hormones). 2. **Tian Ma Tu Chung Seven Leave Ginseng, Vall-Boon Tongkat Al,** and **Pao Ni Kang** The Singapore Health Sciences Authority warned that these traditional herbal products contain prescription and over-the-counter drugs (dexamethasone, ketoconazole, repaglinide, pheniramine, and chlorpheniramine). 3. **Slimming Kapsul** The Hong Kong Department of Health warned that this weight-loss product contains an unauthorized drug (sibutramine) and a prescription drug (spironolactone). 4. **Pancre-Plus** The Hong Kong Department of Health warned that this counterfeit Chinese medicine contains an unauthorized drug (phenformin) and a prescription drug (glyburide).

Health Canada Jan/12 advises: 1)**17 weight loss products (see Alert for a complete list)** A-Slim 100% Natural Slimming Capsule, Acai Berry Soft Gel ABC, Advanced Slim 5 >DaiDaiHuaJiaoNang, Dream Body Slimming Capsule, Fruit Plant Lossing Fat Capsule, Health Slimming Coffee, Ja Dera 100% Natural Weight Loss Supplement, Leisure 18 Slimming Coffee, Lishou, Magic Slim Tea, Magic Slim Weight Reduction Capsule, P57 Hoodia, Pai You Guo Slim Tea, PhentraBurn Slimming Capsules, Slender Slim 11 Tengda. The U.S. Food and Drug Administration warned that these weight loss products contain unauthorized drugs (sibutramine, phenolphthalein). **2. Slimina weightloss capsules, S-shape slim capsules** The Australian Therapeutic Goods Administration warned that these weight loss products contain prescription drugs (propranolol, nifedipine) and/or unauthorized drugs (sibutramine, fenfluramine, phenolphthalein). **3. Cardiotium, Paidusu, SlimEasy Herbs Capsule, Tianran Zuanshi Xianweisu** The Hong Kong Department of Health warned that these health products contain prescription drugs (losartan, atorvastatin, thyroxine) and/or unauthorized drugs (sibutramine, phenolphthalein).

Health Canada May/12 1. **CanSui; Lexscl Fat Rapid Loss Capsule; The Extreme-thin Fat Burning Bomb; Xiu Zhi Su L-Carnitine Slimming Capsule** The Hong Kong Department of Health warned that these weight loss products contain unauthorized drugs (sibutramine, phenolphthalein). 2. **Lipro Diet Pills; Xiyouji Qingzhi** weight loss capsules The Australian Therapeutic Goods Administration warned that these weight loss products contain an unauthorized drug (sibutramine).

Health Canada June/12 **1. Japan Weight Loss Blue, Japan Rapid Weight Loss Diet Pills Green; Japan Rapid Weight Loss Diet Pills Yellow:** The U.S. Food and Drug Administration warned that these weight loss products contain prescription drugs (sibutramine, ephedrine alkaloids) and unauthorized drugs (phenolphthalein, and substances similar to sibutramine). **2. Mince Belle; Everlax; Ever Slim; Ever Slim Shake Mix (Strawberry); Ever Slim Shake Mix (Chocolate); Acai-Man Mangosteen Herbal Drink; Perfect Men:** The U.S. Food and Drug Administration informed of a recall because these weight loss and sexual enhancement products contain prescription drugs (sibutramine or tadalafil).

Health Canada Jun/12 testing has identified that the weight loss product "**ZXT Gold**" bee pollen capsules contain hidden pharmaceutical ingredients (sibutramine and phenolphthlalein).

Health Canada Aug/12: Burnaby, B.C. Store (**U-Box**) Selling Potentially Dangerous Weight Loss Products. Further to our previous communications, Health Canada is advising Canadians that four products promoted for weight loss have been seized from "U-Box," a store in Burnaby, B.C. Health Canada testing has identified they contain hidden drug ingredients (sibutramine and phenolphthalein) that may pose serious health risks. Caffeine was also found in some of the products and was not listed on the product label.

Health Canada is advising Canadians that three unauthorized products "**Goya Bittermelon", "S-organic Cocoa+L-carnitine", or "KaBaNa L-Carnitine 360 Slimming Coffee**", promoted for weight loss have been seized from "Cube Inc.", a box-store in Richmond, B.C. These products contain hidden drug ingredients (sibutramine and phenolphthalein) that may pose serious health risks. Caffeine was also found in two products and was not listed on the product label.

Health Canada Apr/13 **1. Diet Garcinia Forte; Shan Dian Shou; Aulura Energy Dietary Supplement** The Hong Kong Department of Health has advised consumers not to use these products after they were found to contain sibutramine and phenolphthalein, drug ingredients that were not declared on their product label.

Health Canada Aug/13 is advising Canadians not to use these foreign health products as they may pose a health risk. **1. Brazilian Slimming Coffee, Leisure 18 Slimming Coffee, 7 Days Slimming Coffee, Brazilian 7 Days Slimming Coffee, Beauty Secret Slimming Coffee, Body Beauty 5 Days Slimming Coffee, Leisure 18 Slimming Mango Juice, Leisure 18 Slimming Orange Juice, Authentic Leisure 18 Slimming Orange Juice, Super Slim Orange Juice, Coffee Fashion Slimming** The Hong Kong Department of Health has advised consumers not to use these products after they were found to contain the undeclared drug ingredients sibutramine and/or phenolphthalein. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/34859a-eng.php **5. Best Slim capsules, Meizi Evolution Botanical Slimming soft gel capsules** The Australian Therapeutic Goods Administration warned consumers not to use these products after they were found to contain the undeclared drug sibutramine.

Health Canada Nov/13 is advising Canadians not to use these foreign health products as they may pose a health risk. These products have been found by regulators in other countries to contain drug ingredients or soy milk allergens that are not declared on the product labels, or a high level of microbial contamination. Prescription drugs should only be taken under the supervision of a healthcare professional. These products are not authorized for sale in Canada and have not been found on the Canadian market, but they may have been brought into the country by travellers or purchased over the Internet:

1. **Aisiyuan V26 Slimming Granules, AcaiBerry Living-XS, and 4C Cosmoslim** , http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36269a-eng.php ;
2. **MAXILOSS Weight Advanced** http://healthycanadians.gc.ca/recall-alert- rappel-avis/hc-sc/2013/36197a-eng.php;
3. **ESV Extra Strong Version, MSV Strong Version, RL Rapid Loss, My Slimmer Me (MSM) soft gel capsules, Natural Miaotiaoyishen capsules, and Paiyouji Natural Slimming Capsules** http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36521a-eng.php.

Health Canada Feb/14: 1. **Lightning 10.0+, LV Shou Reduces Fat, and STB Summit of the Thin Body S Woman Degreasing Burning Pill** The Hong Kong Department of Health warned consumers not to use this product after it was found to contain sibutramine, phenolphthalein, and indomethacin.

Health Canada Apr/14 has seized the unauthorized drug, "**L-Showm Weight Loss Pills**", being sold at the U-Box store, located at 2809-4500 Kingsway, Burnaby, BC. Health Canada testing: contained an undisclosed ingredient, phenolphthalein.

Health Canada Apr/14: Four unauthorized drugs being sold at two SVN FUEL stores - one in Burnaby and one in Coquitlam, B.C. - were seized by Health Canada as they contain ingredients that are potentially dangerous to the health of consumers. The products, and the unapproved ingredients they contain, include **Jack3d** (DMAA (1, 3-dimethylamylamine), **Red Rockets** (ephedrine and caffeine), **West Pharm Therma Lean** (ephedrine and caffeine), and **OxyElite Pro** (1, 3-dimethylamylamine HCl and Yohimbe Bark extract). They were being promoted for weight management.

Health Canada May/14 **Esbelin siloutte te, Esbelin Siloutte Herbal blend with L-Carnitine, Esbelder man, Esbelder fem, Esbelder siloutte** contains Sibutramine, N-Desmethylsibutramine, and N-di-Desmethylsibutramine; **Instant Slim** contains sibutramine and phenolphthalein.

Health Canada May/14 One lot of **Lite Fit USA** (Lot Number 13165, Exp. 05/17) is being voluntarily recalled in the U.S. after analysis by the U.S. Food and Drug Administration revealed the lot contains the undeclared prescription drug sibutramine.

Health Canada May/14: 1. **Slim Fortune, Lidiy & Slim Expert:** FDA found sibutramine; 2. **Dr. Mao Slimming capsules, Perfect Body Solutions, Burn 7**: FDA found sibutramine; **Bella Vi Insane Amp'd Up, Be Inspired, Goodliness Fat Reducing capsules, Jimpness Beauty Fat Loss capsules**: FDA found sibutramine and phenolphthalein.

Health Canada June/14: **Asset Extreme, Asset Extreme Plus, Meizitang Citrus, Slimming Diet Berry Plus, Citrus Fit Gold, Hot Detox, Thinogenics** contains sibutramine. **Tonic Life BP & Slimfast** capsules contains phenolphthalein . **Dr. Ming's Chinese Capsule, Magic Slim and Apple's Quick Impact Weight Loss** contains sibutramine and phenolphthalein.

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MHRA Feb/12 Herbal sliming products found to contain potentially dangerous undeclared pharmaceuticals: **Expelling Grease Slimming Abdomen, V12 Fruit Slimming, 100% Natural Weight Loss Coffee, Leisure 18 Slimming Orange Juice, Fashion Slimming Milk Shake, Langli, Ya Buk & Fruit and vegetables lose weight**. MHRA has received advice from the Danish Medicines Agency that these unlicensed products have been tested and found to contain the Prescription Only Medicine Sibutramine.

MHRA Feb/12 Following a safety alert issued in October 2010 about slimming products containing Paiyouji the Agency has received a further complaint about a product called **'Paiyouji Plus - Fast Acting Slimming Tea'**. This product has been tested by the Agency and, as in the case of other Paiyouji products, found to contain sibutramine.

MHRA Nov/12 has received advice from the Danish Medicines Agency that this unlicensed product, **Ultra Slim** has been tested and found to contain the Prescription Only Medicine Sibutramine.

MHRA Feb/13 is advising consumers not to use the products specified below due to sibutramine content. Product: **Fashion Slimming Coffee, L-Carnitine + P57, L-CarnitinL 360 Slimming Coffee, Brazil Potent Slimming Coffee sachets, Coffee 26 Original sachets, Coffee Nature Fashion Slimming sachets, Slender Capsule, Slim-1.**

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Useful websites:

American Heart Association: Healthy Lifestyle www.americanheart.org/presenter.jhtml?identifier=1200009
Centers for Disease Control and Prevention: Overweight and Obesity www.cdc.gov/nccdphp/dnpa/obesity/index.htm
Cochrane reviews www.cochrane.org
Lifestyle changes week by week plan for patients taking sibutramine www.changeforlifeonline.com
Heart Healthy Diet(s): http://www.**mayoclinic**.com/health/**mediterranean**-diet/CL00011 ; http://www.**cfp**.ca/content/57/8/894.full#ref-20

National Heart, Lung, and Blood Institute: Aim for a Healthy Weight! www.nhlbi.nih.gov/health/public/heart/obesity/lose_wt/index.htm
Obesity drug news www.obesity-news.com
Surgeon General: Physical activity and health: A report of the Surgeon General www.cdc.gov/nccdphp/sgr/sgr.htm
Rimonabant support site www.itswhatyougain.co.uk
UK multicentre obesity management project www.counterweight.org

Extras (RxFiles Herbal Weight Loss

Energy Drinks

Health Canada: Safe Use of Energy Drinks. Accessed online at http://www.hc-sc.gc.ca/hl-vs/iyh-vsv/food-aliment/boissons-energ-drinks-eng.php. {Excessive drinking of energy drinks or mixing them with alcohol can have serious health effects. Energy drinks are meant to supply mental and physical stimulation for a short period of time. They usually contain caffeine, taurine (an amino acid, one of the building blocks of protein), vitamins and glucuronolactone, a carbohydrate. Energy drinks should not be confused with sports drinks such as Gatorade® or Powerade®. Sports drinks re-hydrate the body and provide sugars, which the body burns to create energy and replenish electrolytes.}

Glucomannan (in PGX PolyGlycopleX) Plant fibre water-soluble: unabsorbable polysaccharide (glucose + mannose). May ↓LDL, ↓gastric emptying & improve BG control. Conflicting evidence. SE: gas, bloating, etc.

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FDA Dec/08 alerted consumers nationwide not to purchase or consume more than **25 different products** marketed for weight loss because they contain undeclared, active pharmaceutical ingredients that may put consumers' health at risk. The undeclared active pharmaceutical ingredients in some of these products include sibutramine (a controlled substance), rimonabant (a drug not approved for marketing in the United States), phenytoin (an anti-seizure medication), and phenolphthalein (a solution used in chemical experiments and a suspected cancer causing agent). The weight loss products, some of which are marked as "dietary supplements," are promoted and sold on various web sites and in some retail stores. FDA advises consumers who use the

products to stop taking them and consult their healthcare professional immediately as the health risks posed by these products can be serious (for example, high blood pressure, seizures, tachycardia, palpitations, heart attack or stroke). FDA also encourages consumers to seek guidance from healthcare professional before purchasing weight loss products. See the FDA News Release for a listing of the names of the 25 referenced products. Read the MedWatch 2008 safety summary, including links to http://www.fda.gov/medwatch/safety/2008/safety08.htm#Weight

FDA May/09 warned consumers to immediately stop using **Hydroxycut products by Iovate Health Sciences**, Inc. Hydroxycut products are associated with a number of **serious liver injuries**. Hydroxycut products are dietary supplements that are marketed for weight-loss, as fat burners, as energy-enhancers, as low carb diet aids, and for water loss under the Iovate and MuscleTech brand names. FDA has received 23 reports of serious health problems ranging from jaundice and elevated liver enzymes, an indicator of potential liver injury, to liver damage requiring liver transplant. One death due to liver failure has been reported to FDA. Other health problems reported include seizures; cardiovascular disorders; and rhabdomyolysis, a type of muscle damage that can lead to other serious health problems such as kidney failure.

FDA Jan/10 notified consumers and healthcare professionals about a counterfeit and potentially harmful version of **Alli 60 mg capsules** (120 count refill kit). The **counterfeit version** contained the controlled substance sibutramine and did not contain orlistat, the active ingredient.

FDA July/10 analysis of **Que She** found that it contains: fenfluramine – a stimulant drug withdrawn from the U.S. market in 1997 after studies demonstrated that it caused serious heart valve damage, propranolol – a prescription beta blocker drug that can pose a risk to people with bronchial asthma and certain heart conditions, sibutramine – a controlled substance and prescription weight loss drug, sibutramine was the subject of a recent study whose preliminary findings showed an association between sibutramine use and increased risk of heart attack and stroke in patients who have a history of heart disease, & ephedrine –a stimulant drug that is legally marketed over-the-counter for temporary asthma relief but can pose a risk to people with cardiovascular disease.

FDA Aug/10 lab analysis of **Solo Slim** was found to contain the undeclared drug ingredient Didesmethyl Sibutramine.

FDA July/10 lab analysis of **Slim-30** Herb Supplement distributed by the company was found to contain undeclared N-Desmethyl Sibutramine & Sibutramine.

FDA July/10 lab analysis of this herb supplement, **Joyful Slim** Herb Supplement, was found to contain the undeclared drug, desmethyl sibutramine.

FDA Oct/10 notified consumers that **Slimming Beauty Bitter Orange Slimming Capsules** contain sibutramine, a prescription-only drug which is a stimulant.

FDA Dec/10 has received multiple reports of adverse events associated with the use of **Fruta Planta**, including several cardiac events and one death. FDA lab analysis confirmed that Fruta Planta contains sibutramine.

FDA Jan/11 laboratory analysis confirmed that **Celerite Slimming Capsules** contain sibutramine

FDA Mar/11 lab analysis of **Svelte 30** orange & gray capsules determined that the product contains Sibutramine.

FDA Mar/11 notified Biotab Nutraceuticals, Inc. that two lots of counterfeit product purporting to be **Extenze** contain undeclared drug ingredients. Specifically, lot 0709241 contains tadalafil and sildenafil, and lot 0509075 contains tadalafil and sibutramine.

FDA Mar/11 laboratory analyses of **Celerite Slimming Tea**: Recall - were found to contain undeclared Sibutramine.

FDA May/11 laboratory analysis confirmed that "**Slim Xtreme Herbal Slimming Capsule**" contains sibutramine.

FDA July/11 is advising consumers not to purchase or use "**Slim Forte Slimming Capsules**," "**Slim Forte Slimming Coffee**," and "**Botanical Slimming Soft Gel & Slim Forte Double Power Slimming Capsules**. FDA laboratory analysis confirmed that these products contain sibutramine.

FDA Dec/11 took joint action against several companies selling over-the-counter **hCG products** that falsely and illegally claim to promote weight loss. Labeled "homeopathic" by the seven companies who received the letters, the products contain human chorionic gonadotropin (hCG), a hormone produced during pregnancy by cells that form the placenta. 1. HCG Diet Direct LLC- HCG Diet Homeopathic Drops, 2. The hCG Drops LLC- Homeopathic HCG, 3. HCG Platinum LLC; RightWay Nutrition- HCG Platinum, HCG Platinum X-30, HCG Platinum X-14, 4. Nutri Fusion Systems LLC- HCG Fusion 30, HCG Fusion 43, 5. www.resetthebody.com; www.theoriginalhcgdrops.com-Homeopathic Original HCG, Homeopathic HCG, 6. Hcg-miracleweightloss.com- HCG Extra Weight Loss Homeopathic Drops, 7. Natural Medical Supply- Alcohol Free hCG Weight Loss Formula.

FDA Feb/12 is advising consumers not to purchase or use "**Japan Weight Loss Blue**," a product for weight loss sold on various websites, laboratory analysis confirmed that "Japan Weight Loss Blue" contains sibutramine, analogs of sibutramine, and ephedrine alkaloids.

FDA Apr/12 laboratory analysis confirmed that "**Japan Rapid Weight Loss Diet Pills Yellow**" contains sibutramine and phenolphthalein.

FDA Dec/12 is advising consumers not to purchase or use "SLIMDIA Revolution," a product promoted and sold for weight loss on various websites, including www.pinkfatty.com, and in some retail stores since it contains Sibutramine.

FDA Jan/13 is advising consumers not to purchase or use "**MAXILOSS** Weight Advanced," a product promoted and sold for weight loss on various websites, includingwww.dreamlifeweightloss.com, and in some retail stores since it contains sibutramine.

FDA Feb/13 Olaax Corp announced a nationwide recall of the company's dietary supplement sold under the brand name **Maxiloss Weight Advanced Softgels** to the user level, because FDA testing found the Maxiloss Weight Advanced product to contain Sibutramine.

FDA Jun/13 FDA laboratory analysis confirmed that "**Bethel 30", & "XIYOUJI QINGZHI CAPSULE**" & **JaDera** contains sibutramine. .

FDA Jun/13 A sample of **Extreme Body Slim, Fat Zero, Fruit & Plant Slimming, & Paiyouji Plus** all contains silbutramine.

FDA Jun/3 Beta Labs has recalled certain lots of **Oxyphen, Phentalene, Phen FX, and Red Vipers** because they contain 1,3 dimethylamylamine (DMAA), the

FDA announced over the weekend. The products are used as pre-workout stimulants and for weight loss, but the agency has previously warned that DMAA can be dangerous: it can elevate blood pressure and lead to cardiovascular complications. One distributor, GNC, faces FDA seizure of over 3000 cases of two other DMAA-containing products, **Jack3d and OxyElitePro**. Although the manufacturer of those supplements has ceased production, GNC continues to sell its remaining stocks, according to the New York Times.

FDA July/13 **Meizi Revolution, Strawberry Balance** contains silbutramine.

FDA Aug/13 Herbal Give Care LLC issued a voluntarily recall of all lots of **Esbelin silouttete** and **Esbelin siloutte Herbal Blend with L-Carnitine** (30 Capsules), to the consumer level. The products have been found to contain undeclared Sibutramine, N-Desmethylsibutramine, and N-di-Desmethylsibutramine.

FDA Aug/13 Bethel Nutritional Consulting, Inc., New York, NY, is voluntarily recalling **Quick Thin and Bethel Advance** to the consumer level. These products have been found to contain Sibutramine and Phenolphthalein, and may pose a threat to consumers.

FDA Aug/13 CTV Best Group announced that it is conducting a voluntary nationwide recall of all lots of a dietary supplement products distributed by the company under the names **BEST SLIM 40 Pills** to the consumer level. Testing by FDA revealed the presence of Sibutramine in Best Slim.

FDA Aig/13 Herbal Give Care LLC is voluntarily recalling all lots of **Esbelder man (30 capsules), Esbelder fem (30 capsules) and Esbelder siloutte** (30 capsules) to the consumer level. The products have been found to contain undeclared Sibutramine, N-Desmethylsibutramine, and N-di-Desmethylsibutramine.

FDA Sep/13 laboratory analysis confirmed that **Shou Fu Ti Tun Guo Xiang Xing Jian Fei Jiao Nang** contains sibutramine.

FDA Oct/13: B@B Trade, Inc., Florida is voluntarily recalling all lots of **Slim Fortune, Lidiy, and Slim Expert** to the consumer level. The FDA laboratory analysis of these dietary supplements found to contain undeclared Sibutramine.

FDA Oct/13 is advising consumers not to purchase or use **Perfect Body Solutions or Burn 7.** FDA laboratory analyses confirmed that Perfect Body Solutions and Burn 7 contain sibutramine.

FDA Oct/13 is advising consumers not to purchase or use **Dr. Mao Slimming Capsules**. FDA laboratory analysis confirmed that Dr. Mao Slimming Capsules contain sibutramine.

FDA Oct/13 is advising consumers not to purchase or use **Bella Vi Insane Amp'd or Bella Vi Amp'd Up.** FDA laboratory analyses confirmed that Bella Vi Insane Amp'd and Bella Vi Amp'd Up contain sibutramine.

FDA Nov/13 **SlimExtra Herbal** capsules contain silbutramine.

FDA Dec/13 laboratory analysis found the **Burn 7 Capsules** to contain undeclared Sibutramine.

FDA Jan/14 is advising consumers not to purchase or use **Magic Slim or Dream Body Slimming Capsule**, products promoted and sold for weight loss and sold on various websites and in some stores, since FDA lab analysis confirmed they contains sibutramine.

FDA Jan/14 **Citrus Fit Gold, Hot Detox & Thinogenics** contains sibutramine. **Tonic Life BP contains** phenolphthalein.

FDA Mar/14 is advising consumers not to purchase or use **Vitaccino Coffee**, a product promoted and sold for weight loss. FDA laboratory analysis confirmed that Vitaccino Coffee contains sibutramine.

FDA Mar/14: New Life Nutritional Center is recalling all lots of "**Super Fat Burner capsules, Maxi Gold capsules and Esmeralda softgels**" to the user level after FDA analysis revealed the products contain undeclared active pharmaceutical ingredients: sibutramine, phenolphthalein or a combination of both sibutramine and phenolphthalein.

FDA Mar/14: **Bella Vi Insane Bee Pollen Capsules, Bella Vi BTrim Ultimate Boost, Bella Vi BTrim Max, Bella Vi Extreme Accelerator, Bella Vi Insane Amp'd, and Bella Vi Amp'd U**, contain silbutramine with or without phenolphthalein.

FDA Apr/14: FDA analysis on **New You** contains silbutramine.

FDA Apr/14 has tested multiple **Zi Xiu Tang Bee Pollen** products from various distributors in the United States (US). All products that have been tested, including those that claim to be "genuine" and "anti-counterfeit," have been found to contain one or both of the undeclared drug ingredients sibutramine and Phenolphthalein.

FDA Apr/14 laboratory analysis confirmed that **Infinity & Lite Fit** USA contains sibutramine.

FDA Apr/14: Nature's Universe notified the public it is recalling all lots of **Thinogenics** product sold prior to February 6, 2014 to the user level after FDA analysis revealed that the affected product contained undeclared sibutramine.

FDA May/14 laboratory analysis confirmed that **Slim Trim U & Natural Body Solution** contains sibutramine.

FDA May/14 is advising consumers not to purchase or use **Asset Bee Pollen**, a product promoted and sold for weight loss because it contains sibutramine.

FDA May/14 is advising consumers not to purchase or use **Asset Bold**, a product promoted and sold for weight loss. FDA laboratory analysis confirmed that Asset Bold contains sibutramine.

FDA Jun/14 laboratory analysis confirmed that **La Jiao Shou Shen** contains sibutramine.

FDA Jun/14 laboratory analysis confirmed that **Sliming Diet** contains sibutramine.

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and epidemiological studies with 960 country-years and 9.1 million participants. Lancet 2011; DOI: 10.1016/S0140-6736(10)62035-5.

Folkvord F, Anschütz DJ, Nederkoorn C, et al. **Impulsivity, "Advergames**," and Food Intake. Pediatrics. 2014 May 5.

Health Canada April 2007: The **Safe Use of Health Products** for Weight Loss. http://www.hc-sc.gc.ca/iyh-vsv/med/weight-amaigr_e.html

Health Canada Apr/07 is warning consumers about **Bitter orange** & cardiovascular reactions in the Canadian Adverse Reactions April 2007 Newsletter.

Health Canada Apr/07 is warning consumers from the Hong Kong Department of Health found **Lexscl Fat Rapid Loss capsules to be adulterated with sibutramine** and thyroid hormones.

Health Canada via July/07 Medsafe also advised the public not to use the product **Dai Dai Hua Jiao Nang** because it was found to contain sibutramine.

Health Canada Aug/07 is advising Canadians of a recall in the United States of one lot of **Metaboslim Apple Cider Vinegar**, which is marketed as a dietary supplement, because it has been found to contain sibutramine, a prescription medication that should only be taken under medical supervision.

Health Canada Sept/07 is advising consumers not to use foreign health products due to concerns about possible side-effects: **Jacaranda**, **Queenmer Fat Loss**, **Li Da Dai Dai Hua Jiao Nang**, **J-minus** and **Jelimel Slimming Capsules**. These products are promoted for weight loss and have been found to be adulterated with the prescription drug sibutramine. Sibutramine is used for treating obesity and should only be taken under the supervision of a health professional. **Junyu Jiaonanyihao** has been found to contain the undeclared prescription drugs sibutramine and dexamethasone, as well as phenolphthalein, which is currently prohibited in Canada.. **Heng Tong Jiangtangning Jiaonang** was found to contain the prohibited drug phenformin, and the prescription drug glibenclamide (glyburide) which should only be taken under the supervision of a health professional.

Health Canada Jan/08 is warning Canadians not to use the unauthorized product **Physio Care Lida Dai Dai Hua Jiao Nang Slimming Capsules** (batch number 28012007 / expiration date: Jan 2009). This product is promoted for weight loss and has been found to contain a derivative of the prescription drug sibutramine.

Health Canada April/08 is advising consumers not to use **Xian Zhi Wei II** was found to contain sibutramine and phenolphthalein, which are not meant for self-care and may cause serious side effects.

Health Canada Aug/08 is advising consumers not to use 9 foreign health products due to concerns about possible side-effects: **Dan Bai Shou Shen Su** was found to contain undeclared thyroid hormones and sibutramine. **Karntien and Karntien Easy to Slim** were adulterated with sibutramine and a compound that is similar in structure to sibutramine (N-desmethylsibutramine). **More Slim** was found to contain the undeclared pharmaceutical ingredient sibutramine. **Soloslim** was found to contain an undeclared substance similar in structure to the prescription drug sibutramine. It also contains the prescription drug L-carnitine, as well as synephrine, which is not authorized for sale in weight loss products in Canada.

Health Canada Aug/08 is advising consumers not to use 8 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned against the use of Natural (Xin Yi Dai) and Lasmi because Natural (Xin Yi Dai) was found to contain sibutramine and phenolphthalein, and Lasmi was found to contain sibutramine and spironolactone. The Hong Kong Department of Health warned against the use of AA Qu Feng Shu Jin Wan because it was found to contain the undeclared pharmaceutical ingredient dexamethasone. Apisate contained fenfluramine and Energy ll contained sibutramine. Obat Asam Urat and Asam Urat both contained dexamethasone, phenylbutazone and piroxicam. The Hong Kong Department of Health warned against the use of Slim 3in1 (Xiao Nan zhi Bao) because it was found to contain the undeclared pharmaceutical ingredients sibutramine and phenolphthalein.

Health Canada Sep/08 is advising consumers not to use 2 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned against the use of **Hanguo shoushen yihao** (meiti xing) because it was found to contain the undeclared pharmaceutical ingredient sibutramine. The Hong Kong Department of Health warned against the use of **ARMA - Sin Gang San** and New ARMA - Sin Gang San because they were found to contain the undeclared pharmaceutical ingredients sibutramine and fenfluramine.

Health Canada Nov/08 is advising that the Hong Kong Department of Health warned consumers not to buy or use **Fat Killer, Carbohydrate Cut and Sugar-Carbohydrate Cut** because they contain sibutramine and an unauthorised substance similar in structure to sibutramine.

Health Canada Jan 2009 is advising consumers not to use 4 foreign products: **Zhuang Tjar Gere** because it contains the undeclared prescription drugs sildenafil & tadalafil, **Zhixhue** Capsules manufactured by Vital Pharmaceutical Holdings Ltd. due to concerns of serious side- effects including liver dysfunction, **Tonik Warisan Banjar** because it contains undeclared dexamethasone & **Healthily Slim** because it contains sibutramine.

Health Canada Mar/09 Foreign Product: **68 Weight Loss Products**; Best-life Fat Burning Capsules; Bevidan;Huiji Yin Chiao Chieh Tu Pien & Relacore. Plus Lami, Linglongquxian, Menergy M-Essence, Nyal Day & Night Cold & Flu Fighter (AUST L 146264), Nyal Cold & Flu Fighter (AUST L 146263), 999 Radix Notoginseng, Batch no. 0807021, Slim Pure, Carbohydrate, Kalomee, K Carbohydrate, K Tighten Slim, & K Slimming Pills. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_fpa-ape_2009/index-eng.php

Health Canada June/09 Foreign Product Alerts: **Jia Yi Jian** (undeclared sibutramine & tadalafil); **Shan Dian Qiang Xiao Shou** (undeclared sibutramine & phenolphthalein).

Health Canada June/09 is warning consumers not to use the unauthorized product **Slim Magic Herbal**, which is promoted as a weight-loss product, as it was

found to contain an undeclared pharmaceutical ingredient similar to the prescription drug sibutramine.

Health Canada is warning consumers not to use the unauthorized product **Nutural Slim**, which is promoted as a weight-loss product, as it was found to contain the undeclared pharmaceutical ingredient sibutramine and also an undeclared pharmaceutical ingredient similar to sibutramine.

Health Canada June/09 warns of foreign Product Alerts: ***Herbal Xenicol*** because it contains undeclared cetilistat. ***BioEmagrecim***, which the FDA had previously warned contained sibutramine, was also found to contain fluoxetine, furosemide and fenproporex. Products: ***Slimbionic***, ***Xsvelten***, ***999 Fitness Essence***, ***24" ince***, ***Light Some***, ***Paiyouji***, ***Pearl White Slimming***, & ***Reducing Weight Easily*** contain undeclared pharmaceutical ingredients (sibutramine and/or phenolphthalein) and/or excessive levels of lead, and may cause serious health effects..

Health Canada Aug/09 is advising via Singapore Health Sciences Authority (HSA) that **Delima Raja Urat** contains undeclared dexamethasone, chlorpheniramine, pheniramine and sibutramine.

Health Canada Dec/09 is advising Canadians not to use certain Acai Berry products after a large number of shipments of adulterated products were stopped at the border. The product names include: **Anti-Aging Acai Berry, Guarana Blast, Brazillian Pure, Anti-aging Vital Rez V, Weight Loss VitalAcai, Dietary Supplement Acai Power Blast and Muscle Mass**. These products for anti-aging and weight loss were found to contain undeclared sildenafil.

Health Canada Dec/09 is warning consumers not to use "**RevolutionDS Weight Loss**", an unauthorized health product promoted for weight loss, because it contains benzylpiperazine (BZP), and may pose serious health risks.

Health Canada Dec/09 is advising consumers not to use **Show Party**: Hong Kong Department of Health warned consumers not to buy or consume [shou-shen pai] after it was found to contain undeclared sibutramine and phenolphthalein.

Health Canada Jan/10 informs that U.S. FDA: **Pai You Guo** contains sibutramine and phenolphthalein. Hong Kong Department of Health: **Ku Xiu Ba Xiang Jian Fei Wan** contains sibutramine and an unauthorized substance similar to sibutramine; **Super Slim (Yani)** contains sibutramine and phenolphthalein; **SHoufsy** contains sibutramine & **MIGAC (sic) FAT BURMING (sic) FACTOR** contains sibutramine.

Health Canada Jan/10 is warning consumers not to use the unauthorized product "**The Slimming Coffee**," which was previously sold as "**Lose Weight Coffee**," because it was found to contain sibutramine.

Health Canada Mar/10 is warning Canadians that an unauthorized health product, "**Herbal Diet Natural**" has been found on the Canadian market and contains an undeclared pharmaceutical ingredient similar to the prescription drug sibutramine.

Health Canada is warning Canadians that an unauthorized health product, "**West Pharm Therma Lean Fat Burner Energizer**" was found on the Canadian market. West Pharm Therma Lean Fat Burner Energizer contains Ephedrine and caffeine, which combined together, may cause serious and possibly fatal adverse effects.

Health Canada Apr/10 is warning Canadians that an unauthorized health product, "**Slim-30**" distributed in Ontario and Quebec by Duxx Enterprises Inc., contains an undeclared pharmaceutical ingredient similar to the prescription drug, sibutramine.

Health Canada May/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **Ba Bao Xiao Ke Da**n The Hong Kong Department of Health warned consumers not to buy or use Ba Bao Xiao Ke Dan after it was found to contain undeclared glibenclamide. 2. **Seven Slim 7 Seshou** (Qingchun Shaonüxing, Jieshixing, Guifurenxing, Songchixing), Shoushen Jiaoguan-Tinei Yundong Wan (Jian Xiabanshen, Jian Quanshen Feipang) The Hong Kong Department of Health warned consumers not to buy or use the six products listed above after they were found to contain undeclared sibutramine and phenolphthalein.

Health Canada May/10 is advising consumers not to use 1. **Botanical Slimming 100% Natural Soft Gel, also sold as Meizitang** Australian Therapeutic Goods Administration warned consumers not to buy or use this product after it was found to contain undeclared sibutramine. 2. **Marsha Slim Plus** Hong Kong Department of Health warned consumers not to buy or use Marsha Slim Plus after it was found to contain undeclared sibutramine, an unauthorized substance similar to sibutramine and phenolphthalein. 3. **S&S Super Slender** The Hong Kong Department of Health warned consumers not to buy or use S&S Super Slender after two samples were found to contain agent similar to sibutramine. One of the tested samples also contained undeclared sibutramine and phenolphthalein.

Health Canada June/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **COMECOO**, **ZHONGCAOYAO-JIANKANGJIANFEI** The Hong Kong Department of Health warned consumers not to buy or consume these two products after they were found to contain undeclared phenolphthalein, sibutramine and two unauthorized substances similar to sibutramine. 2. **Qingzhi Santian Shou** The Hong Kong Department of Health warned consumers not to buy or consume Qingzhi Santian Shou after it was found to contain undeclared sibutramine and an unauthorized substance similar to sibutramine.

Health Canada July/10 is advising consumers not to use the following foreign health product(s) 1. **Po Chai Pills** (capsule form) The Hong Kong Department of Health warned consumers not to buy or use this product after it was found to contain undeclared sibutramine and phenolphthalein. Sibutramine is a prescription drug and should only be used under the supervision of a health care practitioner while phenolphthalein is no longer authorized for sale in Canada because it may cause cancer. Po Chai Pills (capsule form) has been recalled by the manufacturer. 2. **LiPO-8 Cap and Glucomi 600 Cap**

The Hong Kong Department of Health warned consumers not to buy or use these products because they contain undeclared sibutramine.

Health Canada July/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1 Body Beautiful** The Hong Kong Department of Health warned consumers not to buy or consume *1 Body Beautiful* after it was found to contain undeclared phenolphthalein and sibutramine. 2. **USA Yaku Cell Slimming Capsules, Dong Gua Pai You Su, Qing Gua Pai You Su, and Mu Gua Pai You Su** The Hong Kong Department of Health warned consumers not to buy or consume these four products after they were found to contain undeclared phenolphthalein, sibutramine and an unauthorized substance similar to sibutramine.

Health Canada Aug/10 is advising consumers not to use the following foreign health product(s): **Que She** The U.S. FDA warned consumers not to buy or use Que She after it was found to contain undeclared fenfluramine, propranolol, sibutramine and ephedrine. **Sheng Yuan Fang** The Hong Kong Department of Health (HKDH) warned consumers not to buy or use Sheng Yuan Fang after it was found to contain undeclared phenolphthalein and sibutramine.

Health Canada Sep/10 is advising consumers not to use : **Joyful Slim** Herb Supplement The U.S. FDA informed consumers of a recall of one lot (#101408) of Joyful Slim Herb Supplement after FDA tests found it to contain undeclared desmethyl sibutramine. The lot is being voluntarily recalled nationwide in the U.S. by the company J & H Besta Corp.

Health Canada Nov/10 **Amana Care Seven Slim Herbal Capsules**: The Israel Ministry of Health informed consumers that it found the product Amana Care Seven Slim Herbal Capsules to contain undeclared sibutramine and residue of sildenafil.

Health Canada Nov/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Goya–Bitter Melon - Miyura Fit'x Capsules** contained undeclared phenolphthalein and sibutramine **2. Solo Slim Extra Strength - Revivexxx Extra Strength** contained undeclared didesmethyl sibutramine

Health Canada Nov/10 "**Fat Burner No. 1**" (labelled in Chinese characters translated as "**Qian Mei Yin Zi**", an unauthorized Chinese herbal weight loss medicine, is being voluntarily recalled by Ying Tai TCM Supplying Ltd. after Health Canada lab tests revealed the product contains two pharmaceutical ingredients: a chemical similar to sibutramine (N,N- didesmethylsibutramine), and sildenafil.

Health Canada Dec/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **Slimming Beauty Bitter Orange Slimming Capsule (Slimming Beauty)** The U.S. Food and Drug Administration warned consumers not to buy or use Slimming Beauty after FDA lab tests revealed that this product contains undeclared sibutramine.

Health Canada Jan/11 The product **Synerate**, manufactured for Strive and distributed by Upper 49th, is being voluntarily recalled from the Canadian market because of the risk of serious, potentially fatal adverse effects from the combination of the ingredients in the product. Synerate, a product used for weight loss or body building, contains caffeine and synephrine, which is similar to ephedrine.

Health Canada Feb/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Fruta Planta, Reduce Weight Fruta Planta** The U.S. FDA warned consumers not to buy or use Fruta Planta and Reduce Weight Fruta Planta after FDA lab tests revealed that this product contains undeclared sibutramine. **2. Slimming Factor** The Australian TGA warned consumers not to buy or use Slimming Factor after TGA lab tests confirmed the presence of the undeclared substances sibutramine, fenfluramine and phenolphthalein. According to the TGA release, the product is sold over the Internet.

Health Canada Mar/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **Celerite Slimming Capsules**: The U.S. FDA informed consumers of a company recall of CeleriteTM Slimming Capsules after it was found to contain undeclared sibutramine. 2. **Herbal Flos Lonicerae** (Herbal Xenicol) Natural Weight Loss Formula: The product was found to contain undeclared sibutramine at more than twice the dose that was normally prescribed before sibutramine was removed from the UK market in 2010.

Health Canada May/11 is advising consumers not to use: 1. **Dr. Health Series CM Factor** The Hong Kong Department of Health warned consumers not to buy or use this product after found to contain substance similar to sibutramine.

Health Canada July/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **Slim Xtreme Herbal Slimming Capsules** The U.S. Food and Drug Administration informed consumers of a voluntary recall after Slim Xtreme Herbal Slimming Capsules was found to contain undeclared sibutramine.

Health Canada Aug/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Celerite Slimming Tea** The U.S. FDA informed consumers of a company recall of Celerite Slimming Tea after it was found to contain undeclared sibutramine. **2. Pink Lady for Women Capsules, St Nirvana Herbal Slimming Capsules** The Australian TGA warned consumers not to use these products after Pink Lady for Women Capsules was found to contain undeclared tadalafil while St Nirvana Herbal Slimming Capsules was found to contain undeclared sibutramine and phenolphthalein. According to the TGA advisories, these products are sold over the Internet. **3. Fifteen products promoted for weight loss** The Hong Kong Department of Health (HKDH) warned consumers not to buy or use these 15 products after they were found to contain at least one of the following undeclared substances: phenolphthalein, sibutramine, and/or an unauthorized substance similar to sibutramine.

Health Canada Oct/11 is advising Canadians not to use these foreign health products as they may pose a health risk. **Slim Forte Slimming Capsules**, **Slim Forte**

Double Power Slimming Capsules, **Slim Forte Slimming Coffee** and **Meizitang Botanical Slimming Soft Gel**-The U.S. Food and Drug Administration warned that these weight loss products contain an unauthorized drug (sibutramine). **OxyELITE Pro capsules and Pure Fat Three Days Reduce Weight capsules**- The Australian Therapeutic Goods Administration warned that these weight loss products contain an unauthorized drug (sibutramine), or a prescription drug (yohimbine).

Health Canada Nov/11 is advising Canadians not to use these foreign health products as they may pose a health risk. 1. **Metabolic Advantage** The Singapore Health Sciences Authority warned that this weight-loss product contains prescription drugs (thyroid hormones). 2. **Tian Ma Tu Chung Seven Leave Ginseng, Vall-Boon Tongkat Al,** and **Pao Ni Kang** The Singapore Health Sciences Authority warned that these traditional herbal products contain prescription and over-the-counter drugs (dexamethasone, ketoconazole, repaglinide, pheniramine, and chlorpheniramine). 3. **Slimming Kapsul** The Hong Kong Department of Health warned that this weight-loss product contains an unauthorized drug (sibutramine) and a prescription drug (spironolactone). 4. **Pancre-Plus** The Hong Kong Department of Health warned that this counterfeit Chinese medicine contains an unauthorized drug (phenformin) and a prescription drug (glyburide).

Health Canada Jan/12 advises: 1)**17 weight loss products (see Alert for a complete list)** A-Slim 100% Natural Slimming Capsule, Acai Berry Soft Gel ABC, Advanced Slim 5 >DaiDaiHuaJiaoNang, Dream Body Slimming Capsule, Fruit Plant Lossing Fat Capsule, Health Slimming Coffee, Ja Dera 100% Natural Weight Loss Supplement, Leisure 18 Slimming Coffee, Lishou, Magic Slim Tea, Magic Slim Weight Reduction Capsule, P57 Hoodia, Pai You Guo Slim Tea, PhentraBurn Slimming Capsules, Slender Slim 11 Tengda. The U.S. Food and Drug Administration warned that these weight loss products contain unauthorized drugs (sibutramine, phenolphthalein). **2. Slimina weightloss capsules, S-shape slim capsules** The Australian Therapeutic Goods Administration warned that these weight loss products contain prescription drugs (propranolol, nifedipine) and/or unauthorized drugs (sibutramine, fenfluramine, phenolphthalein). **3. Cardiotium, Paidusu, SlimEasy Herbs Capsule, Tianran Zuanshi Xianweisu** The Hong Kong Department of Health warned that these health products contain prescription drugs (losartan, atorvastatin, thyroxine) and/or unauthorized drugs (sibutramine, phenolphthalein).

Health Canada May/12 1. **CanSui; Lexscl Fat Rapid Loss Capsule; The Extreme-thin Fat Burning Bomb; Xiu Zhi Su L-Carnitine Slimming Capsule** The Hong Kong Department of Health warned that these weight loss products contain unauthorized drugs (sibutramine, phenolphthalein). 2. **Lipro Diet Pills; Xiyouji Qingzhi** weight loss capsules The Australian Therapeutic Goods Administration warned that these weight loss products contain an unauthorized drug (sibutramine).

Health Canada June/12 **1. Mince Belle; Everlax; Ever Slim; Ever Slim Shake Mix (Strawberry); Ever Slim Shake Mix (Chocolate); Acai-Man Mangosteen Herbal Drink; Perfect Men:** The U.S. Food and Drug Administration informed of a recall because these weight loss and sexual enhancement products contain prescription drugs (sibutramine or tadalafil). **2. Japan Weight Loss Blue, Japan Rapid Weight Loss Diet Pills Green; Japan Rapid Weight Loss Diet Pills Yellow:** The U.S. Food and Drug Administration warned that these weight loss products contain prescription drugs (sibutramine, ephedrine alkaloids) and unauthorized drugs (phenolphthalein, and substances similar to sibutramine).

Health Canada Jun/12 testing has identified that the weight loss product "**ZXT Gold**" bee pollen capsules contain sibutramine and phenolphthlalein.

Health Canada is advising Canadians that three unauthorized products "**Goya Bittermelon", "S-organic Cocoa+L-carnitine", or "KaBaNa L-Carnitine 360 Slimming Coffee**", promoted for weight loss have been seized from "Cube Inc.", a box-store in Richmond, B.C. These products contain hidden drug ingredients (sibutramine and phenolphthalein) that may pose serious health risks. Caffeine was also found in two products and was not listed on the product label.

Health Canada Aug/13 is advising Canadians not to use these foreign health products as they may pose a health risk. **1. Brazilian Slimming Coffee, Leisure 18 Slimming Coffee, 7 Days Slimming Coffee, Brazilian 7 Days Slimming Coffee, Beauty Secret Slimming Coffee, Body Beauty 5 Days Slimming Coffee, Leisure 18 Slimming Mango Juice, Leisure 18 Slimming Orange Juice, Authentic Leisure 18 Slimming Orange Juice, Super Slim Orange Juice, Coffee Fashion Slimming** The Hong Kong Department of Health has advised consumers not to use these products after they were found to contain the undeclared drug ingredients sibutramine and/or phenolphthalein. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/34859a-eng.php **5. Best Slim capsules, Meizi Evolution Botanical Slimming soft gel capsules** The Australian Therapeutic Goods Administration warned consumers not to use these products after they were found to contain the undeclared drug sibutramine.

Health Canada Nov/13 is advising Canadians not to use these foreign health products as they may pose a health risk. These products have been found by regulators in other countries to contain drug ingredients or soy milk allergens that are not declared on the product labels, or a high level of microbial contamination. Prescription drugs should only be taken under the supervision of a healthcare professional. These products are not authorized for sale in Canada and have not been found on the Canadian market, but they may have been brought into the country by travellers or purchased over the Internet:

1. **Aisiyuan V26 Slimming Granules, AcaiBerry Living-XS, and 4C Cosmoslim** , http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36269a-eng.php ;
2. **MAXILOSS Weight Advanced** http://healthycanadians.gc.ca/recall-alert- rappel-avis/hc-sc/2013/36197a-eng.php;
3. **ESV Extra Strong Version, MSV Strong Version, RL Rapid Loss, My Slimmer Me (MSM) soft gel capsules, Natural Miaotiaoyishen capsules, and Paiyouji Natural Slimming Capsules** http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36521a-eng.php.

Health Canada Feb/14: 1. **Lightning 10.0+, LV Shou Reduces Fat, and STB Summit of the Thin Body S Woman Degreasing Burning Pill** The Hong Kong Department of Health warned consumers not to use this product after it was found to contain sibutramine, phenolphthalein, and indomethacin.

Health Canada Apr/14 has seized the unauthorized drug, "**L-Showm Weight Loss Pills**", being sold at the U-Box store, located at 2809-4500 Kingsway, Burnaby, BC. Health Canada testing found that it contained an undisclosed ingredient, phenolphthalein.

Health Canada Apr/14: Four unauthorized drugs being sold at two SVN FUEL stores - one in Burnaby and one in Coquitlam, B.C. - were seized by Health Canada as they contain ingredients that are potentially dangerous to the health of consumers. The products, and the unapproved ingredients they contain, include **Jack3d** (DMAA (1, 3-dimethylamylamine), **Red Rockets** (ephedrine and caffeine), **West Pharm Therma Lean** (ephedrine and caffeine), and **OxyElite Pro** (1, 3-dimethylamylamine HCl and Yohimbe Bark extract). They were being promoted for weight management.

Health Canada May/14 **Esbelin siloutte te, Esbelin Siloutte Herbal blend with L-Carnitine, Esbelder man, Esbelder fem, Esbelder siloutte** contains Sibutramine, N-Desmethylsibutramine, and N-di-Desmethylsibutramine; **Instant Slim** contains sibutramine and phenolphthalein.

Health Canada May/14 One lot of **Lite Fit USA** (Lot Number 13165, Exp. 05/17) is being voluntarily recalled in the U.S. after analysis by the U.S. Food and Drug Administration revealed the lot contains the undeclared prescription drug sibutramine.

Health Canada May/14: 1. **Slim Fortune, Lidiy & Slim Expert**: FDA found sibutramine; 2. **Dr. Mao Slimming capsules, Perfect Body Solutions, Burn 7**: FDA found sibutramine; **Bella Vi Insane Amp'd Up, Be Inspired, Goodliness Fat Reducing capsules, Jimpness Beauty Fat Loss capsules**: FDA found sibutramine and phenolphthalein.

Health Canada June/14: **Asset Extreme, Asset Extreme Plus, Meizitang Citrus, Slimming Diet Berry Plus, Citrus Fit Gold, Hot Detox, Thinogenics c**ontains sibutramine. **Tonic Life BP & Slimfast capsules** contains phenolphthalein . **Dr**. **Ming's Chinese Capsule**, **Magic Slim and Apple's Quic**k **Impact Weight Loss** contains sibutramine and phenolphthalein.

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MHRA Feb/12 Herbal sliming products found to contain potentially dangerous undeclared pharmaceuticals: **Expelling Grease Slimming Abdomen, V12 Fruit Slimming, 100% Natural Weight Loss Coffee, Leisure 18 Slimming Orange Juice, Fashion Slimming Milk Shake, Langli, Ya Buk & Fruit and vegetables lose weight**. MHRA has received advice from the Danish Medicines Agency that these unlicensed products have been tested and found to contain the Prescription Only Medicine Sibutramine.

MHRA Feb/12 Following a safety alert issued in October 2010 about slimming products containing Paiyouji the Agency has received a further complaint about a product called '**Paiyouji Plus - Fast Acting Slimming Tea**'. This product has been tested by the Agency and, as in the case of other Paiyouji products, found to contain sibutramine.

MHRA Nov/12 has received advice from the Danish Medicines Agency that this unlicensed product, **Ultra Slim** has been tested and found to contain the Prescription Only Medicine Sibutramine.

MHRA Feb/13 is advising consumers not to use the products specified below due to sibutramine content. Product names: **Fashion Slimming Coffee, L-Carnitine + P57, L-CarnitinL 360 Slimming Coffee, Brazil Potent Slimming Coffee sachets, Coffee 26 Original sachets, Coffee Nature Fashion Slimming sachets, Slender Capsule, Slim-1.**

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Given these potential adverse effects, the FDA issued an alert on June 4, 2009 that noted the risk of serious liver injury, including liver failure and death, with the use of PTU in adult (1:10,000) and pediatric (1:2,000) patients. These conferences focused on the relative safety of methimazole compared with PTU.[11-14,16] Approximately 30% of patients treated with PTU will have 1- to 2-fold elevations of serum aminotransferase levels. The liver disease associated with PTU can be severe. In the Adverse Event Reporting System (AERS), approximately 22 adult (12 deaths, 5 hepatic transplants) and 10 pediatric (1 death, 6 hepatic transplants) cases of serious hepatic injury associated with PTU treatment were reported. Methimazole, by contrast, was associated with 5 adult cases of serious hepatic injury with 3 deaths. In a system that may overlap with AERS, the United Network for Organ Sharing reported 23 hepatic transplants from 1990 to 2007 (16 adult, 7 children) related to PTU-associated hepatic failure.[11-13,16] Concurrently, no liver transplants related to the use of methimazole were reported. The average PTU dose in children and adults requiring liver transplant was 300 mg daily. Liver failure occurred between 6 and 450 days after starting treatment (median 120 days). Furthermore, there were 2 reports of serious maternal liver disease during pregnancy and 2 reports of liver injury in fetuses of mothers who ingested PTU during pregnancy.[11-14,16]

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Other Agents	Prednisone (Glucocorticoid) 1, 5ᶜ, 50ᶜmg tab; 1mg/ml soln	-Suppresses adrenal function	Classic & Nonclassic congenital adrenal hyperplasia (NCCAH)	-Less effective compared to OCs or anti-androgens[1]	Uncontrolled diabetes, Obesity	Changes typical of Cushing syndrome (weight gain, bone loss), adrenal atrophy	5-7.5mg po daily $8 (5mg tab)
	Ketoconazole NIZORAL 200ᶜmg tab ☎▼	-Adrenal enzyme inhibitor	For patients with Cushing's syndrome while waiting definite therapy	-Similar efficacy to CPA 2-50mg[20]	Hepatic dysfunction Pregnancy, BF	Gynecomastia, dry skin, hepatotoxicity, adrenocortical suppression	200mg po daily $38 (200mg tab)
	Leuprolide acetate depot (GnRH analog) LUPRON & DEPOT ☎▼ 5mg/ml vial ✗⊗; Depot: 3.75,7.5,11.25,22.5 ✗ &30✗ mg	-Potent inhibitor of ovarian steroidogenesis by suppressing LH & FSH	Severe hyperandrogenism of ovarian origin that does not respond to other drugs	-Similar efficacy to CPA 2-50mg, but more adverse effects[20]	Pregnancy, BF Osteoporosis	Osteoporosis Reversable induced menopause	3.75-7.5mg monthly IM, with 25-50ug transdermal estradiol $445 $415 + $24-30
	Metformin GLUCOPHAGE 500ᶜ, 850mg tab	-improves insulin sensitivity	Used in polycystic ovary syndrome (PCOS). Not effective for idiopathic hirsutism	-Small benefit compared to placebo[23] -Inferior to OC or anti-androgen therapy for idiopathic hirsutism[23]	Renal failure	Gastrointestinal upset (minimize by starting low dose 250mg daily, then titrate)	500-2000mg/day (given 250-1000mg BID) $18-28 (500mg tab)

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http://www.rxfiles.ca/rxfiles/uploads/documents/members/Hirsutism-Treatment-Figure-Drug-Chart.pdf

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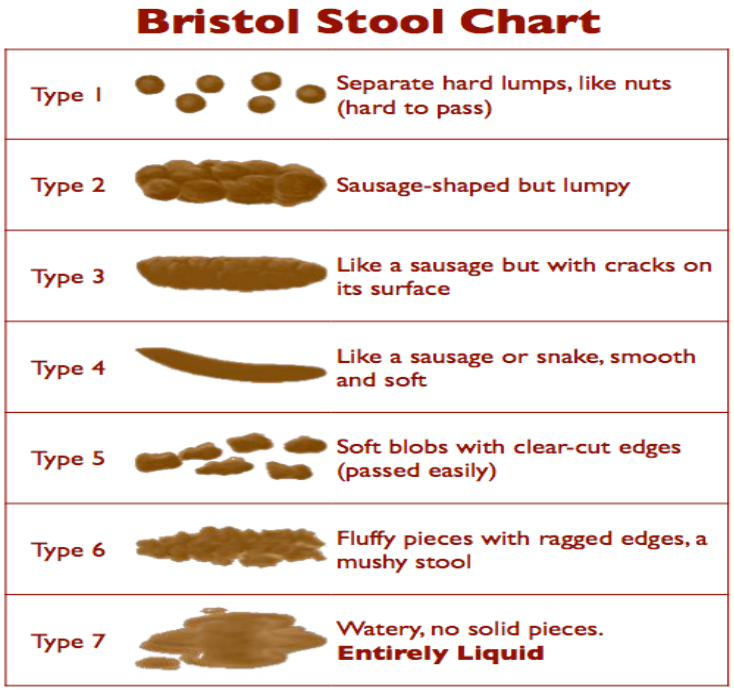

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Additional:

FDA Jan/14 is warning that the over-the-counter constipation drug sodium phosphate (marketed as Fleet, and generics) has been tied to heart and kidney damage and even death when patients exceed the recommended dose. The agency has identified over 50 serious adverse events related to dehydration and electrolyte disturbances (sodium, calcium, and phosphate) with both the oral and rectal formulations. Most cases occurred in older adults and children younger than 5 years.

Cochrane reviews CD:

- TNF-a for induction: data not combined. One RCT indicates single infusion may induce remission. CDP571 may induce remission; no evidence for etanercept. Need longer f/u to assess SE such as TB & lymphoma.
- MTX for induction: data not combined. Evidence from a single large trial suggests benefit of MTX 25 mg IM weekly for induction of remission & complete withdrawal from steroids in refractory disease. No evidence supports lower dose PO MTX.
- CsA for induction: low dose PO CsA does not induce remission. Higher PO or IV doses not adequately evaluated, but ↑risk SE such as nephrotoxicity. One study found clinical improvement on unvalidated scale, but remission not assessed.
- AZA and 6-MP effective for inducing remission (NNT=5); OR increases after 17 weeks of tx; NNT=3 for steroid sparing effect; NNT for SE=14.
- Budesonide: superior to placebo for induction & superior to mesalamine; budesonide was inferior to prednisone/prednisolone, but fewer SE. Note: in disease limited to ileum or ascending colon.
- Natalizumab: superior to placebo for induction, but trials halted after 2 cases fatal progressive multifocal leukoencephalopathy in MS.
- Corticosteroids superior to enteral nutrition therapy for induction.
- 5-ASA not superior to placebo in maintaining remission in CD.
- PO budesonide 6 mg/day not effective in maintaining remission.
- Anti-tubercular tx for maintaining remission: may be effective when remission induced by corticosteroids combined with anti-TB tx; however, this is based on subgroup analyses of 2 trials with small numbers
- Corticosteroids (maintenance): not effective and increased AE.
- Probiotics (maintenance): Lactobacilli GC, E. coli strain Nissle 1917, VSL#3, Saccharomyces boulardii-all not effective, but may be due to small sample size
- AZA (maintenance): effective NNT=7 for maintenance; NNT=3 for steroid sparing; NNH=19.

Cochrane reviews UC:

- 5-ASA superior to placebo to induce remission in UC & trended towards benefit over sulfasalazine (SSZ). However, cost an issue, therefore SSZ generally preferred. 5-ASA has fewer SE than SSZ. 5-ASA not associated with male infertility, but SSZ is.
- 5-ASA superior to placebo in maintaining remission for UC (NNT=6). 5-ASA NOT superior to SSZ (NNT= -19), indicating SSZ superior. HOWEVER, many trials required tolerance of SSZ as part of inclusion criteria (Bergman 2006)
- Transdermal nicotine superior to placebo for inducing remission in UC, however no benefit was seen when compared to standard therapy (oral prednisone or mesalamine). More patients on transdermal nicotine withdrew due to AE then placebo or standard therapy.
- Only 2 small trials identified for CsA; could not be pooled as major differences in design & patients involved. Quick response rates in severe disease appear beneficial, but long-term effects unknown.
- In moderate-severe, refractory disease, infliximab induces remission. NNT=5 at 8 weeks (based on ACT studies alone)
- Systematic review: Combination topical & oral 5ASA superior to oral 5ASA for induction of remission of mild-mod UC. Intermittent topical 5ASA superior to oral for prevention of relapse of quiescent UC.[Ford et al.]

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RxFiles - Acid Suppression - Comparison Chart Supplement

EXTRAs

Sample NG Tube admin instructions for giving a MUPS formulation of a PPI: administering via feeding tube is as follows: "Pre-flush tube with 20 mL SW. Prepare & give immediately: put tab in catheter tip syringe. Draw up 25 mL SW for 14 French tubes or 50 mL SW for 8-13 French. Shake to disperse tab. Hold syringe tip up & check tip for clogging. Attach syringe keeping tip up. Point tip down & give 5-10 mLs. Remove, shake again & give remaining susp. Refill syringe with 25 mL SW, shake to suspend any remaining sediment & give. Post-flush with 40 mL SW for ND, NJ, PGJ and PG tubes and 20-30 mL for all other tube types."

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FDA Apr/11: Teva's lansoprazole **delayed-release orally disintegrating tablet has clogged** and blocked oral syringes and feeding tubes, including both gastric and jejunostomy types, when administered as a suspension.

FDA Feb/12 notified the public that the use of stomach acid drugs known as **proton pump inhibitors** (PPIs) may be associated with an increased risk of **Clostridium difficile**–associated diarrhea (CDAD).

FDA Mar/12 **LINX Reflux Management System** is a surgically-placed string of magnetic titanium beads that is placed at the lower esophageal sphincter. When a person swallows, the device expands to accommodate the liquid or food. Once the food passes, the device keeps a weak lower esophageal sphincter closed, thus preventing material from flowing back into the esophagus.

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Health Canada **Aug/07** is advising consumers that it is currently reviewing new preliminary safety information regarding **serious cardiac events** in patients using Losec (omeprazole) and Nexium (esomeprazole), two prescription drugs used to treat acid-related stomach disorders. (**Feb 27, 2008** Health Canada Completes Safety Review of Losec (omeprazole) and Nexium (esomeprazole) OTTAWA - Further to its Information Update dated August 9, 2007, Health Canada is informing Canadians of the results of its review of safety information for Losec (omeprazole) and Nexium (esomeprazole), two prescription drugs used to treat conditions where a reduction of gastric acid secretion is required, such as ulcers and reflux. In Canada, omeprazole is also sold in generic form as Apo-omeprazole, Ratio-omeprazole and Sandoz-omeprazole. Esomeprazole is only sold under the trade name Nexium. Nexium (esomeprazole) Based on its review of the data available at this time, Health Canada has concluded that there is no evidence supporting an increased cardiovascular risk associated with the long-term use of esomeprazole. The Department will continue to monitor safety issues related to esomeprazole by conducting further analysis of ongoing long-term studies as this data becomes available. Losec (omeprazole) After a thorough analysis, based on the data available to us at this time, we are unable to definitively conclude if there is a potential for increased cardiovascular risk associated with the long-term use of omeprazole. We will continue to evaluate should more conclusive data become available, and will advise Canadians if any further regulatory actions are required.)

Health Canada Aug/09 **Plavix & PPI Interaction** http://www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/medeff/advisories-avis/prof/2009/plavix_hpc-cps-eng.pdf

Health Canada Feb/12 is informing Canadians of a possible association between the use of prescription stomach antacids known as proton pump inhibitors (PPIs) and an increased risk of **Clostridium difficile**-associated diarrhea (CDAD).

Health Canada Oct/12 is informing Canadians that the labelling for **methotrexate and Proton Pump Inhibitors** is being updated to include information on a potential interaction between these products.

Health Canada Apr/13 is informing Canadians and Canadian health care professionals of the potential risk of **bone fractures** associated with the use of drugs known as **proton pump inhibitors**.

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Laine L. Proton pump inhibitors and bone fractures? Am J Gastroenterol 2009;104:S21-S26.

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signs of bleeding in ulcers and reduced the need for endoscopic therapy. (InfoPOEMs: An overnight infusion of omeprazole prior to endoscopy in patients with acute upper GI hemorrhage reduces the need for intervention and speeds discharge from the hospital. (LOE = 1b))
Lau JY, Barkun A, Fan DM, et al. Challenges in the management of **acute peptic ulcer bleeding**. Lancet. 2013 Jun 8;381(9882):2033-43.
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Lee SJ, Shin DH, Hwang HJ et al. **Bleeding Risk and Major Adverse Events in Patients With Previous Ulcer on Oral Anticoagulation** Therapy. Am J Cardiol. 2012 Apr 18.
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***The Rx Files* - *H. pylori* Eradication**
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Extras:

Discontinued Drugs: Alosetron LOTRONEX (2000 -severe constipation & ischemic colitis) avail. in USA ♀ special access 5HT3 antagonist. Not avail. in Canada.

Tegaserod ZELNORM: Mar07- suspended due to CV ischemic events; but Apr08-FDA for Emergency IND situations only use in IBS-constipation & chronic idiopathic constipation in ♀<55yr with no hx of heart problems. 6 mg po bid $160 (NNT=14) 5HT4 agonist Not avail in Canada.

Acupuncture: no difference in IBS symptom severity or IBS-related quality of life when compared to shame-acupuncture.[81]

Patient Handout http://www.nice.org.uk/nicemedia/live/11927/40608/40608.pdf

Notes:

- Children with IBS or functional abdominal pain: probiotic Lactobacillus rhamnosus GG 3 billion colony forming units twice daily reduced # of pain episodes & pain intensity by ≥50% more in Tx vs Pl group (8wks; ave age 6).[53]
- A high-fibre diet and increased frequency of bowel movements may not protect against diverticulosis.[72]

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(IBS) as a supplement to the **January 2009** issue of *The American Journal of Gastroenterology*. "For the gastroenterologist seeing patients with IBS, the new ACG recommendations specify whether or not the range of potential therapies are better than placebo for resolving IBS symptoms," said Lawrence J. Brandt, MD, ACG IBS Task Force, Bethesda, Maryland. The ACG Evidence-Based Systematic Review on IBS can be accessed here: **http://www.acg.gi.org/media/releases/ajg_ibs_supp_0109.pdf**

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N/V EXTRAS:

Alarm signs - "Red Flags" for more severe GI disease:

- age >55, unintended ↓ weight, progressive dysphasia, persistent vomiting, evidence for GI bleed, family hx of GI cancer, altered mental status, abdom pain, feculent vomiting, hematochezia, melena, focal neurologic deficit.

Links:

NHS – CKS: Nausea and Vomiting in Pregnancy - management: http://www.cks.library.nhs.uk/nausea_vomiting_in_pregnancy ; NGC: ACCC Netherlands: http://www.guideline.gov/summary/summary.aspx?doc_id=11793
CINV Guidelines: 1) MASCC: http://www.mascc.org/content/1.html ; 2) ASCO: http://www.asco.org/portal/site/ASCO/
BWH-Overtreatment of PONV: 1) low doses of ondansetron, 1mg iv q6h, adequate ; 2) allow for onset, 30 minutes http://www.brighamandwomens.org/pharmacoepid/Research/EduMaterials/antiemetics3.05.04-web.pdf

Other:

- Fosapreitant: Injectible form of EMEND, 150mg vial in Canada.

Hyperemesis gravidarum

- N/V in pregnancy common, but hperemesis gravidarum likely affects <1%
- Tx: fluids & electrolytes, thiamine (or IV if prolonged & unable to take po), antiemetics.

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Adapted from Timmins Palliative Care (P. Critchley MD, T. Dolanjski Pharmacist) Prepared by: *L. Regier* BSP, BA, B. *Jensen* BSP

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FDA Sep/09 notified healthcare professionals that a Boxed Warning is being added to the prescribing information for **Promethazine** Hydrochloride products, describing the risks of severe tissue injury, including gangrene, requiring amputation following intravenous administration of promethazine.
FDA Dec/09 The Texas Department of State Health Services and FDA notified healthcare professionals and consumers, especially pregnant or breastfeeding women, to avoid consuming a product called "**Nzu**", taken as a traditional remedy for morning sickness,because of the potential health risks from high levels of lead and arsenic, noted on laboratory analysis by Texas DSHS. Nzu, which is sold at African specialty stores is also called Calabash clay, Calabar stone, Mabele, Argile and La Craie. It generally resembles balls of clay or mud and is usually sold in small plastic bags with a handwritten label identifying it as "Nzu" or "Salted Nzu."
FDA Dec/10 The injectable form of **dolasetron** mesylate (Anzemet) should not be used to prevent nausea or vomiting related to chemotherapy because the drug increases the risk for torsade de pointes. The FDA recommends against using Anzemet injections in patients with congenital long-QT syndrome. The warning does not apply to Anzemet tablets because the risks for developing an abnormal heart rhythm are not as high as with the injections. FDA MedWatch alert (Free)
FDA Sep/11 The U.S. Food and Drug Administration (FDA) is informing the public of an ongoing safety review of the anti-nausea drug Zofran (**ondansetron**, ondansetron hydrochloride and their generics). Ondansetron may increase the risk of developing abnormal changes(QT prolongation & torsades) in the electrical activity of the heart
FDA Dec/12 is working with the manufacturers of all **32 mg dose Ondansetron Injectable** Products (brand and generic) to voluntarily recall them from the market due to QT serious cardiac toxicity.
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Health Canada May/11 ANZEMET (**dolasetron** mesylate) - Withdrawal of **20 mg/mL Intravenous** Injection Due to Potential Risk of Arrhythmias. New data suggest that intravenous administration of the injectable form of ANZEMET (dolasetron mesylate) may result in serious arrhythmias.
Health Canada July/11 is informing health professionals and consumers that the labelling information for the drug **metoclopramide** is being updated to include stronger warnings on the risk of a movement disorder known as "**tardive dyskinesia**."
Health Canada Mar/12: **Domperidone** should be used at the lowest possible dose. The risk of serious ventricular arrhythmias (QT) and sudden cardiac death may be higher in patients taking daily doses greater than 30 mg, and in patients over 60 years old.
Health Canada Oct/12: Ondansetron can cause a dose-dependent prolongation of the electrocardiographic-corrected QT interval (QTc), which can lead to Torsade de Pointes, a potentially life-threatening heart rhythm abnormality. The new maximum recommended single intravenous (IV) dose of ZOFRAN®is 16 mg infused over 15 minutes.
Health Canada May/14 has completed a safety review of the serotonin blocking drugs **dolasetron** (ANZEMET), **granisetron** (KYTRIL and generics), **ondansetron** (ZOFRAN and generics) and palonosetron (ALOXI), which are used for treating nausea and vomiting. This review identified a potential risk of **serotonin syndrome**.
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See also: Sexual Dysfunction Chart: http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-Sexual-Dysfx-Drugs-Overview.pdf

Erectile Dysfunction Comparison Chart (ED) Treatment Chart

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Apomorphine (CR sublingual tabs) **ApoKyn** (USA)	Centrally acting agent stimulates dopamine sites in the hypothalamus C	SE: nausea (↓with time, CR SL tabs);headache, dizziness, sedation, yawning Not affected by food or alcohol	Onset <30min Peak ~1h Duration ~1-2h Safe with nitrates so may be preferred in select cardiac patients Can be used in combination with PDE5 inhibitors for increased effect Limited efficacy compared to PDE5 inhibitors generally [39]	2-3mg 6mg	

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FDA May 2007 FDA chemical analysis revealed that **Energy Max** contains thione analog of sildenafil, a substance with a structure similar to sildenafil, the active ingredient in Viagra, an FDA-approved drug for ED.Substances like this are called analogs because they have a structure similar to another drug and may cause similar side effects and drug interactions. **True Man** contains a thione analog of sildenafil or piperadino vardenafil, an analog of vardenafil, the active ingredient in Levitra, another FDA-approved prescription drug for ED. Neither the thione analog of sildenafil nor piperadino vardenafil are components of approved drug products.

FDA: Sept 21, 2007 -- TWC Global LLC, Inc., issued nationwide recall of **Axcil** and **Desirin**, both marketed as dietary supplements, because they contain potentially harmful, undeclared ingredients. FDA laboratory analysis of **Axcil and Desirin** found that the lot of 02B07 contained 3mg/g of sildenafil, the active ingredient of a FDA approved drug used for erectile dysfunction (ED).

FDA Feb/08 Palo Alto Labs and FDA notified consumers and healthcare professionals of a voluntary nationwide recall of two dietary supplements, **Aspire36** and **Aspire Lite**. The products were recalled because they were found to contain Aildenafil in trace amounts and Dimethyl sildenafil thione, an analog of Sildenafil, a drug used to treat erectile dysfunction.

FDA May/08 The U.S. Food and Drug Administration is advising consumers not to purchase or use "**Blue Steel**" or "**Hero**" products, marketed nationally as dietary supplements, because these products contain undeclared ingredients similar to sildenafil.

FDA May/08 is requesting that the manufacturer of **Xiadafil** — an "all natural" dietary supplement sold to treat erectile dysfunction — recall all its stock from natural food stores & discontinue marketing it on the Web since it contains an analog of sildenafil.

FDA May/08 notified consumers and healthcare professionals that supplement products sold under the brand name of **Viril-ity Power** (VIP) Tablets is being recalled because one lot was found to contain a potentially harmful undeclared ingredient, hydroxyhomosildenafil, an analog of sildenafil.

FDA July/08 Jack Distribution, LLC issued a voluntary nationwide recall of selected lots of **Rize 2 The Occasion Capsules** and **Rose 4 Her Capsules**, marketed as dietary supplements. The products were recalled because certain lots contained thiomethisosildenafil, an undeclared analog of sildenafil, a FDA-approved drug used for Erectile Dysfunction.

FDA July/08 not to buy or use **Viapro** 375mg Capsules because one lot of the product was found to contain a potentially harmful undeclared ingredient, thio-methisosildenafil, an analog of sildenafil.

FDA Aug/08 chemical analysis of **Xiadafil VIP** tablet lots 6K029 and 6K029-SEI found that the product contained an undeclared ingredient, hydroxyhomosildenafil

FDA Mar/09- Bodee LLC and FDA notified consumers and healthcare professionals of a nationwide recall of all the company's supplement product sold under the name **Zencore Plus**. FDA lab analysis of Zencore Plus samples found the product contains benzamidenafil, an undeclared drug product and a PDE5 inhibitor.

FDA Apr/09 Nature & Health Co. and FDA notified healthcare professionals of a recall of a supplement product, **Libimax**. FDA analysis found the product contains tadalafil.

FDA July/09 and Haloteco notified healthcare professionals and consumers of a nationwide voluntary recall of Libipower Plus. Lab analysis of **Libipower Plus** samples were found to contain undeclared Tadalalafil.

FDA July/09 found **Steam** (Nutracoastal Trading LLC's dietary supplement) product contains sulfoaildenafil, an analog of sildenafil.

FDA Nov/09 notified consumers that **Stiff Nights**, a product sold as a dietary supplement, contains sulfoaildenafil, a chemical similar to sildenafil (Viagra).

FDA Nov/09 & RockHard Laboratories notified consumers that **RockHard Weekend**, a product sold as a dietary supplement, contains sulfoaildenafil, an analogue of sildenafil.

FDA Dec/09 warned that **Atlas Operations, Inc**. notified consumers of a nationwide recall of the company's dietary supplements for sexual enhancement. These products are sold as dietary supplements throughout the USA. FDA lab analyses found that the products tested from certain batches contain Sulfoaildenafil.

FDA Mar/10 & Natural Wellness notified consumers that **MasXtreme**, a product sold as a dietary supplement contains aildenafil close in structure to sildenafil and is expected to possess a similar pharmacological and adverse event profile as well as the drug phentolamine which is an alpha-adrenergic blocker.

FDA Apr/10 & Kanec USA notified healthcare professionals of a nationwide recall of **Stud Capsule For Men** [Lot #060607-01/060108-01, Exp 6-2013], after being informed by FDA that laboratory analysis of a sample found the product to be adulterated with sildenafil, an FDA approved drug.

FDA June/10 **Magic Power Coffee**: Product marketed as a dietary supplement for sexual enhancement contains the drug ingredient hydroxythiohomosildenafil.
FDA Aug/10 lab analysis of **Revivexxx Extra Strength** was found to contain undeclared tadalafil.
FDA Aug/10 notified Novacare LLC that certain products appear to contain sulfoaildenafil: **Stiff Nights, Aziffa, Size Matters, Erex, Mojo, Hard Drive, Eyeful, Red Magic, Straight Up, Zotrex, Monster Excyte, WOW, Xaitrex, Verect, Prolatis, Xytamax, Maxyte, Libidinal, OMG, OMG45, and Zilex (with Golden Spear) summers.**
FDA July/10 & Good Health, Inc. is conducting a voluntary recall after FDA lab analyses found that the product tested from certain batches of **Vialipro** contain Sulfoaildenafil.
FDA July/10 notified consumers that lab analysis of lots of ejaculoid **XXTREME** and **stimuloid II** found that the products, sold as dietary supplements, contain sulfoaildenafil
FDA Aug/10 had Lab analysis of **Mr. Magic** to contain hydroxythiohomosildenafil and sulfoaildenafil.
FDA Aug/10 analyzed **TimeOut** and determined that it contains hydroxythiohomosildenafil.
FDA Nov/10 ISSUE: Lab analysis has found **Duro Extend Capsules for Men** to contain Sulfoaidenafil, an analogue of Sildenafil
FDA Dec/10 warned consumers not to use **Man Up Now** capsules, marketed as a dietary supplement for sexual enhancement, because FDA analysis determined that the product contains sulfoaildenafil
FDA Dec/10 notified the public that testing determined that **RockHard Weekend** Lot Numbers 100159 and 100260 sold as blister packs, 3ct bottles and 8ct bottles & **Pandora** Lot Numbers 100378 sold as blister packs & **Passion Coffee** contain an analogue of sildenafil.
FDA Mar/11 notified Biotab Nutraceuticals, Inc. that two lots of counterfeit product purporting to be **Extenze** contain undeclared drug ingredients. Specifically, lot 0709241 contains tadalafil and sildenafil, and lot 0509075 contains tadalafil and sibutramine.
FDA Mar/11 laboratory analysis confirmed that **Black Ant** contains sildenafil.
FDA Mar/11 ISSUE: FDA lab analysis of **X-Hero** found the product contains sulfosildenafil, the analogue of the active ingredient of an FDA-approved drug. In addition, FDA analysis of **Male Enhancer** sample found the product contains tadalafil.
FDA Apr/11 Lab analyses of **Best Enhancer** found that the products to contain Sulfoaildenafil.
FDA May/11 **Regenerect**: Recall - Undeclared Drug Ingredient of lab confirmed the presence of Sulfoaildenafil.
FDA June/11 lab analyses found Via **Xtreme Ultimate Sexual Enhancer Dietary** Supplement for Men to contain sulfoaildenafil methanesulfonate.
FDA Nov/11 lab analysis for Lot 10090571 found **Virility Max** to contain sulfoaildenafil.
FDA Feb/12 Healthy People Co. notified the public of a recall of the company's dietary supplements sold under the brand names Healthy People Co. FDA lab confirmed presence of Sibutramine & Tadalafil, making these products unapproved new drugs. (Mince Belle Dietary Supplement, PERFECT Men Dietary Supplement , EVERLAX Dietary Supplement, EVER Slim Dietary Supplement, Herbal Drink Acai-man Mangosteen Dietary Supplement, EVER SLIM Shake Mix Dietary Supplement)
FDA Feb/12 Regeneca, Inc. notifed the public of a nationwide recall of **RegenArouse**, Lot Number 130100. FDA lab analysis confirmed the presence of Tadalafil.
FDA Feb/12 is advising consumers not to purchase or use "**Hard Ten Days**," & "**Man King**" a product for sexual enhancement sold on various websites. FDA laboratory analysis confirmed that "Hard Ten Days" contains sildenafil
FDA Apr/12 laboratory analysis confirmed that "**France T253**" contains sildenafil.
FDA Apr/12 is advising consumers not to purchase or use "**X-Rock**," a product for sexual enhancement manufactured by CRM Laboratories and sold on various websites, including www.xrockme.com. FDA laboratory analysis confirmed that "X-Rock" contains sildenafil and hydroxythiohomosildenafil.
FDA Apr/12 laboratory analysis confirmed that "**Instant Hard Rod**" contains aminotadalafil. FDA laboratory analysis confirmed that "**ZenMaxx**" contains aminotadalafil. FDA laboratory analysis confirmed that "**RigiRx Plus**" contains aminotadalafil.
FDA May/12 is advising consumers not to purchase or use "**VMaxx Rx**," a product for sexual enhancement sold on various websites, including www.vmaxxrx.com. FDA laboratory analysis confirmed that "VMaxx Rx" contains the undeclared ingredient sulfoaildenafil. FDA is also advising consumers not to purchase or use "**Boost — Ultra Sexual Enhancement Formula**." This product is promoted and sold on various websites, includingwww.boostultra.biz. FDA laboratory analysis confirmed that "Boost—Ultra Sexual Enhancement Formula" contains sildenafil. FDA is also advising consumers not to purchase or use "**Firminite**," a product for sexual enhancement sold on various websites, including **www.firminite.com.** FDA laboratory analysis confirmed that "Firminite" contains tadalafil.
FDA May/12 West Coast Nutritionals, Ltd. is conducting a recall of all lots of their dietary supplements **Firminite, Extra Strength Instant Hot Rod, & Libidron** to the consumer. FDA lab analysis of Firminite was found to contain undeclared Tadalafil.
FDA May/12 is advising consumers not to purchase or use "**EreXite**," a product for sexual enhancement sold on various websites, including www.amazon.com. FDA laboratory analysis confirmed that "EreXite" contains tadalafil.
FDA Aug/12 CRM Laboratories is conducting a consumer/user level recall of all **X-ROCK 3 Day Pill For Men and Z-ROCK** products sold between October, 2011 and April, 2012. Finished product of X-ROCK 3 Day Pill for Men and Z-ROCK was tested and found to contain an analogue of an ingredient in an FDA-approved drug. Analytical tests conducted by the FDA concluded that the products contained sildenafil and hydroxythiohomosildenafil.
FDA Aug/12 Revatio (**sildenafil**) should **not be prescribed to children and adolescents** with pulmonary arterial hypertension, according to an FDA MedWatch alert. The warning is based on the results of a trial published in Circulation that showed increased mortality at medium and high doses of Revatio, compared with low-*dose treatment, among patients aged 1 to 17 years. Low-dose Revatio did not improve exercise capacity.*
FDA Sep/12: Body Basics Inc. announced that it is conducting a voluntary nationwide recall of **ACTRA-Sx 500 Dietary Supplement** Capsules, Lot 008-A, Expiration December 2013. The Company, through independent lab analysis, has confirmed the presence of Sildenafil Citrate.
FDA Sep/12 Evol Nutrition Associates, Inc./Red Dawn ("Evol Nutrition") notified the public of a nationwide recall of all lots of two dietary supplement products distributed by the company under the names **Mojo Nights and Mojo Nights for Her** to the consumer level. Testing by the FDA revealed the presence of undeclared tadalafil and sildenafil in Mojo Nights (Evol Nutrition is also recalling Mojo Nights for Her).
FDA Dec/12: **Libigrow, Libigrow XXXtreme, Blue Diamond, Blue Diamond Platinum, Mojo Nights, Mojo Nights Supreme, And Casanova**: Recall - Undeclared Ingredients Sulfoaildenafil and Thioaildenafil.
FDA Jan/13 Freedom Trading is conducting a voluntary consumer recall of a product sold as a dietary supplement under the brand name of **Super Power**. This product was sold between August 2012 and January 2013 nationwide & the products contained trace amounts of sildenafil.
FDA Mar/13 Green Planet, Inc. notified the public of a recall of its dietary supplement product **Night Bullet**. Analytical tests conducted by the FDA found that the product contains trace amounts of Sulfohydroxyhomosildenafil and Aminotadalafil, which are analogues of sildenafil.
FDA Apr/13 laboratory analysis confirmed that "**Ninja Mojo"& "Love Rider**" contains tadalafil. FDA also confirmed that "**AFFIRM XL**" contains the undeclared ingredient sulfoaildenafil.
FDA Apr/13 Consumer Concepts, Inc. notified the public of a consumer/user level recall of all **ROCK-It MAN** Male Enhancement Capsules sold between October, 2012 and April, 2013. Analytical tests conducted by the FDA concluded that the product contained hydroxythiohomosildenafil.
FDA Apr/13 **Affirm XL**, Inc. is conducting a voluntary recall to the consumer level after FDA lab analysis testing found the product to contain an analogue of sildenafil.
FDA Apr/13 laboratory analysis confirmed that "**Sex Plus**" contains undeclared sildenafil, tadalafil, sulfosildenafil and dimethylacetildenafil. FDA laboratory analysis confirmed that "**Zoom-Zooma-Zoom**" contains sildenafil, the active ingredient in the FDA-approved prescription drug Viagra.
FDA May/13 American Lifestyle is announcing that it is conducting a voluntary recall of all lots of **Vicerex** UPC 893490820087 and **Black Ant** UPC 4026666142546. Laboratory analysis conducted by the FDA has determined the Vicerex product contains undeclared tadalafil and the Black Ant product contains undeclared sildenafil.
FDA May/13 is advising consumers not to purchase or use "**Bullet Proof**," a product promoted and sold for sexual enhancement on various websites and in some retail stores. FDA laboratory analysis confirmed that "Bullet Proof" contains tadalafil. Plus Chang Kwung announced today that it is conducting a voluntary nationwide recall of the company's dietary supplements sold under the brand name **Lightning Rod** (500 mg per capsule packaged in 3-count, UPC 6 89076 20257 2 and 12-count bottles, UPC 6 89076 20297 8), because FDA testing found the Lightning Rod Capsules to contain an analogue of Sildenafil.
FDA May/13: BeaMonstar Products notified the public that it is recalling its **SexVoltz, Velextra, and Amerect** capsules. Laboratory analysis conducted by the FDA on SexVoltz and Velextra has determined these products contain undeclared tadalafil.
FDA Jun/13 laboratory analysis confirmed that "**Reload**" , "**Cave Diver**" , "**Super Cheetah**", "**Nights to Remember**" , & "**X Zen Platinum**", contains sildenafil.
FDA Jun/13 A sample of **Royal Dragon Herbal Tonic Balls** contains vardenafil.
FDA July/13 **Clalis, Exten 1300 & MaxTreme Zen** contains sildenafil, while **MVP Mega** contains talalafil.
FDA July/13 **Silver Sword** & **Clalis** contains sildenafil.
FDA Aug/13 Volcano Company is recalling all lots of **Volcano Male Enhancement Liquid and Volcano Male Enhancement Capsules** to the consumer level. FDA test results revealed the Volcano Male Enhancement Liquid has been found to contain undeclared Desmethyl Carbodenafil, Dimethylsildenafil, and Dapoxetine.
FDA Aug/13: Jack Rabbit Inc. announced that it is conducting a voluntary nationwide recall of one lot of the company's dietary supplement product sold under the name **Jack Rabbit**. FDA lab analysis of the product was found to contain Sildenafil and Tadalafil.
FDA Aug/13 Hardmenstore.com is voluntarily recalling 1000 lots of **72HP, Evil Root and Pro Power Max** at the consumer level. According to representatives of the FDA, 72HP, Evil Root and Pro Power Max have reportedly been found to contain

amounts of the PDE-5 Inhibitor, sildenafil.

FDA Sep/13 is advising consumers not to purchase or use **XZone Premium**, a product promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that XZone Premium contains sildenafil, tadalafil, and dapoxetine.

FDA Sep/13 is advising consumers not to purchase or use **Wood-E**, a product promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that Wood-E contains sildenafil.

FDA Sep/13 is advising consumers not to purchase or use **Xzen 1200, Xzen Gold or Xzen XPress,** products promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that it contains either sildenafil & tadalafil.

FDA Sep/13 Haute Health, LLC is voluntarily recalling all lots of **Virilis Pro, PHUK and Prolifta** at the retail and consumer level. Virilis Pro, PHUK and Prolifta have been found to contain amounts of the PDE-5 Inhibitor sildenafil.

FDA Nov/13: Fossil Fuel Products, LLC, is recalling lots QL110714A102 and QL110408B046 of "**RezzRX**." Laboratory analysis conducted by the FDA determined the RezzRX lot QL110714A102 contains undeclared hydroxylthiohomosildenafil and aminotadalafil and RezzRX lot QL110408B046 contains undeclared hydroxylthiohomosildenafil.

FDA Nov/13: Jobbers Wholesale is recalling Lot No. KWAKPMC030505175957019 of **Rhino 5 Plus**, Lot No. JBP-L-1270-70 of **Maxtremezen** and Lot No. KWAKPMC03050517 of **Extenzone**. FDA analysis found these products to contain undeclared desmethylcarbondenafil and dapoxetine, making these products unapproved new drugs.

FDA Nov/13 Vitality Research Labs is recalling lots K58Q and F50Q of **VitaliKOR Fast Acting**. FDA laboratory analysis on VitaliKOR has determined that this product contains undeclared Vardenafil and Tadalafil.

FDA Nov/13: Tendex is voluntarily recalling Lot# F51Q of P-Boost and Lot # F51Q of NatuRECT to the consumer level. FDA laboratory analysis on Lot# F51Q of **P-Boost**, which the firm also labels as **NatuRECT**, has determined that this product contains undeclared tadalafil.

FDA Nov/13 **Alpha Male** contains sildenafil & other analogs.

FDA Jan/14 Midwest Wholesale is voluntarily recalling the following products Boost**: Ultra, XZone Gold, Sexy Monkey, Triple MiracleZen Platinum, Magic for Men, "New" Extenze, and New XZen Platinum**. FDA analysis found these products to contain undeclared Sildenafil and/or Tadalafil.

FDA Jan/14: **JINQIANGBUDOR Red Dragon** & **Tiger King** contains sildenafil; **Bali Mojo** & **Vimax** contains tadalafil; SexRx Contains both sildenafil and tadalafil.

FDA Mar/14 is clarifying its previous recommendation related to prescribing Revatio (**sildenafil**) for children with pulmonary arterial hypertension (PAH). Revatio is FDA-approved only to treat PAH in adults, not in children; however, health care professionals must consider whether the benefits of treatment with the drug are likely to outweigh its potential risks for each patient.

FDA Mar/14: Nova Products, Inc. issued a voluntary recall of the following products: **African Black Ant (Lot# 2006-000926), Black Ant (Lot# 2006-3627878), XZen Gold (Lot# 130310GL), ZXen Platinum (Lot# 130520PL), XZen 1200 (Lot# 13051012), XZone Gold (Lot# 131110GL), and XZone 1200 (Lot# 13071012)** at the retail level. FDA laboratory analysis on these products has determined that they contain undeclared amounts of sildenafil and tadalafil.

FDA apr/14 is advising consumers not to purchase or use **S.W.A.G**, a product promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that S.W.A.G contains sildenafil.

FDA May/14: Eugene Oregon, Inc. is voluntarily conducting this recall because FDA analysis of **African Black Ant, Black Ant, and Mojo Risen** distributed to a third party revealed that the distributed products contained undeclared amounts of the active pharmaceutical ingredients sildenafil and tadalafil.

FDA May/14 is advising consumers not to purchase or use **MV5 Days**, a product promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that MV5 Days contains sildenafil,

FDA Jun/14: advising consumers not to purchase or use **Eyeful** contains hydroxythiohomosildenafil; **Liu Bian Li** contains sildenafil; **Dick's Hard Up** contains tadalafil; **3 Hard Knights** contains sildenafil and thiosildenafil; **Full Throttle On Demand** contains propoxyphenyl sildenafil; GoldReallas contains sildenafil and thiosildenafil.

FDA June/14 laboratory analysis confirmed that **Zhen Gong Fu** contains sildenafil.

FDA Jun/14 laboratory analysis confirmed that **Gold Vigra & Miraculous Evil Root** contains sildenafil.

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Goldstein I, Lue TF, Padma-Nathan H, et al.; Sildenafil Study Group. Oral sildenafil in the treatment of erectile dysfunction. *N Engl J Med* 1998;338:1397-404. (**low 25mg dose effective**)

Guazzi M, Vicenzi M, Arena R, et al. **Pulmonary hypertension** in heart failure with preserved ejection fraction: a target of phosphodiesterase-5 inhibition (sildenafil) in a 1-year study. Circulation. 2011 Jul 12;124(2):164-74.

Gupta BP, Murad MH, Clifton MM, et al. The effect of **lifestyle modification and cardiovascular risk factor reduction** on erectile dysfunction: a systematic review and meta-analysis [Sept 12, 2011]. Arch Intern Med. 2011

Health Canada Jan/06 Natural health product **Libidfit** may pose health risks (promoted for sexual enhancement and erectile dysfunction, but contains an undeclared amount of a pharmaceutical ingredient similar to sildenafil) http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_02_e.html

Health Canada May/06 is warning consumers not to use the product **Nasutra** because it has been found to contain the undeclared ingredient sildenafil (chemical name for Viagra) that could lead to serious health risks, especially for patients with existing medical conditions such as heart problems, those who may be taking heart medications, or those who may be at risk for strokes.

Health Canada Feb/07 is advising consumers not to use the following product listed in the table below due to concerns about possible side-effects. More info **Power 58; Platinum Power 58; Ehanix; Jolex; Onyo; Deguozonghengtianxia** because they contained acetildenafil. Acetildenafil is an analogue of sildenafil, a prescription medication indicated for treatment of erectile dysfunction.

Health Canada Mar/07 is warning consumers not to use the unauthorized natural health product **XOX For Men**, because it contains an undeclared pharmaceutical ingredient, tadalafil, an ingredient found in the prescription drug Cialis. The use of XOX For Men could pose serious health risks, especially for patients with existing medical conditions such as heart problems, those taking heart medication, or those at risk of stroke.

Health Canada Mar/07 is warning consumers not to use the unauthorized product **Vigorect** Oral Gel Shooter, because it contains an undeclared drug substance tadalafil, which should only be available by prescription.

Health Canada Apr/07 is warning consumers from the United States FDA found **V.MAX and Rhino Max (Rhino V Max) to contain undeclared amounts of aminotadalafil**, an analogue of tadalafil, used to treat erectile dysfunction.

Health Canada May/07 is warning consumers **Urat Madu** capsules are marketed for the treatment of erectile dysfunction. The product is adulterated with **sildenafil**, a prescription drug that has been associated with serious side effects including sudden vision loss, penile tissue damage and urinary tract infection.

Health Canada May/07 is advising consumers that **HS Joy of Love** product is marketed as a dietary supplement and was found to contain piperadino **vardenafil**.

Health Canada May/07 is advising consumers not to use 6 foreign health products due to concerns about possible side-effects: **Power 58 Extra, Platinum Power 58 Extra, Enhanix New Extra Men's Formula, Valentino, King Power Oral Solution, and Stretch Up** Capsules are marketed as treatments for erectile dysfunction. The products contain analogues of **sildenafil** and **vardenafil**, which are prescription drugs used for the treatment of erectile dysfunction.

Health Canada June/07 is warning consumers not to use the product **Encore Tabs for Men**, because it contains an undeclared pharmaceutical ingredient similar to the approved drug tadalafil.

Health Canada July/07 is warning consumers not to use **Zencore** Tabs, a product advertised as a dietary supplement for sexual enhancement, because it contains an undeclared pharmaceutical ingredient similar to the approved drug tadalafil.

Health Canada July/07 & the US Food and Drug Administration (FDA) found ***Liviro3*** to contain tadalafil, a prescription drug that should only be taken under the guidance of a health professional.

Health Canada Aug/07 via Medsafe, the New Zealand health regulatory authority, advised the public not to use the products **Darling Capsules, Dali Capsules, Spanish Fly** Capsules, and an unnamed product, because they were found to contain sildenafil.

Health Canada Aug/07 Consumers who use **Excite for women or Ultimates for men** may be at risk of serious side effects similar to those associated with sildenafil.

Health Canada Sept/07 is advising consumers not to use **Satis 60 Hours Ever Lasting Formula** is used for the treatment of erectile dysfunction/sexual enhancement. It was found to contain piperidenafil an analogue of vardenafil.. **True Man** and **Energy Max** are used as sexual enhancement/ erectile dysfunction products and were found to contain an analogue of sildenafil or vardenafil.

Health Canada Sept/07 is advising consumers not to use 5 foreign health products due to concerns about possible side-effects: **Top Gun for Men Herbal Extracts** has been found to contain a substance similar to tadalafil. **Oyster Plus** has been found to contain tadalafil. **Deguozhanjiang** contains sildenafil and tadalafil, prescription drugs used for the treatment of erectile dysfunction. **Chongcaoliubian Jiaonang** and **Santi Scalper Penis Erection** Capsule contain sildenafil.

Health Canada Nov/07 is advising consumers not to use **Axcil** and **Desirin**, are promoted as natural sexual enhancement/ erectile dysfunction products. Consumers are warned not to use Axcil and Desirin because both products were found to contain the prescription drug sildenafil.

Health Canada Mar/08 is warning consumers not to use **ADAM**, an unauthorized product that contains an undeclared pharmaceutical ingredient similar to the prescription drug sildenafil.

Health Canada Mar/08 is warning consumers not to use **Libidus**, an unauthorized product promoted on the web site of the manufacturer for the treatment of erectile dysfunction. The product may pose serious health risks, as it was found to contain the undeclared prescription drug sildenafil.

Health Canada April//08 warns that Singapore's Health Sciences Authority (HSA) advised the public not to use the product **Power 1 Walnut**, because it was found to contain the prescription drugs sildenafil and glibenclamide

Health Canada April//08 is advising consumers not to use 2 foreign health products, **Aspire 36** and **Aspire Lite**, because they were found to contain undeclared sildenafil analogues.

Health Canada April/08 is warning consumers not to use **Vigoureux**, an unauthorized product promoted for the treatment of erectile dysfunction. The product may pose serious health risks, as it was found to contain the prescription drug sildenafil

Health Canada April/08 is advising consumers not to use 2 foreign health products due to concerns about possible side-effects: **Tian Li** was found to contain tadalafil and hydroxyhomosildenafil. Xian Zhi Wei II was found to contain sibutramine and phenolphthalein, which are not meant for self-care and may cause serious side effects.

Health Canada May/08 is advising consumers not to use **vpxl No1** Dietary Supplement for Men was found to contain tadalafil

Health Canada May/08 is warning consumers not to use **Desire**, an unauthorized product promoted to enhance male sexual performance as this product may pose serious health risks in certain patients. Lot 0070263 of the product was found to contain the prescription drug phentolamine.

Health Canada June/08 **Nangen Zengzhangsu** (may also be known as Nangen or Nangeng), Sanbianwan, Jiu Bian Wang, Tian Huang Gu Shen Dan, Zui Xian Dan Gong Shi Zi, and Power Up. The Hong Kong Department of Health has warned consumers not to use these herbal/proprietary Chinese medicine products promoted for erectile dysfunction because they have been found to contain sildenafil and/or glibenclamide.

Health Canada June/08 **Zhong Hua Niu Bian**. Zhong Hua Niu Bian is an herbal/proprietary Chinese medicine product promoted for erectile dysfunction. Singapore's Health Sciences Authority has warned against the use of this product because it has been found to contain sildenafil, glibenclamide, tadalafil and sibutramine

Health Canada July/08 Foreign Product Alerts: **Super Shangai,Strong Testis, Shangai Ultra, Shangai Ultra X, Lady Shangai, Shangai Regular (also known as Shangai Chaojimengnan), Actra-Sx, An unknown product containing the plant Lycium barbarum L., Adam Free, NaturalUp, Erextra, Yilishen, Blue Steel, Hero, & Naturalë Super Plus.** These products have been found to contain sildenafil or an unapproved substance similar to sildenafil.

Health Canada July/08 is advising consumers not to use foreign health products due to concerns about possible side-effects: Wodibo. **Wodibo** is promoted as an all-natural Chinese potency-enhancing product for the treatment of erectile dysfunction. The Danish Medicines Agency has warned against the use of Wodibo because it was found to contain sildenafil and tadalafil, prescription drugs authorized for treatment of erectile dysfunction. **Viril-Ity-Power** (VIP) Tabs. The U.S. Food and Drug Administration has warned consumers not to use Viril-Ity-Power (VIP) Tabs because it was found to contain an undeclared ingredient similar to the prescription drug sildenafil.

Health Canada Aug/08 is warning consumers not to use **Rize 2 The Occasion** capsules (Rize2), an unauthorized product promoted for the treatment of erectile dysfunction, because it may pose serious health risks. Rize 2 contains an undeclared pharmaceutical ingredient similar to the prescription drug sildenafil.

Health Canada Aug/08 is advising consumers not to use 5 foreign health products due to concerns about possible side-effects: **Oyster Extract** Caps. The Hong Kong Department of Health has recalled Oyster Extract Caps because they were found to contain an undeclared ingredient similar to the prescription drug sildenafil. **Xiadafil** VIP Tabs. At the request of the U.S. Food and Drug Administration, U.S. federal authorities seized all Xiadafil VIP Tabs sold in 8 tablet bottles (Lot #6K029) and blister cards of 2 tablets (Lot #6K029-SEI) because they were found to contain an undeclared ingredient similar to the prescription drug sildenafil. **Herb Vigour, Natural Vigour and China Vigour**. The Netherlands Health Care Inspectorate, the U.K. Medicines and Healthcare Products Regulatory Agency, and the Danish Medicines Agency has warned against the use of Herb Vigour, Natural Vigour and China Vigour because they were found to contain undeclared pharmaceutical ingredients used for the treatment of erectile dysfunction that should only be taken under the supervision of a health care professional.

Health Canada Aug/08 is advising consumers not to use 9 foreign health products due to concerns about possible side-effects: **Armstrong Natural Herbal Supplement, Enhanix New Extra Men's Formula, Power 58 Extra, and Platinum Power 58 Extra** were adulterated with tadalafil or unapproved substances with structures similar to tadalafil and vardenafil.

Health Canada Sep/08 is advising consumers not to use 3 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned consumers not to buy or use **Lover Liquid Nutriment Herbal Supplement and Onyo** because they were found to contain undeclared pharmaceutical ingredients. Lover Liquid Nutriment Herbal Supplement was found to contain sildenafil while Onyo was found to contain sildenafil, as well as unapproved substances with structures similar to sildenafil and vardenafil. The U.S. Food and Drug Administration warned consumers not to use the product **Rose 4 Her** because it was found to contain an undeclared ingredient similar to the prescription drug sildenafil.

Health Canada Sep/08 is advising consumers not to use 6 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned consumers not to buy or use **Dr. Life or Chong Cao Ju Wang** because they were found to contain undeclared pharmaceutical ingredients. Dr. Life contains an unauthorised substance similar in structure to tadalafil while Chong Cao Ju Wang contains sildenafil.

Health Canada Oct/08 is advising consumers not to use 2 foreign health products due to concerns about possible side-effects: Swissmedic warned consumers not to buy or use the product **Powertabs** because it contains an unauthorised substance similar in structure to sildenafil. The Hong Kong Department of Health warned consumers not to buy or use **Sweet Energizer Vitality** Candy because it was found to contain an unauthorised substance similar in structure to tadalafil.

Health Canada Oct/08 is warning consumers not to use **Eros Fire**, a product promoted to enhance sexual performance, as this product may pose serious health risks. The product was found to contain xanthoanthrafil (also known as benzamidenafil), which is not indicated on the label.

Health Canada Nov/08 is advising consumers not to use 5 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned consumers not to buy or use **Lu Quan** because it contains undeclared glibenclamide and sildenafil. The Hong Kong Department of Health warned consumers not to buy or use **Fat Killer, Carbohydrate Cut and Sugar-Carbohydrate Cut** because they contain sibutramine and an unauthorised substance similar in structure to sibutramine, and **Zhuang Yao Gu Shen** Capsule because it contains sildenafil.

Health Canada Nov/08 is warning consumers not to use **Firm Dose** and **Granite Rooster**, two products promoted to enhance male sexual performance, as these products may pose serious health risks. Firm Dose was found to contain an undeclared pharmaceutical ingredient similar to sildenafil, while the product Granite Rooster was found to contain an undeclared pharmaceutical ingredient similar to tadalafil.

Health Canada Jan 2009 is advising consumers not to use 4 foreign products: **Zhuang Tjar Gere** because it contains the undeclared prescription drugs sildenafil & tadalafil, **Zhixhue** Capsules manufactured by Vital Pharmaceutical Holdings Ltd. due to concerns of serious side- effects including liver dysfunction, **Tonik Warisan Banjar** because it contains undeclared dexamethasone & **Healthily Slim** because it contains the undeclared prescription drug sibutramine.

Health Canada Mar/09 Foreign Product Alerts: 68 Weight Loss Products; Best-life Fat Burning Capsules; Bevidan;Huiji Yin Chiao Chieh Tu Pien; Relacore
http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_fpa-ape_2009/index-eng.php

Health Canada June/09 Foreign Product Alerts: **Jia Yi Jian** (undeclared sibutramine & tadalafil); **Zencore Plus** (undeclared benzamidenafil) & **Zhong Guo Shen Fang** (undeclared med like sildenafil).

Health Canada July/09 is warning that the Singapore Health Sciences Authority (HSA) warned consumers to not buy or use **XP Tongkat Ali Supreme** after it was found to contain undeclared tadalafil.

Health Canada Oct/09: **Dynasty Worldwide Jinglida So Young Formula**- The Singapore Health Sciences Authority (HSA) warned consumers to not buy or use since contained undeclared aminotadalafil.

STEAM lot#80214, 90260 -The U.S. FDA informed consumers of a voluntary manufacturer recall of two lots of STEAM after FDA testing found these lots to contain undeclared sulfoaildenafil (lot# 80214) & undeclared tadalafil (lot# 90260).

Syntrax Fyre (contained Yohimbine), **Kam Yuen Brand Wan Ying Yang Gan Wan (contained sildenafil)** - The Hong Kong Department of Health warned consumers not to buy or use these products.

Health Canada Nov/09 is warning consumers not to use Herblex "**Once More**"since it was found to contain sildenafil.

Health Canada Dec/09 is advising Canadians not to use certain Acai Berry products after a large number of shipments of adulterated products were stopped at the border. The product names include: **Anti-Aging Acai Berry, Guarana Blast, Brazillian Pure, Anti-aging Vital Rez V, Weight Loss VitalAcai, Dietary Supplement Acai Power Blast and Muscle Mass**. These products advertised for anti-aging and weight loss were found to contain undeclared sildenafil.

Health Canada Dec/09 is advising consumers not to use the following foreign health products: 1. **Power-Plus P**: The Singapore Health Sciences Authority issued a recall notice for Power-Plus P (expiry date 03/03/2011) after it was found to contain undeclared tadalafil. 2. **Zeng Da Yan Shi Wan**: The Hong Kong Department of Health warned consumers not to buy or use after it was found to contain undeclared sildenafil.

Health Canada Jan/10 informs that Finish Food Safety Authority: **Full Contact Max Potency** contains thio-sildenafil and thio-homosildenafil; Singapore Health Sciences Authority: **M-Action** contains desmethylacetildenafil and acetilacid. U.S. FDA: **RockHard Weekend** contains sulfoaildenafil.

Health Canada Jan/10 is advising consumers not to use the unauthorized product "**Stiff Nights**" after the U.S Food and Drug Administration (FDA) found that this product contains an undeclared substance similar to the prescription drug sildenafil.

Health Canada Feb/10: **2H & 2D-** Hong Kong Department of Health (HKDH) warned consumers not to buy or use 2H & 2Dafter it was found to contain undeclared tadalafil. Products distributed by **Atlas Operations Inc**. The FDA informed consumers of a voluntary recall by Atlas Operations Inc. of certain lots of some products that were found to contain undeclared sulfoaildenafil, which is an unauthorized substance similar to sildenafil. **STRO Emperor** Capsules The Irish Medicines Board warned consumers not to buy or use STRO Emperor Capsules after it was found to contain undeclared tadalafil.

Health Canada Mar/10 is warning Canadians that an unapproved health product, **POWER-MAX** that contains sildenafil.

Health Canada May/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **Man Power** The Hong Kong Department of Health warned consumers not to buy or use Man Power product after it was found to contain undeclared tadalafil.

Health Canada June/10 is warning Canadians that the unauthorized health products "**Vigofit**" and "**Once More**," which are promoted to enhance male sexual performance, have been seized by Health Canada inspectors from retail stores in Abbotsford and Surrey, British Columbia. These two products contain sildenafil.

Health Canada July/10 is advising consumers not to use the following foreign health product(s) due to concerns about possible adverse reactions: 1. **Stud Capsule For Men** The U.S. FDA informed consumers of a voluntary recall of one lot (Lot #060607-01/060108-01 Exp 6-2013) after it was found to contain undeclared Sildenafil.

Health Canada July/10 is advising Canadians about "**UP Ultimate Performance for Men**", an unauthorized health product containing undeclared sildenafil.

Health Canada July/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1 Body Beautiful** The Hong Kong Department of Health warned consumers not to buy or consume 1. **Atlas Operations Inc. expands its U.S. recall of over 30 sexual enhancement supplements** The U.S. FDA informed consumers of an expanded recall of certain lots of products after some were found to contain undeclared sulfoaildenafil. The products are being voluntarily recalled nationwide in the U.S. by the company Atlas Operations Inc. 2. **Stallion, SZM Formula for Men, Tomcat Ali and Volcanic** New Zealand's Medsafe warned consumers not to buy or use these four products after they were found to contain undeclared tadalafil. 3. **Vitalex for men and Vitalex for women** The U.S. FDA informed consumers that the *Vitalex*products were found to contain acetildenafil, which is an unauthorized substance similar to sildenafil.

Health Canada Aug/10 is advising **Magic Power Coffee** The U.S. FDA warned consumers not to buy or use Magic Power Coffee after it was found to contain undeclared hydroxythiohomosildenafil.

Health Canada Aug/10: "**SeXXX DRIVE**", promoted as a herbal supplement to enhance male sexual performance, was tested by Health Canada and found to contain undeclared hydroxyhomosildenafil.

Health Canada Aug/10 has seized the unauthorized sexual enhancement supplements "**Male Enhancement ExtenZe**" and "**Women ExtenZe**" imported and sold by the Happy Paradise Adult Store in Burnaby, British Columbia. The labels of each of these unauthorized products list the prescription ingredient pregnenolone and the controlled drug, DHEA dehydroepiandrosterone). The labels of the unauthorized "Male Enhancement ExtenZe Nutritional Supplements" list the ingredient yohimbe extract (bark).

Health Canada Sep/10 **E.O.D. Erection on Demand**" being promoted as a herbal to enhance male sexual performance, the product was tested by Health Canada and found to contain tadalafil.

Health Canada Sep/10 is advising consumers not to use : 1. **Golden aryuru, Baisheng wei ge, Zhonghua niubian, Ten ka dai 1 bou, Kuai gan bei zeng chao yue zi wo (Happy felling doubly increase [sic]), Ling tou lang, SkyFruit, Chu bi ho ken, Jinbolang, Suika Koso, Lov, I ka ou (2009 nen sin hoso) and/or I ka ou (saisinsui shutsu hoso)** The Japanese Ministry of Health, Labour and Welfare warned consumers not to buy or use the 12 products listed above because they were found to contain undeclared sildenafil and/or other unauthorized substances similar to sildenafil that may pose similar health risks (norhongdenafil, acetil acid, and tioqinapiperifil). 2. **Vialipro** The U.S. FDA informed consumers of a recall of certain lots of Vialipro after FDA tests found product samples to contain undeclared sulfoaildenafil, which is an unauthorized substance similar to sildenafil and may pose similar health risks.

Health Canada Nov/10 **Amana Care Seven Slim Herbal Capsules**: The Israel Ministry of Health informed consumers that it found the product Amana Care Seven Slim Herbal Capsules to contain undeclared sibutramine and residue of sildenafil.

Health Canada Nov/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. MasXtreme** contains undeclared aminotadalafil while the other (#911035) contains undeclared aildenafil and phentolamine **2. Mr. Magic Male Enhancer from Don Wands** contained hydroxythiohomosildenafil and sulfoaildenafil **3. So Hard for Men - Pulse8 for Women - The Rock - Tonic 66** contained the undeclared pharmaceutical substances tadalafil, sildenafil, and/or hydroxyhomosildenafil **4. TimeOut** contained undeclared hydroxythiohomosildenafil.

Health Canada Nov/10 "**Fat Burner No. 1**" (labelled in Chinese characters translated as "**Qian Mei Yin Zi**", an unauthorized Chinese herbal weight loss medicine, is being voluntarily recalled by Ying Tai TCM Supplying Ltd. after Health Canada lab tests revealed the product contains two pharmaceutical ingredients: a chemical similar to sibutramine (N,N- didesmethylsibutramine), and sildenafil.

Health Canada Dec/10 "**Durazest**" and "**Once More**": Certain lots of two male sex enhancement products recalled as they may pose serious health risks. Certain lots (listed below) of two health products promoted for male sexual enhancement, "Durazest for Men" and "Once More," have been voluntarily recalled by Natural Performance Products Ltd. Health Canada laboratory tests identified the presence of a chemical similar to tadalafil (nortadalafil) in one lot of each product.

Health Canada Dec/10 is informing Canadians that NorthRegentRx has begun to voluntarily recall its product, **ResurreXX** from the Canadian market. NorthRegentRx is requesting that wholesalers, distributors and retailers stop sale of this product since contained an undeclared substance "hydroxyhomosildenafil".

Health Canada Dec/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **Shaguar, Signature Signergy, VIGRX (green capsule), VIGRX (white capsule), VigRx, VigRX Plus** New Zealand's MedSafe warned consumers to not buy or use these products after they were found to contain undeclared sildenafil, hydroxyhomosildenafil, thiosildenafil, and/or tadalafil. .

Health Canada Feb/11 is advising consumers not to use the following foreign health products promoted for sexual enhancement due to the presence of unauthorized substances (PDE5 derivatives eg. sildenafil): **1. Aziffa, Erex, Eyeful, Hard Drive, Libidinal, Maxyte, Mojo, Monster Excyte, OMG, OMG45, Prolatis, Red Magic, Size Matters, Stiff Nights, Straight Up, Verect, WOW, Xaitrex, Xytamax, Zilex (with Golden Spear), Zotrex 2. Prolatis' Duro Extend Capsules For Men 3. Tiger King 4. Vigor-25, Man Up Now**

Health Canada Feb/11 is advising consumers not to use the following foreign health product **RockHard Weekend (lots 100159 and 100260 sold as blister packs, 3-count bottles and 8-count bottles)** The U.S. FDA informed consumers of a nationwide voluntary recall of certain lots (see above) of RockHard Weekend and Pandora after lab tests confirmed the products contain an unauthorized substance similar to sildenafil.

Health Canada Mar/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Nite Rider Maximum Sexual Enhancer for Men - STUD Capsule for Men:** The U.S. FDA informed consumers of a company recall of these products after they were found to contain undeclared sildenafil.

Health Canada May/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Gold Seagull Long Zhi Wan, Venergy** The Hong Kong Department of Health advised consumers not to buy or use these products after Gold Seagull Long Zhi Wan was found to contain undeclared glibenclamide, while Venergy was found to contain undeclared sildenafil. **2. Rock Hard Extreme, Passion Coffee** The U.S. FDA advised consumers not to buy or use these products after they were found to contain undeclared sulfoaildenafil, which is an unauthorized substance similar to sildenafil and may pose similar health risks.

Health Canada July/11 "**Man Up Now**" Removed From Sale at Delta and Surrey Stores: May Pose Serious Health Risks to Canadians, was removed from sale at "O! Behave" retail stores in Delta and Surrey, B.C. after Health Canada's testing identified undeclared sildenafil.

Health Canada July/11 is advising Canadians that we have updated our list of unauthorized health products. These products were also removed from sale at Male and Female Harmony retail stores in Richmond and Burnaby, B.C., along with the Happy Paradise Adult Store in Burnaby. {**Sildenafil: in BAOLONG Switzerland Rolex 168 Prolong Time, BAOLONG Yilishen, Black Gold, Herbal Viagra, "Jin Chong Chao – Golden Cordyceps", Lubiangaowansu, MAGNA-RX, MAXMAN II capsules, Shenrong dabuwan, Traditional Chinese Medicine Viagra, V100, VIGER, VigRX for Men, VINIX capsules, Wolf, "XiongBaTian", Zang Gong Mi Lian Nan Bao} & Zeng Bei Jiu Zhan-Tadalafil.**

Health Canada July/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Black Ant** The U.S. Food and Drug Administration warned consumers to immediately stop using *Black Ant* after it was found to contain undeclared sildenafil at an amount three times the starting dosage for the approved prescription drug product. **2. Natural Vigra VIAGRA Tablets and Satibo Capsules** The Australian Therapeutic Goods Administration (TGA) advised consumers to stop using *Natural Vigra VIAGRA Tablets* after it was found to contain undeclared sildenafil, and *Satibo Capsules* after it was found to contain undeclared tadalafil and hydroxyhomosildenafil. **3. X-Hero and Male Enhancer** The U.S. Food and Drug Administration informed consumers of a voluntary recall after *X-Hero* was found to contain undeclared sulfosildenafil while *Male Enhancer* was found to contain undeclared tadalafil.

Health Canada July/11 is advising Canadians that we have updated our list of unauthorized health products to include a new product, **Tibet Babao**, which was found to contain undeclared sildenafil, a prescription erectile dysfunction drug. This product and several others have been removed from sale at the **Happy Paradise Adult Store in Burnaby, B.C**.

Health Canada Aug/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Pink Lady for Women Capsules, St Nirvana Herbal Slimming Capsules** The Australian TGA warned consumers not to use these products after Pink Lady for Women Capsules was found to contain undeclared tadalafil while St Nirvana Herbal Slimming Capsules was found to contain undeclared sibutramine and phenolphthalein. According to the TGA advisories, these products are sold over the Internet.

Health Canada Oct/11 is advising Canadians not to use these foreign health products as they may pose a health risk. **SXL Sexcellence sachets**- The Australian Therapeutic Goods Administration warned that this sexual enhancement product contains an unauthorized drug (sulfosildenafil).

Health Canada Nov/11 is advising Canadians not to use these foreign health products as they may pose a health risk. **1. Maxidus capsules, Chao Jimengnan SuperPowerful Man tablets, Fu Yuan Chun capsules, and Qing Tian Zhu tablets** The Australian Therapeutic Goods Administration warned that these sexual enhancement products contain prescription drugs (sildenafil, tadalafil) and/or unauthorized drugs (sulfohydroxyhomosildenafil, sulfosildenafil).

Health Canada Nov/11: An unauthorized health product, "**Stiff One Hard 169**" is being voluntarily recalled from the Canadian market after Health Canada's testing identified an undeclared prescription medication in the product (thiodimethylsildenafil, an undeclared substance similar to the prescription medication sildenafil).

Health Canada Dec/11 is advising "**Yanshiwang**", "**Jin Kong Fu**" and "**Chong Cao She Bian Zhuang Yang Dan**". These products were removed from sale at Male and Female Harmony retail stores in Richmond and Burnaby, B.C., along with the Happy Paradise Adult Store in Burnaby. These contained sildenafil.

Health Canada Jan/12 advises: **1. Get Stiff, Maxi Mize** New Zealand's Medsafe warned that these sexual enhancement products contain prescription drugs (tadalafil, vardenafil, yohimbine) and/or unauthorized drugs (hydroxyhomosildenafil, hydroxythiohomosildenafil). **2. Ying Da Wang tablets** The Australian Therapeutic Goods Administration warned that this sexual enhancement product contains sildenafil.

Health Canada seized a variety of **Stiff4Ever** and **PurePillz** products from The Love Shop retail outlets located in Ontario. These products are unauthorized drugs and are considered potentially dangerous to the health and safety of Canadians. Health Canada tested the Stiff4Ever products, advertised as male sexual stimulants, and identified sildenafil. The labels of the PurePillz products (see below) state that they contain BZP and TFMPP.

Health Canada Mar/12 **Power-X**" has been removed from a Canadian retail location after Health Canada's testing identified undeclared thiodimethylsildenafil which is similar to the prescription medication sildenafil.

Health Canada May/12: Unauthorized health products, **"X-Rock", "Kaboom" and "One For Her"** have been removed from sale from various retail outlets in British Columbia and Saskatchewan. Health Canada's testing identified undeclared prescription drugs sildenafil and tadalafil, and an undeclared substance, hydroxythiohomosildenafil, which is similar to sildenafil.

Health Canada May/12 **1. AdvanceMen capsules; Miraculous Evil Root tablets** The Australian Therapeutic Goods Administration warned that these sexual enhancement products contain either a prescription drug (sildenafil) or an unauthorized drug (sulfoaildenafil).

Health Canada June/12 **1. African Black Ant; France T253; Hard Ten Days; Man King; Stree Overlord** : The U.S. Food and Drug Administration warned that these sexual enhancement products contain prescription drugs (sildenafil. One product also contains tadalafil). **2. RegenArouse; RegenErect:** The U.S. Food and Drug Administration informed of a recall because these sexual enhancement products contain a prescription drug (tadalafil). **3. Mince Belle; Everlax; Ever Slim; Ever Slim Shake Mix (Strawberry); Ever Slim Shake Mix (Chocolate); Acai-Man Mangosteen Herbal Drink; Perfect Men:** The U.S. Food and Drug Administration informed of a recall because these weight loss and sexual enhancement products contain prescription drugs (sibutramine or tadalafil).

Health Canada June/12 **Natural Vigor Maximum** (Exemption Number: 138273) has been removed from sale from various retail outlets in Ontario after testing by Health Canada identified a hidden ingredient (dimethylhomosildenafil).

Health Canada July/12 **Lightning Rod**, an unauthorized sexual enhancement product, has been removed from sale from various retail outlets in Ontario, British Columbia and Saskatchewan after testing by Health Canada identified a hidden ingredient (hydroxythiohomosildenafil).

Health Canada Aug/12 These products are not authorized for sale in Canada and have not been found on the Canadian market, but they may have been brought into the country by travellers or purchased over the Internet. **1. Boost – Ultra Sexual Enhancement Formula; EreXite; Mojo Nights:** The U.S. Food and Drug Administration advised consumers not to buy or use these products after they were found to contain one or more of the following undeclared drug ingredients: tadalafil, sildenafil, and unauthorized substances similar to sildenafil that may pose similar health risks. **2. Firminite; Extra Strength Instant Hot Rod; Libidron:** The U.S. Food and Drug Administration informed consumers of a company recall after these products were found to contain undeclared tadalafil. **3. Instant Hard Rod; RigiRx Plus; ZenMaxx**: The U.S. Food and Drug Administration advised consumers not to buy or use these products after they were found to contain undeclared aminotadalafil, which is similar to tadalafil and may pose similar health risks. **4. VMaxx Rx:** The U.S. Food and Drug Administration informed consumers of a company recall of certain lots of *VMaxx Rx* after found to contain undeclared sulfoaildenafil.

Health Canada Dec/12 Three unauthorized health products -- "**Man Up Now", "Black Ant", "Triple Power Zen Gold 1200mg**"-- are being recalled by DVDXPRO after testing by Health Canada identified undeclared ingredients-sildenafil and/or tadalafil.

Health Canada Dec/12 is advising Four unauthorized natural health products have been removed from sale as they may pose serious risks to the health of Canadians. The "**ExtenZe**" products are promoted as sexual enhancement products and contain ingredients that legally require they be sold with a prescription in Canada. ExtenZe Max Strength Gelcaps, ExtenZe Original Tablets, ExtenZe Natural Female Tablets, and ExtenZe Big Cherry Flavour Liquid: Three of these unauthorized products list the prescription ingredient pregnenolone and the controlled drug DHEA (dehydroepiandrosterone) & three of these unauthorized products contain the prescription medication yohimbine (either as yohimbine HCl or as yohimbe extract).

Health Canada Feb/13: Two unauthorized health products "**18 Again" and "Stiff 4 Hours**" were tested by Health Canada and were found to contain hidden ingredients (sildenafil or tadalafil) that may pose serious risks to the health of Canadians.

Health Canada Feb/13 A Toronto retail outlet (Handy Variety, 591 Sherbourne St.) has voluntarily handed over **counterfeit Viagra and Cialis** to Health Canada following a compliance and enforcement action by the Department. The counterfeit Viagra product is labelled as 100mg tablets (lot number 314833021), and has 11 blister packs of 4 tablets and one incomplete blister of 2 tablets per package. The counterfeit Cialis product is labelled as 20mg tablets (lot number 05668) and contains five blister packs of 2 tablets.

Health Canada Mar/13: An unauthorized natural health product, "**Libigrow**" was tested by Health Canada and found to contain hidden ingredients (sildenafil and tadalafil) that may pose serious risks to the health of Canadians. "Libigrow" was being sold at two retail locations in the province of Québec: Boutique Sexie folie Inc. (Sainte-Catherine) and at Boutique Érotique 5ième avenue Inc. (Valleyfield).

Health Canada Apr/13 **Shan Dian Shou** The Hong Kong Department of Health has advised it contains the undeclared prescription drug sildenafil.

Health Canada May/13 Two unauthorized health products — "**Stiff Nights" and "Stiff 4 Hours**" — were tested by Health Canada & were found to contain hidden ingredients (sildenafil and/or tadalafil) that may pose serious risks to the health of Canadians. The products were being sold at Saints N Sinners Ltd, 1715 Centre Street N.W., Calgary, Alberta.

Health Canada June/13 is advising Canadians not to use these foreign health products as they may pose a health risk. **1. Flutulang, Kapsul Gaut (Asam Urat), and True ProLife Vegrow** The Health Science Authority of Singapore advised consumers not to use these products after they were found to contain phenylbutazone, chlorpheniramine, dexamethasone, and a chemical compound similar to the prescription drug sildenafil. **2. Jinmaoshiwang tablets, Naturally Kouxan Best Slim capsules, and Majestic Slimming capsules** The Australian Therapeutic Goods Administration advised consumers not to use these

products after they were found to contain sildenafil, sibutramine and phenolphthalein. **3. WOW, Super Power and SLIMDIA Revolution** The U.S. Food and Drugs Administration (FDA) warned consumers not to use these products after they were found to contain diclofenac sodium, methocarbamol, dexamethasone, sildenafil and sibutramine.
4. Libigrow XXXtreme, Blue Diamond, Blue Diamond Platinum, Mojo Nights Supreme, and Casanova The U.S. Food and Drugs Administration warned consumers not to use these products after they were found to contain sildenafil, sulfoaildenafil and thioaildenafil.

Health Canada Aug/13 **2. Steelman Capsules 2** The Hong Kong Department of Health has advised consumers not to use this product after it was found to contain undeclared aminotadalafil. **6. Libigirl capsules** The Australian Therapeutic Goods Administration warned consumers not to use this product after it was found to contain the undeclared prescription drugs sildenafil and tadalafil

Health Canada Aug/13 **Prema G** (Granules packaged in tea packets, NPN: 80035944) was tested by Canada Border Services Agency and found to contain a hidden ingredient (hydroxyhomosildenafil thione).

Health Canada Oct/13 wishes to inform Canadians that seized natural health products being sold by Lion King Health Enterprises Group Ltd., 1328-8368 Capstan Way, Richmond, BC. were tested and found to contain hidden ingredients and unauthorized substances similar to the prescription drug, sildenafil. (**North America Dami Ana 600mg, South America Maca 600mg, Ashwagandha 600mg, Optimusman 350mg, Superman 350mg, Innerget Instant Erection (NPN#80041194), Innerget Prolonged Performance (NPN#80041194), Innerget Everlasting Strength (NPN#80041194), Megaton 2080**.)

Health Canada Nov/13 is advising Canadians not to use these foreign health products as they may pose a health risk.

1. **14 sexual enhancement products** http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36233a-eng.php ; SexVoltz (Regular and Maximum Strength); Velextra (Regular and Maximum Strength); Amerect* (Regular and Maximum Strength); Night Bullet; Bullet Proof; Vicerex; Zoom-Zooma-Zoom; Sex Plus; Affirm XL; Ninja Mojo; Love Rider; Stiff Days; ROCK-IT MAN; Libido Sexual Enhancer.
2. **Ziyinzhuangyang tablets, Maxman III, and Mojo Risen** http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36519a-eng.php.

Health Canada Dec/13 has updated the list of natural health products seized from **Lion King Health Enterprises Group** Ltd., 1328 - 8638 Capstan Way, Richmond, B.C. that have been tested and found to contain hidden ingredients and unauthorized substances similar to the prescription drug tadalafil.

Health Canada Dec/13 testing of an unauthorized natural health product, **MaxHIMize**, found it to contain bacteria (Enterococcus durans and Bacillus spp) and undeclared caffeine that could present a risk to health. MaxHIMize is being promoted as a dietary supplement and for erectile dysfunction.

Health Canada Feb/14: 1. **Li Long Mei Guo Mo Bang, and Ginseng Tu chong Wan Lin Heong** The Singapore Health Sciences Authority warned consumers not to use this product after it was found to contain sildenafil.

Health Canada Mar/14 is advising Canadians not to use these foreign health products as they may pose a health risk. 1. **Xiang Gang Tian Long Sheng Wu Ke Ji Di Qi Dai Chi Jiu Zhan Shen** http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2014/38599a-eng.php was found to contain sildenafil. 2. **Various Sexual Enhancement Products** http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2014/38577a-eng.php was found to have sildenafil andtadalafil. 3. **Majestic Slim Perfect and Yixiu L-Carnitine Slimming Capsules** http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2014/38609a-eng.php was found to contain sildenafil andphenolphthalein.

Health Canada Apr/14: **Volcano Male Enhancement** liquid & caps: The U.S. Food and Drug Administration warned consumers not to use these products after they were found to contain desmethyl carbodenafil, dimethylsildenafil and dapoxetine**.**

Health Canada May/14 **Blue Stinger** contains sulfoaildenafil**; 72 HP, Evil root and Pro Power Max** contains sildenafil**; Jack Rabbit** contains sildenafil and tadalafil.

Health Canada May/14: 1. **VitaliKOR**: FDA found vardenafil and tadalafil**;** 2. **Vigor Tea sachets:** Australian Therapeutic Goods Administration found sulfoaildenafil**;** 3. **Prolifta capsules, PHUK and Virilis Pro:** FDA found **sildenafil;** 4. **Wood-E, Xzen Gold, Xzen XPress, XZen 1200, and XZone Premium**: FDA found Wood-E contains sildenafil, Xzen Gold and Xzen XPress contain sildenafil and tadalafil, & XZen 1200 contains tadalafil.

Health Canada June/14: **Bali Mojo & Vimax** contains tadalafil., **LOVher capsule**s contains tadalafil, sildenafil and diclofenac. **Erec-Bull,** contains yohimbine. **Best Whips & JINQIANGBUDOR Red Dragon** contains sildenafil. **Super Hard t**ablets contains sildenafil. **CONTROL All Natural Sexual Enhancement** contains sulfoaildenafil and dimethylsildenafil.

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MHRA Feb/12 has received advice from AGES PharmMed in Austria and the Danish Medicines Agency, warning that these unlicensed products have been tested and found to contain Tadalafil and/or Sildenafil:
AH Free/Reflexit, Stree Overlord, Man King, VigRX, Maxman, Maxman III, Viriya, & Imbiza for Men.
MHRA: Austrian Sep/12 authorities have issued a warning for **Ramlostan Forte** manufactured by SC Parapharm, Romania. Ramlostan comes in white and blue packaging, with a picture of a ram at the top. Inside, there are ten blue capsules. The Austrian authority (AGES) has issued a warning for this product after finding it to contain Tadalafil.
MHRA Nov/12 has received advice from the Ministry of Health, Jerusalem warning that this unlicensed product, **Shark Essence** has been tested and found to contain Tadalafil and Sildenafil.
MHRA May/14: Singapore Health Sciences Department **Li Long Mei Guo Mo Bang** because it contains sildenafil.
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Recommendation 2: The American College of Physicians recommends that clinicians base the choice of a specific PDE-5 inhibitor on the individual preferences of men with erectile dysfunction, including ease of use, cost of medication, and adverse effects profile (Grade: weak recommendation; low-quality evidence).
Recommendation 3: The American College of Physicians does not recommend for or against routine use of hormonal blood tests or hormonal treatment in the management of patients with erectile dysfunction (Grade: insufficient evidence to determine net benefits and harms).
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Web Links:

American Academy of Family Physicians Web site: http://familydoctor.org
American Urological Association Foundation Web site: http://www.urologyhealthorg/adult/index.cfm?cat=11&topic=174
National Institutes of Health Web site: http://www.nlm.nih.gov/medlineplus/erectiledysfunction.html

Reviewers: Dr. K. Knox (SHR Rehabilitation), C Bell (UofS-SDIS), A Kuntz (SK Health), M Jin (PharmD, Hamilton), & the RxFiles Advisory Committee.

Extras:
Europe/Australia: dapoxetine *Priligy* (30-60mg po taken 1-3 hours prior to intercourse) has official indication for Premature Ejaculation. {short acting SSRI}

Additional references: Sexual Dysfunction: Overview & Drug Considerations (www.RxFiles.ca)

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RxFiles Urinary Incontinence On-Line Extras:

Other Medications:

1) AChs, Other: **propantheline** - less effective & ↑ AE than flavoxate & oxybutynin.[11] NICE states not to use[1]; Adult: 7.5mg TID, 7.5-30mg 3-5x/day, 60mg QID; Geriatric: 7.5mg TID; Peds: 7.5-15mg q4-6h.
2) Adrenoreceptor agonists (**phenylpropanolamine** predominantly studied but use extended to **ephedrine**, **pseudoephedrine**): studied for SUI. But cardiac arrhythmias & HTN outweigh benefits.[31]
3) **Belladonna & opium suppositories:** used to relieve **pain of uretal spasms** & pain associated with bladder tenesmus that can occur post-op.[32] Some report use in nocturnal diuresis.[11]
Dicyclomine - insufficient data to recommend over other agents, dose 20-40mg QID.[11]
4) **Flavoxate**: Not used for OAB currently[1] but may be used in discomfort associated with BPH. Efficacy might be comparable to propantheline according to older, short-term studies.[11]
Dose: Adult: 100-200mg TID-QID. May reduce dose with sx improvement. One trial found 1200mg to be superior to 600mg/day. May be effective in children from 6-12 yrs experiencing nocturnal enuresis (33% vs 17% response in placebo).[11] Pediatrics > 12 yr: 100-200mg TID-QID. May reduce dose with sx improvement.[11]
5) **Phenazopyridine:**[11] used strictly as a **urinary analgesic**. The necessity of this medication would suggest pathology different from UI. Dose: Adult: 200mg TID after meals. If renal GFR > 50mL/min 200mg q8-16h. Avoid if GFR < 50mL/min. Geriatrics: ↑risk of accumulation & toxicity. AE: discolor urine
6) **Propiverine:**[53] tertiary amine with ACh & calcium channel antagonist activity; has active metabolites; dose: 15mg IR BID or 30mg ER daily; available United Kingdom.[2006]

Oxybutynin (OXY) vs Tolterodine (TOLT) in OAB

- OBJECT: OXY ER 10mg daily vs TOLT IR 2mg BID; 12 week; ♂ & ♀; Oxy ER slightly more effective (e.g. total incontinence episodes/wk: NNT=45); no difference in overall AEs (dry mouth, CNS effects).[52]
- OPERA: OXY ER 10mg vs TOLT ER 4mg daily; 12 week; ♀ only with severe symptoms; OXY ER somewhat more effective (e.g. 23 vs 16.8% no UI; NNT=16); but also more dry mouth (Any 29.7% vs 22.3%; NNH=13; mod-severe 7.4% vs 5.0%, NS).[50]
- ACET: OXY ER 5 or 10mg vs TOLT ER 2 or 4mg daily; 8 week; ♂ & ♀; TOLT 4mg more effective than OXY 10 70 vs 60% improvement; but lower doses efficacy still ~60% & less dry mouth but similar for TOLT 4mg vs OXY 5mg ; open label trial & subjective assessments subject to bias.[51]

Other Urinary Incontinence Patient Resources:

- Bladder Retraining: http://www.fmpe.org/en/documents/doc_aids/UI-Patient-Handout-4.pdf ; or http://www.fmpe.org/en/documents/handouts/handout_ui_retraining.pdf
- Pelvic Muscle Exercises (Kegel Exercises): http://www.fmpe.org/en/documents/doc_aids/UI-Patient-Handout-3.pdf
- Voiding Diary: http://www.fmpe.org/en/documents/doc_aids/UI-Patient-Handout-2.pdf
- Patient Information - Urinary Incontinence: http://www.fmpe.org/en/documents/doc_aids/UI-Patient-Handout-1.pdf
- CFPC: www.cfpc.ca/English/cfpc/programs/patient%20education/urinary%20incontinence
- American (ACOG): www.acog.com/publications/patient_education/bp081.cfm

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CDR=Common Drug Review (http://cadth.ca//index.php/en/cdr)
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243. FDA: Apr/12 The labels of the alopecia drug Propecia (**finasteride** 1 mg) and the benign prostatic hyperplasia drug Proscar (finasteride 5 mg) are being updated with an expanded list of adverse **sexual effects**, the FDA has announced. Propecia label will include libido, ejaculation, and orgasm disorders that persist after treatment ends; Proscar label will include decreased libido that persists posttreatment & both labels will note reports of male infertility or poor semen quality that improved after drug discontinuation.
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1) Breaking the "cold chain"

Canadian Guidelines: Refrigerated vaccines should be stored between +2°C and +8°C. Frozen vaccines should be stored at -15°C or colder. Store light sensitive vaccines away from light. Follow manufacturer recommendations for storage & transport. Administration requires someone trained to give im/sc injections.

Fridges:

-Fridge used should be dedicated to the storage of vaccines only.

-**Use of bar fridges for vaccine storage is the leading cause of cold chain breaks in Canada. Bar fridges are not recommended for the purpose of storing vaccines.**

- Keeping temperature of fridge stable **(2-8° C)**: Avoid opening refrigerator door unnecessarily, store containers of water in refrigerators, or ice packs in the freezer

NEVER store vaccines in the vegetable bin section of the refrigerator. Ideal storage location for vaccine: In the middle compartment, away from floor, coils, walls, and venting for the freezer or cold air.

-Temperature of the compartments of the refrigerator where the vaccine is stored should be checked and logged at least twice a day. Fridge temperatures outside of the 2 to 8 degree C range must be reported immediately to obtain recommendation on the stability of the affected product.

- Fridge temperature recording logs should be retained for 2 years.

- Min-Max thermometer batteries should be routinely changed twice a year: December 1 and June 1 and the date of changing noted on the device.

Transporting Refrigerated Vaccines: Avoid breaking the cold chain

1) Transport vaccines in insulated containers at all times. Hard sided plastic insulated containers, or Styrofoam containers with walls at least 2 inch thick walls should be used. Icepacks should be placed inside the transport container to maintain the cold chain. To prevent freezing the vaccine should never be placed directly onto an ice pack. Instead an insulating barrier (i.e. bubble wrap, Styrofoam peanuts) should be placed between vaccine and ice pack.
2) Make sure vaccine is never placed in trunk of vehicle, or in direct contact with sunlight. Also the vaccine should not be placed in line with the air from the vehicles heater or air conditioner. Vaccine should never be left in a vehicle unattended.
3) If a break in the cold chain identified prior to administration of the vaccine, contact your local public health authority about the appropriate course of action. While waiting for a decision, ensure that the vaccine is stored in appropriate cold chain conditions. The vaccine should not be administered until a decision has been reached.
4) If a break in the cold chain is identified after administration of the vaccine, contact your local public health authority. The type of vaccine, duration and temperature of the exposure will be taken into account in order to determine the course of action. Serological testing or revaccination may be suggested.

Further information: available from the Public Health Agency of Canada's Website. References:

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2) Anaphylaxis Management with vaccine administration:

1) Patients should be kept under supervision for 15 minutes (JE-VAX: 30 minutes) following administration.
2) In order to treat anaphylaxis perform the following steps (note steps a-d should be performed rapidly or simultaneously, however the priority is to complete step a):
   a) **Promptly administer 0.01 mL/kg (maximum 0.5 mL) of aqueous epinephrine 1:1000 by intramuscular (or subcutaneous) injection in the opposite limb to that in which the vaccination was given (or the vastus lateralis). Prompt administration is essential.**
   b) Call for an ambulance
   c) Place the patient in a recumbent position, and elevate their feet.
   d) If necessary, establish an oral airway.
   e) Patients with severe reactions such as cyanosis, dyspnea, should be given oxygen if it is available. Pulse oximetry can be used to monitor if available.
   f) If the vaccine was administered subcutaneously, an additional dose of 0.005 mL/kg (maximum 0.3 mL) of aqueous epinephrine 1:1000, can be injected into the vaccination site to slow down absorption. This should be done shortly after administration of the first dose of epinephrine in moderate to severe cases, and generally should not be repeated. Local injection of epinephrine into an intramuscular vaccination site is contraindicated, as it speeds up absorption of the vaccine.
   g) A dose of diphenhydramine hydrochloride (Benadryl®) can be given as an adjunct to epinephrine. The oral route of diphenhydramine is preferred for conscious patients who are not seriously ill (as the intramuscular injection is painful). Oral dose: 1-2 mg/kg to a maximum single dose of 50 mg.
   h) An inhaled β-agonist should be considered if there is a bronchospasm resistant to an adequate dose of epinephrine (e.g., nebulized salbutamol 2.5-5.0 mg in 3 mL of saline or 1 puff per 3 kg to a maximum of 10 puffs by metered dose inhalers).
   i) Vital signs should be monitored continuously.
   j) Patient should be transported to emergency department for long term monitoring.

◆Epinephrine dosing can be repeated twice at 5-minute intervals if necessary, for a total of three doses. The limb in which the vaccination was given should be avoided. A different limb is preferred for each dose to maximize drug absorption.

3) **Breastfeeding and Vaccinations:** Immunizations for actively breastfeeding women are considered safe, with the exception of smallpox vaccine and yellow fever, by both the CDC and the American academy of pediatrics. Breastfeeding does not appear to influence the maternal immune response. Vaccines do not appear to affect the safety of breast milk for infants.[10,11]

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Anti-inflammatory properties of topical antifungal preparations:

It is difficult to determine the anti-inflammatory effects of topical antifungals in humans as the majority of studies are completed as *in vitro* studies or in animal models. Some studies compared antifungal drugs alone to a combination of antifungal plus steroid combination and had similar efficacies in treatment. A small study (n=20) assessed and compared *in vivo* anti-inflammatory effects of terbinafine, ciclopirox, ketoconazole and other antifungals (econazole, oxiconazole- not commonly used in Canada) with hydrocortisone 2.5%. This study looked at the ability to decrease erythema due to UVB exposure which is thought to mimic the response in dermatophyte infections. It did not study the effects in an actual dermatophyte–induced inflammatory reaction. Terbinafine, ciclopirox, and ketoconazole all demonstrated anti-inflammatory effects. Terbinafine and ciclopirox exhibited statistically significant difference in erythema when compared to control than ketoconazole, econazole, oxiconazole, and hydrocortisone. Ketoconazole exhibited intermediate anti-inflammatory effects. May consider use of these antifungals if there is an inflammatory component to the fungal infection.

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Official Warnings

June 2014: TERAZOL 7 Vaginal Cream 0.4% (**terconazole**); TERAZOL 3 Dual-Pak - Vaginal Cream 0.8%/Vaginal Ovules 80 mg (terconazole) - Risk of Anaphylaxis and Toxic Epidermal Necrolysis - Janssen Inc. Very rare cases of serious adverse reactions of anaphylaxis or Toxic Epidermal Necrolysis have been reported during treatment with TERAZOL. Patients should discontinue use of the product if signs or symptoms of serious allergic reactions occur. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2014/39911a-eng.php; http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2014/39915a-eng.php

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American Academy of Pediatric Dentistry Clinical Affairs Committee, American Academy of Pediatric Dentistry Council on Clinical Affairs. Guideline on antibiotic prophylaxis for **dental** patients at risk for infection. Pediatr Dent 2008-2009;30(7 Suppl):215-8. http://www.aapd.org/media/Policies_Guidelines/G_AntibioticProphylaxis.pdf
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The present systematic review, including meta-analyses for select outcomes, suggests that although individual studies vary in their findings, there is no evidence to support a consistent, clinically important impact of antibiotics in reducing the main morbid outcomes following tonsillectomy (i.e. pain, need for analgesia and secondary haemorrhage rates). Limited benefit apparent with antibiotics may be a result of positive bias introduced by several important methodological shortcomings in the included trials. Based on existing evidence therefore, we would advocate against the routine prescription of antibiotics to patients undergoing tonsillectomy. Whether a subgroup of patients who might benefit from selective administration of antibiotics exists is unknown and needs to be explored in future trials.
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Each column represents a group of Beta-lactams with similar side chains:

Amoxicillin	Ampicillin	Cefprozil	Cefotaxime	Penicillin G
Cefadroxil	Cephalexin	Aztreonam	Ceftriaxone	Cefoxitin
Cefprozil	Cefaclor	Ceftazidine	Cefepime	

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Extras

Combos to Avoid: Early virologic failure: abacavir + lamivudine (or emtricitabine) + tenofovir ; didanosine + lamivudine (or emtricitabine) + tenofovir; didanosine + tenofovir + NNRTI; didanosine + emtricitabine(lamivudine) + atazanavir; Caution: emtricitabine(or lamivudine) + tenofovir + nevirapine [71] (early virologic failure in small clinical trials; ARTEN [72] trial: may be okay)
↑AE: Didanosine + stavudine (peripheral neuropthy, pancreatitis & lactic acidosis); ATV + IDV ↑ bilirubin; 2 NNRTI regimen Antagonism: stavudine + zidovudine

- Oral contraceptives + non-ritonavir boosted atazanavir (may ↑ hormone levels; ⇨use lowest dose OC)[73] or indinavir (will maintain hormone levels)

{Refractory large volume diarrhea, HIV related: octreotide (50-500mcg sc TID)$$$ }[74,75]

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Extras:

1) Clinical Decision Rule for Point of Care Testing of Influenza Patients: *fever* (2 points), *myalgia* (2 points), *symptoms <48hrs* (1 point), *chills/sweats* (1 point). **0-2points** = 8%; **3 points** = 30%; **4-6 points** = 59%.

Rx Files – Drugs for Influenza
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Since the 2011-12 influenza season, NACI has recommended that egg-allergic individuals may be vaccinated against influenza using TIV, without a prior influenza vaccine skin test, based on an assessment of risk for a severe allergic reaction to guide the method of vaccination. (NACI recommendation Grade A)Footnote bb Details of the vaccine delivery protocols are found below. Because of the lack of data, the use of FluMist® in egg-allergic persons is not recommended at this time. However, ovalbumin concentrations in FluMist® are documented to be very low and a study is currently underway to assess the use of FluMist® in egg-allergic persons. Its use will be re-evaluated when further data become available. Although ovalbumin content in influenza vaccine manufactured in eggs may vary from year to year, between vaccine products or between lots of the same vaccine,Footnote 6363-Footnote 6565 vaccines marketed in Canada are approved under the European specification for ovalbumin content, which is currently <1.2 µg/mL, the level associated with low risks of adverse events.Footnote 6666 An egg-allergic individual is considered to be at higher risk for severe allergic reactions by CSACI if they have had a previous respiratory or cardiovascular reaction or generalized hives when exposed to egg, or have poorly controlled asthma. Two vaccine delivery protocols can be used for egg-allergic individuals, depending on their level of risk for an allergic reaction.Footnote 6767 Egg-allergic individuals at lower risk for severe allergic reaction can be vaccinated for influenza using a single vaccine dose. The two-step graded protocol is recommended for individuals who are at higher risk for severe allergic reaction. These protocols are as follows:

Full dose - A single vaccine dose without the use of a graded challenge. Individuals should be observed for 30 minutes following administration for symptom development.

Two-step graded dosing - A two-step graded process, whereby 10% of the dose is administered followed by 30 minutes of observation. If no symptoms develop, or symptoms are self-resolving, administer the remaining 90% with another 30 minute observation period. If sustained or severe reactions arise after the initial dose, the vaccine is withheld and the individual should be re-evaluated for receipt of the influenza vaccine.

***More recent studies suggest that the absolute risk of GBS in the period following seasonal and A(H1N1)pdm09 influenza vaccination is about one excess case per 1 million vaccines

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tested viruses showed resistance (data on Canada were not provided, but reported in Pharmacy Bulletin Board Feb 4/08 at **10%**). "We don't know right now if this is a trend on the upswing or just a small blip," the CDC's chief of epidemiology and prevention told the Associated Press. Officials from the U.S. and World Health Organization told the *Times* they do not currently advise changes in Tamiflu use. In addition, the flu vaccine is still effective against the mutant virus.

Dec/08: Clinicians should remain alert for changes in recommendations that might occur as the 2008--09 influenza season progresses. Recommendations regarding the use of antiviral medications might be revised if surveillance data indicate a substantial and widespread increase in the prevalence of oseltamivir-resistant influenza viruses in the United States. In fact, the interim CDC guidance provides advice for clinicians on how to treat patients with influenza antiviral medications this season. Clinicians can use influenza test results and information, if available, about which viruses are circulating, to help decide which antiviral(s) should be used. If H1N1 viruses are circulating in the community, or it's not clear which viruses are circulating, health care providers are recommended to use an alternative antiviral, zanamivir (Relenza®), or to use combination therapy of oseltamivir and rimantadine. Use of zanamivir or dual therapy with oseltamivir and rimantadine would provide effective treatment against all circulating influenza viruses. In some instances, oseltamivir alone can still be used, such as when influenza B is diagnosed, or H1N1 viruses are not circulating.

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FDA April /08 GlaxoSmithKline informed healthcare professionals of changes to the WARNINGS AND PRECAUTIONS sections of prescribing information for **Relenza** regarding information from postmarketing reports (mostly from Japan) of **delirium and abnormal behavior** leading to injury in patients with influenza who are receiving neuraminidase inhibitors, including Relenza. These events were reported primarily among pediatric patients and often had an abrupt onset and rapid resolution. The contribution of Relenza to these events has not been established. Influenza can be associated with a variety of neurologic and behavioral symptoms which can include seizures, hallucinations, delirium, and abnormal behavior, in some cases resulting in fatal outcomes. These events may occur in the setting of encephalitis or encephalopathy but can occur without obvious severe disease.

FDA June/10 notified consumers and healthcare professionals about a potentially harmful product represented as "**Generic Tamiflu" sold over the Internet**. FDA tests revealed that the fraudulent product does not contain Tamiflu's active ingredient, oseltamivir, but cloxacillin, an ingredient in the same class of antibiotics as penicillin.

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WEBSITES & Updates:

Update: Influenza Activity --- United States, September 28--November 29, 2008

During September 28--November 29, 2008, influenza activity remained low in the United States. Of the few influenza viruses characterized thus far this season, **most are antigenically** related to the strains included in the 2008--09 influenza **vaccine**. Oseltamivir-resistant influenza A (H1N1) viruses have been detected, but currently available data are insufficient to predict their prevalence for the 2008--09 season. This report summarizes U.S. influenza activity* since the last update (1) and reviews new influenza vaccine recommendations for the current season. During September 28--November 29, 2008, approximately 150 World Health Organization (WHO) and National Respiratory and Enteric Virus Surveillance System collaborating laboratories in the United States tested 24,657 respiratory specimens for influenza viruses; 365 (1.5%) were positive (Figure 1). Of these, 282 (77.3%) were influenza A viruses, and 83 (22.7%) were influenza B viruses. One hundred twenty-eight (45.4%) of the 282 influenza A viruses were subtyped; 112 (87.5%) of these were influenza A (H1) viruses, and 16 (12.5%) were influenza A (H3) viruses. Influenza-positive tests have been reported from 26 states in eight of the nine surveillance regions since September 28.

Enhanced surveillance for oseltamivir-resistant viruses is ongoing at CDC. Alternatives for antiviral treatment in the context of widely circulating **oseltamivir-resistant** viruses have been suggested. These treatment options, which might include preferential use of zanamivir or therapy with a combination of antivirals for certain patients, have been outlined in the ACIP 2008 influenza recommendations.†† Currently, the neuraminidase inhibitors oseltamivir and zanamivir remain the recommended medications for treatment and chemoprophylaxis of influenza. Clinicians should **remain alert for changes in recommendations** that might occur as the 2008--09 influenza season progresses. Recommendations regarding the use of antiviral medications might be revised if surveillance data indicate a substantial and widespread increase in the prevalence of oseltamivir-resistant influenza viruses in the United States. http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5749a3.htm?s_cid=mm5749a3_e

CDC Flu Update:

http://www.cdc.gov/flu/

http://www.cdc.gov/flu/about/season/index.htm

Public Health Agency of Canada- FluWatch:

http://www.phac-aspc.gc.ca/fluwatch/

Swine Flue Outbreak – 2009 (Mexico & worldwide extension)

http://www.who.int/mediacentre/news/statements/2009/h1n1_20090427/en/index.html
http://www.cdc.gov/swineflu/

Primaquine 26.3mg tab (= 15mg base) ✗▼ PL

Terminal prophylaxis: effective against P. *vivax* & P. *ovale*. Used for pts that have had long exposure to malaria endemic areas (>8wks)[36]. Not required for travel to Haiti or the Dominican Republic as of July06 [2].

- **Chloroquine/doxycycline/mefloquine prophylaxis**: primaquine taken in conjunction with the last 2 wks of post-exposure prophylaxis, but may be taken immediately after.
- **Atovaquone/proguanil prophylaxis:** primaquine is taken during atovaquone/ proguanil post-exposure prophylaxis & then for an additional 7-14 days after.

Primaquine eradicates latent parasites in the liver & rapidly kills mature gametocytes (even falciparum).

Pediatric Dosing age >9yrs for prevention; any age for tx

Prophylaxis: 0.5 mg(base)/kg/day
Terminal Prophylaxis: 0.5 mg/kg/day x14d

Adult Dosing

Prophylaxis: 52.6 mg (30 mg base) DAILY $9
Terminal Proph.: 30 mg base/d x 14d $9

For prophylaxis: begin 1-2d prior to entering

Comments

Second-line for chloroquine resistant areas

- 85- 95% effective against P. *falciparum* & P. *vivax*
- **Only therapy to prevent relapse from P. vivax & P.ovale** due to dormant hypnozoites in liver (relapse may occur within 5 years of exposure)

CI: **G6PD deficiency**/favism, pregnancy,rh. arthritis, lupus
SE: Well tolerated. GI upset; Take with food.
Missed Dose: Take next dose ASAP. However, if it is almost time for your next dose, skip the missed dose & go back to your regular dosing schedule. Do not double doses. **Take with food; not grapefruit juice**

Drug Treatment of Malaria: Tx will vary depending on species of malaria. For severe: (IV quinine or artesunate) + (Atovaquone/proguanil or doxycycline or clindamycin)

Other Investigational Drugs: **IV artesunate**: investigational in the USA for treatment of severe malaria. {May be accessed in Canada through the Canadian Malarial Network. It is an alternative to quinine with less side effects, although limited long term experience with potential side effects from recurrent use.}

{Recent historical resistance trends: {choroquine sensitive areas: travel to **Caribbean** including Haiti and rural areas of Dominican Republic; travelers visiting resort areas not generally at risk; travel to Central America except Panama, Mexico, Argentina; parts of China / Middle east; geographic risk and resistance trends change over time.}

Approximate malaria risk (1 month stay without chemoprophylaxis): (source: CCDR 2000 Malaria Recommendations, p.3)

-	Oceania (Papua New Guinea, Irian Jaya, Solomon Islands, and Vanuatu)	1:30 or higher
-	Sub-Saharan Africa	1:50
-	Indian Subcontinent	1:250
-	Southeast Asia	1:1000
-	South America	1:2,500
-	Central America	1:10,000

- Risk also ↑'d with >6month stay, in part due to underuse of protection measures.
- Stand-By Emergency Treatment (self-admin) may be recommended in select cases.

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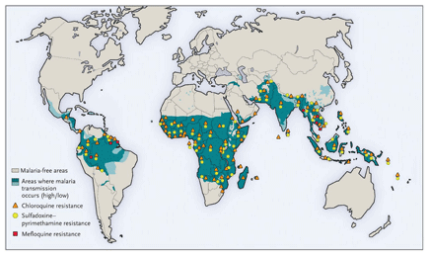

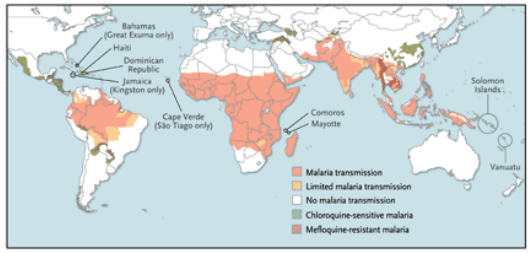

Thumbnails: Areas of Malaria Transmission and Antimalarial Drug Resistance. Data on malaria transmission are for 2007 and are from the World Health Organization. Data on drug resistance are for 2004 and are from the Roll Back Malaria partnership.**NEJM** June 5,2008. 2nd Map Thumbnail: NEJM Aug 7, 2008. **CDC Map**: http://cdc-malaria.ncsa.uiuc.edu/

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Hydroxychloroquine PLAQUENIL,g 200mg tab

{Not used very often! Licensed for malaria in USA**}**

Second-line: chloroquine sensitive malaria

PL

- Only in chloroquine-sensitive P. *falciparum* malaria prevention

{Opthalmological exam periodically if used weekly low dose long term; risk very low in first 5yrs; if >5yrs (BMJ,CDC), or high risk (ACP)}.

Pediatric: 5 mg base/kg weekly (200 mg tab = 155 mg base) (Do not exceed adult dose)

- Adult: 400 mg **weekly**
- Begin **2 wks prior** to entering MRZ, continue during stay & **8 wks after** leaving MRZ

19

- **Caution**: pts with hepatic failure, **G6PD** deficiency, pre-existing auditory damage; psoriasis, prophyria {Pregnancy: considered safe} {May have lower retinal risk than chloroquine.}
- SE: N/V/D(↓ by giving with food or milk), pruritus, fatigue, seizures, headache & dizziness. Uncommon: alopecia, hair depigmentation, skin eruptions & seizures.
- DI: antacids, cimetidine, digoxin (increase dig level)
- Vaccine Interaction[17]: Assume same as chloroquine

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COMMUNITY ACQUIRED PNEUMONIA – Empiric Antibiotic Selection

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Treatment of Low Back Pain [21, 22]

Red Flags (assessment considerations):

- pain when recumbent
- saddle anesthesia
- pseudoclaudication
- age >55y or <20
- recent UTI
- trauma (major
- pain persisting >1mo

Tx Guidelines:

- symptomatic relief can be accomplished with OTC medication and/or spinal manipulation
- during acute phase, bed rest >4 days may further debilitate the patient
- low-stress aerobic activity & exercise OK in first 2 weeks; may delay trunk muscle exercises
- recommend return to work/normal activities as soon as possible
- if problems persist, reassessment required
- address nonphysical factors (psych/socioeconomic)

Meds: acetaminophen 1st line; NSAIDs option if necessary & not contraindicated; strong opioids may be necessary for some but consider addiction risk, use treatment agreement and set appropriate boundaries; consider referral.

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Extras:

- **Renal Failure** – Considerations: that need to alter approach to drug selection will depend on degree of renal dysfx (e.g. GFR ≥20ml/min, 10-20ml/min, <10ml/min), pain severity & drug dose required, use of dialysis.
  A) Less problematic options may include: acetaminophen, tramadol, topicals (capsaicin, nitro spray?); hydromorphone, fentanyl, methadone. {Always include non-drug techniques.}
- **Cisplatinin** related neuropathy: prevention with Vitamin E 400mg/day starting before, and going for 3 months after cisplatinin treatment.
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  Pain Training – Online: http://www.algo-md.com/en/index.php (fee for course)
  Pain Approaches: Distinctives in the Acute vs Palliative vs CNCP use of Opioids: http://www.rxfiles.ca/rxfiles/uploads/documents/members/CHT-Pain-Approaches-Acute-Palliative-CNCP.pdf
  Methadone dosing in pain management: http://pain-topics.org/pdf/OralMethadoneDosing.pdf

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Glucosamine seems to be safe}

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National Institute of Arthritis and Musculoskeletal and Skin Diseases: Questions and Answers About Gout

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Gout and Uric Acid Education Society www.gouteducation.org/

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GENERIC/TRADE (Strengths & formulations)	LOWEST ANTI-INFLAMMATORY, USUAL RANGE & MAXIMUM DOSE	$/30d	Class/Comments
Acetaminophen TYLENOL, g **OTC** ✘ (=paracetamol) Chewable tablet: 160mg ✘ ▼ Rapid-dissolving tablet: 80, 160mg ✘ ▼ PL Immediate release caplet/tablet: 160, 325, 500mg ✘ ▼ Extended release caplet: TYLENOL ARTHRITIS 650mg ✘ ⊗ Gelcap: 500mg ✘ ⊗ Drops: 80mg/mL ✘ ▼ Liquid: 16mg/mL, 80mg/mL, 32mg/mL ✘ ▼ Suppository: 120, 160, 325,650mg ✘ ▼ **Caution: ingredient of many products! Unintentional duplication of use sometimes with overdose is common!**	**Lowest Anti-inflammatory:** 650mg po QID 1,300mg ER po TID **Usual Range:** 325-1000mg po TID-QID **Maximum:** 4g/day. Consider limiting dose to ≤3250mg/day if elderly or chronic use, or ≤2600mg/day if hepatic/renal disease or chronic alcohol use. **Pediatrics:** 10-15mg/kg q4-6hr; **Max**: 75mg/kg/day	$20 $25	**NON-ANTI-INFLAMMATORY ANALGESIC** • Compared to NSAIDs/COXIBs, lowest risk for CV events & GI ulcer/bleed • Option in osteoarthritis • **D**: warfarin ↑ INR with scheduled chronic use of acetaminophen • **M**: **LFTs** with chronic use & if ↑ alcohol use [Larson'05] • **Acute Overdose: hepatotoxic** (#1 cause of drug-induced transplant) >140mg/kg or >7.5g - Level within 24 hours predictive [Rumack-Matthew Nomogram 36]

Combination Product to Reduce Dyspepsia: ASPIRIN STOMACH GUARD: ASA 325/500mg & Ca^{++} Carbonate 227.5/350mg **OTC** ✘ ⊗

New Drugs/Formulations:

◆ low-dose **diclofenac submicron** particles (ZORVOLEX) [Not in Canada] – 18, 35mg capsules. Reduction in particle size ↑'s surface area resulting in faster dissolution & absorption.

Discontinued Products:

NSAIDs: Choline Mg^{++} Trisalicylate TRILISATE, Fenoprofen NALFON, Piroxicam BREXIDOL, Salsalate DISALCID, Tolmentin TOLECTIN.

COX-2 Inhibitors:

- Lumiracoxib PREXIGE 100mg daily. Discontinued October 2007. Rare severe hepatic toxicity at doses ≥200mg/day.
- Rofecoxib VIOXX 12.5mg (OA) to 25mg (OA/RA) daily. Discontinued September 2004. VIGOR: CV events NNH=83, GI NNT=129/8 months.
- Valdecoxib BEXTRA 10-20mg daily (OA, RA). Discontinued April 2005 in Canada, USA. Rare severe skin reactions e.g. exfoliative dermatitis & Stevens Johnson Syndrome.

Trials to watch:

- PRECISION: CV risk of celecoxib vs ibuprofen vs naproxen (estimated study completion date - Sept 2015) http://clinicaltrials.gov/ct/show/NCT00346216?order=4

NSAIDS, COXIBs & OTHER ANALGESICS: Comparison Chart

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Long-term use of NSAIDs is associated with a reduced incidence of oral cancer (including in active smokers), but also with an increased risk of death due to cardiovascular disease. These findings highlight the need for a careful risk-benefit analysis when the long-term use of NSAIDs. (Jan/06 The Norwegian daily newspaper Dagbladet reports that a number of **statistical improbabilities** were found in the data set of the cancer trial, published in the Lancet in October last year. Lancet editor Dr Richard Horton told the BBC he would be speaking to the coauthors of the study to seek their permission to retract the paper. One example of the improbabilities" is the fact that of the 908 people in the trial, 250 shared the same birthday.)

36. **Acetaminophen Overdose**: Medscape article: http://www.medscape.com/viewarticle/459187_4 ; Merck Manual's Online Medical Manual: http://www.merck.com/mmpe/sec21/ch326/ch326c.html {Rumack-Matthew nomogram for predicting (Caution with units of measure!) } (10ug/ml = 66.2umol/L) {Acetaminophen level: 4hrs post ingestion & repeat in 4hrs; if ≥150mg/kg and 8hr post, may start n-acetylcysteine while awaiting levels; TOXIC levels: 4hr level >993umol/L; 6hr >728umol/L; 8hr >496.5umol/L; 24hr >29.8umol/L } {LFTs: AST usually ↑ first}
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Hitchings AW, Wood DM, Dargan PI. Dissemination and uptake of a new treatment pathway for paracetamol poisoning in the UK: a survey of healthcare professionals. Br J Clin Pharmacol. 2013 Mar 14.
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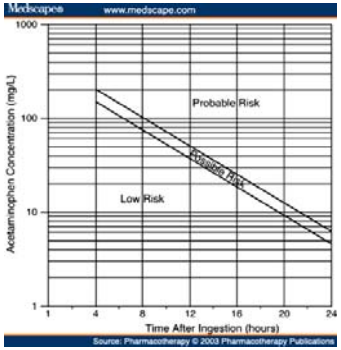
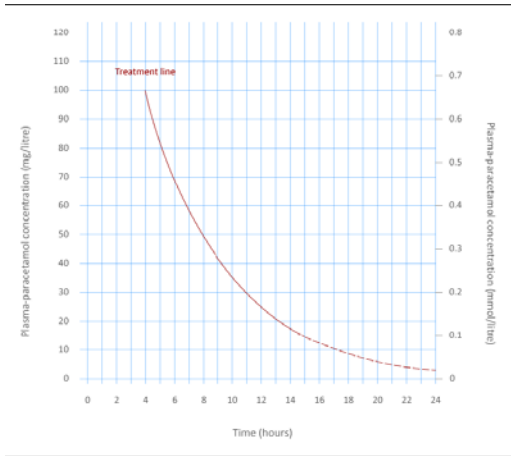
This modified acetylcysteine regimen infused a total dose of 300 mg/kg over 12 hours, versus roughly 20 hours; it used a lower initial dose (100 mg/kg over 2 hours, vs. 150 mg/kg over 15 minutes in the U.K. and 1 hour in the U.S.).



MHRA Sept 2012: Paracetamol (acetaminophen) overdose: Simplification of the use of intravenous acetylcysteine



{There is some evidence for the use of fomepizole as a CYP2E1 inhibitor and for decreased hepatotoxicity in the setting of acetaminophen overdose... To date, the evidence is all animal models but when the patient will otherwise die, the potential benefit outweighs the lack of human evidence.}

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Chan FKL, et al Clopidogrel versus **Aspirin and Esomeprazole** to Prevent Recurrent Ulcer Bleeding. N Engl J Med 2005;352:238-44. (InfoPOEMs: For patients with a history of bleeding peptic ulcer, the combination of aspirin and a proton pump inhibitor twice a day was safer in terms of bleeding side effects than clopidogrel. While esomeprazole was used in this study, generic omeprazole 20 mg give twice a day provides nearly the same degree of acid suppression at a much lower cost. This study calls into question the overall safety of clopidogrel, which has been promoted as not increasing the risk of bleeding significantly. (LOE = 1b))

Chan FK, et al. Preventing recurrent upper gastrointestinal bleeding in patients with Helicobacter pylori infection who are taking low-dose aspirin or naproxen. N Engl J Med. 2001 Mar 29;344(13):967-73. CONCLUSIONS: Among patients with H. pylori infection and a history of upper gastrointestinal bleeding who are taking low-dose aspirin, the eradication of H. pylori is equivalent to treatment with omeprazole in preventing recurrent bleeding. Omeprazole is superior to the eradication of H. pylori in preventing recurrent bleeding in patients who are taking other NSAIDs.

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FDA- **Acetaminophen and Liver Injury**: Q & A for Consumers 2009 http://www.fda.gov/downloads/ForConsumers/ConsumerUpdates/UCM172664.pdf

FDA Dec/09 , Endo, & Novartis revised the Hepatic Effects section of the Prescribing Information to add new warnings and precautions about the potential for elevation in liver function tests during treatment with all products (**including diclofenac gel**) on **diclofenac** sodium. In postmarketing reports, cases of drug-induced **hepatotoxicity** have been reported in the first month but can occur at any time during treatment with diclofenac. Postmarketing surveillance has reported cases of severe hepatic reactions, including liver necrosis, jaundice, fulminant hepatitis with and without jaundice, and liver failure. Some of these reported cases resulted in fatalities or liver transplantation.

FDA June/12 cautioned late last week against using **Reumofan Plus**, a dietary supplement marketed as a "natural" pain reliever for arthritis, osteoporosis, and other conditions. The drug, which is made in Mexico but available online, contains unlabeled and potentially harmful pharmaceutical ingredients: diclofenac, methocarbamol & sometimes dexamethasone. (Dec/12 FDA: Reumofan Plus is being relabeled and sold under the name "**WOW**.")

FDA Aug/12 is issuing an updated alert that **Reumofan Plus and Reumofan Plus Premium** contain undeclared active ingredients found in prescription drugs that should be used only under the supervision of a health care professional. It contains Diclofenac Sodium and Methocarbamol.

FDA Aug/13 laboratory analysis confirmed that **Ortiga contains the prescription drug ingredient, diclofenac**.

FDA Jan/14 is recommending health care professionals **discontinue prescribing and dispensing prescription combination drug products that contain more than 325 milligrams (mg) of acetaminophen** per tablet, capsule or other dosage unit.

FDA Feb/14 analysis of **Arth-Q supplement** contains hidden ingredient ibuprofen.

FDA Mar/14: Pain Free By Nature is recalling "**Reumofan Plus**" Tablets purchased through their website at www.painfreebynature.com, after FDA discovered that the product was distributed in packaging that did not reveal the presence of the active pharmaceutical ingredients methocarbamol and **diclofenac**, making it an unapproved drug.

FDA Apr/14: Nano Well-being Health Inc. issued a voluntary recall of **Super Arthgold**, 500 mg capsules to the consumer level. FDA laboratory analysis has found the product to contain chlorzoxazone, diclofenac and indomethacin.

Felson DT. Clinical practice. **Osteoarthritis of the knee**. N Engl J Med. 2006 Feb 23;354(8):841-8.

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Gaujoux-Viala C, Dougados M, Gossec L. Efficacy and safety of **steroid injections** for shoulder and elbow tendonitis: a meta-analysis of randomized controlled trials. Ann Rheum Dis. 2009 Dec;68(12):1843-9. Epub 2008 Dec 3. In the first 3 months of tendinitis of either the elbow or shoulder, injected corticosteroids are more effective than placebo or physical therapy, but no more effective than treatment with nonsteroidal anti-inflammatory drugs (NSAIDs). In the longer term they are no more effective than any treatment. What hasn't been studied is the effectiveness of steroid injections in patients for whom NSAID treatment isn't effective, since this is the usual progression of treatment of these painful conditions. (LOE = 1a-)

Gislason GH, et al. **Risk of Death or Reinfarction** Associated With the Use of Selective Cyclooxygenase-2 Inhibitors and Nonselective Nonsteroidal Antiinflammatory Drugs After Acute Myocardial Infarction. Circulation. 2006 Jun 19; [Epub ahead of print] For any use of rofecoxib, celecoxib, ibuprofen, diclofenac, and other NSAIDs, the hazard ratios and 95% confidence intervals for death were 2.80 (2.41 to 3.25; for rofecoxib), 2.57 (2.15 to 3.08; for celecoxib), 1.50 (1.36 to 1.67; for ibuprofen), 2.40 (2.09 to 2.80; for diclofenac), and 1.29 (1.16 to 1.43; for other NSAIDS); there were dose-related increases in risk of death for all of the drugs. There were trends for increased risk of rehospitalization for MI associated with the use of both the selective COX-2 inhibitors and the nonselective NSAIDs. CONCLUSIONS: Selective COX-2 inhibitors in all dosages and nonselective NSAIDs in high dosages increase mortality in patients with previous MI and should therefore be used with particular caution in these patients.

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Goldstein JL, Cryer B, Amer F, Hunt B. Celecoxib plus aspirin versus naproxen and lansoprazole plus aspirin: a randomized, double-blind, endoscopic trial. Clin Gastroenterol Hepatol. 2007 Oct;5(10):1167-74. n=854 In patients with osteoarthritis taking low-dose aspirin, the use of celecoxib or naproxen plus lansoprazole resulted in similar rates of gastroduodenal ulceration.

Goldstein LH, Berlin M, Berkovitch M, Kozer E. Effectiveness of oral vs rectal acetaminophen: a meta-analysis. Arch Pediatr Adolesc Med. 2008 Nov;162(11):1042-6. Among 4 small studies, oral and rectal acetaminophen for fever control were comparable in effectiveness. The authors could only find 1 study comparing **oral and rectal acetaminophen** for pain. It appeared that oral administration was more effective, but the effect may not have been clinically meaningful. The authors don't report on adverse effects. (LOE = 1a-)

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González ELM et al. **Variability** among nonsteroidal antiinflammatory drugs in risk of upper **gastrointestinal bleeding**. Arthritis Rheum 2010 Jun; 62:1592.

Gouyon JB, Kibleur Y. Efficacy and tolerability of enteral formulations of **ibuprofen** in the treatment of **patent ductus arteriosus** in preterm infants. Clin Ther. 2010 Sep;32(10):1740-8.

Gossec L, Smolen JS, Gaujoux-Viala C, et al. European League Against Rheumatism (**EULAR**) recommendations for the management of **psoriatic arthritis** with pharmacological therapies. Ann Rheum Dis. 2011 Sep 27.

Graham GG, Scott KF, Day RO. Tolerability of **paracetamol**. Drug Saf. 2005;28(3):227-40.

Graham DJ, et al. Risk of acute myocardial infarction and sudden cardiac death in patients treated with cyclo-oxygenase 2 selective and non-selective non-steroidal anti-inflammatory drugs: nested case-control study. Lancet. 2005 Feb 5-11;365(9458):475-81.

Graham DY, Agrawal NM, Campbell DR, et al. NSAID-Associated Gastric Ulcer Prevention Study Group. Ulcer prevention in long-term users of nonsteroidal anti-inflammatory drugs: results of a double-blind, randomized, multicenter, active- and placebo-controlled study of **misoprostol vs lansoprazole**. Arch Intern Med. 2002 Jan 28;162(2):169-75.

Gulmez SE, Larrey D, Pageaux GP, Lignot S, Lassalle R, Jove J, et al. **Transplantation** for acute liver failure in patients exposed to **NSAIDs or paracetamol acetaminophen**): the multinational case-population SALT study. Drug Saf 2013;36:135-44.

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Harris RE, Beebe-Donk J, Alshafie GA. Reduction in the risk of human **breast cancer** by selective cyclooxygenase-2 (COX-2) inhibitors. BMC Cancer. 2006 Jan 30;6:27.

Hay EM, et al. Effectiveness of community **physiotherapy** and enhanced **pharmacy review** for knee pain in people aged over 55 presenting to primary care: pragmatic randomized trial. BMJ. 2006 Oct 20; [Epub ahead of print] Evidence based care for older adults with knee pain, delivered by primary care physiotherapists and pharmacists, resulted in short term improvements in health outcomes, reduced use of non-steroidal anti-inflammatory drugs, and high patient satisfaction.

Hay AD, Costelloe C, Redmond NM, et al. Paracetamol plus ibuprofen for the treatment of fever in children (**PITCH**): randomised controlled trial. BMJ. 2008 Sep 2;337:a1302. doi: 10.1136/bmj.a1302. Parents, nurses, pharmacists, and doctors wanting to use medicines to supplement physical measures to maximise the time that children spend without fever should use **ibuprofen first** and consider the relative benefits and risks of using paracetamol plus ibuprofen over 24 hours.

Hawkey CJ, et al. Omeprazole compared with misoprostol for ulcers associated with nonsteroidal antiinflammatory drugs. **Omeprazole** versus Misoprostol for NSAID-induced Ulcer Management (**OMNIUM**) Study Group. N Engl J Med. 1998 Mar 12;338(11):727-34.

Hawton K, Bergen H, Simkin S, et al. Long term effect of reduced **pack sizes of paracetamol (acetaminophen)** on poisoning deaths and liver transplant activity in England and Wales: interrupted time series analyses. BMJ 2013;346:f403.

Health Canada Prohits sale of Bextra http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2005/2005_134_e.html

Health Canada June/06 two documents as part of its ongoing evaluation of COX-2-selective drugs: its official comments on the advice provided by the COX-2 Expert Advisory Panel and a report on the Department's scientific review of certain COX-2s. http://www.hc-sc.gc.ca/dhp-mps/prodpharma/activit/sci-consult/cox2/index_e.html

Health Canada Aug/07 reports that the Therapeutic Goods Administration (TGA), the federal regulatory authority in Australia, recently withdrew market authorization for **Prexige due to eight reports of serious liver adverse events** in Australia linked to the drug, including two deaths and two liver transplants. These adverse events were primarily with use of 200 mg and 400 mg doses daily.

Health Canada Sept/07 reports that **Qiangli Zhuanggutongbiling** has reportedly been used for joint pain and stiffness. It was found to contain the undeclared prescription drugs prednisolone acetate, cortisone acetate, piroxicam, and diclofenac.

Health Canada Sept/07: **Khun-Phra** is a health product promoted for pain relief that has been found to contain the undeclared drugs dexamethasone, prednisolone, phenylbutazone, diazepam, cyproheptadine and mebhydrolin.. **Asam Urat Flu Tulang, PJ Dewandaru** is a health product promoted to treat joint pain, rheumatism and arthritis. It has been found to contain the undeclared drugs dexamethasone, diclofenac and acetaminophen.

Health Canada Oct/07 Foreign Product Alerts: ***Zhen Feng Da Brand Xi Tong Wan*** is promoted as a pain reliever. Lot #060908 has been found to contain undeclared indomethacin, a prescription anti-inflammatory drug that should only be taken under the guidance of a health professional. ***Wellring Brand Yin Qiao Jie Du*** is a health product promoted to treat cold and flu symptoms. Lot#51005 has been found to contain undeclared acetaminophen. ***Gu Ci Dan*** and ***Xu Log Bou*** are promoted as pain relievers and have been found to contain indomethacin.

Health Canada Oct/07 is advising consumers that it has stopped the sale of the anti-inflammatory drug **Prexige** (lumiracoxib) in Canada and will cancel the drug's market authorization due to the potential for serious liver-related adverse events. (2 new severe cases in Canada)

Health Canada July/08 is advising consumers not to use 2 foreign health products due to concerns about possible side-effects: **3rd Generation In Homoeopathy Arthrit Indica Tablet**. The product is labelled for "intense joint pain." The Health Sciences Authority of Singapore has warned consumers not to use the product because it contains **nimesulide**, a pharmaceutical ingredient that has been associated with liver damage.

Health Canada Aug/08 is advising consumers not to use foreign health products due to concerns against the use of **AA Qu Feng Shu Jin Wan** because it was found to contain the undeclared pharmaceutical ingredient dexamethasone. **Obat Asam Urat** and **Asam Urat** both contained dexamethasone, phenylbutazone and piroxicam.

Health Canada June/09 is informing Canadian health care professionals and consumers of recent restrictions regarding the use of the prescription drug piroxicam. Health Canada has conducted a safety review and concluded that **piroxicam** should no longer be used to treat short-term pain and inflammation due to an increased risk of serious skin reactions and gastrointestinal problems relative to other similar drugs.

Health Canada July/09 is warning consumers not to use the unauthorized health product labelled as **Specific-Formula Arthro-Ace** as it was found to contain undeclared dexamethasone and may cause serious health effects.

Health Canada July/09 is warning that the Singapore Health Sciences Authority (HSA) warned consumers to not buy or use **Air Ikan Haruan** after it was found to contain undeclared dexamethasone. The Hong Kong Department of Health warned consumers not to buy or use the product **Neovidan** after it was found to contain undeclared prednisolone and mefenamic acid.

Health Canada Aug/09 is advising via Singapore Health Sciences Authority (HSA) that **Delima Raja Urat** contains undeclared dexamethasone, chlorpheniramine, pheniramine and sibutramine, while **Cao Gen Bai Lin Wan** contains undeclared dexamethasone and chlorpheniramine.

Health Canada Aug/10 **Huo Luo Jing Dan** The Singapore Health Sciences Authority warned consumers not to buy or consume Huo Luo Jing Dan after it was found to contain undeclared indomethacin, dexamethasone and prednisolone.

Health Canada Oct/11 **Huo Li Bao and Ren Sem Tu Chon Chin Kuo Pill** - The Singapore Health Sciences Authority warned that these Chinese pain-relief products contain prescription and/or over-the-counter drugs (furosemide, piroxicam, chlorpheniramine, and/or dexamethasone).

Health Canada Dec/11 is advising Canadians that Vita Health's product, "**Compliments Muscle and Back Pain Relief Regular Strength**" contains a significant labelling error in the French dosing directions that may pose serious risks to children (less than 12 years of age).

Health Canada Apr/13 **1. Diet Garcinia Forte; Shan Dian Shou; Aulura Energy Dietary Supplement** The Hong Kong Department of Health has advised consumers not to use these products after they were found to contain sibutramine and phenolphthalein, drug ingredients that were not declared on their product label. Shan Dian Shou also contains the undeclared prescription drug sildenafil. **2. Snake Powder Capsule for Rheumatism; Jia Rong Zhuang Gu Tong Bi Jiaonang; Long Ren Tang Fu She Gu Rang Jiao Nang** The Hong Kong Department of Health advised consumers not to use these products after they were found to contain multiple prescription and non-prescription drugs that were not declared on their product label. (prednisone, indomethacin, diclofenac, hydrochlorothiazide, cimetidine, prednisone, theophylline, dexamethasone etc). **3. Tinea Schwartz's; Tiao Jing Bu Xue Pills; Yeung Ng Tong Tin Hee Pills** The Hong Kong Department of Health advised consumers not to use these products after they were found to contain prescription drugs that were not declared on their product label (prednisone, indomethacin, diclofenac). **4. Quan Xie Jin Gu Tong; Xinhuang Pian; Jin Gu Feng Shi Kang Jiao Nang** The Hong Kong Department of Health advised consumers not to use these products after they were found to contain multiple prescription and non-prescription drugs that were not declared on their product label. (prednisone, piroxicam, diclofenac, indomethacin, naproxen).

Health Canada Apr/14: Nano Well-being Health Inc. issued a voluntary recall of **Super Arthgold**, 500 mg capsules to the consumer level. FDA laboratory analysis has found the product to contain chlorzoxazone, diclofenac and indomethacin, making it an unapproved new drug.

Health Canada May/14 **Ortiga** contains diclofenac.

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Celecoxib was not associated with an elevated risk of vascular occlusion, summary relative risk 1.06 (95% CI, 0.91-1.23). Among older nonselective drugs, diclofenac had the highest risk with a summary relative risk of 1.40 (95% CI, 1.16-1.70). The other drugs had summary relative risks close to 1: naproxen, 0.97 (95% CI, 0.87-1.07); piroxicam, 1.06 (95% CI, 0.70-1.59); and ibuprofen, 1.07 (95% CI, 0.97-1.18). CONCLUSIONS: This review confirms the findings from randomized trials regarding the risk of cardiovascular events with rofecoxib and suggests that celecoxib in commonly used doses may not increase the risk, contradicts claims of a protective effect of naproxen, and raises serious questions about the safety of diclofenac, an older drug. (InfoPOEMs: Rofecoxib (Vioxx), diclofenac (Voltaren, Cataflam), and indomethacin (Indocin) are associated with a significant increased risk of CVD. It is likely that all NSAIDs carry some risk, but the risks may vary between medicines. Current evidence does not point to an increased risk for low dose (over the counter) ibuprofen and this remains safe to use at recommended doses. (LOE = 2a-))

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OPIOID ANALGESIC: COMPARISON CHART

Extras:

- Buprenorphine Transdermal System (BuTrans Patch) Q&A – Aug 2010: http://www.rxfiles.ca/rxfiles/uploads/documents/BuTrans-QandA.pdf
- Fentanyl Nasal Spray (LAZANDA): available in USA, for cancer related breakthrough pain; 100ug/100mcL, 400ug/100mcL; time to onset =11 minutes; always start at 100ug spray, allow 2 hrs between doses, stepwise ↑ in dosage, max 4 doses in 24hrs.
- Fentanyl Sublingual Tablet (PALADIN, ProStrakan in USA): 100, 200, 300, 400, 600, 800 ug.
- Hydrocodone + Ibuprofen (REPREXAIN, VICOPROFEN, others): available in USA. (5/200, 7.5/200, 10/200 mg)
- Methadone injection (IV): available via special access program (SAP) in Canada
- Morphine + naltrexone (EMBEDA): available in USA; naltrexone added to ↓ abuse risk.
- Oxycodone: new products USA: (OXECTA), (ROXYCODONE)
- Oxycodone + Ibuprofen (COMBUNOX): available in USA. (5 / 400 mg)
- Oxymorphone (OPANA, OPANA ER): available in USA; IM, rectal, & recently oral; 3x more potent than oral morphine; avoid alcohol as ↑↑↑ peak concentrations. (IR tabs: 5,10mg; e.g 5mg q4-6h prn. ER tabs: 5, 7.5, 10,15,20,30, 40mg; e.g. 10mg q12h).
  - Oxymorphone OPANA ER Abuse Thrombotic thrombocytopenic purpura (TTP) strongly associated with injection drug abuse of OPANA ER.
- See also RxFiles Substance Abuse Chart: http://www.rxfiles.ca/rxfiles/uploads/documents/CHT-Substance-Abuse.pdf (sections: 4- Addiction screening; 5-Universal Precautions in Pain Medicine; 6-Red Flags for Aberrant Rx Drug Use)
- Oral Morphine for Cancer Pain: Systematic Review (Cochrane): Somewhat effective in 9/10 patients; 6/10 patients, very satisfied; 1/20 stopped due to AEs, Common AE: constipation, N&V.

Fentanyl Patches: "Attempting to give 1/2 patch"

The rate of medication delivery from Duragesic® patches is in proportion to the surface area of drug reservoir in contact with the skin. Prior to the availability of the 12.5 mcg/hr strength, the following procedure was occasionally used to achieve this rate:

1. An occlusive dressing like Opsite was put on the skin.
2. A 25 mcg/hr patch was then applied on top with half on the skin and half on the dressing.

This approach lacks documentation and can not be routinely recommended.

Fentanyl / Opioid Patch Exchange Tool: http://www.rxfiles.ca/rxfiles/uploads/documents/Opioid-Patch-Exchange-Disposal-Tool.pdf

Opioid Intolerance:

- **Pseudoallergy**
  - **COMMON**! May use non-opioid, lower opioid dose, alternate opioid even from same class; add H1 $_{\text{diphenhydramine}}$ +/- H2 $_{\text{ranitiidine}}$ blocker, moisturizers, cold compresses
    - Flushing, itching, hives, sweating, and/or mild hypotension
    - Itching, flushing or hives at injection site only

These symptoms **may** be due to a *pseudoallergy*. It's a result of histamine release, a pharmacologic side effect of some opioids. Options for this patient include:

1. A nonopioid analgesic (e.g., acetaminophen, an NSAID)
2. Avoidance of codeine, morphine, and meperidine, the opioids most commonly associated with pseudoallergy
3. Use of a more potent opioid less likely to release histamine. Potency, from lower to higher:
   meperidine<codeine<morphine<hydrocodone<oxycodone<hydromorphone<levorphanol<fentanyl
4. If needed, concurrent administration of an antihistamine…an H1 (e.g., diphenhydramine) and perhaps an H2 blocker (e.g., cimetidine)
5. Dose reduction, if tolerated

- **Potential true opioid allergy**
  - **RARE**! - would require change to non-opioid or opioid from different chemical class – see below
    - Severe hypotension
    - Skin reaction other than (Flushing, itching, hives)
    - Breathing, speaking, swallowing difficulties
    - Swelling of the face, lips, mouth, tongue, pharynx or larynx

Opioid Reversal Agent for Overdose: Naloxone (IV, IM, SC; sometimes intranasal off-label). Dose, initial 0.4-2mg IV for adults, may repeat q2-3 minutes up to total maximum of 10mg. Will precipitate withdrawal.
- Used to treat life threatening respiratory depression, and sometimes, since short acting, just to temporarily bring patient to consciousness to gather information, then allow back into unconsciousness while drug is eliminated from system.

Opioid Chemical Class

1. **Phenylpiperidines**: meperidine, fentanyl, sufentanil, remifentanil
2. **Diphenylheptanes**: methadone, propoxyphene
3. **Morphine group**: morphine, codeine, hydromorphone, oxycodone, oxymorphone, nalbuphine, butorphanol, levorphanol, pentazocine

New Drugs {Not yet in Canada)

- **Oral Oxymorphone**
  i. (Opana, Opana ER): **Potency** is about 10x more potent than morphine! Caution!. [Immediate release: 5, 10mg tabs; Extended release; 5, 10, 20, 40 mg tabs]

Additional References & Links:

- **Canadian Guidelines for Safe and Effective Use of Opioids**: http://nationalpaincentre.mcmaster.ca/index.html
- **Responsible Physician Opioid Prescribing Resources (USA) Links:** http://www.responsibleopioidprescribing.org
- Health Canada – Company – Dosage Conversion Guidelines for Fentanyl; Revised Mar 2010: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/pdf/medeff/advisories-avis/prof/2010/fentanyl_2_hpc-cps-eng.pdf
- **Opioid Manager Tool**: Point of care tool summarizing Canadian Guidelines:
  - **From CEP**: http://www.effectivepractice.org/index.cfm?pagePath=CEP_TOOLS/Opioid_Manager&id=23515
  - **From NPC:** http://nationalpaincentre.mcmaster.ca/opioidmanager/
- Tramadol warning (FDA): http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm213264.htm
- **AFP article Aug 2012 - on Rational Use of Opioids for Management of Chronic Nonterminal Pain** http://www.aafp.org/afp/2012/0801/p252.html

Treatment Agreements:

Medscape discussion on use in primary care. http://www.medscape.com/viewarticle/711659?src=mp&spon=30&uac=93517FV

Canadian Guideline sample at http://nationalpaincentre.mcmaster.ca/opioid/cgop_b_app_b05.html

RxFiles 1 page version at http://www.rxfiles.ca/rxfiles/uploads/documents/Pain-CNMP-Opioid-TreatmentAGREEMENT.pdf ; Customizable MS-Word versionhttp://www.rxfiles.ca/rxfiles/uploads/documents/Pain-CNMP-Opioid-TreatmentAGREEMENT.doc

RxFiles 2 page version at: ♦customizable MS Word: http://www.rxfiles.ca/rxfiles/uploads/documents/Opiod-Informed-Consent-And-Agreement.docx ♦pdf: http://www.rxfiles.ca/rxfiles/uploads/documents/Opiod-Informed-Consent-And-Agreement.pdf

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FDA July/09 notified healthcare professionals that it is taking several actions to reduce the risk of overdose in patients using pain medications that contain propoxyphene because of data linking propoxyphene and fatal overdoses. The agency will require manufacturers of propoxyphene-containing products to strengthen the label, including the boxed warning, emphasizing the potential for overdose when using these products and to provide a medication guide to patients stressing the importance of using the drugs as directed.

FDA Nov/10 is requesting that manufacturers of the painkiller propoxyphene pull the drug from the market because of concerns over cardiotoxicity. (Propoxyphene is marketed alone as Darvon and combined with acetaminophen as Darvocet.) The agency's request is based on data showing that, even when taken at therapeutic doses, the drug can lead to potentially dangerous changes in the heart's electrical activity, including prolonged PR and QT intervals and widened QRS complex. The FDA advises clinicians to stop prescribing propoxyphene and to ask current users to discontinue the drug. FDA's MedWatch alert (Free)

FDA: July/12 Clinicians who prescribe extended-release and long-acting opioids may receive training as part of an FDA effort to curb misuse. With the risk evaluation and mitigation strategy, pharmaceutical companies must develop programs to train clinicians on how to choose patients for opioid therapy appropriately, how to weigh the risks and benefits for a given patient, how to counsel patients against misuse, and how to spot signs of opioid misuse and addiction. The first training programs are expected to be available by March 2013. Currently, this training is optional, but the Obama administration has endorsed a mandatory training plan.

FDA Aug/12 is reviewing reports of children who developed serious adverse effects or died after taking codeine for pain relief after tonsillectomy and/or adenoidectomy for obstructive sleep apnea syndrome. Recently, three pediatric deaths and one non-fatal but life-threatening case of respiratory depression were documented in the medical literature.

FDA Sep/13 Extended-release and long-acting (ER/LA) opioid pain relievers are no longer indicated for merely moderate pain, the US Food and Drug Administration (FDA) announced today as part of a sweeping move to stem the deadly misuse and abuse of the drugs. Previously, the labels for ER/LA opioid analgesics stated that they were indicated for "moderate to severe pain in patients requiring continuous, around-the-clock opioid treatment for an extended period of time." The labels now will state that the drugs are indicated "for the management of pain severe enough to require daily, around-the-clock opioid treatment and for which alternative treatments are inadequate."

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Opioid Treatment Agreements

- Useful for:
  - Identifying drug abuse
  - Reducing doctor shopping
  - Outlining how "requests" will be handled
    - E.g. early refills? Running out due to "borrowing from tomorrow"
  - Educating patients on:
    - What to expect?
    - What not too expect?
      - realistic expectations for 30-50% reduction in pain
    - Importance of non-drug interventions
    - Role or lack thereof for "prns" in therapeutic plan
  - Outline responsibilities and expectations
    - monitoring plans, especially functional goals
    - how opioids will be obtained and taken
    - use of concomitant drugs
    - storage and security requirements
    - consequences for non-adherence or aberrant behaviour
  - option of including informed consent components
  - proactive managing of highly functioning, charming and convincing individuals with borderline personality traits – to pre-empt typical conflict that can arise
- The more routine the clinicians use of an agreement, the easier it is!
  - Removes stigma of "suspicion" and any issues of trust
  - Offers best practice protection to all

Education Programs of Interest

- *Inventory of Pain and Addiction Education Programs for Canadian Prescribers*
  - From the National Pain Centre in collaboration with CCSA
  - Link: http://nationalpaincentre.mcmaster.ca/tools.html

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Additional information:

CAMH: Video discussion of issues around how to taper. http://knowledgex.camh.net/videos/Pages/tapering_presopioids_selby2013.aspx

Opioid Taper Template & related materials at: www.RxFiles.ca

Opioid Manager tool from Canadian CNCP guideline group: http://nationalpaincentre.mcmaster.ca/opioidmanager/

RxFiles Opioid Taper Template TOOL: http://www.rxfiles.ca/rxfiles/uploads/documents/Opioid-Taper-Template.pdf

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FDA Nov/10 has approved **denosumab** (marketed as **Xgeva**) for the prevention of fracture and bone pain in patients with cancer that has metastasized to the bone. FDA news release (Free) Xgeva prescribing information (Free PDF)

FDA July/11 notified healthcare professionals and patients about its ongoing review of data from published studies to evaluate whether use of **oral bisphosphonate** drugs is associated with an **increased risk of cancer of the esophagus**. FDA has not concluded that taking an oral bisphosphonate drug increases the risk of esophageal cancer. There are insufficient data to recommend endoscopic screening of asymptomatic patients.

FDA Sep/11 notified healthcare professionals and patients of an update to the drug label for **Reclast (zoledronic acid)** regarding the risk of kidney failure. Cases of acute renal failure requiring dialysis or having a fatal outcome following Reclast use have been reported to FDA. The revised label states that Reclast is contraindicated in patients with creatinine clearance less than 35 mL/min or in patients with evidence of acute renal impairment.

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Health Canada Dec/11 is updating Canadians with respect to its review of bisphosphonate drugs, used to treat osteoporosis, and the risk of a rare but serious type of thigh bone fracture known as an "**atypical femur fracture** <1% ."

Health Canada May/12: Cases of severe, sometimes **fatal, symptomatic hypocalcemia associated with XGEVA (denosumab)** treatment have been reported in cancer patients with bone metastases

Health Canada Nov/12 **PROLIA (denosumab)** - Association with the Risk of **Atypical Femoral Fractures** - Amgen Canada Inc. Cases of atypical femoral fractures associated with PROLIA (denosumab) treatment have been reported in patients participating in an ongoing clinical trial involving postmenopausal women with osteoporosis.

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Calculating Bone Mineral Densitometry, BMD fracture risk http://www.halls.md/bone-mineral-densitometry/bmd.htm
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QFractureScore http://www.qfracture.org/
Simple Calculated Osteoporosis Risk Estimation (SCORE) tool http://osteoed.org/tools.php (sensitivity 91%, specificity 40%)[BMD]

Extras, Links & References:

- **AMETOP**: **tetracaine** (amethocaine) **4% Gel** : Adults (including geriatrics) & children over 1 month of age: **Apply** contents of the tube to the skin starting from the centre of the area to be anesthetized & cover with an occlusive dressing. The contents expellable from 1 tube (approximately 1 g) will cover & anesthetize an area of up to 30cm^2 (6×5 cm {~ 3/4 area of a credit card}). Smaller areas of anesthetized skin may be adequate in infants & small children. Adequate anesthesia can usually be achieved for venepuncture following a 30-minute application time, & for venous cannulation following a 45-minute application time; after which the gel should be removed with a gauze swab & the site prepared with an antiseptic wipe in the normal manner. It is not necessary to apply tetracaine gel for longer than the above times & anesthesia is maintained for 4 to 6 hrs in most patients after a single application. [Clinical Trial in progress: Ametop vs Maxilene: http://www.druglib.com/trial/02/NCT00353002.html]

- **EMLA (lidocaine and prilocaine)** - for intact skin, requires occlusion, needs to be applied for at least one hour Dose — To attain adequate anesthesia, 1 to 2 g of EMLA cream should be applied per 10 sq cm (approximate size of a Canadian "toonie") of skin and covered with an occlusive dressing for 45 to 60 minutes. The maximum application areas recommended for children are Less than 10 kg —100 sq cm {~ 2.5x area of a credit card};10 to 20 kg — 600 sq cm; Greater than 20 kg — 2000 sq cm ; causes vasoconstriction.

See www.usask.ca/pediatrics/services/pain for information for parents on children's pain

- **acetaminophen use with vaccination:** may ↓ immunogenicity ∴ avoid if possible.
- **Benzocaine** –in NG tube placement controversial[10] Causes methemoglobinemia!!! AVOID!
- **Lidocaine iontophoresis** {Numby Stuff}: mild electric current penetrates skin more quickly; effective in 10-20min.[43] EMLA similar or slightly better.[44,45] (Tingle may be bothersome.)
- **TAC** tetracaine 0.5% / epinephrine 0.05% / cocaine ≤ 11.8%; AE: seizures, arrhythmias, fatal; requires narcotic storage (LET preferred)
- **Cancer Pain:** Reference [46]
- **Urethral Catheterization**: lidocaine gel 2 min prior to insertion while setting up then use as the lubricant as well (video: http://www.uihealthcare.com/topics/medicaldepartments/urology/catheterization/index.html)
- **Acetaminophen vs ibuprofen**: http://www.cps.ca/English/statements/DT/dt98-01.htm For fever:[47]
- **SHR Peds Pain Links**: http://www.usask.ca/pediatrics/services/pain/
- CADTH. Short-Acting Agents for Procedural Sedation and Analgesia in Canadian Emerg.: A Review of Clinical Outcomes and Economic Evaluation http://cadth.ca/media/pdf/O0428_Short-Acting-Procedural-Sedation_to_e.pdf

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Pain Intensity Scoring:

- Chose a scale that is age appropriate to patient & become familiar with using!
- Interpret in light of any other pain related physical factors (e.g. heart rate)
- Also interpret according to trends for improvement or worsening of pain control
- Sherbrooke algorithm for acute pain in children (post-op): gave regular analgesic according to pain scale: {0-3: acetaminophen; 3-6: naproxen + acetaminophen; 6-9: morphine + naproxen + acetaminophen; 9-10: notify MD. Overall ↓ in pain scores & a ↓ in opioid requirement.}
- Other links: **Visual Analogue Scale**: suitable for age 7+ {McGrath PA, Seifert CE, Speechley KN, et al. A new analogue scale for assessing children's pain: an initial validation study. Pain. 1996 Mar;64(3):435-43.} **Oucher Scale**: age 3-12: http://www.oucher.org/history.html
BMJ Clinical Review: Pain Management and Sedation for Children in the Emergency Setting: http://www.bmj.com/cgi/content/full/339/oct30_1/b4234

FLACC SCALE – for assessing pain in very young children non-verbal; suitable for cognitively impaired

Face	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant quivering chin, clenched jaw
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimpers; occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

- Each of the five categories (F) Face; (L) Legs; (A) Activity; (C) Cry; (C) Consolability is scored from 0-2, which results in a total score between zero and ten.
- From ***The FLACC****: A behavioral scale for scoring postoperative pain in young children*, by S Merkel and others, 1997, Pediatr Nurse 23(3), p. 293-297. Copyright 1997 by Jannetti Co. University of Michigan Medical Center.

Faces Pain Scale – Revised (FPS-R) – age 4+

This is a thumbnail image. The full-size FPS-R with instructions is available on page 3 at http://www.iasp-pain.org/FPSR Numbers are not shown to children.

0 2 4 6 8 10

From: Hicks CL, von Baeyer CL, Spafford PA, Van Korlaar I, Goodenough B. The *Faces Pain Scale – Revised*. Toward a common metric in pediatric pain measurement. *Pain* 2001;93:173-183. ©2001 International Association for the Study of Pain. Reprinted with permission.

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RA - EXTRAS

Approach & Considerations for Drug Tx in RA

- Initial: DMARD + NSAID +/- Corticosteroid for symptoms. MTX often the DMARD of choice, however, HCQ is safer but suitable only for mild cases.
  -NSAIDs now used primarily for bridging and pain management.
  -Oral corticosteroids associated with complications, so use controversial. Short courses &/or low doses for ≤2yrs sometimes used (↓ joint pain & systemic symptoms). Intra-articular injections useful & few AEs.
  -Earlier combo DMARD or biologic tx warranted for those with high disease activity & poor prognostic factors.
  {Features of poor prognosis include: functional limitation, extraarticular disease rheumatoid nodules, RA vasculitis, Felty's syndrome, +'ve rheumatoid factor, anti-cyclic citrullinated peptide antibodies, bony erosions radiographic.}
- TNF inhibitors - 1st line biologics after an inadequate response to a DMARD. They are given +/- MTX (synergistic). Note, infliximab given with MTX (not recommended for monotherapy).
  - ◆Initial TNF inhibitor choice: varies with clinician (often etanercept rapid onset, short t ½ or infliximab)
  - ◆Relative to other agents, TNF-inhibitors may be more effective in relieving symptoms & limiting joint destruction. They often also act more rapidly.
  - ◆AEs: 1) Injection site reactions (back pain, fever, urticaria, dyspnea, ↓BP): common with etanercept, golimumab, certolizumab, & adalimumab.
    2) Cytopenia: uncommon, but can occur with any anti-TNF tx. Monitor CBC.
    3) The potential for Serious Infections: (eg. bacterial sepsis, TB reactivated & disseminated, fungal, viral & opportunistic unusual eg. *p. jiroveci*) are important; screen for active infection, latent TB, etc.
    4) Malignancies (esp. lymphomas): reported but causality not established. The condition of RA ↑ lymphoma risk on its own. Avoid anti-TNF tx in patients with recent ca.
    5) Other AEs: (rare) – CHF, reversible lupus-like syndrome, demyelinating conditions eg. M.S. (avoid if hx), hepatoxicity (caution with infliximab).
  - ◆If 1st TNF inhibitor is not effective, switching to a 2nd TNF inhibitor may be effective; however, many specialists will opt for a non-TNF biologic for a different mechanism of action.
- Non-TNF Biologics – include rituximab co-admin with a DMARD; pre-treat to prevent infusion reaction, abatacept +/- a DMARD, tocilizumab may work in ≥2wks, AEs (many; severe complications reported), anakinra less effective.
- Aggressive early therapy with MTX &/or a biologic ⇨ longer remissions, less joint destruction & improved quality of life.
- Combination Tx with 2-3 DMARDs (or a DMARD + biologic): often more effective than monotherapy without more toxicity.
  - ◆Triple DMARD Tx: MTX +SSZ + HCQ (+/- prednisone low-dose ≤7.5-10mg/day) effective. ◆MTX + Biologic more efficatious than either alone. ◆Combination of 2+ Biologics NOT recommended as ↑ toxicity!
- Comorbidity & biologics ACR RA 2012:
  - 1) Hepatitis
    a) Hep C ⇨ potentially recommend etanercept;
    b) Hep B: untreated chronic or treated chronic with Child-Pugh class B or higher: avoid any biologic!
  - 2) Malignancy
    a) treated solid malignancy >5yrs or non-melanoma skin ca >5ys ago – recommend any biologic;
    b) treated solid malignancy <5yr or treated non-melanoma skin ca within 5yr – recommend rituximab;
    c) treated skin melanoma, & treated lymphoproliferative malignancy – recommend rituximab;
  - 3) CHF
    a) NYHA class III-IV with ejection fraction ≤50%: avoid anti-TNF biologics!

Vaccinations: before DMARD or biologic, immunize for influenza, pneumococcal, hep-B & HZV. Live vaccines should not be given to patients on biologics (should be given ≥1 month prior to starting tx).

Pain Management in RA:

- Neuromodulators: Cochrane Review RCT, placebo controlled - few trials, all short term (~2-5 weeks) with high risk of bias (ie. Weak evidence)
  1) Nefopam (ACUPAN): not in Canada; 5HT, NE & DA receptor blocking; NNT=2 for pain relief, offset by significant SE's
  2) Topical capsaicin: reasonable add-onn option; NNT=2-3 for pain relief, offset by some burning at application site
  3) Oromucosal cannabis: small reduction in pain, highly offset by SE's leading to withdrawal (NNH=3) including dizziness 26%, dry mouth 13% & lightheadedness (10%)
  4) Lack of data for other agents included: anticonvulsants, ketamine, bupropion, methylphenidate

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FDA Sep/11 notified healthcare professionals that the Boxed Warning for the entire class of **Tumor Necrosis Factor-alpha (TNFα) blockers** has been updated to include the risk of infection from two bacterial pathogens, **Legionella and Listeria**. In addition, the Boxed Warning and Warnings and Precautions sections of the labels for all of the TNFα blockers have been revised so that they contain consistent information about the risk for serious infections and the associated disease-causing pathogens.
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Health Canada June/11 **RITUXAN (rituximab) - Fatal Infusion Related Reactions** in Patients with Rheumatoid Arthritis
Health Canada Oct/12 is informing Canadians and Canadian health care practitioners that the labelling for **methotrexate and Proton Pump Inhibitors** (eg. Omeprazole) will include information on a potential interaction between these products.
Health Canada Feb/13 Severe skin reactions such as Toxic Epidermal Necrolysis (TEN) and Stevens-Johnson Syndrome (**SJS**) have been reported very rarely in patients who were given **RITUXAN** for the treatment of cancer or disorders of the immune system such as rheumatoid arthritis (RA). Some cases resulted in death.
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Behavioural & Psychological Symptoms of DEMENTIA (BPSD) Treatment Chart

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Useful Web sites:

Alzheimer Society Canada www.alzheimer.ca

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Essential Tremor (ET) & Restless Legs Syndrome (RLS) - Treatment Options

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RxFiles provides objective comparisons for optimal drug therapy decision making via:

- Academic Detailing (to Saskatchewan physicians, pharmacists, & nurse practitioners)
- RxFiles Drug Comparison Charts book {8th Edition coming - Summer 2010; see http://www.rxfiles.ca/rxfiles/modules/druginfoindex/druginfo.aspx}
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- Newsletters, Q&As, Trial Summaries, Charts; participation in continued professional learning (http://www.usask.ca/cme/)
- Contributions to Canadian and international evidence informed drug therapy discussions and academic detailing developments.

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Recommendations for determining the level of concern when considering treatment modification based on **relapse**:

Criteria	Level of Concern		
	Low	Medium	High
Rate	1 relapse in 2nd year of tx	1 relapse in 1st yr of tx	>1 relapse in the 1st yr of tx
Severity	**Mild**	**Moderate**	**Severe**
	-steroids not required	-steroids required	-steroids/ hospitalization required
	-minimal effect on ADL	-moderate effect on ADL	-severe effect on ADL
	-1 functional domain affected	->1 functional domain affected	->1 functional domain affected
	-no or mild motor/cerebellar involvement	-moderate motor/cerebellar involvement	-severe motor/cerebellar involvement
Recovery	-prompt recovery	-incomplete recovery at 3 months	-incomplete recovery at 6 months
	-no functional deficit	-some functional impairment	-functional impairment

Recommendations for determining the level of concern when considering treatment modification based **disability progression**:

Criteria	Level of Concern		
EDSS score:	Low	Medium	High
≤ 3.5	≤ 1 points	2 points at 6months	>2 points at 6months 2 points at 12months
4-5	<1 point	1 point at 6 months	>1 point at 6months 1 point at 12months
≥5.5		0.5 points at 6months	>0.5 points at 6 months
Clinically Documented Progression	No motor Minor sensory	Some motor, cerebellar or cognitive Multiple EDSS domains affected	Pronounced motor, cerebellar or cognitive Multiple EDSS domains affected
T25FW	≤ 20% confirmed at 6months	>20% and ,100% increase confirmed at 6months	≥ 100% increase confirmed at 6 months

Recommendations for determining the level of concern when considering treatment modification based on annual MRI findings:

Criteria	Level of Concern		
	Low	Medium	High
Activity on MRI:			
New Gd-enhancing Lesions OR accumulation Of new T2 lesions per year	1 lesion	2 lesion	≥3 lesions

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Pucci E, Giuliani G, Solari A, Simi S, Minozzi S, Di Pietrantonj C, Galea I. **Natalizumab** for relapsing remitting multiple sclerosis. Cochrane Database of Systematic Reviews 2011, Issue 10. Art. No.: CD007621. DOI: 10.1002/14651858.CD007621.pub2. Although one trial did not contribute to efficacy results due to its duration, we found robust evidence in favour of a reduction in relapses and disability at 2 years in RRMS patients treated with NTZ. The drug was well tolerated. There are current significant safety concerns due to reporting of an increasing number of PML cases in patients treated with NTZ. This review was unable to provide an up-to-date systematic assessment of the risk due to the maximum 2 year-duration of the trials included. An independent systematic review of the safety profile of NTZ is warranted. NTZ should be used only by skilled neurologists in MS centres under surveillance programs.
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(Yousry TA, Major EO, Ryschkewitsch C, et al. Evaluation of patients treated with natalizumab for progressive multifocal leukoencephalopathy. N Engl J Med. 2006 Mar 2;354(9):924-33.) (May 3, 2007 - Biogen Idec (NASDAQ: BIIB) and Elan Corporation, plc (NYSE: ELN) announced today that new data from the TOUCH Prescribing Programä and TYGRIS safety study confirm the safety profile from previous clinical studies of TYSABRI® (natalizumab). Also presented at the 59th annual meeting of the American Academy of Neurology in Boston, MA were extension study data that showed that TYSABRI has a sustained treatment effect on clinical relapses and the risk of disability progression in multiple sclerosis (MS) patients treated for up to three years. The companies recently reported that as of mid-April 2007 approximately 12,500 patients have been prescribed TYSABRI worldwide. The companies estimate that in both commercial use and clinical trials, there are currently over 10,000 patients on TYSABRI therapy worldwide. No New PML Cases 10 Months After Tysabri Allowed Back on Market. The drug is currently being used by more than 10,00 patients worldwide -- including roughly 6600 in the U.S. -- the manufacturer said.) July 31/08 Biogen, Elan Report Brain Infections in Patients Shares of Biogen Idec Inc. and Elan Corp. fell sharply in late trading Thursday, after the companies said their multiple sclerosis drug Tysabri has been linked to **two new cases** of a rare and often fatal brain inflammation.
Goodin DS, Cohen BA, O'Connor P, Kappos L, Stevens JC; Therapeutics and Technology Assessment Subcommittee of the **American Academy of Neurology**. Assessment: the use of natalizumab (Tysabri) for the treatment of multiple sclerosis (an evidence-based review): report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2008 Sep 2;71(10):766-73. The **PML** risk in a pooled clinical trial cohort has been estimated to be 1 person for every 1,000 patients treated for an average of 17.9 months, although this figure could change in either direction with more experience with the drug.
December 17, 2008 — Biogen Idec and Élan reported to the United States Securities and Exchange Commission (SEC) that "relevant regulatory agencies" had been informed of another case of progressive multifocal leukoencephalopathy (PML) with natalizumab (Tysabri) monotherapy in a patient with multiple sclerosis (MS). The case was found through surveillance, the companies note, and the patient is stable. The male patient is from Germany and had been on natalizumab monotherapy for 26 months. He is reported to be stable and under the care of his physician. The companies released information on their December 11 Form 8-K report to the SEC December 15.
Health Canada Feb/09 New Safety Information Regarding Progressive Multifocal Leukoencephalopathy (PML) Associated with Tysabri (natalizumab) http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-_avis/prof/_2009/tysabri_2_hpc-cps-eng.php
Biogen http://phx.corporate-ir.net/External.File?item=UGFyZW50SUQ9ODc0MXxDaGlsZElEPS0xfFR5cGU9Mw==&t=1
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FDA Sep/09 documents 13 PML cases http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm107198.htm
October 27, 2009 — The European Medicines Agency (EMEA) disclosed October 23 that it has begun a review of the risk–benefit balance for use of natalizumab (*Tysabri*, Biogen Idec/Elan) in relapsing-remitting multiple sclerosis in light of new cases of progressive multifocal leukoencephalopathy (PML) with treatment. The EMEA notes it started a review of the benefits and risks of natalizumab because reports of PML cases worldwide have climbed now to 23 since the drug was reinstated in the market in 2006. "This review is initiated to discuss any additional measures necessary to ensure the safe use of Tysabri and how to balance the risks to the patients against the benefits of the treatment," a press release from EMEA notes. The release was a round-up of EMEA activities as of October 2009. Natalizumab was taken off the market in February 2005 after the first 3 cases of PML were reported. On September 23, 2009, the US Food and Drug Administration (FDA) reported that the count for confirmed cases of PML worldwide in patients treated with natalizumab as monotherapy had reached 13. They have now confirmed the new total case count at 23.
Jan 21,2010 (Dow Jones)--As of Wednesday, there have been 31 cases of a rare brain infection in multiple sclerosis patients on Tysabri, sold by Biogen Idec Inc. (BIIB) and Elan Corp. (ELN), according to a review by a European regulatory panel. The European Medicines Agency's Committee for Medicinal Products for Human Use, known as CHMP, reported the cases of progressive multifocal leukoencephalopathy, or PML, in a review of the drug that concluded its rewards outweigh its risks and the drug should stay on the market. Of the **31 cases**, 23 of the patients were on the drug for more than two years, which puts the infection rate at about 1 in 1,000 patients for those exceeding that duration.
This assertion is the same held by the company and implied by the drug's label.
FDA Feb/10 notified healthcare professionals and patients that the risk of developing progressive multifocal leukoencephalopathy (PML) increases with the number of Tysabri infusions received. This new safety information, based on reports of 31 confirmed cases of PML received by the FDA as of January 21, 2010, will now be included in the Tysabri drug label and patient *Medication Guide*.
March 18, 2010 9:22 AM EDT Biogen Idec (Nasdaq: BIIB) disclosed that the number of PML cases involving those taking its Tysabri drug has increased to 42 patients with 9 who have died.
May/10 Biogen Idec Canada Inc., has updated the Tysabri product information with new information on Progressive Multifocal Leukoencephalopathy (PML). The risk of PML increases with increasing duration of treatment with Tysabri. After 24 infusions, physicians are to review with their patients, the benefits and risk of continuing Tysabri treatment.
Schröder A, Lee DH, Hellwig K, Lukas C, Linker RA, Gold R. **Successful Management of Natalizumab**-Associated Progressive Multifocal Leukoencephalopathy and Immune Reconstitution Syndrome in a Patient With Multiple Sclerosis. Arch Neurol. 2010 Jul 12.
Oct 22/10 - Two more patients taking Biogen Idec Inc's multiple sclerosis drug Tysabri (natalizumab) have developed progressive multifocal leukoencephalopathy (PML), the company said on Wednesday. The Cambridge, Massachusetts-based biotechnology company said in its latest monthly update that as of Oct. 1, there have been **70 confirmed cases of PML**, up from 68 as of Sept. 2. Of those, 14 have died and 56 are alive with varying degrees of disability ranging from mild to severe. There were no additional deaths in October. As of June 30, about 71,400 patients had received Tysabri since it was launched.
Vermersch P, Kappos L, Gold R, et al. Clinical outcomes of natalizumab-associated progressive multifocal leukoencephalopathy. Neurology. 2011 May 17;76(20):1697-704.
FDA Jan/12 JC virus is common and usually harmless, the agency said, but its presence — along with either of the other two PML risk factors — can be dangerous in patients taking immunomodulating drugs like natalizumab. The other risk factors are treatment with natalizumab for longer than 2 years, and previous treatment with immunosuppressant drugs such as methotrexate or cyclophosphamide. The FDA estimates that patients with all three risk factors face about a 1% risk for PML (11 cases per 1000 patients treated).
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For cladribine versus placebo, the relative risk reduction in the annualized relapse rate was 57.6% for the group receiving 3.5 mg per kilogram of body weight and 54.5% for those receiving 5.25 mg per kilogram. Adverse effects were similar in all three trials of cladribine and fingolimod, and rates of events leading to discontinuation of a study drug were low but still at least twice as frequent with high-dose cladribine (7.9% for the 5.25-mg dose) and fingolimod (10% and 14% for the 1.25-mg dose). Side effects: herpetic infections, ?cancer & lymphocytopenia.

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Kappos L, Radue EW, O'Connor P et al. **FREEDOMS** Study, A Placebo-Controlled Trial of Oral **Fingolimod** in Relapsing Multiple Sclerosis. N Engl J Med 2010 0: NEJMoa0909494.. (n=1272, 2yr, 1.25 or 0.5mg po od vs placebo)
For fingolimod versus placebo, the relative risk reduction was 54% for the 0.5-mg dose and 60% for the 1.25-mg dose. For fingolimod versus interferon beta-1a, the relative risk reduction was 52% for the 0.5-mg dose and 39% for the 1.25-mg dose. Adverse effects were similar in all three trials of cladribine and fingolimod, and rates of events leading to discontinuation of a study drug were low but still at least twice as frequent with high-dose cladribine (7.9% for the 5.25-mg dose) and fingolimod (10% and 14% for the 1.25-mg dose). Side effects: herpetic infections, ?cancer, macular edema, bradycardia & lymphocytopenia.

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EMA Jan/12 European and U.S. regulators are reviewing Novartis AG's (NOVN) **Gilenya** pill for multiple sclerosis after reports of **11 deaths** among patients who took the drug.

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FDA Dec/11 has received a report of a patient with multiple sclerosis (MS) who **died** within 24 hours of taking the first dose of **Gilenya (fingolimod).** At this time, FDA cannot conclude whether the drug resulted in the patient's death.

FDA May/12 warned clinicians on Thursday that "**liberation therapy**," an experimental procedure that uses angioplasty balloons or stents to open narrowed veins in the chest and neck, has not been approved to treat chronic cerebrospinal venous insufficiency (**CCSVI**) and could be dangerous. Liberation therapy has been associated with one death due to a brain hemorrhage and one stroke, says the FDA. Other possible risks include blood clots, cranial nerve damage, and migrating stents.

FDA is alerting the public that a patient in Europe diagnosed with possible multiple sclerosis (MS) has developed a rare and serious brain infection after taking the drug Gilenya (fingolimod). This is the first case of progressive multifocal leukoencephalopathy (**PML**), reported following the administration of **Gilenya** to a patient who had not previously received Tysabri (natalizumab), an MS drug associated with a higher risk of PML.

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Approach to Migraine: Considerations

- ACUTE: - may consider metoclopramide or domperidone 1st; NSAID and/or triptan also recommended first line;
  - in very severe attacks, SC sumatriptan likely to be most effective & rapid; consider need for rapid onset vs recurrence, GI tolerance of po form, etc.
  - Link to Review Article in AFP Feb 2011: http://www.aafp.org/afp/2011/0201/p271.html
- PROPHYLAXIS: 1st line: beta-blockers (propranolol, metoprolol), TCAs, valproic acid, topiramate.
- MENSTRUAL Related Migraine (MRM): - severity may be increased; duration of headache may be longer and may be harder to treat than regular migraine
  - may consider NSAID or triptan for short-term treatment, several days before and during menstruation [20].

Agents not effective or too many side effects:

- SSRIs, clonidine, methylsergide, oxcarbazepine, melatonin

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- **EXTRAS:**

Alternative Therapies: behavioural therapies include the mastery of relaxation techniques, cognitive behavioural therapy including stress management, biofeedback, and the mastery of pacing and self monitoring skills

Patient Factors	**Red Flags for Serious Headaches**[17] "This is the worst headache ever…"
Age of onset	middle-aged to elderly patients
Type of onset	severe & abrupt; presents suddenly "like a thunderclap"
Temporal sequence	progressive severity or increased frequency
Pattern	significant change in headache pattern
Neurologic signs	stiff neck, focal signs, reduced consciousness
Systemic signs	fever, appears sick, abnormal exam, myalgias, weight loss
Caution: If headache does not fit typical pattern, a serious diagnosis can be missed.	

The **diagnosis of migraine** is clinically based upon a compatible history, physical examination, and fulfillment of diagnostic criteria.
Gold Standard for Diagnosis: The International Classification of Headache Disorders (2nd ed.)[18]
http://www.ihs-headache.org/upload/ct_clas/ihc_II_main_no_print.pdf

How to distinguish a migraine from other headache types?[19]
Findings suggest that the best criteria differentiating migraine with other headache types are the presence of nausea and/or vomiting in combination with 2 of the following 3 symptoms: photophobia[light], phonophobia[loud noises], and osmophobia[odour] *{see no evil, hear no evil, smell no evil}*

Different types of headache
1° migraine (included hormone related) with or without aura, tension-type headache, cluster headache & other trigeminal autonomic cephalgias, others (cough, exertion, etc…)
2° attributed to head and/or neck trauma, attributed to a substance or its withdrawal, attributed to a psychiatric disorder, etc…

Clinical Features of Migraine
Many patients with chronic migraine have a pattern of daily or near-daily headaches of low to moderate severity, associated with less prominent migrainous features. Superimposed on this baseline are exacerbations of pain with more prominent migrainous features such as photophobia, phonophobia, osmophobia, nausea, vomiting, and cutaneous allodynia (ie, the perception of pain produced by innocuous stimulation of normal skin).

ER setting[20]
- Use parenteral NSAIDS, sumatriptan, metoclopramide, or neuroleptics for initial symptom control
- Consider dihydroergotamine for severe cases
- Dexamethasone for possible prophylaxis against recurrence

Other resources:

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Headache Network Canada http://www.headachenetwork.ca

Migraine Quebec www.migrainequebec.com

American Headache Society
http://www.americanheadachesociety.org/professionalresrouces/TriggerAvoidanceInformation.asp

Chronic Daily Headache: AAFP Patient Page: http://www.aafp.org/afp/2014/0415/p642-s1.html

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FDA Mar/11 notified healthcare professionals and patients of an increased risk of development of cleft lip and/or cleft palate (oral clefts) in infants born to women treated with Topamax (topiramate) during pregnancy. Because of new human data that show an increased risk for oral clefts, topiramate is being placed in Pregnancy Category D.
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Adverse Effect on:		Most; and Least Likely Agents
Brain	Cognition	Barbs, Benzos
	Coordination	Barbs, Benzos, CBZ Phenytoin; 2nd gen less so and least with Levetiracetam, Gabapentin
	Language	Topiramate
	Behavior, Personality	Barbs, Levetiracetam, Topiramate, Vigabatrin (+ psychiatric history increase risk)
Blood		CBZ, Phenytoin, Valproate
Bone		CBZ, Valproate
Liver, Pancreas		Valproate
Skin		CBZ, OxyCarb, Lamotrigine, Phenytoin (also related to Asian/genetics, age – Peds and Geriatrics, prior hx of skin rx, high initial dose or rapid dose esculation, immune system disorders, Herpes virus reactivation)
Weight (gain also associated with ↑ risk of CVD)		↑: Gabapentin, Pregabalin, Vigabatrin, Valproate, CBZ (moderate); ↓:Topiramate
Pregnancy		Barbs, Topiramate,Valproate; CBZ, Phenytoin, Lamotrigine
Female Hormones		Valproate (↑Polycystic Ovarian Syndrome and Hirsuitism in ♀);Levetiracetam least effect on OCs
Metabolic Enzyme **Induction** (**Increased** metabolic clearance of other substrates and reduced efficacy)		Barbs, CBZ, Phenytoin (reduce levels of antimicrobials, immunosuppressants, OCs, cardiovascular meds, psychotropics, antineoplastics, antiepileptics)
Metabolic Enzyme **Inhibition** (**Decreased** metabolic clearance of other substrates and increased/prolonged effects)		Valproate (TCAs, Barbs, Benzos, CBZ, lamotrigine, warfarin, zidovudine)

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Further investigations for Special Circumstances

Bleeding Disorders- ↑ suspicion when initial onset of menses is heavy & regular bleeding patterns or presents with suggestive sx: postpartum hemorrhage; surgery-related bleeding, & bleeding associated with dental procedures; or frequent bruising, epistaxis, and bleeding gums. Further investigations: platelet count, PTT, INR, von Willebrand factor,& ristocetin factor

Peri-menopausal- consider endometrial sampling first line due to ↑ risk of endometrial hyperplasia/carcinoma in patients >45yrs or <45 WITH hx of unopposed estrogen exposure, failed medical management, or persistent AUB

Uterine Fibroids & AUB Treatment[32,33,34,35]

Uterine fibroids are commonly found in women in the middle to later reproductive years & are associated with symptoms such as heavy bleeding, menstrual pain, pressure in the lower abdomen, infertiliy, & recurrent miscarriages. Uterine fibroids are thought to be estrogen and progesterone dependent because they shrink after menopause. Traditionally treatment has been the surgical route (myomectomy or hysterectomy), but drug treatments are becoming more relevant:

Agents currently used for Uterine Fibroids

1. GnRH agonists: ↓ uterine fibroid size (by ≤50%) & ↓ uterine fibroid-related symptoms, but treatment restricted to 3-6 months due to hypoestrogenic AE & fibroids return to pretreatment size once agents are stopped
2. LNG-IUS MIRENA: ↓ menstrual blood loss related to uterine fibroids & ↑ hemoglobin in women with anemia, but is not beneficial for uterine regression
3. Ulipristal FIBRISTAL: selective progesterone receptor modulator; ↓ uterine fibroid volume (≤31% vs placebo ↑ 3%); controls bleeding & faster onset of amenorrhea (noninferior & more sustained effect than leuprolide acetate); no serious side effects

Agents in the Clinical Trial Pipeline for the indication of Uterine Fibroid Associated Abnormal Uterine Bleeding:

- Mifepristone MIFEPREX: competitively binds & antagonizes progesterone receptors; inconsistent evidence on effect of uterine size reduction (0 to 50%); ↑ endometrial hyperplasia with no atypia (unsure of clinical implications)
- Asoprisnil: selective progesterone receptor modulator with high receptor & tissue specificity; 25mg/day ↓ volume by ≤36%; ↓ bloating, pelvic pain, & uterine artery blood flow; minimal hypoestrogenic effects
- Telapristone PROELLEX: selective progesterone modulator; doses of 12.5, 25, & 50mg ↓ fibroid size by 10.6, 32.6, & 40.3% respectively (leuprolide acetate 32.6% & placebo 10.6% ↓)
- Aromatase inhibitors (letrozole, anastrozole, fadrozole): antiestrogen; ↓ size of fibroid & symptoms (menstrual volume, duration of menstruation, & dysmenorrhea); no serious side effects reported

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RxFiles – Abnormal Uterine Bleeding – Tx Chart (Developed by Kellie Towriss, BSP (Pharmacy Resident, Saskatoon Health Region (2013)

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Health Canada Dec/11 has completed a safety review of drospirenone-containing oral contraceptives (marketed under the brand names Yasmin and Yaz) with respect to the risk of blood clots (venous thromboembolism, or VTE). The review determined that **drospirenone-containing birth** control pills may be associated with a risk of blood clots that is **1.5 to 3 times higher than other birth control pills**.
Health Canada May/13: **Diane-35** supports current labelling and use. The review of the safety of the anti-acne medication Diane-35 has found that the drug's benefits continue to outweigh the risks, when used as authorized.
Health Canada Sep/13 **Freya-28**, an oral contraceptive (birth control product), is being voluntarily recalled from the Canadian market by Mylan Pharmaceuticals after a pharmacy reported that a placebo pill was found in place of an active pill in one package.
Health Canada Sep/13 **Esme-28** (DIN 02388146), an oral contraceptive (birth control product), is being voluntarily recalled from the Canadian market by Mylan Pharmaceuticals.
Health Canada Mar/14 has asked companies to add new warnings to product packages advising that Emergency contraceptive pills, also known as the "morning after" pill,are less effective in **women weighing 165 to 176 pounds (75-80 kg),** and are **not effective** in women over 176 pounds (**80 kg**).
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Health Canada Dec/11 has completed a safety review of drospirenone-containing oral contraceptives (marketed under the brand names Yasmin and Yaz) with respect to the risk of blood clots (venous thromboembolism, or VTE). The review determined that **drospirenone-containing birth** control pills may be associated with a risk of blood clots that is **1.5 to 3 times higher than other birth control pills**.
Health Canada Sep/13 **Freya-28**, an oral contraceptive (birth control product), is being voluntarily recalled from the Canadian market by Mylan Pharmaceuticals after a pharmacy reported that a placebo pill was found in place of an active pill in one package.
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Pearls for post-menopausal hormone therapy (HT):

- ♀ without hx of hysterectomy who are on estrogen should use a progestogen to protect against endometrial hyperplasia & carcinoma
- If last menstrual period < 1yr prior, a sequential combined regimen recommended (e.g. continuous estrogen with 12-14 days progestogen/month)
- If last menstrual period > 1yr prior, ♀ who wish to avoid monthly withdrawal bleed, may start continuous combined regimen
- If breakthrough bleeding occurs following switch to continuous combined & does not settle within 3-6months, consider switch back to sequential for 1 or more years
- If bleeding is heavy or erratic on sequential regimen, consider ↑ dose of progestagen (e.g. double)
- Persistent bleeding beyond 6 months warrant referral/investigation
- 90% of ♀ persisting with regimens will eventually be bleed free
- If AEs 2° to progestagen (mood swings, PMS like effects, androgenic effects), may ↓ dose by ½ &/or ↓ duration to 7 -10 days
- HT prescribed before age 60 has a favorable benefit/risk profile
- If using HT after age 60 lower doses (lowest effective dose) especially prudent due to gradually increasing risk
- Venlafaxine (75mg/day) was equal to low dose estrogen (estradiol 0.5mg/day) for treatment of vasomotor symptoms in a RCT.[Joffe H et al., 2014.]

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Health Canada Aug/06 & Jan/10 is advising consumers about a possible link between health products containing herbal medicine **black cohosh** and liver damage. A number of international case reports of liver damage suspected to be associated with the use of black cohosh, including three case reports in Canada and one published case of death in the United States. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_72_e.html , http://www.hc-sc.gc.ca/dhp-mps/medeff/bulletin/carn-bcei_v20n1-eng.php#_Black_cohosh_products

Health Canada Jan/08 is warning Canadians not to use the unauthorized product **RGC-RMC Rheumax Capsule** (batch number REM1-SI93016N). This batch of RGC-RMC Rheumax Capsule has been found to contain **progesterone**, a steroid hormone that can have adverse effects on the brain, breast and skin and should only be taken if prescribed by a health professional.

Health Canada Dec/13 General Nutrition Centres Company (GNC), in consultation with Health Canada, is voluntarily recalling its natural health product "**Women's Phytoestrogen Formula**" – used for the relief of menopausal symptoms – due to possible contamination with chloramphenicol.

Health Canada May/14 has requested that Christmas Natural Foods Ltd. stop selling and recall its unauthorized health product, **Heartland Natural Wild Yam Moisturizing Cream**, after testing conducted by the Department identified a undisclosed prescription drug ingredient, progesterone.

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Health Canada May 2006: The **RUTH** study demonstrated an **increase in mortality due to stroke** for Evista compared to placebo. The incidence of stroke mortality was 1.5 per 1,000 women per year for placebo versus 2.2 per 1,000 women per year for Evista (p=0.0499). The incidence of stroke, myocardial infarction, hospitalized acute coronary syndrome, cardiovascular mortality, or overall mortality (all causes combined) was comparable for Evista and placebo. http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2006/evista_hpc-cps_e.html Barrett-Connor E, et al.; Raloxifene Use for The Heart (**RUTH**) Trial Investigators. Effects of raloxifene on cardiovascular events and breast cancer in postmenopausal women. N=10,101 5.6yrs N Engl J Med. 2006 Jul 13;355(2):125-37. (InfoPOEMs: For every 1000 women who take raloxifene for 5 years, we can expect 4 to 5 additional strokes, 6 additional episodes of venous thromboembolism (VTE), 6 fewer invasive breast cancers, and 6 to 7 fewer clinical vertebral fractures. The cost for this mixed bag of benefits and harms would be approximately $1000 per woman per year, for a total cost of $5,000,000 at current drug prices. (LOE = 1b))

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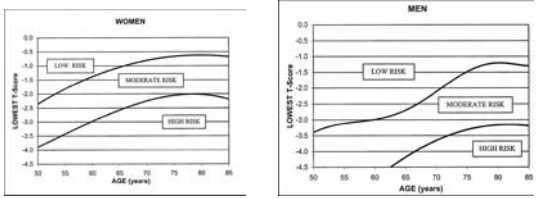

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TSH Trimester Specific Targets for Hypothyroidism

The 2011 American Thyroid Association (ATA) Guideline recommends a first trimester TSH target of <2.5mIU/L, and second & third trimester TSH targets of <3mIU/L.[12] These goals are often attainable with an increase in the levothyroxine dose, especially when the targets are met in early pregnancy. However, in clinical practice, there may be the rare occasion when it is difficult to reach the second & third trimester TSH target of <3mIU/L. This may occur when the levothyroxine dose required to achieve a TSH <3mIU/L results in symptoms of hyperthyroidism (e.g. maternal palpitations, failure to gain weight in either mother and/or fetus, or the development of maternal mood disorders). It may also result when pregnant patients are non-compliant with their levothyroxine as they are hesitant to take medications or increase their doses during pregnancy. In these rare situations, if a second and third trimester TSH <3mIU/L cannot be tolerated or attained, a TSH of <3.5mIU/L may be reasonable.

In 2012, the ATA & American Association of Clinical Endocrinologists released guidelines suggestion the following TSH targets: first trimester ≤ 2.5mIU/L, second trimester ≤ 3mIU/L & third trimester ≤ 3.5mIU/L.[12]

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Complementary and alternative medicine-what people ≥50 are using & discussing with their doctor Jan/07 Nearly two-thirds of older people in the U.S. use complimentary or alternative therapies, but less than a third of the users discuss the practice with their physicians, according to a survey commissioned by the NIH and the AARP. The survey was based on interviews last year with about 1600 people aged 50 and older. The leading reason people said they don't discuss alternative therapies -- which include herbal and dietary supplements, massage, and chiropractic manipulation -- is that physicians never ask. Others said, among other reasons, that they did not know they should or they did not have enough time during the office visit. In addition, nearly 75% of respondents report taking one or more prescription medications, and nearly 60% said they take over-the-counter medications. http://assets.aarp.org/rgcenter/health/cam_2007.pdf

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De Silva V, El-Metwally A, Ernst E, et al. Evidence for the efficacy of complementary and alternative medicines in the management of **osteoarthritis**: a systematic review. Rheumatology (Oxford). 2011 May;50(5):911-20. The available data for most complementary and alternative medicine (CAM) in treating patients with degenerative joint disease is limited. Topical capsaicin and S-adenosyl methionine (SAMe) appear to be effective in treating pain, but even these data are limited and potentially subject to bias in favor of publishing positive results. (LOE = 1a-)

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Dhiman RK, Chawla YK. Herbal medicines for liver diseases. Dig Dis Sci. 2005 Oct;50(10):1807-12. (InfoPOEMs: There is insufficient evidence to recommend most commonly used herbal medicines for the treatment of liver disease. Of the 4 products evaluated in this review -- Phyllanthus, Silybum marianum (milk thistle), **glycyrrhizin** (licorice root extract), and Liv 52 (a mixture of herbs) -- available evidence supports only the use of the **licorice root extract** in the treatment of subacute liver failure and the prevention of hepatocellular carcinoma in patients with chronic hepatitis C. (LOE = 2a))

DMAA: July 25/12- Manufacturers of some sports supplements are falsely claiming a compound known as DMAA is a natural substance derived from geraniums, researchers say. Instead, research shows that DMAA is synthetic, consisting of four compounds called stereoisomers. DMAA (1,3-dimethylamylamine) is a stimulant found in some nutritional and sport supplements.

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Elderberry extract has long been used as a folk remedy for cold and influenza symptoms. A recent randomized trial provides evidence for its efficacy (level 2 [mid-level] evidence). During the spring 2009 influenza season in China, 64 patients with ≥ 3 influenza-like symptoms (fever, headache, myalgias, coughing, nasal mucus discharge, nasal congestion) were randomized within 24 hours of symptom onset to elderberry extract lozenge (175 mg) vs. placebo orally 4 times daily for 2 days. After 48 hours, the rate of complete symptom relief was higher in the elderberry group (28% vs. 0%, no p value reported), with at least some symptom relief (only 0-2 mild symptoms remaining) reported in 88% vs. 16% for placebo (no p value reported). Elderberry extract was associated with significantly improved symptom severity scores for headache, nasal congestion, muscle aches, and fever at 24 hours ($p < 0.001$) and for all symptoms at 48 hours ($p < 0.001$). The elderberry group had higher symptom scores at baseline, however, suggesting that the groups may have been at different stages in their overall illness course despite randomization within 24 hours (Online J Pharmacol Pharmacokin 2009;5:32).

Ernst E. **Cardiovascular adverse effects of herbal medicines**: a systematic review of the recent literature. Can J Cardiol. 2003;19:818-27.

Fava M, Alpert J, et al. A Double-blind, Randomized Trial of **St John's Wort**, Fluoxetine, and Placebo in Major Depressive Disorder. J Clin Psychopharmacol. 2005 Oct;25(5):441-447.

FDA May 2007 FDA chemical analysis revealed that **Energy Max** contains thione analog of sildenafil, a substance with a structure similar to sildenafil, the active ingredient in Viagra, an FDA-approved drug for ED.Substances like this are called analogs because they have a structure similar to another drug and may cause similar side effects and drug interactions. **True Man** contains a thione analog of sildenafil or piperadino vardenafil, an analog of vardenafil, the active ingredient in Levitra, another FDA-approved prescription drug for ED. Neither the thione analog of sildenafil nor piperadino vardenafil are components of approved drug products.

FDA Feb/08 Palo Alto Labs and FDA notified consumers and healthcare professionals of a voluntary nationwide recall of two dietary supplements, **Aspire36** and **Aspire Lite**. The products were recalled because they were found to contain Aildenafil in trace amounts and Dimethyl sildenafil thione, an analog of Sildenafil, a drug used to treat erectile dysfunction.

FDA Mar/08 The U.S. Food and Drug Administration is advising consumers not to purchase or use "**Blue Steel**" or "**Hero**" products, marketed nationally as dietary supplements, because these products contain undeclared ingredients similar to sildenafil.

FDA April/08 **Herbal Science International**, Inc. and FDA informed consumers and healthcare professionals of a nationwide recall of twelve dietary supplements that contain ephedra, aristolochic acid or human placenta because they may present a serious health hazard to consumers. FDA has long regarded dietary supplements containing ephedra, a botanical that contains ephedrine alkaloids, as a potential health hazards because the alkaloid raises blood pressure and otherwise stress the circulatory system.

FDA May/08 is requesting that the manufacturer of **Xiadafil** — an "all natural" dietary supplement sold to treat erectile dysfunction — recall all its stock from natural food stores & discontinue marketing it on the Web since it contains an analog of sildenafil.

FDA May/08 notified consumers and healthcare professionals that supplement products sold under the brand name of **Viril-ity Power** (VIP) Tablets is being recalled because one lot was found to contain a potentially harmful undeclared ingredient, hydroxyhomosildenafil, an analog of sildenafil.

FDA May/08 The US Food and Drug Administration advised consumers not to use the products **Total Body Formula** in Tropical Orange and Peach Nectar flavours, and **Total Body Mega Formula** in Orange/Tangerine flavour, because they contain high doses of selenium and chromium.

FDA July/08 Jack Distribution, LLC issued a voluntary nationwide recall of selected lots of **Rize 2 The Occasion Capsules** and **Rose 4 Her Capsules**, marketed as dietary supplements. The products were recalled because certain lots contained thiomethisosildenafil, an undeclared analog of sildenafil, a FDA-approved drug used for Erectile Dysfunction.

FDA July/08 not to buy or use **Viapro** 375mg Capsules because one lot of the product was found to contain a potentially harmful undeclared ingredient, thio-methisosildenafil, an analog of sildenafil.

FDA Nov/08 Balanced Health Products, Inc. announced a recall of **STARCAPS** due to the presence of an undeclared drug ingredient, Bumetanide. Bumetanide is a diuretic indicated for the treatment of edema associated with congestive heart failure, hepatic and renal disease including nephrotic syndrome.

FDA Nov/08 Fashion Sanctuary announced a recall of **Zhen De Shou Fat Loss** Capsules because FDA analysis found the product to contain undeclared sibutramine, an FDA approved drug used as an appetite suppressant for weight loss.

FDA Dec/08 alerted consumers not to purchase or consume more than **25 different products** marketed for weight loss because they contain undeclared, active pharmaceutical ingredients that may put consumers' health at risk. The undeclared active pharmaceutical ingredients in some of these products include sibutramine (a controlled substance), rimonabant (a drug not approved for marketing in the USA), phenytoin (an anti-seizure medication), and phenolphthalein (a solution used in chemical experiments and a suspected cancer causing agent). The weight loss products, some of which are marked as "dietary supplements," are promoted and sold on various web sites and in some retail stores. FDA advises consumers who use the products to stop taking them and consult their healthcare professional immediately as the health risks posed by these products can be serious (for example, high blood pressure, seizures, tachycardia, palpitations, heart attack or stroke). FDA also encourages consumers to seek guidance from healthcare professional before purchasing weight loss products. See the FDA News Release for a listing of the names of the 25 referenced products. Read the MedWatch 2008 safety summary, including links to the News Release and Questions and Answers, at: http://www.fda.gov/medwatch/safety/2008/safety08.htm#Weight

FDA Jan/09 notified consumers not to take **Venom HYPERDRIVE 3.0**, a product sold as a dietary supplement but containing sibutramine.

FDA Apr/09: **ABC Beauty Supply** & FDA notified consumers and healthcare professionals of a recall of 34 dietary supplement products. FDA lab analyses identified undeclared **sibutramine**, an FDA- approved drug, used as an appetite suppressant for weight loss. http://www.fda.gov/oc/po/firmrecalls/universalabc04_09.html

FDA Apr/09 Nature & Health Co. and FDA notified healthcare professionals of a recall of a supplement product, **Libimax**. FDA analysis found the product contains tadalafil

FDA May/09 warned consumers to immediately stop using **Hydroxycut** products by Iovate Health Sciences, Inc. Hydroxycut products are associated with a number of serious **liver injuries**. Hydroxycut products are dietary supplements that are marketed for weight-loss, as fat burners, as energy-enhancers, as low carb diet aids, and for water loss under the **Iovate and MuscleTech brand** names. FDA has received 23 reports of serious health problems ranging from jaundice and elevated liver enzymes, an indicator of potential liver injury, to liver damage requiring liver transplant. One death due to liver failure has been reported to FDA. Other health problems reported include seizures; cardiovascular disorders; and rhabdomyolysis, a type of muscle damage that can lead to other serious health problems such as kidney failure.

FDA June/09 notified consumers and healthcare professionals to discontinue use of three **Zicam Nasal Gel/Nasal Swab** products sold over-the-counter as cold remedies because they are associated with the loss of sense of smell that may be long-lasting or permanent.

FDA July/09 and Haloteco notified healthcare professionals and consumers of a nationwide voluntary recall of Libipower Plus. Lab analysis of **Libipower Plus** samples were found to contain undeclared Tadalalafil.

FDA July/09 notified healthcare professionals that four weight loss dietary supplements sold and marketed by the firm (**Slimbionic, One Weight Loss Pill, SlimDemand Capsules, Botanical Weight Loss**) contain sibutramine.

FDA Aug/09 not to use body-building products marketed as containing steroids or steroid-like substances. The affected products are TREN-Xtreme, MASS Xtreme, ESTRO Xtreme, AH-89-Xtreme, HMG Xtreme, MMA-3 Xtreme, VNS-9 Xtreme, and TT-40-Xtreme..

FDA Nov/09 notified consumers that **Stiff Nights**, a product sold as a dietary supplement, contains sulfoaildenafil, a chemical similar to sildenafil (Viagra).

FDA Nov/09 & GMP Herbal Products notified consumers and healthcare professionals of a recall of **Pai You Guo**, a weight loss dietary supplement, due to the presence sibutramine & phenolphthalein.

FDA Nov/09 & RockHard Laboratories notified consumers that **RockHard Weekend**, a product sold as a dietary supplement, contains sulfoaildenafil, an analogue of sildenafil.

FDA Nov/09 & IDS Sports notified consumers that five of the IDS's dietary supplement products (**Bromodrol, Dual Action Grow Tabs, Grow Tabs, Mass Tabs, and Ripped Tabs TR**) contain the following undeclared substances, which FDA considers to be steroids: "Madol," "Turinabol," "Superdrol," &/or "Androstenedione."

FDA Dec/09 for **S-DROL**: a voluntary recall by the manufacturer of one lot (lot# 810481, expiry date 01/2012) of S-DROL after FDA testing found it to contain undeclared desoxymethyltestosterone.

FDA Dec/09 warned consumers to stop using bodybuilding products manufactured by American Cellular Labs after they were found to contain unauthorized synthetic steroids in **TREN-Xtreme, MASS Xtreme, ESTRO Xtreme, AH-89-Xtreme, HMG Xtreme, MMA-3 Xtreme, VNS-9 Xtreme, TT-40-Xtreme.**

FDA Dec/09 warned that **Atlas Operations, Inc**. notified consumers of a nationwide recall of the company's dietary supplements for sexual enhancement. These products are sold as dietary supplements throughout the USA. FDA lab analyses found that the products tested from certain batches contain Sulfoaildenafil.

FDA Dec/09 The Texas Department of State Health Services and FDA notified healthcare professionals and consumers, especially pregnant or breastfeeding women, to avoid consuming a product called "**Nzu**", taken as a traditional remedy for morning sickness,because of the potential health risks from high levels of lead and arsenic, noted on laboratory analysis by Texas DSHS. Nzu, which is sold at African specialty stores is also called Calabash clay, Calabar stone, Mabele, Argile and La Craie. It generally resembles balls of clay or mud and is usually sold in small plastic bags with a handwritten label identifying it as "Nzu" or "Salted Nzu."

FDA Jan/10 & **MuscleMaster(dot)com**, Inc. notified consumers and healthcare professionals of the voluntary nationwide recall of all lots and expiration dates of the seventeen dietary supplements listed in the firm press release, sold between June 1, 2009 and November 17, 2009. FDA informed MuscleMaster(dot)com that it believes that the recalled products contain ingredients that are **steroids**.

FDA Jan/10 notified consumers and healthcare professionals about a counterfeit and potentially harmful version of **Alli 60 mg capsules** (120 count refill kit). The **counterfeit** version contained the controlled substance sibutramine and did not contain orlistat, the active ingredient.

FDA Mar/10 & Natural Wellness notified consumers that **MasXtreme**, a product sold as a dietary supplement contains aildenafil close in structure to sildenafil and is expected to possess a similar pharmacological and adverse event profile as well as the drug phentolamine which is an alpha-adrenergic blocker.

FDA Apr/10 & Kanec USA notified healthcare professionals of a nationwide recall of **Stud Capsule For Men** [Lot #060607-01/060108-01, Exp 6-2013], after being informed by FDA that laboratory analysis of a sample found the product to be adulterated with sildenafil, an FDA approved drug.

FDA May/10 notified healthcare professionals, their patients, and consumers not to consume **Vita Breath**, a dietary supplement manufactured by American Herbal Lab and marketed at health fairs and on the Internet, because the product may contain hazardous levels of lead.

FDA June/10 **Magic Power Coffee**: Product marketed as a dietary supplement for sexual enhancement contains the drug ingredient hydroxythiohomosildenafil.

FDA July/10 analysis of **Que She** found that it contains: fenfluramine – a stimulant drug withdrawn from the U.S. market in 1997 after studies demonstrated that it caused serious heart valve damage, propranolol – a prescription beta blocker drug that can pose a risk to people with bronchial asthma and certain heart conditions, sibutramine – a controlled substance and prescription weight loss drug, sibutramine was the subject of a recent study whose preliminary findings showed an association between sibutramine use and increased risk of heart attack and stroke in patients who have a history of heart disease, & ephedrine – a stimulant drug that is legally marketed over-the-counter for temporary relief of asthma but can pose a risk to people with certain cardiovascular conditions.

FDA Aug/10 lab analysis of **Solo Slim** was found to contain the undeclared drug ingredient Didesmethyl Sibutramine.

FDA Aug/10 lab analysis of **Revivexxx Extra Strength** was found to contain undeclared tadalafil.

FDA Aug/10 notified Novacare LLC that certain products appear to contain sulfoaildenafil: **Stiff Nights, Aziffa, Size Matters, Erex, Mojo, Hard Drive, Eyeful, Red Magic, Straight Up, Zotrex, Monster Excyte, WOW, Xaitrex, Verect, Prolatis, Xytamax, Maxyte, Libidinal, OMG, OMG45, and Zilex (with Golden Spear) summers**.

FDA July/10 lab analysis of **Slim-30** Herb Supplement distributed by the company was found to contain undeclared N-Desmethyl Sibutramine and traces of Sibutramine.

FDA July/10 & Good Health, Inc. is conducting a voluntary recall after FDA lab analyses found that the product tested from certain batches of **Vialipro** contain Sulfoaildenafil.

FDA July/10 lab analysis of this herb supplement, **Joyful Slim** Herb Supplement, was found to contain the undeclared drug, desmethyl sibutramine.

FDA July/10 warned consumers not to consume or use **Miracle Mineral Solution**, an oral liquid solution also known as "Miracle Mineral Supplement" or "**MMS**." The product, when used as directed, produces an industrial bleach.

FDA July/10 notified consumers that lab analysis of lots of ejaculoid **XXTREME** and **stimuloid II** found that the products, sold as dietary supplements, contain sulfoaildenafil FDA Aug/10 had Lab analysis of **Mr. Magic** to contain hydroxythiohomosildenafil and sulfoaildenafil.

FDA Aug/10 analyzed **TimeOut** and determined that it contains hydroxythiohomosildenafil.

FDA Sep/10: Products marketed as dietary supplements contain **aromatase inhibitors**, commonly known as "ATD." Adverse events associated with the use of aromatase inhibitors could include the following: decreased rate of bone maturation and growth, decreased sperm production, infertility, aggressive behavior, adrenal insufficiency, kidney failure, and liver dysfunction. Advanced Muscle Science (Arom-X, Arom-X UTT, Arom-XL, 4-AD, and Decavol), ArimaDex, Clomed, Off Cycle II Hardcore, iForce – Reversitol.

FDA Oct/10 advised consumers to avoid "**chelation**" products that are marketed over-the-counter (OTC) to prevent or treat diseases. There are serious safety issues associated with chelation products. Depending on the condition, when relying on unproven OTC chelation products to treat serious conditions, patients may delay seeking effective medical care. Even when used under medical supervision, these products can cause serious harm, including dehydration, kidney failure, and death.

FDA Nov/10 ISSUE: Lab analysis has found **Duro Extend** Capsules for Men to contain Sulfoaidenafil, an analogue of Sildenafil.

FDA Dec/10 warned consumers not to use **Man Up Now** capsules, marketed as a dietary supplement for sexual enhancement, because FDA analysis determined that the product contains sulfoaildenafil.

FDA Dec/10 notified the public that testing determined that **RockHard Weekend** Lot Numbers 100159 and 100260 sold as blister packs, 3ct bottles and 8ct bottles &

Pandora Lot Numbers 100378 sold as blister packs & **Passion Coffee** contain an analogue of sildenafil.

FDA Dec/10 has received multiple reports of adverse events associated with the use of **Fruta Planta**, including several cardiac events and one death. FDA laboratory analysis confirmed that Fruta Planta contains sibutramine.

FDA Jan/11 laboratory analysis confirmed that **Celerite Slimming Capsules** contain sibutramine

FDA Mar/11 lab analysis of **Svelte 30** orange & gray capsules determined that the product contains Sibutramine.

FDA Mar/11 notified Biotab Nutraceuticals, Inc. that two lots of counterfeit product purporting to be **Extenze** contain undeclared drug ingredients. Specifically, lot 0709241 contains tadalafil and sildenafil, and lot 0509075 contains tadalafil and sibutramine.

FDA Mar/11 laboratory analysis confirmed that **Black Ant** contains sildenafil.

FDA Mar/11 **:** USA Far Ocean Group, Inc. issues voluntary nationwide recall of **U-Prosta**, a product marketed as a dietary supplement that contains undeclared terazosin.

FDA Mar/11 ISSUE: Tested samples of **Soladek** contained levels of vitamin A and vitamin D that were many times the recommended daily allowances for these vitamins.

FDA Mar/11 laboratory analyses of **Celerite Slimming Tea**: Recall - were found to contain undeclared Sibutramine.

FDA Mar/11 ISSUE: FDA lab analysis of **X-Hero** found the product contains sulfosildenafil, the analogue of the active ingredient of an FDA-approved drug. In addition, FDA analysis of **Male Enhancer** sample found the product contains tadalafil.

FDA Apr/11 Lab analyses of **Best Enhancer** found that the product contain Sulfoaildenafil.

FDA Apr/11 "**U-Prosta Natural support for prostate health**" is being voluntarily recalled in Canada by Sunnylife International Inc. after the U.S. Food and Drug Administration (FDA) found the product contains undeclared terazosin.

FDA May/11 **Regenerect**: Recall - Undeclared Drug Ingredient of lab confirmed the presence of Sulfoaildenafil.

FDA May/11 laboratory analysis confirmed that "**Slim Xtreme Herbal Slimming Capsule**" contains sibutramine.

FDA June/11 lab analyses found Via **Xtreme Ultimate Sexual Enhancer Dietary** Supplement for Men to contain sulfoaildenafil methanesulfonate.

FDA June/11 Nature Relief and FDA notified the public of a recall of **Nature Relief Instant Wart and Mole Remover**. FDA has advised that the active ingredient, calcium oxide, can cause severe burns of the skin, particularly to areas of thin or sensitive skin, such as the face, area around the eyes, and genitalia.

FDA July/11 is advising consumers not to purchase or use "**Slim Forte Slimming Capsules**," "**Slim Forte Slimming Coffee**," and "**Botanical Slimming Soft Gel & Slim Forte Double Power Slimming Capsules.** FDA laboratory analysis confirmed that these products contain sibutramine.

FDA Oct/11 notified the manufacturer that lab analyses found that the product; **Uprizing 2.0** , sold as a testosterone booster, contains superdrol, a synthetic steroid, making it an unapproved new drug.

FDA Nov/11 lab analysis for Lot 10090571 found **Virility Max** to contain sulfoaildenafil.

FDA Dec/11 Eclectic Institute is voluntarily recalling specific lots of its freeze-dried capsules containing **Gotu Kola** (Centella asiatica) and **Bladderwrack** (Fucus vesiculosus) capsules because of potential Salmonella contamination.

FDA Feb/12 Healthy People Co. notified the public of a recall of the company's dietary supplements sold under the brand names Healthy People Co. FDA lab analysis confirmed the presence of Sibutramine and Tadalafil, making these products unapproved new drugs. (Mince Belle Dietary Supplement, PERFECT Men Dietary Supplement , EVERLAX Dietary Supplement, EVER Slim Dietary Supplement, Herbal Drink Acai-man Mangosteen Dietary Supplement, EVER SLIM Shake Mix Dietary Supplement)

FDA Feb/12 Regeneca, Inc. notifed the public of a nationwide recall of **RegenArouse**, Lot Number 130100. FDA lab analysis confirmed the presence of Tadalafil.

FDA Feb/12 is advising consumers not to purchase or use "**Hard Ten Days**," & "**Man King**" a product for sexual enhancement sold on various websites. FDA laboratory analysis confirmed that "Hard Ten Days" contains sildenafil

FDA Feb/12 is advising consumers not to purchase or use "**Japan Weight Loss Blue**," a product for weight loss sold on various websites, laboratory analysis confirmed that "Japan Weight Loss Blue" contains sibutramine, analogs of sibutramine, and ephedrine alkaloids.

FDA Mar/12 notified healthcare professionals and warned consumers not to use skin creams, beauty and antiseptic soaps, or lotions that might contain **mercury**. The products are marketed as **skin lighteners and anti-aging** treatments that remove age spots, freckles, blemishes and wrinkles. Adolescents also may use these products as acne treatments.

FDA Apr/12 laboratory analysis confirmed that "**Japan Rapid Weight Loss Diet Pills Yellow**" contains sibutramine and phenolphthalein.

FDA Apr/12 laboratory analysis confirmed that "**France T253**" contains sildenafil.

FDA Apr/12 is advising consumers not to purchase or use "**X-Rock**," a product for sexual enhancement manufactured by CRM Laboratories and sold on various websites, including www.xrockme.com. FDA laboratory analysis confirmed that "X-Rock" contains sildenafil and hydroxythiohomosildenafil.

FDA Apr/12 laboratory analysis confirmed that "**Instant Hard Rod**" contains aminotadalafil. FDA laboratory analysis confirmed that "**ZenMaxx**" contains aminotadalafil. FDA laboratory analysis confirmed that "**RigiRx Plus**" contains aminotadalafil.

FDA May/12 is advising consumers not to purchase or use "**VMaxx Rx**," a product for sexual enhancement sold on various websites, including www.vmaxxrx.com. FDA laboratory analysis confirmed that "VMaxx Rx" contains the undeclared ingredient sulfoaildenafil. FDA is also advising consumers not to purchase or use "**Boost — Ultra Sexual Enhancement Formula**." This product is promoted and sold on various websites, including www.boostultra.biz. FDA laboratory analysis confirmed that "Boost—Ultra Sexual Enhancement Formula" contains sildenafil. FDA is also advising consumers not to purchase or use "**Firminite**," a product for sexual enhancement sold on various websites, including **www.firminite.com.** FDA laboratory analysis confirmed that "Firminite" contains tadalafil.

FDA May/12 West Coast Nutritionals, Ltd. is conducting a recall of all lots of their dietary supplements **Firminite, Extra Strength Instant Hot Rod, and Libidron** to the consumer level. An FDA lab analysis of Firminite was found to contain undeclared Tadalafil.

FDA May/12 is advising consumers not to purchase or use "**EreXite**," a product for sexual enhancement sold on various websites, including www.amazon.com. FDA laboratory analysis confirmed that "EreXite" contains tadalafil.

FDA June/12 cautioned late last week against using **Reumofan Plus**, a dietary supplement marketed as a "natural" pain reliever for arthritis, osteoporosis, and other conditions. The drug, which is made in Mexico but available online, contains unlabeled and potentially harmful pharmaceutical ingredients: diclofenac, methocarbamol & sometimes dexamethasone. (Dec/12 FDA: Reumofan Plus is being relabeled and sold under the name "**WOW**.")

FDA June/12 Botanical Laboratories Inc. and FDA notified consumers and healthcare professionals of a recall of **Wellesse Digestive 3 in 1 Health liquid dietary supplement**. A supplier of one of the ingredients indicated the ingredient has the potential to be contaminated with Salmonella.

FDA Aug/12 CRM Laboratories is conducting a consumer/user level recall of all X-ROCK 3 Day Pill For Men and Z-ROCK products sold between October, 2011 and April, 2012. Finished product of

X-ROCK 3 Day Pill for Men and Z-ROCK was tested and found to contain an analogue of an ingredient in an FDA-approved drug. Analytical tests conducted by the FDA concluded that the products contained sildenafil and hydroxythiohomosildenafil.

FDA Aug/12 is issuing an updated alert that **Reumofan Plus and Reumofan Plus Premium** contain undeclared active ingredients found in prescription drugs that should be used only under the supervision of a health care professional. It contains Diclofenac Sodium and Methocarbamol.

FDA Sep/12 Brand New Energy and FDA notified the public of a recall of all lot codes of **EphBurn 25**. One lot of EphBurn 25 sampled by the FDA was found to contain ephedrine alkaloids, making it an unapproved drug.

FDA Sep/12: Body Basics Inc. announced that it is conducting a voluntary nationwide recall of **ACTRA-Sx 500 Dietary Supplement Capsules**, Lot 008-A, Expiration December 2013. The Company, through independent lab analysis, has confirmed the presence of Sildenafil Citrate.

FDA Sep/12 is warning consumers not to use **Intestinomicina**, a drug product manufactured in El Salvador, because it contains the prescription drug ingredient, Chloramphenicol.

FDA Sep/12 Evol Nutrition Associates, Inc./Red Dawn ("Evol Nutrition") notified the public of a nationwide recall of all lots of two dietary supplement products distributed by the company under the names **Mojo Nights and Mojo Nights for Her** to the consumer level. Testing by the FDA revealed the presence of undeclared tadalafil and sildenafil in Mojo Nights (Evol Nutrition is also recalling Mojo Nights for Her).

FDA Oct/12 is advising consumers not to purchase or use "**Ultimate Formula Bee Pollen Capsules (Ultimate Formula)**," or "**Zi Xiu Tang Bee Pollen Capsules**," also referred to as "**Zi Xiu Tang Beauty, Face & Figure Capsule**," a product promoted and sold for weight loss because they contain sibutramine.

FDA Dec/12: **Libigrow, Libigrow XXXtreme, Blue Diamond, Blue Diamond Platinum, Mojo Nights, Mojo Nights Supreme, And Casanova**: Recall - Undeclared Ingredients Sulfoaildenafil and Thioaildenafil.

FDA Dec/12 is advising consumers not to purchase or use "**SLIMDIA Revolution**," a product promoted and sold for weight loss on various websites, including www.pinkfatty.com, and in some retail stores since it contains Sibutramine.

FDA Jan/13 is advising consumers not to purchase or use "**MAXILOSS** Weight Advanced," a product promoted and sold for weight loss on various websites, includingwww.dreamlifeweightloss.com, and in some retail stores since it contains sibutramine.

FDA Jan/13 Freedom Trading is conducting a voluntary consumer recall of a product sold as a dietary supplement under the brand name of **Super Power**. This product was sold between August 2012 and January 2013 nationwide & the products contained trace amounts of sildenafil.

FDA Feb/13 Olaax Corp announced a nationwide recall of the company's dietary supplement sold under the brand name **Maxiloss Weight Advanced Softgels** to the user level, because FDA testing found the Maxiloss Weight Advanced product to contain Sibutramine.

FDA Mar/13 Green Planet, Inc. notified the public of a recall of its dietary supplement product **Night Bullet**. Analytical tests conducted by the FDA found that the product contains trace amounts of Sulfohydroxyhomosildenafil and Aminotadalafil, which are analogues of sildenafil.

FDA Apr/13 laboratory analysis confirmed that "**Ninja Mojo"& "Love Rider**" contains tadalafil. FDA also confirmed that "**AFFIRM XL**" contains the undeclared ingredient sulfoaildenafil.

FDA Apr/13 Consumer Concepts, Inc. notified the public of a consumer/user level recall of all **ROCK-It MAN** Male Enhancement Capsules sold between October, 2012 and April, 2013. Analytical tests conducted by the FDA concluded that the product contained hydroxythiohomosildenafil.

FDA Apr/13 **Affirm XL**, Inc. is conducting a voluntary recall to the consumer level after FDA lab analysis testing found the product to contain an analogue of sildenafil.

FDA Apr/13 says it wants to make sure that supplements containing the **stimulant dimethylamylamine (DMAA)** are not distributed or sold in the U.S. The agency's action comes after reports of illness and death associated with DMAA-containing supplements. It has warned companies that use of DMAA in dietary supplements is illegal. One company, USPLabs, has defended its use. The company makes "**Jack3d**," which contains DMAA and is described as a "pre-exercise CNS-carnosine-ATP augmentor." It's sold on the Web.

FDA Apr/13 laboratory analysis confirmed that "**Sex Plus**" contains undeclared sildenafil, tadalafil, sulfosildenafil and dimethylacetildenafil. FDA laboratory analysis confirmed that "**Zoom-Zooma-Zoom**" contains sildenafil, the active ingredient in the FDA-approved prescription drug Viagra.

FDA May/13 American Lifestyle is announcing that it is conducting a voluntary recall of all lots of **Vicerex** UPC 893490820087 and **Black Ant** UPC 4026666142546. Laboratory analysis conducted by the FDA has determined the Vicerex product contains undeclared tadalafil and the Black Ant product contains undeclared sildenafil.

FDA May/13 is advising consumers not to purchase or use "**Bullet Proof**," a product promoted and sold for sexual enhancement on various websites and in some retail stores. FDA laboratory analysis confirmed that "Bullet Proof" contains tadalafil. Plus Chang Kwung announced today that it is conducting a voluntary nationwide recall of the company's dietary supplements sold under the brand name **Lightning Rod** (500 mg per capsule packaged in 3-count, UPC 6 89076 20257 2 and 12-count bottles, UPC 6 89076 20297 8), because FDA testing found the Lightning Rod Capsules to contain an analogue of Sildenafil.

FDA May/13: BeaMonstar Products notified the public that it is recalling its **SexVoltz, Velextra, and Amerect** capsules. Laboratory analysis conducted by the FDA on SexVoltz and Velextra has determined these products contain undeclared tadalafil.

FDA Jun/13 FDA laboratory analysis confirmed that "**Bethel 30**", & "**XIYOUJI QINGZHI CAPSULE**" & **JaDera** contains sibutramine. .

FDA Jun/13 laboratory analysis confirmed that "**Reload**" , "**Cave Diver**" , "**Super Cheetah**", "**Nights to Remember**" , & "**X Zen Platinum**", contains sildenafil.

FDA Jun/13 A sample of **Extreme Body Slim, Fat Zero, Fruit & Plant Slimming, & Paiyouji Plus** all contains silbutramine.

FDA Jun/13 A sample of **Royal Dragon Herbal Tonic Balls** contains vardenafil.

FDA Jun/13 Beta Labs has recalled certain lots of **Oxyphen, Phentalene, Phen FX, and Red Vipers** because they contain 1,3 dimethylamylamine (DMAA), the FDA announced over the weekend. The products are used as pre-workout stimulants and for weight loss, but the agency has previously warned that DMAA can be dangerous: it can elevate blood pressure and lead to cardiovascular complications. One distributor, GNC, faces FDA seizure of over 3000 cases of two other DMAA-containing products, **Jack3d and OxyElitePro**. Although the manufacturer of those supplements has ceased production, GNC continues to sell its remaining stocks, according to the *New York Times*.

FDA July/13 **Clalis, Exten 1300 & MaxTreme Zen** contains sildenafil, while **MVP Mega** contains talalafil.

FDA July/13 **Meizi Revolution, Strawberry Balance** contains silbutramine. **Silver Sword** & **Clalis** contains sildenafil.

FDA Aug/13 Volcano Company is recalling all lots of **Volcano Male Enhancement Liquid and Volcano Male Enhancement Capsules** to the consumer level. FDA test results revealed the Volcano Male Enhancement Liquid has been found to contain undeclared Desmethyl Carbodenafil, Dimethylsildenafil, and Dapoxetine.

FDA Aug/13 Purity First Health Products is recalling two lots of **Healthy Life Chemistry B-50** (100 capsules), one lot of **Healthy Life Chemistry Multi-Mineral** (200 capsules) and all lot numbers for **Healthy Life Chemistry Vitamin C** (200 capsules). The B-50 capsules were found on testing by FDA to contain Methasterone (a schedule III controlled substance) and Dimethazine. Testing of the Multi-Mineral and Vitamin C capsules appear to indicate the presence of Dimethyltestosterone.

FDA Aug/13 Herbal Give Care LLC issued a voluntarily recall of all lots of **Esbelin silouttee** and **Esbelin siloutte Herbal Blend with L-Carnitine** (30 Capsules), to the consumer level. The products have been found to contain undeclared Sibutramine, N-Desmethylsibutramine, and N-di-Desmethylsibutramine.

FDA Aug/13 Bethel Nutritional Consulting, Inc., New York, NY, is voluntarily recalling **Quick Thin and Bethel Advance** to the consumer level. These products have been found to contain Sibutramine and Phenolphthalein, and may pose a threat to consumers.

FDA Aug/13 Health and Beyond LLC is voluntarily recalling quantity lots of product **Tranquility**. The products have been found to contain a trace of Doxepin which is a pharmaceutical for sleep and Chlorpormazine for psychotic disorders.

FDA Aug/13 CTV Best Group announced that it is conducting a voluntary nationwide recall of all lots of a dietary supplement products distributed by the company under the names **BEST SLIM 40 Pills** to the consumer level. Testing by FDA revealed the presence of Sibutramine in Best Slim.

FDA Aig/13 Herbal Give Care LLC is voluntarily recalling all lots of **Esbelder man (30 capsules), Esbelder fem (30 capsules) and Esbelder siloutte** (30 capsules) to the consumer level. The products have been found to contain undeclared Sibutramine, N-Desmethylsibutramine, and N-di-Desmethylsibutramine.

FDA Aug/13: Jack Rabbit Inc. announced that it is conducting a voluntary nationwide recall of one lot of the company's dietary supplement product sold under the name **Jack Rabbit**. FDA lab analysis of the product was found to contain Sildenafil and Tadalafil.

FDA Aug/13 laboratory analysis confirmed that **Ortiga** contains the prescription drug ingredient, diclofenac.

FDA Aug/13 Hardmenstore.com is voluntarily recalling 1000 lots of **72HP, Evil Root and Pro Power Max** at the consumer level. According to representatives of the FDA, 72HP, Evil Root and Pro Power Max have reportedly been found to contain amounts of the PDE-5 Inhibitor, sildenafil.

FDA Sep/13 Ge Pharma, LLC is recalling **Creafuse Powder Grape** Lot# GE4568 and Creafuse Powder Fruit Punch Lot #GE4570, because they contain 1,3 dimethylamylamine (DMAA). DMAA is commonly used as a stimulant, pre-workout, and weight loss ingredient in dietary supplement products.

FDA Sep/13 laboratory analysis confirmed that **Shou Fu Ti Tun Guo Xiang Xing Jian Fei Jiao Nang** contains sibutramine.

FDA Sep/13 is advising consumers not to purchase or use **XZone Premium**, a product promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that XZone Premium contains sildenafil, tadalafil, and dapoxetine.
FDA Sep/13 is advising consumers not to purchase or use **Wood-E**, a product promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that Wood-E contains sildenafil.
FDA Sep/13 is advising consumers not to purchase or use **Xzen 1200, Xzen Gold or Xzen XPress**, products promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that it contains either sildenafil & tadalafil.
FDA Sep/13 Haute Health, LLC is voluntarily recalling all lots of **Virilis Pro, PHUK and Prolifta** at the retail and consumer level. Virilis Pro, PHUK and Prolifta have been found to contain amounts of the PDE-5 Inhibitor sildenafil.
FDA Oct/13 along with the Centers for Disease Control and Prevention (CDC) and the Hawaii Department of Health (DOH), are investigating a growing number of reports of acute non-viral hepatitis in Hawaii. The Hawaii DOH has reported that 24 of these cases share a common link to a dietary supplement product labeled as **OxyElite Pro**.

FDA Oct/13: B@B Trade, Inc., Florida is voluntarily recalling all lots of **Slim Fortune, Lidiy, and Slim Expert** to the consumer level. The FDA laboratory analysis of these dietary supplements found to contain undeclared Sibutramine,
FDA Oct/13 is advising consumers not to purchase or use **Perfect Body Solutions or Burn 7.** FDA laboratory analyses confirmed that Perfect Body Solutions and Burn 7 contain sibutramine.
FDA Oct/13 is advising consumers not to purchase or use **Dr. Mao Slimming Capsules**. FDA laboratory analysis confirmed that Dr. Mao Slimming Capsules contain sibutramine.
FDA Oct/13 is advising consumers not to purchase or use **Bella Vi Insane Amp'd or Bella Vi Amp'd Up & Be Inspired.** FDA laboratory analyses confirmed that Bella Vi Insane Amp'd and Bella Vi Amp'd Up contain sibutramine.
FDA Nov/13: Fossil Fuel Products, LLC, is recalling lots QL110714A102 and QL110408B046 of "**RezzRX**." Laboratory analysis conducted by the FDA determined the RezzRX lot QL110714A102 contains undeclared hydroxylthiohomosildenafil and aminotadalafil and RezzRX lot QL110408B046 contains undeclared hydroxylthiohomosildenafil.
FDA Nov/13: Jobbers Wholesale is recalling Lot No. KWAKPMC030505175957019 of **Rhino 5 Plus**, Lot No. JBP-L-1270-70 of **Maxtremezen** and Lot No. KWAKPMC03050517 of **Extenzone**. FDA analysis found these products to contain undeclared desmethylcarbondenafil and dapoxetine, making these products unapproved new drugs.
FDA Nov/13 Vitality Research Labs is recalling lots K58Q and F50Q of **VitaliKOR Fast Acting**. FDA laboratory analysis on VitaliKOR has determined that this product contains undeclared Vardenafil and Tadalafil.
FDA Nov/13: Tendex is voluntarily recalling Lot# F51Q of P-Boost and Lot # F51Q of NatuRECT to the consumer level. FDA laboratory analysis on Lot# F51Q of **P-Boost**, which the firm also labels as **NatuRECT**, has determined that this product contains undeclared tadalafil.
FDA Nov/13 **SlimExtra Herbal** capsules contain silbutramine.
FDA Nov/13 **Alpha Male** contains sildenafil & other analogs.
FDA Dec/13 IQ Formulations, of Sunrise, Florida is initiating a recall of all lots of its 45-capsule bottles of **Hydravax** due to potential inclusion of an unlisted ingredient. The FDA has advised IQ Formulations that an analysis of a sample from one lot of Hydravax (Lot # 2458, Exp # 07/16) revealed the presence of an undeclared ingredient – a diuretic.
FDA Dec/13 is advising consumers to immediately stop using a product called **Mass Destruction**, marketed as a dietary supplement for muscle growth. The product is labeled to contain at least one synthetic anabolic steroid and has been linked to at least one reported serious illness.
FDA Dec/13 laboratory analysis found the **Burn 7 Capsules** to contain undeclared Sibutramine.
FDA Jan/14 Midwest Wholesale is voluntarily recalling the following products Boost**: Ultra, XZone Gold, Sexy Monkey, Triple MiracleZen Platinum, Magic for Men, "New" Extenze, and New XZen Platinum**. FDA analysis found these products to contain undeclared Sildenafil and/or Tadalafil.
FDA Jan/14 is advising consumers not to purchase or use **Magic Slim or Dream Body Slimming Capsule**, products promoted and sold for weight loss and sold on various websites and in some stores, since FDA lab analysis confirmed they contains sibutramine.
FDA Jan/14: **JINQIANGBUDOR Red Dragon** & **Tiger King** contains sildenafil; **Bali Mojo** & **Vimax** contains tadalafil; SexRx Contains both sildenafil and tadalafil.
FDA Jan/14 **Citrus Fit Gold**, **Hot Detox** & **Thinogenics** contains sibutramine. **Tonic Life BP** contains phenolphthalein.
FDA Mar/14 is advising consumers not to purchase or use **Vitaccino Coffee**, a product promoted and sold for weight loss. FDA laboratory analysis confirmed that Vitaccino Coffee contains sibutramine.
FDA Mar/14 Terra-Medica, Inc. is voluntarily recalling 56 lots of **Pleo-FORT, Pleo-QUENT, Pleo-NOT, Pleo-STOLO, Pleo-NOTA-QUENT, and Pleo-EX homeopathic** drug products in liquid, tablet, capsule, ointment, and suppository forms to the consumer level. FDA has determined that these products have the potential to contain penicillin or derivatives of penicillin.
FDA Mar/14: New Life Nutritional Center is recalling all lots of "**Super Fat Burner capsules, Maxi Gold capsules and Esmeralda softgels**" to the user level after FDA analysis revealed the products contain undeclared active pharmaceutical ingredients: sibutramine, phenolphthalein or a combination of both sibutramine and phenolphthalein.
FDA Mar/14: **Bella Vi Insane Bee Pollen Capsules, Bella Vi BTrim Ultimate Boost, Bella Vi BTrim Max, Bella Vi Extreme Accelerator, Bella Vi Insane Amp'd, and Bella Vi Amp'd U**, contain silbutramine with or without phenolphthalein.
FDA Mar/14: Nova Products, Inc. issued a voluntary recall of the following products: **African Black Ant (Lot# 2006-000926), Black Ant (Lot# 2006-3627878), XZen Gold (Lot# 130310GL), ZXen Platinum (Lot# 130520PL), XZen 1200 (Lot# 13051012), XZone Gold (Lot# 131110GL), and XZone 1200 (Lot# 13071012)** at the retail level. FDA laboratory analysis on these products has determined that they contain undeclared amounts of sildenafil and tadalafil.

FDA Apr/14: FDA analysis on **New You** contains silbutramine.
FDA Apr/14 has tested multiple **Zi Xiu Tang Bee Pollen** products from various distributors in the United States (US). All products that have been tested, including those that claim to be "genuine" and "anti-counterfeit," have been found to contain one or both of the undeclared drug ingredients sibutramine and Phenolphthalein.
FDA Apr/14 laboratory analysis confirmed that **Infinity** & **Lite Fit** USA contains sibutramine.
FDA apr/14 is advising consumers not to purchase or use **S.W.A.G,** a product promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that S.W.A.G contains sildenafil.
FDA Apr/14: Nature's Universe notified the public it is recalling all lots of **Thinogenics** product sold prior to February 6, 2014 to the user level after FDA analysis revealed that the affected product contained undeclared sibutramine.
FDA Apr/14: Nano Well-being Health Inc. issued a voluntary recall of **Super Arthgold**, 500 mg capsules to the consumer level. FDA laboratory analysis has found the product to contain chlorzoxazone, diclofenac and indomethacin.
FDA May/14 laboratory analysis confirmed that **Slim Trim U** & **Natural Body Solution** contains sibutramine.
FDA May/14: Eugene Oregon, Inc. is voluntarily conducting this recall because FDA analysis of **African Black Ant, Black Ant, and Mojo Risen** distributed to a third party revealed that the distributed products contained undeclared amounts of the active pharmaceutical ingredients sildenafil and tadalafil.
FDA May/14 is advising consumers not to purchase or use **Asset Bee Pollen**, a product promoted and sold for weight loss because it contains sibutramine.
FDA May/14 is advising consumers not to purchase or use **Asset Bold**, a product promoted and sold for weight loss. FDA laboratory analysis confirmed that Asset Bold contains sibutramine.
FDA May/14 is advising consumers not to purchase or use **MV5 Days**, a product promoted and sold for sexual enhancement. FDA laboratory analysis confirmed that MV5 Days contains sildenafil.
FDA Jun/14: advising consumers not to purchase or use **Eyeful** contains hydroxythiohomosildenafil; **Liu Bian Li** contains sildenafil; **Dick's Hard Up** contains tadalafil; **3 Hard Knights** contains sildenafil and thiosildenafil; **Full Throttle On Demand** contains propoxyphenyl sildenafil; GoldReallas contains sildenafil and thiosildenafil.
FDA June/14 laboratory analysis confirmed that **Zhen Gong Fu** contains sildenafil.
FDA Jun/14 laboratory analysis confirmed that **La Jiao Shou Shen** contains sibutramine
FDA Jun/14 laboratory analysis confirmed that **Gold Vigra & Miraculous Evil Root** contains sildenafil. FDA laboratory analysis confirmed that **Sport Burner & Toxin Discharged Tea** contains fluoxetine. FDA laboratory analysis confirmed that **Sliming Diet** contains sibutramine.

Fish Oil Testing: Independent test for contaminants Nutrasource Diagnostics at the University of Guelp www.nutrasource.ca/ifos_new

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Health Canada is warning Aril/06 consumers not to not to use advises consumers not to use unauthorized products containing **anabolic steroids** (Five products containing illegal anabolic steroids, as they can potentially cause serious health issues such as liver disorders and heart problems. The five products are: Anabolic Xtreme Superdrol, Methyl-1-P, Ergomax LMG, Prostanozoland, and FiniGenX Magnum Liquid.)

Health Canada is warning consumers not to not to use **Kaizen Ephedrine HCL tablets for weight loss Dec/05** http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2005/2005_138_e.html

Health Canada is warning consumers not to ingest the herb **chaparral** in the form of loose leaves, teas, capsules or bulk herbal products because of the risk of liver and kidney problems. Dec/05 http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2005/2005_135_e.html

Health Canada is warning consumers not to use certain **Ayurvedic medicinal** products because they contain high levels of heavy metals such as lead, mercury and/or arsenic. July/05 http://www.hc-sc.gc.ca/english/protection/warnings/2005/2005_80.html

Health Canada Jan/06 Natural health product **Libidfit** may pose health risks (promoted for sexual enhancement and erectile dysfunction, but contains an undeclared amount of a pharmaceutical

ingredient similar to sildenafil) http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_02_e.html

Health Canada is warning consumers Feb/06: Not to use the Chinese medicinal product White Peony Scar-repairing pills, manufactured in Hong Kong by White Peony Pharmaceuticals Limited, due to high levels of lead. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_05_e.html

Health Canada is warning consumers Feb/06 not to use 13 Chinese herbal products manufactured by the Hong Kong Chi Chun Tang Herbal Factory due to bacterial contamination that could lead to serious health risks. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_08_e.html

Health Canada advises consumers April/06 not to use Super Fat Burning and LiDa Daidaihua Slimming Capsules for weight loss because they have been found to contain sibutramine http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_15_e.html

Health Canada is advising consumers Apr/06 not to use unapproved products containing **yohimbine or yohimbe bark**, including Strauss Energy SIX capsules. Yohimbine is a prescription substance that can pose serious health risks for people with underlying risk factors. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_16_e.html

Health Canada is advising consumers Apr/06 not to use unapproved Miracle Bion products as it could be contaminated with bacteria such as *E. coli*. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_23_e.html

Health Canada May/06 is warning consumers not to use the product **Nasutra** because it has been found to contain the sildenafil (chemical name for Viagra) that could lead to serious health risks, especially for patients with existing medical conditions such as heart problems, those who may be taking heart medications, or those who may be at risk for strokes.

Health Canada May/06 is advising consumers not to use Ocean Plasma **Isotonic Living Water and Ocean Plasma Hypertonic Living Water** because they are unapproved products that contain unacceptable amounts of aerobic bacteria.

Health Canada June/06 is advising consumers not to use four unapproved **Ayurvedic medicinal products** from India because they contain high levels of lead and/or mercury. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_46_e.html

Health Canada July/06 is advising Fat Rapid Loss Capsules (Xin Yan Zi Pai Mei Zi Jiao Nang) because may contain sibutramine http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_55_e.html

Health Canada July/06 is advising consumers not to use 4 foreign health products due to concerns about possible side-effects: **Zhuifeng Tougu Wan** & **Fufang LuHui Jiaonang**, two traditional Chinese medicines that contain toxic levels of mercury; **Safi**, a herbal product manufactured in India and Pakistan that contains toxic levels of arsenic; and **Baike Wan**, a herbal product from Malaysia that contains the prescription drugs piroxicam and frusemide, and the over-the- counter drug chlorpheniramine.

Health Canada Aug/06 is advising consumers not to use **Salt Spring Herbals Sleep Well Dietary Supplement** because a sample has been found to contain **estazolam.**

Health Canada Warns Consumers August 04, 2006 Not To Use **Neophase** Formula For Men Due To Potential Health Risks which has been found to contain an undeclared ingredient similar to the active pharmaceutical ingredient found in Viagra. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_67_e.html

Health Canada Aug/06 is reminding consumers not to use Miracle II Miracle Neutralizer or any other products exported or sold by Tedco, Inc. of Louisiana because they could contain harmful bacteria. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_68_e.html

Health Canada Aug/06 is advising consumers about a possible link between health products containing the herbal medicine **black cohosh and liver damage**. There have been a number of international case reports of liver damage suspected to be associated with the use of black cohosh, including three case reports in Canada and one published case of death in the United States. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_72_e.html

Health Canada Aug/06 is advising consumers not to use four foreign health products due to concerns about possible side-effects: **Reduce Weight**, a proprietary Chinese Medicine marketed as a weight-loss product. Contains the prescription drug sibutramine (the generic name for Meridia) **Yixinjiaonang**, a proprietary Chinese medicine marketed as a sexual enhancement & erectile dysfunction product, contains the prescription drug tadalafil (the generic name for Cialis) **Meng Rong**, a proprietary Chinese medicine marketed as a sexual enhancement and erectile dysfunction product, contains the prescription drug sildenafil (the generic name for Viagra) **VG**, a proprietary Chinese medicine marketed as a sexual enhancement and erectile dysfunction product, contains the prescription drug sildenafil (the generic name for Viagra) http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/fpa-ape/index_e.html

Health Canada Aug/06 is advising consumers not to use **Salt Spring Herbals Sleep Well** Dietary Supplement because a sample analyzed by Health Canada has been found to contain the undeclared drug Estazolam. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_82_e.html

Health Canada Aug/06 is advising consumers not to use two foreign health products due to concerns about possible side-effects: **Chao Nongsu Qingzhi Jiaonang** (OPC Care) is promoted as a weight-loss product. The product is adulterated with sibutramine and mazindol, two prescription medications used to suppress appetite. **Conting Qianweisu Slimming Herbs** Capsule is marketed as a weight-loss product. The product is adulterated with sibutramine, a prescription medication used to suppress appetite. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/fpa-ape/2006/2006_84_e.html http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/fpa-ape/2006/2006_83_e.html

Health Canada Sept/06 advises against use of the **Ayurvedic medicinal product Jambrulin** due to lead content http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_89_e.html

Health Canada Sept/06 is warning consumers not to use the natural health product **Libidus** because it contains an undeclared pharmaceutical ingredient, a modified form of vardenafil.

Health Canada Oct/06 is advising consumers not to use the unauthorized natural health products **Emperor's Tea Pill (Tian Huang Bu Xin Wan)** and **Hepatico Extract (Shu Gan Wan)** because certain lots of these products contain high levels of lead and mercury. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_98_e.html

Heath Canada Nov/ 06 is warning Canadians not to use the unauthorized product **Embrun de mer** promoted for the treatment of skin irritation in newborns and adults because it contains unacceptable amounts of harmful bacteria.

Health Canada Dec/06 is advising consumers not to use a product called **Eden Herbal Formulations Sleep Ease Dietary Supplement**, because it was found to contain an undeclared drug estazolam http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2006/2006_127_e.html

Health Canada Dec/06 is advising consumers not to use two foreign health products due to concerns about possible side-effects: **Slim & Detox Peptide**, which are weight-loss products. Containing the prescription drug sibutramine (the generic name for Meridia) http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/fpa-ape/index_e.html

Health Canada Jan/07 is advising consumers not to use **Kang Da** and **four unlabelled products** are marketed as herbal sexual enhancements and treatments for erectile dysfunction. The products are adulterated with a prescription medication used in the treatment of sexual dysfunction. **Qing Zhi** and one unlabelled product are marketed as herbal weight-loss products. The products are adulterated with sibutramine, a prescription medication used to suppress appetite.

Health Canada Feb/07 is advising consumers not to use a product called **Sleepees**, because it was found to contain an undeclared drug **estazolam**, which can be habit-forming when used for as little as a few months. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/2007/2007_16_e.html

Health Canada Feb/07 is updating Canadians about adverse reaction reports it has received concerning the use of **EMPowerplus**, a vitamin mineral supplement, for serious medical conditions. Health Canada has received nine case reports of serious adverse reactions associated with the use of EMPowerplus. Most of the adverse reactions relate to worsening of psychiatric symptoms in those patients with serious underlying mental health problems, such as bipolar disorder and depression.

Health Canada Feb/07 is advising consumers not to use the following product listed in the table below due to concerns about possible side-effects. More info **Power 58; Platinum Power 58; Ehanix; Jolex; Onyo; Deguozonghengtianxia** because they contained acetildenafil. Acetildenafil is an analogue of sildenafil, a prescription medication indicated for treatment of erectile dysfunction.

Health Canada Mar/07 is Health Canada is advising consumers not to use **MIAOZI Slimming Capsules** because they have been found to contain sibutramine, a prescription medication that should only be taken under medical supervision.

Health Canada Mar/07 is warning consumers not to use the unauthorized natural health product **XOX For Men**, because it contains an undeclared pharmaceutical ingredient, tadalafil, an ingredient found in the prescription drug Cialis. The use of XOX For Men could pose serious health risks, especially for patients with existing medical conditions such as heart problems, those taking heart medication, or those at risk of stroke.

Health Canada Mar/07 is warning consumers not to use the unauthorized product **Vigorect** Oral Gel Shooter, because it contains an undeclared drug substance tadalafil.

Health Canada Apr/07 is warning consumers about **Bitter orange** & cardiovascular reactions in the Canadian Adverse Reactions April 2007 Newsletter.

Health Canada Apr/07 is warning consumers from The Hong Kong Department of Health found **Lanmei Keili Ji to be adulterated with gliclazide**, a hypoglycaemic agent (lowers blood sugar). The Hong Kong Department of Health found **Lexscl Fat Rapid Loss capsules to be adulterated with sibutramine** and thyroid hormones. The United States Food and Drug Administration found **V.MAX and Rhino Max (Rhino V Max) to contain undeclared amounts of aminotadalafil**, an analogue of tadalafil, used to treat erectile dysfunction.

Health Canada April/07is advising consumers not to use a product called **Eden Herbal Formulations Serenity Pills II** because it contains the undeclared drug **estazolam**.

Health Canada April/07is advising consumers not to use a product **FibreChoice plus Multivitamins** is marketed as a fibre supplement. The product is contaminated with **fish gelatin**, a known allergen that could cause life-threatening reactions in some sensitive individuals.

Health Canada May/07 is warning consumers **Urat Madu** capsules are marketed for the treatment of erectile dysfunction. The product is adulterated with **sildenafil**, a prescription drug that has been associated with serious side effects including sudden vision loss, penile tissue damage and urinary tract infection.

Health Canada May/07 is advising consumers not to use **Xiaokeshuping Jiangtangning Jiaonang** capsules in Hong Kong to contain the undeclared pharmaceutical drugs phenformin, rosiglitazone, and glibenclamide, which may be used in diabetes to lower blood sugar.

Health Canada May/07 is advising consumers that **HS Joy of Love** product is marketed as a dietary supplement and was found to contain piperadino **vardenafil**.

Health Canada May/07 is advising consumers not to use 6 foreign health products due to concerns about possible side-effects: **Power 58 Extra, Platinum Power 58 Extra, Enhanix New Extra Men's Formula, Valentino, King Power Oral Solution, and Stretch Up** Capsules are marketed as treatments for erectile dysfunction. The products contain analogues of sildenafil and vardenafil, which are prescription drugs used for the treatment of erectile dysfunction.

Health Canada June/07 is advising consumers not to use **Optimum Health Care SleePlus TCM** or **BYL SleePlus**, because the products contain the undeclared drug **clonazepam.**

Health Canada June/07 is warning consumers not to use the product **Encore Tabs for Men**, because it contains an undeclared pharmaceutical ingredient similar to the approved drug tadalafil.

Health Canada July/07 is warning Canadians not to use the dietary supplement **MdMt**, or any other supplements containing the synthetic steroids methyl-1-testosterone or methyldienolone that are obtained without a prescription, due to potentially serious health risks including reduced fertility and liver disorders.

Health Canada July/07 is warning consumers not to use **Zencore** Tabs, a product advertised as a dietary supplement for sexual enhancement, because it contains an undeclared pharmaceutical ingredient similar to the approved drug tadalafil.

Health Canada July/07 & the US Food and Drug Administration (FDA) found ***Liviro3*** to contain tadalafil, a prescription drug that should only be taken under the guidance of a health professional.

Health Canada July/07 is advising consumers not to use the sleep supplement product **Optimum Health Care Sleep Easy**, because it contains the undeclared drug clonazepam.

Health Canada July/07 is advising consumers not to use 8 foreign health products due to concerns about possible side-effects: **Jie Jie Pills** and **Chuan Xiong Cha Tiao Wan** are proprietary Chinese medicines that have been found to contain aristolochic acid, a natural toxin known to cause kidney failure and cancer in humans. Medsafe, the New Zealand health regulatory authority, advised the public not to use the products **Darling Capsules**, **Dali Capsules**, **Spanish Fly Capsules**, and an unnamed product, because they were found to contain sildenafil. Medsafe also advised the public not to use the product **Dai Dai Hua Jiao Nang** because it was found to contain sibutramine. The Hong Kong Department of Health [HKDH] found batch #WA00030 of the product K**ui Hua Chut Lee San Bird's Nest & Pearl** to exceed the acceptable limit for microbiological contaminants set out by the HKDH. Further investigation revealed that this product also exceeded the limit for bacterial contamination in Natural Health Products in Canada.

Health Canada Aug/07 Consumers who use **Excite for women or Ultimates for men** may be at risk of serious side effects similar to those associated with sildenafil.

Health Canada Aug/07 is advising Canadians of a recall in the United States of one lot of **Metaboslim Apple Cider Vinegar**, which is marketed as a dietary supplement, because it has been found to contain **sibutramine**, a prescription medication that should only be taken under medical supervision.

Health Canada Sept/07 is advising consumers not to use 13 foreign health products due to concerns about possible side-effects: **Jacaranda**, **Queenmer Fat Loss**, **Li Da Dai Dai Hua Jiao Nang, J-minus** and **Jelimel Slimming Capsules**. These products are promoted for weight loss and have been found to be adulterated with the prescription drug sibutramine. Sibutramine is used for treating obesity and should only be taken under the supervision of a health professional. **Junyu Jiaonanyihao** has been found to contain the undeclared prescription drugs sibutramine and dexamethasone, as well as phenolphthalein, which is currently prohibited in Canada. **Satis 60 Hours Ever Lasting Formula** is used for the treatment of erectile dysfunction/sexual enhancement. It was found to contain piperidenafil an analogue of vardenafil, a drug that should only be used under the supervision of a health professional. **Qiangli Zhuanggutongbiling** has reportedly been used for joint pain and stiffness. It was found to contain the undeclared prescription drugs prednisolone acetate, cortisone acetate, piroxicam, and diclofenac. **Heng Tong Jiangtangning Jiaonang** was found to contain the prohibited drug phenformin, and the prescription drug glibenclamide (glyburide) which should only be taken under the supervision of a health professional. **Endopile Capsules** is used for the treatment of hemorrhoids and piles, and related symptoms and was found to contain potentially toxic levels of lead and mercury. **BuXie PaiDu XiaoDou Su** is used as an acne treatment and was found to contain the prescription drug rifampicin (rifampin). **True Man** and **Energy Max** are used as sexual enhancement/ erectile dysfunction products and were found to contain an analogue of sildenafil or vardenafil which are prescription medications.

Health Canada Sept/07 is advising consumers not to use 5 foreign health products due to concerns about possible side-effects: **Top Gun for Men Herbal Extracts** has been found to contain a substance similar to tadalafil. **Oyster Plus** has been found to contain tadalafil. **Deguozhanjiang** contains sildenafil and tadalafil, prescription drugs used for the treatment of erectile dysfunction. **Chongcaoliubian Jiaonang** and **Santi Scalper Penis Erection** Capsule contain sildenafil.

Health Canada Sept/07: **Khun-Phra** is a health product promoted for pain relief that has been found to contain the undeclared drugs dexamethasone, prednisolone, phenylbutazone, diazepam, cyproheptadine and mebhydrolin.. **Asam Urat Flu Tulang, PJ Dewandaru** is a health product promoted to treat joint pain, rheumatism and arthritis. It has been found to contain the undeclared drugs dexamethasone, diclofenac and acetaminophen.

Health Canada Oct/07 Foreign Product Alerts: ***Zhen Feng Da Brand Xi Tong Wan*** is promoted as a pain reliever. Lot #060908 has been found to contain undeclared indomethacin, a prescription anti-inflammatory drug that should only be taken under the guidance of a health professional. ***Wellring Brand Yin Qiao Jie Du*** is a health product promoted to treat cold and flu symptoms. Lot#51005 has been found to contain undeclared acetaminophen. ***Gu Ci Dan*** and ***Xu Log Bou*** are promoted as pain relievers and have been found to contain undeclared indomethacin. Indomethacin is a prescription anti-inflammatory drug that should only be taken under the guidance of a health professional.

Health Canada Oct/07 is advising, especially pregnant & breastfeeding women, not to use **Calabash chalk** because of the potential health risk due to high levels of lead.

Health Canada Oct/07: Foreign Product Alerts: **Red Yeast Rice, Red Yeast Rice/Policosonal Complex and Cholestrix, and Xie Gan Wan**. Red Yeast Rice, Red Yeast Rice/Policosonal Complex and Cholestrix are promoted as dietary supplements for the treatment of high cholesterol. These products may contain **lovastatin**, a prescription medication for the treatment of high cholesterol that should only be taken under the guidance of a health professional. Xie Gan Wan is a Proprietary Chinese Medicine with unknown indication for use. Xie Gan Wan, was found to contain **Aristolochia** plant species.

Health Canada Oct/07: **Royal Medic No.1 Chinese Caterpillar Fungus** is a proprietary Chinese medicine promoted as a general health tonic, but Health Canada advises Canadians not to use this product due to microbial contamination. **Steripaste Medicated Paste Bandages** may not be sterile therefore there is a possibility the bandage may cause a wound infection.

Health Canada Nov/07 is advising consumers not to use **Axcil** and **Desirin**, are promoted as natural sexual enhancement/ erectile dysfunction products. Consumers are warned not to use Axcil and Desirin because both products were found to contain the prescription drug **sildenafil**.

Health Canada Dec/07 is advising Canadians not to use unauthorized products manufactured by **Wild Vineyard** because of the potential health risk to consumers. Wild Vineyard is not authorized to manufacture, package, label or import natural health products in Canada.

Health Canada Jan/08 is advising consumers not to use 2 foreign health products due to concerns about possible side-effects: **Baby's Bliss Gripe Water** (apple flavour), code

26952V, a natural health product given to infants to ease stomach discomfort and gas, was found to contain the parasite cryptosporidium. Cryptosporidium may cause severe, chronic or even fatal effects, especially in infants. **Zhong Ti Xiao Er Jian Pi San** is a natural health product. Batch number JPS0704 has been recalled due to microbial contamination.

Health Canada Jan/08 is warning Canadians not to use the unauthorized product **Yeniujyn** because the product contains heavy metal contaminants and may pose a serious health risk. Yeniujyn is advertised as a natural health product, for adults and children, to be used "to cure involuntary passage of urine diseases." The product was found to contain high levels of **lead and arsenic**.

Health Canada Jan/08 is warning Canadians not to use the unauthorized product 1- ZhenZhu HouFengSan Penji; Vyling Cornu Saigae Tataricae Cooling Tea; Natorny Kwek's Herb 106; Chinese Herbal Heritage Herbal Slimming Tea; Vyling Urticaria Itch-Killer A; Vyling Water- Melon Pearls Powder; Phoenix Brand Tea For Sore Throat And Fever; Qing Yin Bai Hua Tea; and Yinqiao Flu & Fever Tea. **Nine specific batches** of Chinese medicines and teas manufactured in Singapore that have been recalled due to microbial (bacterial) and/or yeast and mould **contamination**.

Physio Care Lida Dai Dai Hua Jiao Nang Slimming Capsules (batch number 28012007 / expiration date: Jan 2009). This product is promoted for weight loss and has been found to contain a derivative of the prescription drug **sibutramine**.

RGC-RMC Rheumax Capsule (batch number REM1-SI93016N). This batch of RGC-RMC Rheumax Capsule has been found to contain **progesterone**, a steroid hormone that can have adverse effects on the brain, breast and skin and should only be taken if prescribed by a health professional.

Health Canada Feb/08 warning Canadians not to use Foreign Products: 1) **Jingzhi Kesou Tanchuan; Guanxin Suhe capsules**; **Qing Re An Cang Wan**; & **Guan Xin Su He** 2) **Xiao Qin Long Capsules** 3) **Xiao Qin Long Wan**; **Chuan Xiong Cha Tiao Wan Tablets**; **Bai Tou Weng Wan** 4) **Wannianqing Pai Danggui Niantong Tang** (batch number 050401) These products have been found to contain aristolochic acid, a toxin associated with serious and potentially fatal health effects.

Health Canada Feb/08 warning Canadians not to **use VPX 'No Shotgun' and BSN 'Cell Mass' Body Building Powders** These products have been found to contain coumarin.

Health Canada Feb/08 warning Canadians not to use 1) Ding Lu Brand Guipi Wan (batch number 060401); Ding Lu Brand Bushen Yijing Wan (batch number 060401); Ding Lu Brand Shiquan Dabu Wan (batch number 060401); **Ding Lu Brand Xiangsha Liujun Wan** (batch number 060401); Ding Lu Brand Xiaoyao Wan (batch number 060401); Medco Brand Vitality Essence Extract Of Deer Fetus (batch number 61007); Plasmin (batch number 20060102) 2) **Yogaraja Gulgulu Pills** (batch number GK039) and Pilsol Capsule 3) **Conforer Global Yang Tonic-2** (batch number 060117) 4) **Liang Gel San Concentrated Powder** (batch number G3238913) and **Qing Xin Lian Zi Yin Concentrated** Powder (batch number G3239274) These products were found to contain excessive amounts of heavy metals.

Health Canada Mar/08 is warning consumers not to use **Libidus**, an unauthorized product promoted on the web site of the manufacturer for the treatment of erectile dysfunction. The product may pose serious health risks, as it was found to contain the undeclared prescription drug sildenafil.

Health Canada April/08 is warning consumers not to use Foreign Product Alert: **Tetrasil, Genisil, Aviralex, OXi-MED, Beta-mannan Micronutrient, Qina** and **SlicPlus**. They are marketed for the prevention or treatment of a variety of sexually transmitted diseases.

Health Canada April//08 is advising consumers not to use 2 foreign products, **Aspire 36** & **Aspire Lite**, because they were found to contain undeclared sildenafil analogues.

Health Canada April/08 is warning consumers not to use **Vigoureux**, an unauthorized product promoted for the treatment of erectile dysfunction. The product may pose serious health risks, as it was found to contain the prescription drug sildenafil

Health Canada April/08 is advising consumers not to use 2 foreign health products due to concerns about possible side-effects: **Tian Li** was found to contain tadalafil and hydroxyhomosildenafil, and should only be taken under the guidance of a healthcare professional. **Xian Zhi Wei II** was found to contain sibutramine and phenolphthalein, which are not meant for self-care and may cause serious side effects.

Health Canada April/08 is advising consumers not to use The Hong Kong Department of Health advised the public not to use the product **Tian Sheng Yi Bao** because it was found to contain two pharmaceutical products, glibenclamide and phenformin

Health Canada April/08 is advising consumers about The Health Sciences Authority (HSA) of Singapore recalled **Qili Brand Tongbianling Jiaonang, Sincere Brand ChuanXinLian Jiaonang, Xiangyao Brand Xiangyao Weian Jiaonang, Biflora Brand Fufang Danshen Pian (film-coated), Biflora Brand 306 Xiaoyan Jiedu capsules, and Xiang Sha Liu Jun Wan** as they were found to contain high levels of arsenic and/or mercury that exceeded the permissible limits outlined by the HSA standards of safety and quality.

Health Canada May/08 is advising consumers not to use **vpxl No1** Dietary Supplement for Men was found to contain tadalafil

Health Canada May/08 is reminding consumers who choose to use unapproved Ayurvedic medicinal products that some of these products may contain high levels of heavy metals. Consumption of excessive amounts of heavy metals, such as lead, mercury, and arsenic, pose serious health risks.

Health Canada May/08 is warning consumers not to use **Trophic Kelp & Glutamic Acid HCl** due to the health risk posed by exposure to high levels of iodine.

Health Canada May/08 is warning consumers not to use **Desire**, an unauthorized product promoted to enhance male sexual performance as this product may pose serious health risks in certain patients. Lot 0070263 of the product was found to contain the prescription drug phentolamine.

Health Canada June/08 is advising that **Desire** contains Phentolamine, which should only be used under the supervision of a health care professional.

Health Canada June/08 **6-OXO**, which contains the compound 4-androstene-3,6,17-trione, is an unauthorized natural health product in Canada. **1-AD** contains 1-androstenediol, an anabolic steroid that is regulated as a controlled substance in Canada

Health Canada July/08 Foreign Product Alerts: **Super Shangai,Strong Testis, Shangai Ultra, Shangai Ultra X, Lady Shangai, Shangai Regular (also known as Shangai Chaojimengnan), Actra-Sx, An unknown product containing the plant Lycium barbarum L., Adam Free, NaturalUp, Erextra, Yilishen, Blue Steel, Hero, & Naturalë Super Plus.** These products have been found to contain sildenafil or an unapproved substance similar to sildenafil.

Health Canada July/08 is advising consumers not to use 4 foreign health products due to concerns about possible side-effects: Wodibo. **Wodibo** is promoted as an all-natural Chinese potency-enhancing product for the treatment of erectile dysfunction. The Danish Medicines Agency has warned against the use of Wodibo because it was found to contain sildenafil and tadalafil, prescription drugs authorized for treatment of erectile dysfunction. Both of these medications should only be used under the supervision of a health care professional. **Viril-Ity-Power** (VIP) Tabs. The U.S. Food and Drug Administration has warned consumers not to use Viril-Ity-Power (VIP) Tabs because it was found to contain an undeclared ingredient similar to the prescription drug sildenafil. The product has been recalled by the manufacturer in the U.S. **Therma Power** (red and blue varieties) and **Grenade Fat Burner**. The U.K. Medicines and Healthcare products Regulatory Agency (MHRA) warned consumers not to use the ephedrine-containing products Therma Power (red variety) and Grenade Fat Burner after the products were associated with serious adverse reactions. The MHRA also warned consumers to not use the

ephedrine-free Therma Power (blue variety) because it contains synephrine and caffeine, a combination that has been associated with cardiovascular adverse reactions.

Health Canada Aug/08 is advising consumers not to use 9 foreign health products due to concerns about possible side-effects: **Dan Bai Shou Shen Su** was found to contain undeclared thyroid hormones and sibutramine. **Karntien and Karntien Easy to Slim** were adulterated with sibutramine and a compound that is similar in structure to sibutramine (N-desmethylsibutramine). **Armstrong Natural Herbal Supplement, Enhanix New Extra Men's Formula, Power 58 Extra, and Platinum Power 58 Extra** were adulterated with tadalafil or unapproved substances with structures similar to tadalafil and vardenafil. **More Slim** was found to contain the undeclared pharmaceutical ingredient sibutramine. **Soloslim** was found to contain an undeclared substance similar in structure to the prescription drug sibutramine. It also contains the prescription drug L-carnitine, as well as synephrine, which is not authorized for sale in weight loss products in Canada.

Health Canada Aug/08 is advising consumers not to use 8 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned against the use of Natural (Xin Yi Dai) and Lasmi because Natural (Xin Yi Dai) was found to contain sibutramine and phenolphthalein, and Lasmi was found to contain sibutramine and spironolactone. The Hong Kong Department of Health warned against the use of AA Qu Feng Shu Jin Wan because it was found to contain the undeclared pharmaceutical ingredient dexamethasone. Apisate contained fenfluramine and Energy ll contained sibutramine. Obat Asam Urat and Asam Urat both contained dexamethasone, phenylbutazone and piroxicam. The Hong Kong Department of Health warned against the use of Slim 3in1 (Xiao Nan zhi Bao) because it was found to contain the undeclared pharmaceutical ingredients sibutramine and phenolphthalein.

Health Canada Sept/08 is advising consumers not to use any unauthorized health products sold under the brand names **Life Choice, Healthy Choice, Doctor's Choice and Your Choice** as well as other products without a brand name. All of these unauthorized health products have the same identifying image on their label.

Health Canada Sep/08 is advising consumers not to use 3 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned consumers not to buy or use **Lover Liquid Nutriment Herbal Supplement and Onyo** because they were found to contain undeclared pharmaceutical ingredients. **Lover Liquid Nutriment Herbal Supplement** was found to contain sildenafil while Onyo was found to contain sildenafil, as well as unapproved substances with structures similar to sildenafil and vardenafil. The U.S. Food and Drug Administration warned consumers not to use the product **Rose 4 Her** because it was found to contain an undeclared ingredient similar to the prescription drug sildenafil.

Health Canada Sep/08 is advising consumers not to use 6 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned consumers not to buy or use **Dr. Life** or **Chong Cao Ju Wang** because they were found to contain undeclared pharmaceutical ingredients. Dr. Life contains an unauthorised substance similar in structure to tadalafil while Chong Cao Ju Wang contains sildenafil. The Hong Kong Department of Health warned against the use of **Hanguo shoushen yihao** (meiti xing) because it was found to contain the undeclared pharmaceutical ingredient sibutramine. The U.S. Food and Drug Administration alerted consumers to a voluntary recall of 32-ounce plastic bottles of **Liquimax Complete Nutrition Multivitamin Formula** (UPC codes 7497052290, 7497023607 or 7497023696) because the product may contain undeclared fish (not shellfish), tree nuts (almonds, pecans, and/or walnuts), and wheat. People with sensitivities to fish, tree nuts and/or wheat may risk serious or life-threatening allergic reactions if they consume these products. The Hong Kong Department of Health warned against the use of **ARMA - Sin Gang San** and **New ARMA - Sin Gang San** because they were found to contain the undeclared pharmaceutical ingredients sibutramine and fenfluramine.

Health Canada Oct/08 is advising consumers not to use 2 foreign health products due to concerns about possible side-effects: Swissmedic warned consumers not to buy or use the product **Powertabs** because it contains an unauthorised substance similar in structure to sildenafil. The Hong Kong Department of Health warned consumers not to buy or use **Sweet Energizer Vitality** Candy because it was found to contain an unauthorised substance similar in structure to tadalafil.

Health Canada Nov/08 is advising consumers not to use 5 foreign health products due to concerns about possible side-effects: The Hong Kong Department of Health warned consumers not to buy or use **Lu Quan** because it contains undeclared glibenclamide and sildenafil. The Hong Kong Department of Health warned consumers not to buy or use **Fat Killer, Carbohydrate Cut and Sugar-Carbohydrate Cut** because they contain sibutramine and an unauthorised substance similar in structure to sibutramine, and **Zhuang Yao Gu Shen** Capsule because it contains sildenafil.

Health Canada Nov/08 is advising consumers not to use 13 foreign health products due to concerns about possible side-effects: The U.S. FDA warned consumers not to buy or use **Viapro** because it contains an unauthorised substance similar in structure to sildenafil. Sildenafil is a prescription drug used in the treatment of erectile dysfunction and should only be used under the supervision of a health care practitioner.

The U.S. Food and Drug Administration informed consumers of a voluntary manufacturer recall of these 12 products because they contain human **placenta, aristolochic acid and/or ephedra**, and may pose serious health risks. All 12 products are manufactured by **Jen-On Herbal Science** International Inc. (also known as **Herbal Science International Inc**.). Consumers who had purchased these products were advised to discontinue their use immediately and return them to the place of purchase for a full refund.

Health Canada Nov/08 is warning consumers not to use **Firm Dose** and **Granite Rooster**, two products promoted to enhance male sexual performance, as these products may pose serious health risks. Firm Dose was found to contain similar to sildenafil, while Granite Rooster was found to contain similar to tadalafil.

Health Canada Nov/08 is advising consumers not to use the unauthorized product, Kwan Loong Medicated Oil, as it contains chloroform. Foreign Product Alerts: Seng Jong Tzu Tong Tan,Tou Tong San (Headache Formula),Du Huo Ji Sheng ,Tang (Du Huo Joint Relief), Wu Yao Shun Qi San, Qing Bi Tang (Nasal Cleanser), Zhong Fong Huo Luo Wan (Stroke Revito Formula), Xiao Qing Long Tang (Little Green Dragon), Ding Chuan Tang (Breathe Smooth), Xiao Xu Ming Tang, Feng Shi Zhi Tong Wan (Joint Relief),,Guo Min Bi Yan Wan, Fang Feng Tong Sheng San.

Health Canada Jan 2009 is advising consumers not to use 4 foreign products: **Zhuang Tjar Gere** because it contains the undeclared prescription drugs sildenafil & tadalafil, **Zhixhue** Capsules manufactured by Vital Pharmaceutical Holdings Ltd. due to concerns of serious side- effects including liver dysfunction, **Tonik Warisan Banjar** because it contains undeclared dexamethasone & **Healthily Slim** because it contains sibutramine.

Health Canada Mar/09 Foreign Product Alerts: **68 Weight Loss Products**; Best-life Fat Burning Capsules; Bevidan;Huiji Yin Chiao Chieh Tu Pien; Relacore -plus Lami, Linglongquxian, Menergy M-Essence, Nyal Day & Night Cold & Flu Fighter (AUST L 146264), Nyal Cold & Flu Fighter (AUST L 146263), 999 Radix Notoginseng, Batch no. 0807021, Slim Pure, Carbohydrate, Kalomee, K Carbohydrate, K Tighten Slim, & K Slimming Pills. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_fpa-ape_2009/index-eng.php

Health Canada June/09 Foreign Product Alerts: **Fangocur Mineral Drink** (undeclared arsenic); **Jia Yi Jian** (undeclared sibutramine & tadalafil);**Fortodol**, which is also sold under the names (undeclared nimesulide with liver concern) of Donsbach Miradin, Lepicol Miradin, Leppin Miradin, & Miradin; **Shan Dian Qiang Xiao Shou** (undeclared sibutramine & phenolphthalein); **Zencore Plus** (undeclared benzamidenafil) & **Zhong Guo Shen Fang** (undeclared med like sildenafil).

Health Canada June/09 is warning consumers not to use the unauthorized product **Slim Magic Herbal**, which is promoted as a weight-loss product, as it was found to contain an undeclared pharmaceutical ingredient similar to the prescription drug sibutramine.

Health Canada is warning consumers not to use the unauthorized product **Nutural Slim**, which is promoted as a weight-loss product, as it was found to contain the undeclared pharmaceutical ingredient sibutramine and also an undeclared pharmaceutical ingredient similar to sibutramine.

Health Canada June/09 warns of foreign Product Alerts: **Herbal Xenicol** because it contains undeclared cetilistat. **BioEmagrecim**, which the FDA had previously warned contained sibutramine, was also found to contain fluoxetine, furosemide and fenproporex. Products: **Slimbionic, Xsvelten, 999 Fitness Essence, 24" ince, Light Some, Paiyouji, Pearl White Slimming, & Reducing Weight Easily** contain undeclared pharmaceutical ingredients (sibutramine and/or phenolphthalein) and/or excessive levels of lead, and may cause serious health effects..

Health Canada July/09 is warning consumers not to use the unauthorized health product labelled as **Specific-Formula Arthro-Ace** as it was found to contain undeclared dexamethasone and may cause serious health effects.

Health Canada July/09 is warning that the Singapore Health Sciences Authority (HSA) warned consumers to not buy or use **Air Ikan Haruan** after it was found to contain undeclared dexamethasone. The Hong Kong Department of Health warned consumers not to buy or use the product **Neovidan** after it was found to contain undeclared prednisolone and mefenamic acid. Plus the Singapore Health Sciences Authority (HSA) warned consumers to not buy or use **XP Tongkat Ali Supreme** after it was found to contain undeclared tadalafil.

Health Canada Aug/09 is advising via Singapore Health Sciences Authority (HSA) warned that **Delima Raja Urat** contains undeclared dexamethasone, chlorpheniramine, pheniramine and sibutramine, while **Cao Gen Bai Lin Wan** contains undeclared dexamethasone and chlorpheniramine.

Health Canada Oct/09: **Bao Ling**- The Singapore Health Sciences Authority advised consumers not to buy or use since contained undeclared betamethasone, hydrochlorothiazide & chlorpheniramine. **Dynasty Worldwide Jinglida So Young Formula**- The Singapore Health Sciences Authority (HSA) warned consumers to not buy or use since contained undeclared aminotadalafil. **STEAM** lot#80214, 90260 -The U.S. FDA informed consumers of a voluntary manufacturer recall of two lots of STEAM after FDA testing found these lots to contain undeclared sulfoaildenafil (lot# 80214) & undeclared tadalafil (lot# 90260). **Syntrax Fyre (contained Yohimbine)**, **Texiao Fengshi Gutong Ling (contained indomethacin)**, **Kam Yuen Brand Wan Ying Yang Gan Wan (contained sildenafil)** - The Hong Kong Department of Health warned consumers not to buy or use these three products after they were found to contain undeclared pharmaceutical substances.

Health Canada Nov/09 is advising Canadians not to consume Chaotic Beverages sold under the brand names Mind Strike, Fearocity, Elixir of Tenacity and Power Pulse because they are unauthorized products marketed to a vulnerable population (children) with ingredients that may pose a health risk. **Mind Strike:** Contains an unknown amount of caffeine despite advertising that it is not an energy drink and contains several herbs which are not included in Health Canada's list of botanicals with a history of safe use in children. **Fearocity:** Contains an unknown amount of caffeine, several herbs not included in Health Canada's list of botanicals with a history of safe use in children, taurine at an unacceptable level for children, and niacin at a level three times higher than that recommended for children aged 1 to 13 years. **Elixir of Tenacity:** Contains green tea extract, which is not included in Health Canada's list of botanicals with a history of safe use in children, and vitamin A at a level unacceptable for children aged 1 to 8 years. **Power Pulse:** Contains chromium picolinate at levels of possible concern in a product taken by children.

Health Canada Nov/09 is warning consumers not to use Herblex "**Once More**"since it was found to contain sildenafil.

Health Canada Dec/09 is advising Canadians not to use certain Acai Berry products after a large number of shipments of adulterated products were stopped at the border. The product names include: **Anti-Aging Acai Berry, Guarana Blast, Brazillian Pure, Anti-aging Vital Rez V, Weight Loss VitalAcai, Dietary Supplement Acai Power Blast and Muscle Mass**. These products advertised for anti-aging and weight loss were found to contain undeclared sildenafil.

Health Canada Dec/09 is warning consumers not to use "**RevolutionDS Weight Loss**", an unauthorized health product promoted for weight loss, because it contains benzylpiperazine (BZP), and may pose serious health risks.

Health Canada Dec/09 is advising consumers not to use the following foreign health products: 1. **Power-Plus P**: The Singapore Health Sciences Authority issued a recall notice for Power-Plus P (expiry date 03/03/2011) after it was found to contain undeclared tadalafil. 2. **Show Party**: The Hong Kong Department of Health warned consumers not to buy or consume Show Party [shou-shen pai] after it was found to contain undeclared sibutramine and phenolphthalein. 3. **Zeng Da Yan Shi Wan**: The Hong Kong Department of Health warned consumers not to buy or use after it was found to contain undeclared sildenafil.

Health Canada Jan/10 informs that Finish Food Safety Authority: **Full Contact Max Potency** contains thio-sildenafil and thio-homosildenafil; Singapore Health Sciences Authority: **M-Action** contains desmethylacetildenafil and acetilacid. U.S. FDA: **RockHard Weekend** contains sulfoaildenafil; & **Pai You Guo** contains sibutramine and phenolphthalein. Hong Kong Department of Health: **Ku Xiu Ba Xiang Jian Fei Wan** contains sibutramine and an unauthorized substance similar to sibutramine; **Super Slim (Yani)** contains sibutramine and phenolphthalein; **SHoufsy** contains sibutramine & **MIGAC (sic) FAT BURMING (sic) FACTOR** contains sibutramine.

Health Canada Jan/10 is advising consumers not to use the unauthorized product "**Stiff Nights**" after the U.S Food and Drug Administration (FDA) found that this product contains an undeclared substance similar to the prescription drug sildenafil.

Health Canada Jan/10 is warning consumers not to use the unauthorized product "**The Slimming Coffee**," which was previously sold as "**Lose Weight Coffee**," because it was found to contain sibutramine.

Health Canada Jan/10 is advising consumers not to use any unauthorized health products sold under the brand names **Natural Choice Vitamin B-17**, **Natural Choice Kava Kava** and **Natural Choice Lithium Orotate**. The unauthorized Natural Choice Vitamin B-17, according to what is listed on the product label, contains amygdalin which is a compound derived from bitter apricot kernels that has the potential to release cyanide when ingested by humans. The unauthorized Natural Choice Kava Kava, according to what is listed on the product label, contains kava lactones & agencies have received reports associating the use of kava with serious liver dysfunction.

Health Canada Jan/10 is advising Canadians that natural health products containing the ingredient **glucomannan** in tablet, capsule or powder form, which are currently on the Canadian market, have a potential for harm if taken without at least 8 ounces of water or other fluid.

Health Canada Feb/10 is advising consumers that the unauthorized product "**Complete 7-Day Cleanse**" is being recalled because it contains a number of active ingredients with a combined effect that may pose serious health risks. "Complete 7-Day Cleanse" is a multi-ingredient natural health product promoted for "cleansing" or removing toxins from the body. According to package labelling, the product contains over 30 active ingredients, some having a diuretic (water pill) or laxative (stimulant, and bulk-forming) effect.

Health Canada Feb/10: **2H & 2D**- Hong Kong Department of Health (HKDH) warned consumers not to buy or use 2H & 2Dafter it was found to contain undeclared tadalafil. Products distributed by **Atlas Operations Inc**. The FDA informed consumers of a voluntary recall by Atlas Operations Inc. of certain lots of some products that were found to contain undeclared sulfoaildenafil, which is an unauthorized substance similar to sildenafil. Products distributed by **Bodybuilding.com** The FDA informed consumers of a voluntary recall of 65 bodybuilding products as these products may contain the following anabolic steroids: "Superdrol," "Madol," "Tren," "Androstenedione," and/or "Turinabol." **STRO Emperor** Capsules The Irish Medicines Board warned consumers not to buy or use STRO Emperor Capsules after it was found to contain undeclared tadalafil. **Tian Yang Xu Huo Oral Ulcer** Capsule Singapore Health Sciences Authority issued a recall notice for one batch (batch number 0812003, expiry date 11.2011) of Tian Yang Xu Huo Oral Ulcer Capsuleafter it was found to contain undeclared aristolochic acid.

Health Canada Mar/10 is warning Canadians that an unapproved health product, **POWER-MAX** that contains sildenafil.

Health Canada Mar/10 is warning Canadians that an unauthorized health product, "**Herbal Diet Natural**" has been found on the Canadian market and contains an undeclared pharmaceutical ingredient similar to the prescription drug sibutramine.

Health Canada is warning Canadians that an unauthorized health product, "**West Pharm Therma Lean Fat Burner Energizer**" was found on the Canadian market. West Pharm Therma Lean Fat Burner Energizer contains Ephedrine and caffeine, which combined together, may cause serious and possibly fatal adverse effects.

Health Canada Apr/10 is warning Canadians that an unauthorized health product, "**Slim-30**" distributed in Ontario and Quebec by Duxx Enterprises Inc., contains an undeclared pharmaceutical ingredient similar to the prescription drug, sibutramine.

Health Canada May/10 consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **Ba Bao Xiao Ke Dan** The Hong Kong Department of Health warned consumers not to buy or use Ba Bao Xiao Ke Dan after it was found to contain undeclared glibenclamide. 2. **Bao Shu Tang Wu Zi Yan Zong Wan** The Hong Kong Department of Health warned consumers not to buy or use Bao Shu Tang Wu Zi Yan Zong Wan after it was found to contain excessive levels of lead, a heavy metal. 3. **Lin Yan Yin Chiao** The Singapore Health Sciences Authority issued a recall notice for one batch (batch# JI0324, expiry date 03/2011) of Lin Yan Yin Chiao after it was found to contain undeclared chlorpheniramine and paracetamol (acetaminophen). 4. **Man Power** The Hong Kong Department of Health warned consumers not to buy or use Man Power product after it was found to contain undeclared tadalafil. 5. 17 products sold through **MuscleMaster.com** (see Foreign Product Alert for a complete product list) The FDA informed consumers of a voluntary recall of the 17 bodybuilding products as they may contain the following anabolic steroids: "Superdrol," "Madol," "Tren," "Androstenedione," and/or "Turinabol." 6. **Seven Slim 7 Seshou** (Qingchun Shaonüxing, Jieshixing, Guifurenxing, Songchixing), Shoushen Jiaoguan-Tinei Yundong Wan (Jian Xiabanshen, Jian Quanshen Feipang) The Hong Kong Department of Health warned consumers not to buy or use the six products listed above after they were found to contain undeclared sibutramine and phenolphthalein.

Health Canada May/10 is advising consumers not to use 1. **Botanical Slimming 100% Natural Soft Gel, also sold as Meizitang** The Australian Therapeutic Goods Administration warned consumers not to buy or use this product after it was found to contain undeclared sibutramine. 2. **Marsha Slim Plus** The Hong Kong Department of Health warned consumers not to buy or use Marsha Slim Plus after it was found to contain undeclared sibutramine, an unauthorized substance similar to sibutramine and phenolphthalein. 3. **S&S Super Slender** The Hong Kong Department of Health warned consumers not to buy or use S&S Super Slender after two samples were found to contain agent similar to sibutramine. One of the tested samples also contained undeclared sibutramine and phenolphthalein.

Health Canada June/10 is warning Canadians that the unauthorized health products "**Vigofit**" and "**Once More**," which are promoted to enhance male sexual performance, have been seized by Health Canada inspectors from retail stores in Abbotsford and Surrey, British Columbia. These two products contain sildenafil.

Health Canada June/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **COMECOO, ZHONGCAOYAO-JIANKANGJIANFEI** The Hong Kong Department of Health warned consumers not to buy or consume these two products after they were found to contain undeclared phenolphthalein, sibutramine and two unauthorized substances similar to sibutramine. 2. **Qingzhi Santian Shou** The Hong Kong Department of Health warned consumers not to buy or consume Qingzhi Santian Shou after it was found to contain undeclared sibutramine and an unauthorized substance similar to sibutramine. 3. **Vita Breath** The U.S. FDA warned consumers not to buy or consume Vita Breath because it may contain hazardous levels of lead, which is a heavy metal.

Health Canada July/10 is advising consumers not to use the following foreign health product(s) due to concerns about possible adverse reactions: 1. **Stud Capsule For Men** The U.S. FDA informed consumers of a voluntary recall of one lot (Lot #060607-01/060108-01 Exp 6-2013) after it was found to contain undeclared Sildenafil. 2. **Po Chai Pills** (capsule form) The Hong Kong Department of Health warned consumers not to buy or use this product after it was found to contain undeclared sibutramine and phenolphthalein. Sibutramine is a prescription drug and should only be used under the supervision of a health care practitioner while phenolphthalein is no longer authorized for sale in Canada because it may cause cancer. Po Chai Pills (capsule form) has been recalled by the manufacturer. 3. **LiPO-8 Cap and Glucomi 600 Cap** The Hong Kong Department of Health warned consumers not to buy or use these products because they contain undeclared sibutramine.

Health Canada July/10 is advising Canadians about "**UP Ultimate Performance for Men**", an unauthorized health product containing undeclared sildenafil.

Health Canada July/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1 Body Beautiful** The Hong Kong Department of Health warned consumers not to buy or consume *1 Body Beautiful* after it was found to contain undeclared phenolphthalein and sibutramine. 2. **USA Yaku Cell Slimming Capsules, Dong Gua Pai You Su, Qing Gua Pai You Su, and Mu Gua Pai You Su** The Hong Kong Department of Health warned consumers not to buy or consume these four products after they were found to contain undeclared phenolphthalein, sibutramine and an unauthorized substance similar to sibutramine. 3. **Atlas Operations Inc. expands its U.S. recall of over 30 sexual enhancement supplements** The U.S. FDA informed consumers of an expanded recall of certain lots of products after some were found to contain undeclared sulfoaildenafil. The products are being voluntarily recalled nationwide in the U.S. by the company Atlas Operations Inc. 4. **Stallion, SZM Formula for Men, Tomcat Ali and Volcanic** New Zealand's Medsafe warned consumers not to buy or use these four products after they were found to contain undeclared tadalafil. 5. **Vitalex for men and Vitalex for women** The U.S. FDA informed consumers that the *Vitalex*products were found to contain acetildenafil, which is an unauthorized substance similar to sildenafil and may pose similar health risks.

Health Canada Aug/10 says **Fulda Unitang Herbs Sleep Plus**, an unauthorized product promoted as an herbal sleep aid, has been found to contain high levels of estazolam.

Health Canada July/10 Unauthorized Health Products Sold by **Marigold Natural Pharmacy Ltd**. May Pose Health Risks. These products (http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_2010/2010_126bk-eng.php) were made available to Canadians via the company's pharmacy in Courtenay, British Columbia and via their website (http://www.marigoldnaturalpharmacy.com).

Health Canada July/10 is advising consumers not to use the following foreign health product(s): **Huo Luo Jing Dan** The Singapore Health Sciences Authority warned consumers not to buy or consume Huo Luo Jing Dan after it was found to contain undeclared indomethacin, dexamethasone and prednisolone.

Kam Chik San The Hong Kong Department of Health (HKDH) cautioned against the use of **Kam Chik San** after samples were found to contain mercury at a level much higher than permitted by the HKDH. **Magic Power Coffee** The U.S. FDA warned consumers not to buy or use Magic Power Coffee after it was found to contain undeclared hydroxythiohomosildenafil, which is an unauthorized substance similar to sildenafil.
Que She The U.S. FDA warned consumers not to buy or use Que She after it was found to contain undeclared fenfluramine, propranolol, sibutramine and ephedrine. **Sheng Yuan Fang** The Hong Kong Department of Health (HKDH) warned consumers not to buy or use Sheng Yuan Fang after it was found to contain undeclared phenolphthalein and sibutramine.

Health Canada July/10 is informing Canadians that **Marché Euromix**, a retail store in Pierrefonds (Montréal), was found to be selling a health product that was not authorized for sale by Health Canada and that closely resembled in appearance an authorized drug, Viagra.

Health Canada Aug/10: "**SeXXX DRIVE**", promoted as a herbal supplement to enhance male sexual performance, & Health Canada found hydroxyhomosildenafil.
Health Canada Aug/10 has seized the unauthorized sexual enhancement supplements "**Male Enhancement ExtenZe**" and "**Women ExtenZe**" imported and sold by the Happy Paradise Adult Store in Burnaby, British Columbia. The labels of each of these unauthorized products list the prescription ingredient pregnenolone and the controlled drug, DHEA (dehydroepiandrosterone). The labels of the unauthorized "Male Enhancement ExtenZe Nutritional Supplements" list the ingredient yohimbe extract (bark).
Health Canada Sep/10 **E.O.D. Erection on Demand**" being promoted as a herbal to enhance male sexual performance, the product was tested by Health Canada and found to contain tadalafil.
Health Canada Sep/10: "**Arth-Forth**", an unauthorized product promoted as an herbal supplement and distributed by Ka Wing Hong Ltd., was tested by Health Canada and found to contain a steroid prescription drug, dexamethasone.
Health Canada Sep/10 is advising consumers not to use : 1. **Golden aryuru, Baisheng wei ge, Zhonghua niubian, Ten ka dai 1 bou, Kuai gan bei zeng chao yue zi wo (Happy felling doubly increase [sic]), Ling tou lang, SkyFruit, Chu bi ho ken, Jinbolang, Suika Koso, Lov, I ka ou (2009 nen sin hoso) and/or I ka ou (saisinsui shutsu hoso)** The Japanese Ministry of Health, Labour and Welfare warned consumers not to buy or use the 12 products listed above because they were found to contain undeclared sildenafil and/or other unauthorized substances similar to sildenafil that may pose similar health risks (norhongdenafil, acetil acid, and tioqinapiperifil). 2. **Joyful Slim Herb** Supplement The U.S. FDA informed consumers of a recall of one lot (#101408) of Joyful Slim Herb Supplement after FDA tests found it to contain undeclared desmethyl sibutramine. The lot is being voluntarily recalled nationwide in the U.S. by the company J & H Besta Corp. 3. **Vialipro** The U.S. FDA informed consumers of a recall of certain lots of Vialipro after FDA tests found product samples to contain undeclared sulfoaildenafil, which is an unauthorized substance similar to sildenafil and may pose similar health risks.
Health Canada Sep/10 **Exemption number**: This will help with the backlog of applications for a licence. Exemptions will be given to natural products that have passed an initial assessment of safety, quality, and efficacy. These products will be given an exemption number (EN)...instead of a Natural Product Number (NPN) or Drug Identification Number-Homeopathic Medicine (DIN-HM)...until they are fully reviewed by Health Canada.
Health Canada Nov/10 **Amana Care Seven Slim Herbal Capsules**: The Israel Ministry of Health informed consumers that it found the product Amana Care Seven Slim Herbal Capsules to contain undeclared sibutramine and residue of sildenafil. Arrow Brand Medicated Oil & Embrocation: The U.S. FDA warned consumers not to buy or use **Arrow Brand Medicated Oil & Embrocation** because it contains ingredients that are potentially poisonous, particularly in children. **Beijing 101 Hair Consultants: Hair Growth Formula D-2653-Band Hair Growth Tonic E-0583-D**: The Singapore Health Sciences Authority advised consumers to stop using one batch of these products (Beijing 101 Hair Consultants Hair Growth Formula D-2653-B batch# 20091201, and Hair Growth Tonic E-0583-D batch# 20091201) after testing of these batches revealed the presence of undeclared minoxidil.
101 Zhangguang: Gold 101 Super Effective Hair Growth Agentand Fabao 101D Doctor Zhao's Chinese Traditional Herbal Hair Care Formula: The Hong Kong Department of Health warned consumers not to buy or use these two products after they were found to contain undeclared minoxidil.
Health Canada Nov/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Goya–Bitter Melon - Miyura Fit'x Capsules** contained undeclared phenolphthalein and sibutramine **2. MasXtreme** contains undeclared aminotadalafil while the other (#911035) contains undeclared aildenafil and phentolamine **3. Mr. Magic Male Enhancer from Don Wands** contained hydroxythiohomosildenafil and sulfoaildenafil **4. So Hard for Men - Pulse8 for Women - The Rock – Tonic 66** contained the undeclared pharmaceutical substances tadalafil, sildenafil, and/or hydroxyhomosildenafil **5. Solo Slim Extra Strength - Revivexxx Extra Strength** contained undeclared didesmethyl sibutramine **6. TimeOut** contained undeclared hydroxythiohomosildenafil.
Health Canada Nov/10 "**Fat Burner No. 1**" (labelled in Chinese characters translated as "**Qian Mei Yin Zi**", an unauthorized Chinese herbal weight loss medicine, is being voluntarily recalled by Ying Tai TCM Supplying Ltd. after Health Canada lab tests revealed the product contains two pharmaceutical ingredients: a chemical similar to sibutramine (N,N- didesmethylsibutramine), and sildenafil.
Health Canada Dec/10 "**Durazest**" and "**Once More**": Certain lots of two male sex enhancement products recalled as they may pose serious health risks. Certain lots (listed below) of two health products promoted for male sexual enhancement, "Durazest for Men" and "Once More," have been voluntarily recalled by Natural Performance Products Ltd. Health Canada laboratory tests identified the presence of a chemical similar to tadalafil (nortadalafil) in one lot of each product.
Health Canada Dec/10 is informing Canadians that NorthRegentRx has begun to voluntarily recall its product, **ResurreXX** from the Canadian market. NorthRegentRx is requesting that wholesalers, distributors and retailers stop sale of this product since contained an undeclared substance "hydroxyhomosildenafil".
Health Canada Dec/10 has been advised "**Flat Stomach Concept Extra**" is being voluntarily recalled by Les Produits Naturels Leblanc Inc due to missing label statements related to duration of use, risks and contraindications. Information missing from the label of Flat Stomach, a product contained within the Flat Stomach Concept Extra kit, may result in potential chronic use of aloe, which can lead to bowel dependence, and electrolyte imbalance.
Health Canada Dec/10 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: 1. **Slimming Beauty Bitter Orange Slimming Capsule** (Slimming Beauty) The U.S. Food and Drug Administration warned consumers not to buy or use Slimming Beauty after FDA lab tests revealed that this product contains undeclared sibutramine. 2. **Shaguar, Signature Signergy, VIGRX (green capsule), VIGRX (white capsule), VigRx, VigRX Plus** New Zealand's MedSafe warned consumers to not buy or use these products after they were found to contain undeclared sildenafil, hydroxyhomosildenafil, thiosildenafil, and/or tadalafil. 3. **ArimaDex**, **Clomed** The U.S. Food and Drug Administration informed consumers that ArimaDex and Clomed are being recalled in the U.S. because they may contain an aromatase inhibitor. ArimaDex and Clomed are being voluntarily recalled by G.E.T. and KiloSports Inc., respectively.
Health Canada Dec/10 Three Probiotic Natural Health Products May Pose Serious Health Risks to Canadians with Milk or Soy Allergies. Consumers with milk or soy allergies are advised that three probiotic natural health products are being voluntarily recalled from the market because they are labelled as not containing dairy(milk) and/or soy but may contain trace amounts of milk or soy protein from ingredients used in the production process. **Saccharomyces Boulardii** (NPN 80013551) Advanced Orthomolecular Research Inc. (AOR); **Herbasaurs Bifidophilus for Kids** (NPN 80015508) & **Acidophilus Bifidobacterium** (NPN 80015336) by Nature's Sunshine Products of Canada Ltd & **Cultures de Yogourt 2 Milliards** (NPN 80013273 Bio-Dis Inc.
Health Canada Jan/11 The product **Synerate**, manufactured for Strive and distributed by Upper 49th, is being voluntarily recalled from the Canadian market because of the risk of serious, potentially fatal adverse effects from the combination of the ingredients in the product. Synerate, a product used for weight loss or body building, contains caffeine and synephrine, which is similar to ephedrine.
Health Canada Jan/11 **Nutrex Research Lipo 6X** is being voluntarily recalled from the Canadian market because of the risk of serious, potentially fatal adverse effects from the combination of the ingredients in the product. It contains caffeine and synephrine, which is similar to ephedrine.

Health Canada Feb/11 is advising consumers not to use the following foreign health products promoted for sexual enhancement due to the presence of unauthorized substances (PDE5 derivatives eg. sildenafil): **1. Aziffa, Erex, Eyeful, Hard Drive, Libidinal, Maxyte, Mojo, Monster Excyte, OMG, OMG45, Prolatis, Red Magic, Size Matters, Stiff Nights, Straight Up, Verect, WOW, Xaitrex, Xytamax, Zilex (with Golden Spear), Zotrex 2. Prolatis' Duro Extend Capsules For Men 3. Tiger King 4. Vigor-25, Man Up Now**

Health Canada Feb/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Fruta Planta, Reduce Weight Fruta Planta** The U.S. FDA warned consumers not to buy or use Fruta Planta and Reduce Weight Fruta Planta after FDA lab tests revealed that this product contains undeclared sibutramine. **2. RockHard Weekend (lots 100159 and 100260 sold as blister packs, 3-count bottles and 8-count bottles)** The U.S. FDA informed consumers of a nationwide voluntary recall of certain lots (see above) of RockHard Weekend and Pandora after lab tests confirmed the products contain an unauthorized substance similar to sildenafil that may pose similar heath risks. **3. Slimming Factor** The Australian TGA warned consumers not to buy or use Slimming Factor after TGA lab tests confirmed the presence of the undeclared substances sibutramine, fenfluramine and phenolphthalein. According to the TGA release, the product is sold over the Internet.

Health Canada Mar/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Celerite Slimming Capsules:** The U.S. FDA informed consumers of a company recall of Celerite™ Slimming Capsules after it was found to contain undeclared sibutramine. **2. Herbal Flos Lonicerae (Herbal Xenicol) Natural Weight Loss Formula:** The product was found to contain undeclared sibutramine at more than twice the dose that was normally prescribed before sibutramine was removed from the UK market in 2010. **3. Magicream:** The Irish Medicines Board warned consumers not to buy or use Magicream after it was found to contain undeclared clobetasol propionate and ketoconazole. **4. Nite Rider Maximum Sexual Enhancer for Men - STUD Capsule for Men:** The U.S. FDA informed consumers of a company recall of these products after they were found to contain undeclared sildenafil.

Health Canada April/11 Consumers with milk or soy allergies are advised that four probiotic natural health products {**Saccharomyces Boulardii (NPN 80013551), Herbasaurs Bifidophilus for Kids (NPN 80015508), Acidophilus Bifidobacterium (NPN 80015336), Cultures de Yogourt 2 Milliards (NPN 80013273)**} are being voluntarily recalled from the market because they are labelled as not containing dairy (milk) and/or soy but may contain trace amounts of milk or soy protein from ingredients used in the production process.

Health Canada Apr/11 has identified the presence of microbial contamination in "**Mary Ginseng House 100% Pure High Calibre Pow Sum Ontario Ginseng**", that may pose a health risk to immune-compromised individuals.

Health Canada May/11 "**Omega Alpha Kidney Flush**" Being Recalled from the Canadian Market: May Cause Serious Adverse Reactions in Pregnant Women and Kidney Disease Patients.

Health Canada May/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Dr. Health Series CM Factor** The Hong Kong Department of Health warned consumers not to buy or use this product after it was found to contain an unauthorized substance similar to sibutramine that may pose similar health risks. **2. Gold Seagull Long Zhi Wan, Venergy** The Hong Kong Department of Health advised consumers not to buy or use these products after Gold Seagull Long Zhi Wan was found to contain undeclared glibenclamide, while Venergy was found to contain undeclared sildenafil. **3. JianBu HuQian Wan** The HSA warned consumers not to buy or use JianBu HuQian Wan after it was found to contain undeclared dexamethasone and chlorpheniramine. **4. Rock Hard Extreme, Passion Coffee** The U.S. FDA advised consumers not to buy or use these products after they were found to contain undeclared sulfoaildenafil, which is an unauthorized substance similar to sildenafil and may pose similar health risks.

Health Canada July/11 "**Man Up Now**" Removed From Sale at Delta and Surrey Stores: May Pose Serious Health Risks to Canadians, was removed from sale at "O! Behave" retail stores in Delta and Surrey, B.C. after Health Canada's testing identified undeclared sildenafil.

Health Canada July/11 is advising Canadians that we have updated our list of unauthorized health products. These products were also removed from sale at Male and Female Harmony retail stores in Richmond and Burnaby, B.C., along with the Happy Paradise Adult Store in Burnaby. {**Sildenafil: in BAOLONG Switzerland Rolex 168 Prolong Time, BAOLONG Yilishen, Black Gold, Herbal Viagra, "Jin Chong Chao - Golden Cordyceps", Lubiangaowansu, MAGNA-RX, MAXMAN II capsules, Shenrong dabuwan, Traditional Chinese Medicine Viagra, V100, VIGER, VigRX for Men, VINIX capsules, Wolf, "XiongBaTian", Zang Gong Mi Lian Nan Bao} & Zeng Bei Jiu Zhan-Tadalafil.**

Health Canada July/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Beline Capsules** The U.K. Medicine and Healthcare products Regulatory Agency (MHRA) advised consumers not to use *Beline Capsules* after it was found to contain undeclared chlorpheniramine, an over-the-counter antihistamine drug. **2. Black Ant** The U.S. Food and Drug Administration warned consumers to immediately stop using *Black Ant* after it was found to contain undeclared sildenafil at an amount three times the starting dosage for the approved prescription drug product. **3. [Hua Tuo Brand] Youzhi Baoying Dan, [Lee Sze] Texiao Houtong Wan and Prolonged Man Power Essence** The Hong Kong Department of Health (HKDH) warned consumers to not use these products after they were found to contain excessive levels of mercury, lead, or arsenic, which are heavy metals. **4. Natural Vigra VIAGRA Tablets and Satibo Capsules** The Australian Therapeutic Goods Administration (TGA) advised consumers to stop using *Natural Vigra VIAGRA Tablets* after it was found to contain undeclared sildenafil, and *Satibo Capsules* after it was found to contain undeclared tadalafil and hydroxyhomosildenafil. **5. Slim Xtreme Herbal Slimming Capsules** The U.S. Food and Drug Administration informed consumers of a voluntary recall after *Slim Xtreme Herbal Slimming Capsules* was found to contain undeclared sibutramine. **6. X-Hero and Male Enhancer** The U.S. Food and Drug Administration informed consumers of a voluntary recall after *X-Hero* was found to contain undeclared sulfosildenafil while *Male Enhancer* was found to contain undeclared tadalafil.

Health Canada July/11 is advising Canadians that we have updated our list of unauthorized health products to include a new product, **Tibet Babao**, which was found to contain undeclared sildenafil, a prescription erectile dysfunction drug. This product and several others have been removed from sale at the **Happy Paradise Adult Store in Burnaby, B.C**.

Health Canada Aug/11 is advising consumers not to use the following foreign health products due to concerns about possible adverse reactions: **1. Celerite Slimming Tea** The U.S. FDA informed consumers of a company recall of Celerite Slimming Tea after it was found to contain undeclared sibutramine. **2. Pink Lady for Women Capsules, St Nirvana Herbal Slimming Capsules** The Australian TGA warned consumers not to use these products after Pink Lady for Women Capsules was found to contain undeclared tadalafil while St Nirvana Herbal Slimming Capsules was found to contain undeclared sibutramine and phenolphthalein. According to the TGA advisories, these products are sold over the Internet. **3. Fifteen products promoted for weight loss** The Hong Kong Department of Health (HKDH) warned consumers not to buy or use these 15 products after they were found to contain at least one of the following undeclared substances: phenolphthalein, sibutramine, and/or an unauthorized substance similar to sibutramine.

Health Canada Sep/11 **Bi Yan Pian** Recalled Due to Excessive Amount of Mercury. Wing Quon Enterprises Ltd has initiated a stop sale and is voluntarily recalling a natural health product, Bi Yan Pian (NPN# 80023876) from the Canadian market after the product was found to contain an excessive amount of mercury.

Health Canada Oct/11 is advising Canadians not to use these foreign health products as they may pose a health risk. **Slim Forte Slimming Capsules**, **Slim Forte Double Power Slimming Capsules**, **Slim Forte Slimming Coffee** and **Meizitang Botanical Slimming Soft Gel**-The U.S. Food and Drug Administration warned that these weight loss products contain an unauthorized drug (sibutramine). **OxyELITE Pro capsules and Pure Fat Three Days Reduce Weight capsules**- The Australian Therapeutic Goods Administration warned that these weight loss products contain an unauthorized drug (sibutramine), or a prescription drug (yohimbine). **SXL Sexcellence sachets**- The Australian Therapeutic Goods Administration warned that this sexual enhancement product contains an unauthorized drug (sulfosildenafil). [W.S] **Gan Mao Ling and Chaisentomg Baby's Kam Chik San Powder** - The Hong Kong Department of Health warned that these Chinese health products contain excessive levels of heavy metals (lead or arsenic). **Huo Li Bao and Ren Sem Tu Chon Chin Kuo Pill** - The Singapore Health Sciences Authority warned that these Chinese pain-relief products contain prescription and/or over-the-counter drugs (furosemide, piroxicam, chlorpheniramine, and/or dexamethasone).

Health Canada Nov/11 is advising Canadians not to use these foreign health products as they may pose a health risk. **1. Zhui Feng Bao Wei San** The Singapore Health Sciences Authority warned that this health product contains excessive levels of microbial contamination. **2. Metabolic Advantage** The Singapore Health Sciences Authority warned that this weight-loss product contains prescription drugs (thyroid hormones). **3. Majun Dua Istimewa, Raja Maajun-Jerat Dan Seret Angin, and Horkut Chooi Foong Hor Lok Tan** The Singapore Health Sciences Authority warned that these traditional medicines contain undeclared prescription and over-the-counter drugs (dexamethasone, indomethacin, chlorpheniramine, dextromethorphan and acetaminophen). **4. Tian Ma Tu Chung Seven Leave Ginseng, Vall-Boon Tongkat Al, and Pao Ni Kang** The Singapore Health Sciences Authority warned that these traditional herbal products contain prescription and over-the-counter drugs (dexamethasone, ketoconazole, repaglinide, pheniramine, and chlorpheniramine). **5. Slimming Kapsul** The Hong Kong Department of Health warned that this weight-loss product contains an unauthorized drug (sibutramine) and a prescription drug (spironolactone). **6. Pancre-Plus** The Hong Kong Department of Health warned that this counterfeit Chinese medicine contains an unauthorized drug (phenformin) and a prescription drug (glyburide). **7. Maxidus capsules, Chao Jimengnan SuperPowerful Man tablets, Fu Yuan Chun capsules, and Qing Tian Zhu tablets** The Australian Therapeutic Goods Administration warned that these sexual enhancement products contain prescription drugs (sildenafil, tadalafil) and/or unauthorized drugs (sulfohydroxyhomosildenafil, sulfosildenafil).

Health Canada Nov/11: An unauthorized health product, "**Stiff One Hard 169**" is being voluntarily recalled from the Canadian market after Health Canada's testing identified an undeclared prescription medication in the product (thiodimethylsildenafil, an undeclared substance similar to the prescription medication sildenafil).

Health Canada Dec/11 is advising "**Yanshiwang**", "**Jin Kong Fu**" and "**Chong Cao She Bian Zhuang Yang Dan**". These products were removed from sale at Male and Female Harmony retail stores in Richmond and Burnaby, B.C., along with the Happy Paradise Adult Store in Burnaby. These contained sildenafil.

Health Canada Jan/12 advises: 1)**17 weight loss products (see Alert for a complete list)** A-Slim 100% Natural Slimming Capsule, Acai Berry Soft Gel ABC, Advanced Slim 5 > DaiDaiHuaJiaoNang, Dream Body Slimming Capsule, Fruit Plant Lossing Fat Capsule, Health Slimming Coffee, Ja Dera 100% Natural Weight Loss Supplement, Leisure 18 Slimming Coffee, Lishou, Magic Slim Tea, Magic Slim Weight Reduction Capsule, P57 Hoodia, Pai You Guo Slim Tea, PhentraBurn Slimming Capsules, Slender Slim 11 Tengda. The U.S. Food and Drug Administration warned that these weight loss products contain unauthorized drugs (sibutramine, phenolphthalein). **2. Uprizing 2.0** The U.S. Food and Drug Administration warned that this body building product contains a controlled prescription drug (superdrol). **3. Get Stiff, Maxi Mize** New Zealand's Medsafe warned that these sexual enhancement products contain prescription drugs (tadalafil, vardenafil, yohimbine) and/or unauthorized drugs (hydroxyhomosildenafil, hydroxythiohomosildenafil). **4. Ying Da Wang tablets** The Australian Therapeutic Goods Administration warned that this sexual enhancement product contains a prescription drug (sildenafil). **5. Slimina weightloss capsules, S-shape slim capsules** The Australian Therapeutic Goods Administration warned that these weight loss products contain prescription drugs (propranolol, nifedipine) and/or unauthorized drugs (sibutramine, fenfluramine, phenolphthalein). **6. Athri-Eze, Sear Heang Tienchi Tu Chung Wan, Wiku Jahe Kencur (Akur Mujarab), Cap Wijaya Kusuma (An Ki It)** The Singapore Health Sciences Authority warned that these Traditional Chinese or Traditional Malay Jamu products contain prescription and/or over-the-counter drugs (dexamethasone, prednisolone, furosemide, allopurinol, acetaminophen, chlorpheniramine), and/or an unauthorized drug (phenylbutazone). **7. Cardiotium, Paidusu, SlimEasy Herbs Capsule, Tianran Zuanshi Xianweisu** The Hong Kong Department of Health warned that these health products contain prescription drugs (losartan, atorvastatin, thyroxine) and/or unauthorized drugs (sibutramine, phenolphthalein). Consult a health care practitioner immediately if you have taken "Cardiotium" while pregnant. The use of losartan during pregnancy can cause injury and even death to the fetus. **8. [LuShenPai] Specific Hou Ton Qing, [AA] Pe Min Kan Wan** The Hong Kong Department of Health warned that these traditional Chinese health products contain excessive levels of heavy metals (arsenic or mercury).

Health Canada Feb/12 is advising Canadians that using "MMS", also known as **Miracle Mineral Solution or Miracle Mineral Supplement** may cause serious health problems. The product information lists sodium chlorite as an ingredient and is promoted as a substance that can cleanse toxins from the human body.

Health Canada Feb/12 seized a variety of **Stiff4Ever** and **PurePillz** products from The Love Shop retail outlets located in Ontario. These products are unauthorized drugs and are considered potentially dangerous to the health and safety of Canadians. Health Canada tested the Stiff4Ever products, advertised as male sexual stimulants, and identified sildenafil. The labels of the PurePillz products (see below) state that they contain BZP and TFMPP. Benzylpiperazine (BZP) is a synthetic substance with stimulant-like effects, while 3-trifluoromethylphenylpiperazine (TFMPP) is a synthetic substance with hallucinogen-like effects.

Health Canada Mar/12 **Power-X**" has been removed from a Canadian retail location after Health Canada's testing identified undeclared thiodimethylsildenafil which is similar to the prescription medication sildenafil.

Health Canada May/12: Unauthorized health products, **"X-Rock", "Kaboom" and "One For Her"** have been removed from sale from various retail outlets in British Columbia and Saskatchewan. Health Canada's testing identified undeclared prescription drugs sildenafil and tadalafil, and an undeclared substance, hydroxythiohomosildenafil, which is similar to sildenafil.

Health Canada May/12 **1. CanSui; Lexscl Fat Rapid Loss Capsule; The Extreme-thin Fat Burning Bomb; Xiu Zhi Su L-Carnitine Slimming Capsule** The Hong Kong Department of Health warned that these weight loss products contain unauthorized drugs (sibutramine, phenolphthalein). **2. Jin Yu Tang Tai Han Kang Pai Pu Ling Jiao Nang; TangBaoKouFuYiDaoSuJiaoNang; Tangren 365 Kangxunpai sangge huoyisu jiaonang; Tong Ren Xiu Fu Kou Fu Yi Dao Su** The Hong Kong Department of Health warned these products, promoted to control high blood sugar, contain a combination of prescription drugs (metformin, glibenclamide [also known as glyburide], rosiglitazone, glimepiride, hydrochlorothiazide) and unauthorized drugs (phenolphthalein, phenformin). **3. [Chung Lien Kulin Brand] Anshen Bunai Pian** The Hong Kong Department of Health warned that this traditional Chinese health product, used for insomnia, contains excessive levels of the heavy metal mercury. **4. Lipro Diet Pills; Xiyouji Qingzhi weight loss capsules** The Australian Therapeutic Goods Administration warned that these weight loss products contain an unauthorized drug (sibutramine). **5. AdvanceMen capsules; Miraculous Evil Root tablets** The Australian Therapeutic Goods Administration warned that these sexual enhancement products contain either a prescription drug (sildenafil) or an unauthorized drug (sulfoaildenafil).

Health Canada June/12 **1. African Black Ant; France T253; Hard Ten Days; Man King; Stree Overlord** : The U.S. Food and Drug Administration warned that these sexual enhancement products contain prescription drugs (sildenafil. One product also contains tadalafil). **2. RegenArouse; RegenErect:** The U.S. Food and Drug Administration informed of a recall because these sexual enhancement products contain a prescription drug (tadalafil). **3. Mince Belle; Everlax; Ever Slim; Ever Slim Shake Mix (Strawberry); Ever Slim Shake Mix (Chocolate); Acai-Man Mangosteen Herbal Drink; Perfect Men:** The U.S. Food and Drug Administration informed of a recall because these weight loss and sexual enhancement products contain prescription drugs (sibutramine or tadalafil). **4. Japan Weight Loss Blue, Japan Rapid Weight Loss Diet Pills Green; Japan Rapid Weight Loss Diet Pills Yellow:** The U.S. Food and Drug Administration warned that these weight loss products contain prescription drugs (sibutramine, ephedrine alkaloids) and unauthorized drugs (phenolphthalein, and substances similar to sibutramine). **5. Koff & Kold; Kold Sore:** The U.S. Food and Drug Administration informed of a recall because these cough and cold products were found to be non-sterile. **6. Ling Zhi She Xiang Tong Mai Dan:** The Hong Kong Department of Health warned this health product contains a prescription drug (dexamethasone). **7. Q & N Omega Tree:** The Singapore Health Sciences Authority informed of a recall after this product was found to contain controlled drug substances (cannabinol and tetrahydrocannabinol (THC)).

Health Canada June/12 **Natural Vigor Maximum** (Exemption Number: 138273) has been removed from sale from various retail outlets in Ontario after testing by Health Canada identified a hidden ingredient (dimethylhomosildenafil).

Health Canada Jun/12 testing has identified that the weight loss product "**ZXT Gold**" bee pollen capsules contain hidden pharmaceutical ingredients (sibutramine and phenolphthlalein).

Health Canada July/12 **Lightning Rod**, an unauthorized sexual enhancement product, has been removed from sale from various retail outlets in Ontario, British Columbia and Saskatchewan after testing by Health Canada identified a hidden ingredient (hydroxythiohomosildenafil).

Health Canada July/12 "**Fu Fang Zaoren Jiaonang**": A Potentially Dangerous Product for Pregnant Women. "Fu Fang Zaoren Jiaonang," an unauthorized natural health product promoted for anxiety and/or insomnia, has been removed from sale after testing by Health Canada confirmed the presence of the ingredient L-tetrahydropalmatine that could cause damage to vital organs such as the liver, most notably in pregnant women.

Health Canada July/12 **Vine Essence** has been recalled after testing by Health Canada identified a quantity of lead that exceeds Departmental acceptable limits and low levels of undeclared acetaminophen.

Health Canada Aug/12 These products are not authorized for sale in Canada and have not been found on the Canadian market, but they may have been brought into the country by travellers or purchased over the Internet. **1. Boost – Ultra Sexual Enhancement Formula; EreXite; Mojo Nights:** The U.S. Food and Drug Administration advised consumers not to buy or use these products after they were found to contain one or more of the following undeclared drug ingredients: tadalafil, sildenafil, and unauthorized substances similar to sildenafil that may pose similar health risks. **2. Firminite; Extra Strength Instant Hot Rod; Libidron:** The U.S. Food and Drug Administration informed consumers of a company recall after these products were found to contain undeclared tadalafil. **3. [Hu Qiu] Niu Huang Xiao Yan Wan:** The Hong Kong Department of Health warned consumers to not use this product after it was found to contain an excessive level of mercury. **4. Instant Hard Rod; RigiRx Plus; ZenMaxx**: The U.S. Food and Drug Administration advised consumers not to buy or use these products after they were found to contain undeclared aminotadalafil, which is similar to tadalafil and may pose similar health risks. **5. VMaxx Rx:** The U.S. Food and Drug Administration informed consumers of a company recall of certain lots of *VMaxx Rx* after the product was found to contain undeclared sulfoaildenafil.

Health Canada Aug/12: **Burnaby, B.C. Store (U-Box) Selling Potentially Dangerous Weight Loss Products.** Further to our previous communications, Health Canada is advising Canadians that four products promoted for weight loss have been seized from "U-Box," a store in Burnaby, B.C. Health Canada testing has identified they contain hidden drug ingredients (sibutramine and phenolphthalein) that may pose serious health risks. Caffeine was also found in some of the products and was not listed on the product label.

Health Canada Sep/12: **Zhuifeng Tougu Wan**", an unauthorized natural health product, is being voluntarily recalled after testing identified levels of mercury that are far beyond the allowable limit set by Health Canada.

Health Canada Oct/12 The natural health product "**Pollen Allergy**" (NPN 80035736), now sold as "**Tongqiao Biyan Pian**," is being recalled from the Canadian market after testing conducted by

Health Canada identified levels of arsenic that exceed Departmental allowable limits.

Health Canada Dec/12 Three unauthorized health products -- "**Man Up Now", "Black Ant", "Triple Power Zen Gold 1200mg**"-- are being recalled by DVDXPRO after testing by Health Canada identified undeclared ingredients-sildenafil and/or tadalafil.

Health Canada Dec/12 is advising Canadians that three unauthorized products "**Goya Bittermelon", "S-organic Cocoa+L-carnitine", or "KaBaNa L-Carnitine 360 Slimming Coffee**", promoted for weight loss have been seized from "Cube Inc.", a box-store in Richmond, B.C. These products contain hidden drug ingredients (sibutramine and phenolphthalein) that may pose serious health risks. Caffeine was also found in two products and was not listed on the product label.

Health Canada Dec/12 is advising Four unauthorized natural health products have been removed from sale as they may pose serious risks to the health of Canadians. The "**ExtenZe**" products are promoted as sexual enhancement products and contain ingredients that legally require they be sold with a prescription in Canada. ExtenZe Max Strength Gelcaps, ExtenZe Original Tablets, ExtenZe Natural Female Tablets, and ExtenZe Big Cherry Flavour Liquid: Three of these unauthorized products list the prescription ingredient pregnenolone and the controlled drug DHEA (dehydroepiandrosterone) & three of these unauthorized products contain the prescription medication yohimbine (either as yohimbine HCl or as yohimbe extract).

Health Canada Jan/13: 1) **Muscletech Hydroxystim capsules**- The Australian Therapeutic Goods Administration (TGA) warned consumers not to purchase or use this product after it was found to contain 1,3-dimethylamylamine (DMAA), a drug that is not approved for sale in Canada. **2. [W.S.] Tian Ma Toutong Wan; Shi Hu Ye Guang Wan (Ye Guang Wan); Nai Chang Ming Yan Pills (Ming Yan Pills); [Fung Shing Pai] Tian-Ma Wan; Bak Foong Pills (11 products) .** The Hong Kong Department of Health has warned consumers not to purchase or use certain batches of these products after they were found to contain excessive levels of lead or mercury.

Health Canada Feb/13: Two unauthorized health products "**18 Again" and "Stiff 4 Hours**" were tested by Health Canada and were found to contain hidden ingredients (sildenafil or tadalafil) that may pose serious risks to the health of Canadians.

Health Canada Mar/13: An unauthorized natural health product, "**Libigrow**" was tested by Health Canada and found to contain hidden ingredients (sildenafil and tadalafil) that may pose serious risks to the health of Canadians. "Libigrow" was being sold at two retail locations in the province of Québec: Boutique Sexie folie Inc. (Sainte-Catherine) and at Boutique Érotique 5ième avenue Inc. (Valleyfield).

Health Canada Apr/13 **1. Diet Garcinia Forte; Shan Dian Shou; Aulura Energy Dietary Supplement** The Hong Kong Department of Health has advised consumers not to use these products after they were found to contain sibutramine and phenolphthalein, drug ingredients that were not declared on their product label. Shan Dian Shou also contains the undeclared prescription drug sildenafil. **2. Snake Powder Capsule for Rheumatism; Jia Rong Zhuang Gu Tong Bi Jiaonang; Long Ren Tang Fu She Gu Rang Jiao Nang** The Hong Kong Department of Health advised consumers not to use these products after they were found to contain multiple prescription and non-prescription drugs that were not declared on their product label. (prednisone, indomethacin, diclofenac, hydrochlorothiazide, cimetidine, prednisone, theophylline, dexamethasone etc). **3. Tinea Schwartz's; Tiao Jing Bu Xue Pills; Yeung Ng Tong Tin Hee Pills** The Hong Kong Department of Health advised consumers not to use these products after they were found to contain prescription drugs that were not declared on their product label (prednisone, indomethacin, diclofenac). **4. Quan Xie Jin Gu Tong; Xinhuang Pian; Jin Gu Feng Shi Kang Jiao Nang** The Hong Kong Department of Health advised consumers not to use these products after they were found to contain multiple prescription and non-prescription drugs that were not declared on their product label. (prednisone, piroxicam, diclofenac, indomethacin, naproxen).

Health Canada May/13 Two unauthorized health products — **"Stiff Nights" and "Stiff 4 Hours"** — were tested by Health Canada and were found to contain hidden ingredients (sildenafil and/or tadalafil) that may pose serious risks to the health of Canadians. The products were being sold at Saints N Sinners Ltd, 1715 Centre Street N.W., Calgary, Alberta.

Health Canada June/13 is advising Canadians not to use these foreign health products as they may pose a health risk. **1. Flutulang, Kapsul Gaut (Asam Urat), and True ProLife Vegrow** The Health Science Authority of Singapore advised consumers not to use these products after they were found to contain phenylbutazone, chlorpheniramine, dexamethasone, and a chemical compound similar to the prescription drug sildenafil. **2. Jinmaoshiwang tablets, Naturally Kouxan Best Slim capsules, and Majestic Slimming capsules** The Australian Therapeutic Goods Administration advised consumers not to use these products after they were found to contain sildenafil, sibutramine and phenolphthalein. **3. WOW, Super Power and SLIMDIA Revolution** The U.S. Food and Drugs Administration (FDA) warned consumers not to use these products after they were found to contain diclofenac sodium, methocarbamol, dexamethasone, sildenafil and sibutramine. **4. Libigrow XXXtreme, Blue Diamond, Blue Diamond Platinum, Mojo Nights Supreme, and Casanova** The U.S. Food and Drugs Administration warned consumers not to use these products after they were found to contain sildenafil, sulfoaildenafil and thioaildenafil.

Health Canada Aug/13 is advising Canadians not to use these foreign health products as they may pose a health risk. **1. Brazilian Slimming Coffee, Leisure 18 Slimming Coffee, 7 Days Slimming Coffee, Brazilian 7 Days Slimming Coffee, Beauty Secret Slimming Coffee, Body Beauty 5 Days Slimming Coffee, Leisure 18 Slimming Mango Juice, Leisure 18 Slimming Orange Juice, Authentic Leisure 18 Slimming Orange Juice, Super Slim Orange Juice, Coffee Fashion Slimming** The Hong Kong Department of Health has advised consumers not to use these products after they were found to contain the undeclared drug ingredients sibutramine and/or phenolphthalein. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/34859a-eng.php **2. Steelman Capsules 2** The Hong Kong Department of Health has advised consumers not to use this product after it was found to contain undeclared aminotadalafil. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/34861a-eng.php **3. CO Feng Shi Gu Tong Ning Jiao Nang** The Hong Kong Department of Health has advised consumers not to use this product after it was found to contain undeclared prednisone, diclofenac, ibuprofen, hydrochlorothiazide, metoclopramide and trimethoprim. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/34861a-eng.php **4. Fu Fang Feng Shi Gu Kang Ling Jiao Nang** The Hong Kong Department of Health has advised consumers not to use this product after it was found to contain undeclared prednisone, diclofenac, ibuprofen, indomethacin, piroxicam and metoclopramide. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/34861a-eng.php **5. Best Slim capsules, Meizi Evolution Botanical Slimming soft gel capsules** The Australian Therapeutic Goods Administration warned consumers not to use these products after they were found to contain the undeclared drug sibutramine. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/34869a-eng.php **6. Libigirl capsules** The Australian Therapeutic Goods Administration warned consumers not to use this product after it was found to contain the undeclared prescription drugs sildenafil and tadalafil. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/34869a-eng.php **7. Albuterex Xtreme Formula** The Australian Therapeutic Goods Administration has warned consumers not to use this product after it was found to contain undeclared theophylline, yohimbine and high amounts of undeclared caffeine. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/34863a-eng.php **8. Albutarex Xtreme and Albutarex Femme Formula** The Australian Therapeutic Goods Administration has warned consumers not to use these products after they were found to contain undeclared theophylline and high amounts of undeclared caffeine. http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/34863a-eng.php

Health Canada Aug/13 **Prema G** (Granules packaged in tea packets, NPN: 80035944) was tested by Canada Border Services Agency and found to contain a hidden ingredient (hydroxyhomosildenafil thione).

Health Canada Oct/13 is warning consumers not to use unauthorized **Compound Danshen Dripping Pills** after it was associated with a Canadian case of methemoglobinemia, a rare but serious condition which may result in coma or death.

Health Canada Oct/13 Natural health product (**Spectrazyme**) recalled due to potential contamination with the antibiotic chloramphenicol. Metagenics Canada, in consultation with Health Canada, is voluntarily recalling its natural health product "Spectrazyme" – a digestive aid – due to a possible contamination with chloramphenicol, an antibiotic that may pose serious health risks to consumers.

Health Canada Oct/13 Natural health product (**Flora Essentials**) recalled due to potential contamination with the antibiotic chloramphenicol.

Health Canada Oct/13 Natural health products (**Kamizym-U and Kamizym+)** recalled due to potential contamination with the antibiotic chloramphenicol.

Health Canada Oct/13 wishes to inform Canadians that seized natural health products being sold by Lion King Health Enterprises Group Ltd., 1328-8368 Capstan Way, Richmond, BC. were tested and found to contain hidden ingredients and unauthorized substances similar to the prescription drug, sildenafil. (**North America Dami Ana 600mg, South America Maca 600mg, Ashwagandha 600mg, Optimusman 350mg, Superman 350mg, Innerget Instant Erection (NPN#80041194), Innerget Prolonged Performance (NPN#80041194), Innerget Everlasting Strength (NPN#80041194), Megaton 2080**.)

Health Canada Nov/13 is advising Canadians not to use these foreign health products as they may pose a health risk. These products have been found by regulators in other countries to contain drug ingredients or soy milk allergens that are not declared on the product labels, or a high level of microbial contamination. Prescription drugs should only be taken under the supervision of a healthcare professional. These products are not authorized for sale in Canada and have not been found on the Canadian market, but they may have been brought into the country by travellers or purchased over the Internet:

1. **Protein Extract and artiph**en http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36237a-eng.php ;
2. **Aisiyuan V26 Slimming Granules, AcaiBerry Living-XS, and 4C Cosmoslim** , http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36269a-eng.php ;
3. **MAXILOSS Weight Advanced** http://healthycanadians.gc.ca/recall-alert- rappel-avis/hc-sc/2013/36197a-eng.php;
4. **14 sexual enhancement products** http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36233a-eng.php ;
5. **Ginseng Baji Gu Ci Wan, Tu Chong Ginseng Wan Le Seang and X-Tract Nature** http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36359a-eng.php ;
6. **Ziyinzhuangyang tablets, Maxman III, and Mojo Risen** http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36519a-eng.php ;
7. **Kyuwei** http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36515a-eng.php ;
8. **ESV Extra Strong Version, MSV Strong Version, RL Rapid Loss, My Slimmer Me (MSM) soft gel capsules, Natural Miaotiaoyishen capsules, and Paiyouji Natural Slimming Capsules** http://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2013/36521a-eng.php.

Health Canada Dec/13 has updated the list of natural health products seized from **Lion King Health Enterprises Group** Ltd., 1328 - 8638 Capstan Way, Richmond, B.C. that have been tested and found to contain hidden ingredients and unauthorized substances similar to the prescription drug tadalafil.

Health Canada Dec/13 General Nutrition Centres Company (GNC), in consultation with Health Canada, is voluntarily recalling its natural health product "**Women's Phytoestrogen Formula**" – used for the relief of menopausal symptoms – due to possible contamination with chloramphenicol.

Health Canada Dec/13 testing of an unauthorized natural health product, **MaxHIMize**, found it to contain bacteria (Enterococcus durans and Bacillus spp) and undeclared caffeine that could present a risk to health. MaxHIMize is being promoted as a dietary supplement and for erectile dysfunction.

Health Canada Feb/14: 1. **Hairegenerator** The Hong Kong Department of Health warned consumers not to use this product after samples of the product were found to exceed the permissible limit for mercury. The level of mercury exceeds Health Canada's acceptable limits as well. 2. **Li Long Mei Guo Mo Bang, and Ginseng Tu chong Wan Lin Heong** The Singapore Health Sciences Authority warned consumers not to use this product after it was found to contain sildenafil, a drug ingredient that was not declared on the product label. 3. **Lightning 10.0+, LV Shou Reduces Fat, and STB Summit of the Thin Body S Woman Degreasing Burning Pill** The Hong Kong Department of Health warned consumers not to use this product after it was found to contain sibutramine, phenolphthalein, and indomethacin.

Health Canada Mar/14 is advising Canadians not to use these foreign health products as they may pose a health risk. 1. Xiang Gang Tian Long Sheng Wu Ke Ji Di Qi Dai Chi Jiu Zhan Shen http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2014/38599a-eng.php was found to contain **sildenafil**. 2. Various Sexual Enhancement Products http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2014/38577a-eng.php was found to have **sildenafil** and **tadalafil.** 3. Majestic Slim Perfect and Yixiu L-Carnitine Slimming Capsules http://www.healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2014/38609a-eng.php was found to contain **sildenafil** and **phenolphthalein.**

Health Canada Mar/14: **Zyrexin**, tested by Health Canada at the border was found to contain a hidden prescription drug ingredient **(Yohimbine)** .

Health Canada Apr/14 has seized the unauthorized drug, "**L-Showm Weight Loss Pills**", being sold at the U-Box store, located at 2809-4500 Kingsway, Burnaby, BC. Health Canada testing found that it contained an undisclosed ingredient, phenolphthalein.

Health Canada Apr/14: Four unauthorized drugs being sold at two SVN FUEL stores - one in Burnaby and one in Coquitlam, B.C. - were seized by Health Canada as they contain ingredients that are potentially dangerous to the health of consumers. The products, and the unapproved ingredients they contain, include **Jack3d** (DMAA (1, 3-dimethylamylamine), **Red Rockets** (ephedrine and caffeine), **West Pharm Therma Lean** (ephedrine and caffeine), and **OxyElite Pro** (1, 3-dimethylamylamine HCl and Yohimbe Bark extract). They were being promoted for weight management.

Health Canada Apr/14: 1) **San Xiao Ping Tang Jin Qi Jiao Nang**: The Hong Kong Department of Health warned consumers not to use this product after it was found to contain phenformin, pioglitazoneand glibenclamide**. 2) Volcano Male Enhancement** liquid & caps: The U.S. Food and Drug Administration warned consumers not to use these products after they were found to contain desmethyl carbodenafil, dimethylsildenafil and dapoxetine**. 3) Dr. Larry's Tranquility**: The U.S. Food and Drug Administration warned consumers not to use this product after it was found to contain undeclared doxepin and chlorpromazine.

Health Canada Apr/14: Nano Well-being Health Inc. issued a voluntary recall of **Super Arthgold**, 500 mg capsules to the consumer level. FDA laboratory analysis has found the product to contain chlorzoxazone, diclofenac and indomethacin, making it an unapproved new drug.

Health Canada May/14 **Blue Stinger** contains sulfoaildenafil**; 72 HP, Evil root and Pro Power Max** contains sildenafil**; Esbelin siloutte te, Esbelin Siloutte Herbal blend with L-Carnitine, Esbelder man**, **Esbelder fem, Esbelder siloutte** contains Sibutramine, N-Desmethylsibutramine, and N-di-Desmethylsibutramine; **Instant Slim** contains sibutramine and phenolphthalein; **Jack Rabbit** contains sildenafil and tadalafil**; Live Clinical 90 caps** contains milk, **Ortiga** contains diclofenac.

Health Canada May/14 One lot of **Lite Fit USA (**Lot Number 13165, Exp. 05/17) is being voluntarily recalled in the U.S. after analysis by the U.S. Food and Drug Administration revealed the lot contains the undeclared prescription drug sibutramine.

Health Canada May/14 has requested that Christmas Natural Foods Ltd. stop selling and recall its unauthorized health product, **Heartland Natural Wild Yam Moisturizing Cream**, after testing conducted by the Department identified a undisclosed prescription drug ingredient, progesterone.

Health Canada May/14: 1. **VitaliKOR**: FDA found vardenafil and tadalafil**;** 2. **Slim Fortune, Lidiy & Slim Expert** FDA found sibutramine**;** 3. **Vigor Tea sachets:** Australian Therapeutic Goods Administration found sulfoaildenafil**;** 4. **Prolifta capsules, PHUK and Virilis Pro:** FDA found **sildenafil;** 5. **Dr. Mao Slimming capsules, Perfect Body Solutions, Burn 7**: FDA found sibutramine; **Bella Vi Insane Amp'd Up, Be Inspired, Goodliness Fat Reducing capsules, Jimpness Beauty Fat Loss capsule**s: FDA found sibutramine and phenolphthalein; 6. **Nature Most Laboratories Vanilla Almond, and Strawberry Banana Whey Power products**: FDA found undeclared milk, soy and almond allergens**;** 7. **Wood-E, Xzen Gold, Xzen XPress, XZen 1200, and XZone Premium**: FDA found Wood-E contains sildenafil, Xzen Gold and Xzen XPress contain sildenafil and tadalafil, & XZen 1200 contains tadalafil.

Health Canada June/14: **Bali Mojo & Vimax** contains tadalafil., **LOVher capsule**s contains tadalafil, sildenafil and diclofenac. **Erec-Bull,** contains yohimbine. **Best Whips & JINQIANGBUDOR Red Dragon** contains sildenafil. **Super Hard t**ablets contains sildenafil. **CONTROL All Natural Sexual Enhancement** contains sulfoaildenafil and dimethylsildenafil. **Phen Tabz contains dimethylamylamine (DMAA). Asset Extreme, Asset Extreme Plus, Meizitang Citrus, Slimming Diet Berry Plus, Citrus Fit Gold, Hot Detox, Thinogenics** contains sibutramine. **Tonic Life BP & Slimfast capsules** contains phenolphthalein . **Dr**. **Ming's Chinese Capsule**, **Magic Slim and Apple's Quic**k **Impact Weight Loss** contains sibutramine and phenolphthalein. **Pro ArthMax** contains diclofenac, ibuprofen, naproxen, indomethacin, chlorzoxazone. **Adipotrim XT** contains fluoxetine. **StemAlive** contains milk.

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McDonnell WM, Bhattacharya R, Halldorson JB. Fulminant Hepatic Failure After Use of the Herbal Weight-Loss Supplement **Exilis**. Ann Intern Med. 2009 Nov 3;151(9):673-674.

Medical Letter. Dehydroepiandrosterone (**DHEA**). Vol 47 (Issue 1208) May 9, 2005 p.37-38.

Medicines and Healthcare products Regulatory Agency (MHRA) Dec/07 said: **Xiao Qin Long Wan**, a cold and flu medicine; pain reliever **Chuan Xiong Cha Tiao Wan**; **Bai Tou Weng Wan**, sold for stomach problems, and **Xie Gan Wan**, used to treat stress may contain Aristolochicia, which in unlicensed medicines was banned in UK in 1999

Melchart D, Linde K, Fischer P, **Echinacea** for preventing and treating the **common cold**. Cochrane Database Syst Rev. 2000;(2):CD000530. CONCLUSIONS: The majority of the available studies report positive results. However there is not enough evidence to recommend a specific Echinacea product, or Echinacea preparations for the treatment or prevention of common colds.

MHRA Aug 2011 issues warning over traditional Chinese medicines containing **Lei Gong Teng** (**tripterygium wilfordii**)

MHRA Dec/11Health Sciences Authority in Singapore has issued a press release warning the public of four adulterated health products. **ATHRI-Eze** - is marketed as a traditional Chinese medicine and packaged in a bottle of 20 white capsules. **SEAR HEANG TIENCHI TU CHUNG WAN** - claims to treat rheumatic pain and backache and is sold in a bottle of 40 black pills with a red label. **CAP WIJAYA KUSUMA (AN KI IT)** and **WIKU JAHE KENCUR (AKUR MUJARAB)** - are promoted as Malay Jamu (postnatal) medicines, which are packed in foil sachets of brown powder and are labelled to treat rheumatoid and arthritic conditions.These four products have been found to contain undeclared pharmaceutical medicines. Ingredients found include: dexamethasone, furosemide, paracetamol, chlorpheniramine (also known as chlorphenamine), phenylbutazone, allopurinol & prednisolone.

MHRA Dec/11 In response to an urgent notice issued by MHRA, Bee Health Ltd has agreed to stop marketing FSC Black Cohosh 1000 mg due to concerns about the high dosage of black cohosh in the product. The MHRA advises consumers not to take the FSC Black Cohosh product as it equates to 50 times the dose approved for traditional herbal medicinal products used to relieve menopausal symptoms. It is not known what the risks or effects on the body could be associated with such a high level of Black Cohosh.

MHRA Jan/12 Consumers are advised not to take unlicensed **Butterbur (Petasites hybridus)** herbal remedies. Butterbur contains pyrrolizidine alkaloids (PAs) which studies have shown can result in serious liver damage and organ failure. PAs have also been shown to lead to cancer in animals. Butterbur is most commonly used to treat migraine and hayfever. Butterbur products have been associated with cases of liver toxicity; 40 cases have been reported in the literature. Of these cases, nine were of acute hepatitis and two of the nine cases resulted in liver failure requiring transplantation. The cases of liver toxicity appear to have occurred with extracts of Butterbur where the PAs had been removed and only small amounts remained. There is some evidence that other constituents found in Butterbur such as the sesquiterpene constituents for example petasin may be implicated in the liver toxicity.

MHRA Feb/12 Herbal sliming products found to contain potentially dangerous undeclared pharmaceuticals: **Expelling Grease Slimming Abdomen, V12 Fruit Slimming, 100% Natural Weight Loss Coffee, Leisure 18 Slimming Orange Juice, Fashion Slimming Milk Shake, Langli, Ya Buk & Fruit and vegetables lose weight**. MHRA has received advice from the Danish Medicines Agency that these unlicensed products have been tested and found to contain the Prescription Only Medicine Sibutramine.

MHRA Feb/12 has received advice from AGES PharmMed in Austria and the Danish Medicines Agency, warning that these unlicensed products have been tested and found to contain Tadalafil and/or Sildenafil: **AH Free/Reflexit, Stree Overlord, Man King, VigRX, Maxman, Maxman III, Viriya, & Imbiza for Men.**

MHRA Feb/12 Following a safety alert issued in October 2010 about slimming products containing Paiyouji the Agency has received a further complaint about a product called '**Paiyouji Plus - Fast Acting Slimming Tea**'. This product has been tested by the Agency and, as in the case of other Paiyouji products, found to contain sibutramine.

MHRA Mar/12 Traditional Chinese Medicine (TCM) **Anshen Bunao Pian** (Chung Lien Kulin Brand) has been found by the Department of Health in Hong Kong to contain 55 times the level of mercury permitted in China. Acute mercury poisoning can damage the neurological system and kidneys. The product is manufactured in mainland China and imported by Fung Wah (HK) Company.

MHRA July/12 Department of Health in Hong Kong have issued a warning asking members of the public not to buy or consume an oral product called '**Ling Zhi She Xiang Tong Mai Dan'**, as it may contain an undeclared pharmaceutical, dexamethasone.

MHRA Aug/12 **Echinacea should not be given to children under 12 years**: Oral herbal products containing echinacea should not be given to children under 12 years, the Medicines and Healthcare products Regulatory Agency (MHRA) has warned. http://www.mhra.gov.uk/NewsCentre/Pressreleases/CON180627 [Accessed 24 October 2012].

MHRA: Austrian Sep/12 authorities have issued a warning for **Ramlostan Forte** manufactured by SC Parapharm, Romania. Ramlostan comes in white and blue packaging, with a picture of a ram at the top. Inside, there are ten blue capsules. The Austrian authority (AGES) has issued a warning for this product after finding it to contain Tadalafil.

MHRA Oct/12 The UK Medicines and Healthcare products Regulatory Agency (MHRA) has issued a reminder about a potential adverse effect of liver problems when using **Black Cohosh** to relieve symptoms of the menopause. The MHRA has issued a press release reminding people about the risk of liver problems with Black Cohosh, following a serious case of liver failure resulting in a liver transplant suspected to have been caused by a herbal product containing Black Cohosh. The investigation of this case and of the product involved is ongoing. To date, the MHRA has received 53 reports of adverse reactions suspected to be associated with the use of Black Cohosh.

MHRA, Viridian Nutrition has agreed to recall stocks of **Black Cohosh** Root Capsules, as some batches of the product have been found to contain an undeclared plant species in addition to the declared plant species. The product is labelled as containing Black Cohosh, which is the common name of Cimicifuga racemosa, as specified in the European, British and American Pharmacopoeia. However tests carried out on the product have shown that the product also contains other Cimicifuga species, probably Cimicifuga foetida.

MHRA Nov/12 has received advice from the Danish Medicines Agency that this unlicensed product, **Ultra Slim** has been tested and found to contain the Prescription Only Medicine Sibutramine.

MHRA Nov/12 has received advice from the Ministry of Health, Jerusalem warning that this unlicensed product, **Shark Essence** has been tested and found to contain Tadalafil and Sildenafil.

MHRA Dec/12 Medicines and Healthcare products Regulatory Agency, 2012. Liver failure case highlights need to use **Black Cohosh** remedies carefully [online].

Available: http://www.mhra.gov.uk/NewsCentre/Pressreleases/CON199545

MHRA Feb/13 is advising consumers not to use the products specified below due to sibutramine content. Product names**: Fashion Slimming Coffee, L-Carnitine + P57, L-CarnitinL 360 Slimming Coffee, Brazil Potent Slimming Coffee sachets, Coffee 26 Original sachets, Coffee Nature Fashion Slimming sachets, Slender Capsule, Slim-1.**

MHRA Feb/13 Hong Kong Department of Health issues warnings about **Traditional Chinese Medicines (TCM) found to contain heavy** metals. Product names: [W.S.] Tian Ma Toutong Wan; Shi Hu Ye Guang Wan (Ye Guang Wan); Nai Chang Ming Yan Pills (Ming Yan Pills); [Fung Shing Pai] Tian-Ma Wan; Bak Foong Pills (11 products - see below for details).

MHRA Aug/13 has recently been made aware of several unlicensed herbal products which have been found to contain **heavy metals**: **Bak Foong Pills, Hairegenerator, Niu-Huang Chieh-tu-pien, Divya Kaishore Guggul, Chandraprabha Vati.**

MHRA May/14: Advising consumers not to use Ayurvedic Herbal Medicine **Shwasa Sanjeevani** as it has been found to contain dexamethasone. Hong Kong Department of Health found that samples of **Hairegenerator** exceeded the permissible limit for mercury. Singapore Health Sciences Department **Li Long Mei Guo Mo Bang** because it contains sildenafil & **Ginseng Tu chong Wan Lin Heong** contains dexamethasone.

Michel BA, Stucki G, Frey D, et al. **Chondroitins** 4 and 6 sulfate in osteoarthritis of the knee: a randomized, controlled trial. Arthritis Rheum 2005; 52:779-86.
(InfoPOEMs: After 2 years of treatment, chondroitin sulfate had no effect on comfort in patients with severe degenerative arthritis of the knee. Compared with placebo, however, it appears that chondroitin may have a small protective effect on the joint. The clinical relevance of this effect not known. (LOE = 1b))

Mills E, Singh R, Ross C, Ernst E. Sale of **kava** extract in some health food stores. CMAJ. 2003 Nov 25;169(11):1158-9. (January 2002, Health Canada issued an advisory, followed by a ban in August 2002, on the sale of herbal kava. One month after the advisory, 22 (67%) of 33 health food stores approached were selling kava. Two months after the ban, 17 (57%) of 30 stores continued to sell kava. These findings demonstrate that health food stores may need to be better informed about the sale of restricted natural health products.

Misaka S, Yatabe J, Müller F, et al. **Green tea** ingestion greatly reduces plasma concentrations of **nadolol** in healthy subjects. *Clin Pharmacol Ther* 2014.

Miyasaka LS, Atallah AN, Soares BG. **Valerian** for anxiety disorders. Cochrane Database Syst Rev 2006; 4:CD004515. This paper and [17**]

Miyasaka LS, Atallah AN, Soares BG. **Passiflora** for anxiety disorder. Cochrane Database Syst Rev 2007; 1:CD004518.

Mischoulon D. Update and critique of **natural remedies as antidepressant treatments**. Psychiatr Clin North Am 2007; 30:51-68.

Murphy RK, Ketzler L, Rice RD, et al. Oral **Glucosamine Supplements as a Possible Ocular Hypertensive Agent**. JAMA Ophthalmol. 2013 May 23:1-3.

Nahas R, Moher M. **Complementary and alternative medicine** for the treatment of type 2 diabetes. Can Fam Physician. 2009 Jun;55(6):591-6. Chromium, and possibly gymnema, appears to improve glycemic control. Fibre, green tea, and fenugreek have other benefits but there is little evidence that they substantially improve glycemic control. Further research on bitter melon and cinnamon is warranted. There is no complementary and alternative medicine research addressing microvascular or macrovascular clinical outcomes.

Nahas Richard, Sheikh Osmaan. **Complementary and alternative medicine** for the treatment of **major depressive disorder** Can Fam Physician June 2011 57: 659-663. (**St John's wort & exercise**)

Nahin RL, Pecha M, Welmerink DB, et al. Ginkgo Evaluation of Memory Study Investigators. Concomitant use of **prescription drugs and dietary supplements** in ambulatory elderly people. J Am Geriatr Soc. 2009 Jul;57(7):1197-205.

Nair KS, et al. **DHEA** in elderly **women** and **DHEA or testosterone** in elderly men. N Engl J Med. 2006 Oct 19;355(16):1647-59. (see also Pharmacist's Letter: Anti-aging Effects of DHEA. Dec/06)
(n= 2yr 87 males, 57 women) Men who received testosterone had a slight increase in fat-free mass, and men in both treatment groups had an increase in BMD at the femoral neck. Women who received DHEA had an increase in BMD at the ultradistal radius. Neither DHEA nor low-dose testosterone replacement in elderly people has physiologically relevant beneficial

effects on body composition, physical performance, insulin sensitivity, or quality of life. (InfoPOEMs: There is no evidence that supplementation with dehydroepiandrosterone (DHEA) or testosterone has any meaningful clinical benefit for older patients with low serum levels of those hormones. (LOE = 1b))

Neale C, Camfield D, et al. Cognitive effects of two nutraceuticals **Ginseng and Bacopa** benchmarked against modafinil: a review and comparison of effect sizes. Br J Clin Pharmacol. 2012 Oct 9.

Newmaster SG, Grguric M, Shanmughanandhan D, Ramalingam S, Ragupathy S. **DNA barcoding detects contamination and substitution** in North American herbal products. BMC Med. 2013;11:222.

Newton KM, Reed SD, LaCroix AZ, et al. Treatment of vasomotor symptoms ofmenopausewith **black cohosh**, multibotanicals, soy, hormone therapy, or placebo: a randomized trial. Ann Intern Med 2006;145:869–79.

Nicolai SP, Kruidenier LM, Bendermacher BL, et al. **Ginkgo biloba for intermittent claudication**. Cochrane Database Syst Rev. 2013 Jun 6;6:CD006888. doi: 10.1002/14651858.CD006888.pub3. Overall, there is no evidence that Ginkgo biloba has a clinically significant benefit for patients with peripheral arterial disease.

Nieminen TH, Hagelberg NM, Saari TI, Neuvonen M, Laine K, Neuvonen PJ, Olkkola KT. **St John's wort greatly reduces the concentrations of oral oxycodone**. Eur J Pain. 2010 Jan 25.

Ngo MQ, Nguyen NN, Shah SA. Oral **aloe vera** for treatment of diabetes mellitus and dyslipidemia. Am J Health Syst Pharm. 2010 Nov 1;67(21):1804, 1806, 1808.

Oct/13 The workout supplement marketed as "**Craze**" contains a potentially dangerous designer drug — a methamphetamine analog — according to an article in Drug Testing and Analysis. The analog, N,alpha-diethyl-phenylethylamine (N,alpha-DEPEA), was found in three different samples of the product obtained from separate sources and analyzed by two labs. The product's label claims it contains phenylethylamines derived from dendrobium, but the authors say the component identified as N,alpha-DEPEA has never been identified in dendrobium. They say the amounts of N,alpha-DEPEA found "strongly suggest" that it's not a minor contaminant, adding that if their findings are confirmed, the FDA should "remove all N,alpha-DEPEA-containing supplements from the marketplace." The Boston Globe reports that another supplement, "**Detonate**," also contained N,alpha-DEPEA upon analysis.

Ondrizek RR, Chan PJ, Patton WC, King A. Inhibition of human **sperm** motility by specific herbs used in alternative medicine (eg. St. John's Wort). J Assist Reprod Genet. 1999 Feb;16(2):87-91.

Ooi CP, Yassin Z, Hamid TA. **Momordica charantia** for type 2 diabetes mellitus. Cochrane Database Syst Rev. 2010 Feb 17;2:CD007845.

Papakostas GI, Mischoulon D, Shyu I, Alpert JE, Fava M. S-adenosyl methionine (SAMe) augmentation of serotonin reuptake inhibitors for antidepressant nonresponders with major depressive disorder: double-blind, randomized clinical trial. Am J Psychiatry. 2010 Aug;167(8):942-8. These preliminary results suggest that SAMe can be an effective, well-tolerated, and safe adjunctive treatment strategy for SRI nonresponders with major depressive disorder and warrant replication.

Parasrampuria J, Schwartz K, Petesch R. Quality control of **dehydroepiandrosterone** dietary supplement products. JAMA. 1998 Nov 11;280(18):1565.

Peng CC, Glassman PA, Trilli LE, et al. Incidence and severity of **potential drug-dietary supplement interactions** in primary care patients: an exploratory study of 2 outpatient practices. Arch Intern Med. 2004 Mar 22;164(6):630-6.

Perri D, Dugoua JJ, Mills E, Koren G. Safety & efficacy of echinacea (E. angustafolia, purpurea & pallida) during pregnancy & lactation. Can J Clin Pharmacol.2006 Fall;13(3):e262-7.Epub 2006Nov3.

Perry, Rachel, Hunt, Katherine, Ernst, Edzard. Nutritional Supplements and Other Complementary Medicines for **Infantile Colic**: A Systematic Review. Pediatrics 2011 127: 720-733

Pharmacist's Letter: Health Benefits of Drinking **Green Tea.** Nov 2006.

Pharmacist's Letter. Is **Chondroitin** effective for Osteoarthritis. June 2007. (Best evidence is with glucosamine sulfate called DONA by Rotta Pharmaceuticals)

Pharmacist's Letter. **New Health Canada Rules Allow More Health Claims for Natural Products**. April 2008.

Pharmacist's Letter. **Hawthorn for Heart Failure**. April 2008.

Pharmacist's Letter. **Flaxseed**: Is It As Beneficial As Fish Oil? July 2009.

Pharmacist's Letter. **Supplements for Prevention and Treatment of Colds and Influenza**. Nov 2009.

Pittler MH, Ernst E. **Horse chestnut** seed extract for chronic venous insufficiency. Cochrane Database Syst Rev. 2006 Jan 25;(1):CD003230. The evidence presented implies that HCSE is an efficacious & safe short-term treatment for CVI. However, several caveats exist and more rigorous RCTs are required to confirm the efficacy of this treatment option.

Pittler MH, Ernst E. **Kava** extract for treating anxiety. Cochrane Database Syst Rev. 2003;(1):CD003383. CONCLUSIONS: Compared with placebo, kava extract appears to be an effective symptomatic treatment option for anxiety. The data available from the reviewed studies suggest that kava is relatively safe for short-term treatment (1 to 24 weeks), although more information is required. Further rigorous investigations, particularly into the long-term safety profile of kava are warranted.

Pittler MH, Ernst E. **Feverfew** for preventing migraine. Cochrane Database Syst Rev. 2004;(1):CD002286. CONCLUSIONS: There is insufficient evidence from randomised, double-blind trials to suggest an effect of feverfew over & above placebo for preventing migraine. It appears from the data reviewed that feverfew presents no major safety problems.

Pittler MH, Guo R, Ernst E. **Hawthorn extract** for treating chronic heart failure. Cochrane Database Syst Rev 2008; DOI: 10.1002/14651858.CD005312.pub2. (Not included in the review was the survival and Prognosis: Investigation of Crataegus Extract WS1442 in CHF (**SPICE**) trial, which was ongoing as Pittler et al were screening relevant trials. As reported by heartwire when the study was later presented at the American College of Cardiology 2007 Scientific Sessions, adding the herbal to ACE inhibitors, beta blockers, and other components of contemporary therapy failed to alter a composite primary end point that included sudden cardiac death, death due to progressive heart failure, fatal or nonfatal MI, and HF hospitalization at 24 months. The trial did support hawthorn extract's good safety record, however.)

Portnoi G, Chng LA, et al. Prospective comparative study of the safety & effectiveness of **ginger** for the treatment of nausea and vomiting in pregnancy. Am J Obstet Gynecol. 2003 Nov;189(5):1374-7.

Posadzki P, Watson L, Ernst E. **Herb-drug interactions**: an overview of systematic reviews. Br J Clin Pharmacol. 2012 Jun 1.

Prasad K, Sharma V, Lackore K, et al. Use of **Complementary Therapies** in Cardiovascular Disease. Am J Cardiol. 2012 Nov 24.

Predy GN, Goel V, Lovlin R, et al. Efficacy of an extract of North American **ginseng (Cold-fx)** containing poly-furanosyl-pyranosyl-saccharides for preventing upper respiratory tract infections: a randomized controlled trial. CMAJ. 2005 Oct 25;173(9):1043-8. INTERPRETATION: Ingestion of a poly-furanosyl-pyranosyl-saccharide-rich extract of the roots of North American ginseng in a moderate dose **400mg (2 capsules) over 4 months** reduced the mean number of colds per person (0.99 vs 0.71), the proportion of subjects who experienced 2 or more colds (24.8 vs 10%), the severity of symptoms and the number of days cold symptoms were reported (from 11.1 days to only 8.7 days). The number of people with 1 cold was 64.4 vs 56.1% with Cold-fX in **healthy** 18-65yrs old (mean 43yrs), n=323 with a history of at least 2 colds in the previous year. Limitations: not virologically proven influenza or more typical common cold illnesses studied will be important in the future, only most severe illnesses were evaluated, mechanism of action & true active constituents are not known.

Qato DM, Alexander GC, et al. Use of **prescription & over-the-counter medications and dietary supplements** among older adults in the United States. JAMA. 2008 Dec 24;300(24):2867-78.

Qiu GX, Weng XS, Zhang K, et al. [A multi-central, randomized, controlled clinical trial of **glucosamine** hydrochloride/sulfate in the treatment of knee osteoarthritis.] Zhonghua Yi Xue Za Zhi. 2005 Nov;85(43):3067-70.

Quinn JF.; Raman R,Thomas RG.; et al. **Docosahexaenoic Acid (DHA) Supplementation** and Cognitive Decline in Alzheimer Disease: A Randomized Trial. *JAMA*. 2010;304(17):1903-1911.

Rambaldi A, Jacobs BP, Iaquinto G. **Milk thistle** for alcoholic and/or hepatitis B or C virus liver diseases. Cochrane Database Syst Rev. 2005 Apr 18;(2):CD003620. CONCLUSIONS: Our results question the beneficial effects of milk thistle for patients with alcoholic and/or hepatitis B or C virus liver diseases and highlight the lack of high-quality evidence to support this intervention. Adequately conducted and reported randomised clinical trials on milk thistle versus placebo are needed.

Ravindran AV, Lam RW, Filteau MJ, et al. Canadian Network for Mood and Anxiety Treatments (**CANMAT**) clinical guidelines for the management of major depressive disorder in adults. V. Complementary and alternative medicine treatments. J Affect Disord. 2009 Aug 8. [Epub ahead of print]

Red yeast: Most clinical studies have used a specific brand product (Cholestin). However, most other red yeast brands contain similar amount of red yeast, 600 mg. For hypercholesterolemia, a typical dose of red yeast is 1200 mg two times daily with food (2624). A total daily dose of 2400 mg red yeast contains approximately 9.6 mg total statins, of which 7.2 mg is lovastatin (2624). For dyslipidemia related to HIV infection, 1200 mg twice daily has been used (9475). www.naturaldatabase.com

Reeds Dominic N., Patterson Bruce W., Okunade Adewole, et al. **Ginseng and Ginsenoside** Re Do Not Improve β-Cell Function or Insulin Sensitivity in Overweight and Obese Subjects With Impaired Glucose Tolerance or Diabetes. Diabetes Care May 2011 34:1071-1076; published ahead of print March 16, 2011, doi:10.2337/dc10-2299

Reginster JY, Deroisy R, Rovati LC, et al. Long-term eff ects of **glucosamine** sulphate on osteoarthritis progression: a randomised, placebo-controlled clinical trial. Lancet 2001; 357: 251–56.

Reichenbach S, et al. **Meta-analysis: chondroitin** for osteoarthritis of the knee or hip. Ann Intern Med. 2007 Apr 17;146(8):580-90. Large-scale, methodologically sound trials indicate that the symptomatic

benefit of chondroitin is minimal or nonexistent.
Reinhart KM, Coleman CI, Teevan C, et al. Effects of **garlic on blood pressure** in patients with and without systolic hypertension: a meta-analysis. Ann Pharmacother. 2008 Dec;42(12):1766-71. Epub 2008 Nov 18. This meta-analysis suggests that garlic is associated with blood pressure reductions in patients with an elevated SBP although not in those without elevated SBP.
Richy F, et al. Structural and symptomatic efficacy of **glucosamine and chondroitin** in knee osteoarthritis: a comprehensive meta-analysis. Arch Intern Med. 2003 Jul 14;163(13):1514-22.
Ringdahl E, Pandit S. Treatment of **Knee Osteoarthritis**. Am Fam Physician. 2011;83(11):1287-1292.
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Roselle H et al. Symptomatic hepatitis associated with the use of herbal **red yeast rice**. Ann Intern Med 2008; 149:516.
Rosenblatt M, Mindel J. Spontaneous hyphema associated with ingestion of **Ginkgo** biloba extract. N Engl J Med. 1997 Apr 10;336(15):1108.
Rowin J, Lewis SL. Spontaneous bilateral subdural hematomas associated with chronic **Ginkgo** biloba ingestion. Neurology. 1996 Jun;46(6):1775-6.
Rozendaal RM, et al. Effect of **glucosamine sulfate on hip osteoarthritis**: a randomized trial. Ann Intern Med. 2008 Feb 19;148(4):268-77. Glucosamine sulfate was no better than placebo in reducing symptoms and progression of hip osteoarthritis.
Saeed SA, et al. **Herbal and Dietary Supplements** for Treatment of **Anxiety** Disorders. American Family Physician 2007;76:549-56. Kava potential for mild to moderate anxiety. Inositol modest effects with panic or OCD disorder. Not encourage St. John's wort, valerian, Sympathyl or passionflower.
Saito YA, Rey E, Almazar-Elder AE, et al. A randomized, double-blind, placebo-controlled trial of **St John's wort** for treating irritable bowel syndrome. Am J Gastroenterol. 2010 Jan;105(1):170-7. Epub 2009 Oct 6. SJW was a less effective treatment for IBS than placebo.
Samuels N, Finkelstein Y, Singer SR, Oberbaum M. **Herbal medicine and epilepsy**: proconvulsive effects and interactions with antiepileptic drugs. Epilepsia 2008;49:373-80.
Saper RB, Kales SN, Paquin J, Burns MJ, Eisenberg DM, Davis RB, Phillips RS. Heavy metal content of **ayurvedic** herbal medicine products. JAMA. 2004 Dec 15;292(23):2868-73.
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Sawitzke AD, Shi H, Finco MF, Dunlop DD, et al.. Clinical efficacy and safety of **glucosamine, chondroitin sulphate, their combination, celecoxib or placebo** taken to treat osteoarthritis of the knee: 2-year results from **GAIT**. Ann Rheum Dis. 2010 Jun 4.
Schabath MB, Hernandez LM, Wu X, Pillow PC, Spitz MR. Dietary **phytoestrogens** and lung cancer risk. JAMA. 2005 Sep 28;294(12):1493-504.
Schoonees A, Visser J, Musekiwa A, Volmink J. **Pycnogenol**® for the treatment of chronic disorders. Cochrane Database of Systematic Reviews 2012, Issue 2. Art. No.: CD008294. DOI: 10.1002/14651858.CD008294.pub3. Oxidative stress has been implicated in the development of a number of conditions including cancer, arthritic disorders and cardiovascular disease. Pycnogenol®, a herbal dietary supplement derived from French maritime pine bark extract, is standardised to contain 70% procyanidin which is a powerful antioxidant. Pycnogenol® is marketed as a supplement for preventing or treating a wide range of chronic conditions.Current evidence is insufficient to support Pycnogenol® use for the treatment of any chronic disorder. Well-designed, adequately powered trials are needed to establish the value of this treatment.
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Shang A, Huwiler-Müntener K, et al. Are the clinical effects of **homoeopathy** placebo effects? Comparative study of placebo-controlled trials of homoeopathy and allopathy. The Lancet - Vol. 366, Issue 9487, 27 August 2005, Pages 726-732. (InfoPOEMs: High-quality studies demonstrate that homeopathy are no more effective than placebo. (LOE = 1a-))
Shelton RC, Keller MB, et al. Effectiveness of **St John's wort** in major depression: a randomized controlled trial. **JAMA. 2001** Apr 18;285(15):1978-86.
Skalli S, Zaid A, Soulaymani R. **Drug interactions with herbal medicines**. *Ther Drug Monit*. 2007. 29(6): 679–86.
Smith C, Crowther C, Willson K, Hotham N, McMillian V. A randomized controlled trial of **ginger** to treat nausea and vomiting in pregnancy. Obstet Gynecol. 2004 Apr;103(4):639-45.
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Squadrito F, Marini H, Bitto A, et al. **Genistein** in the metabolic syndrome: results of a randomized clinical trial. J Clin Endocrinol Metab. 2013 Aug;98(8):3366-74.
Siegel AB, Stebbing J. **Milk thistle**: early seeds of potential. Lancet Oncol. 2013 Sep;14(10):929-30.
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Stranges S, Marshall JR, Natarajan R, et al. Effects of Long-Term Selenium Supplementation on the Incidence of Type 2 Diabetes: A Randomized Trial. Ann Intern Med. 2007 Jul 9; [Epub ahead of print] Selenium supplementation does not seem to prevent type 2 diabetes, and it may increase risk for the disease.
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Lozoff B et al. Iron-fortified vs low-**iron infant formula: Developmental outcome at 10 years**. Arch Pediatr Adolesc Med2011 Nov 7; [e-pub ahead of print],
Pena-Rosas JP, De-Regil LM, et al. **Intermittent oral iron supplementation during pregnancy.** Cochrane Database Syst Rev. 2012 Jul 11;7:CD009997. The present systematic review is the most comprehensive summary of the evidence assessing the benefits and harms of intermittent iron supplementation regimens in pregnant women on haematological and pregnancy outcomes. The findings suggest that intermittent iron+folic acid regimens produce similar maternal and infant outcomes at birth as daily supplementation but are associated with fewer side effects. Women receiving daily supplements had increased risk of developing high levels of Hb in mid and late pregnancy but were less likely to present mild anaemia near term.
Peña-Rosas JP, De-Regil LM, Dowswell T,Viteri FE. **Daily oral iron supplementation during pregnancy**. Cochrane Database of Systematic Reviews 2012, Issue 12. Art. No.: CD004736.DOI: 10.1002/14651858.CD004736.pub4. Prenatal supplementation with daily iron are effective to reduce the risk of low birthweight, and to prevent maternal anaemia and iron deficiency in pregnancy. Associated maternal side effects and particularly high Hb concentrations during pregnancy at currently used doses suggest the need to update recommendations on doses and regimens for routine iron supplementation.
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These data do **not support** recommending vitamin E supplementation for cardiovascular disease or cancer prevention among healthy women. (InfoPOEMs: Vitamin E does not reduce the risk of cardiovascular disease, cancer, or total mortality among healthy women 45 years or older. (LOE = 1b)) Zhang SM, Cook NR, Albert CM, Gaziano JM, Buring JE, Manson JE. Effect of combined folic acid, vitamin B6, and vitamin B12 on cancer risk in women: a randomized trial. (WAFACS) JAMA. 2008 Nov 5;300(17):2012-21. Combined folic acid, vitamin B(6), and vitamin B(12) treatment had no significant effect on overall risk of total invasive cancer or breast cancer among women during the folic acid fortification era.

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Canadian Paediatric Society. Head lice infestations: a clinical update. http://cps.ca/English/statements/ID/id08-06.pdf
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Health Canada April/07is advising consumers not to use a product called **Eden Herbal Formulations Serenity Pills II** because it contains the undeclared drug **estazolam**.

Health Canada June/07 is advising consumers not to use **Optimum Health Care SleePlus TCM** or **BYL SleePlus**, because the products contain the undeclared drug **clonazepam.**

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Health Canada Aug/06 Lamictal warning with non-syndromic oral clefts**.** Emerging data from the North American Antiepileptic Drug (NAAED) Pregnancy Registry suggest an association between LAMICTAL® (lamotrigine) and an increased risk of non-syndromic oral clefts over the reference population for the registry (ie. Active Malformations Surveillance Program at Brigham and Women's Hospital in Boston, USA)1. Recently published data from the Registry report three cases of isolated, non syndromic cleft palate and two cases of isolated, non syndromic cleft lip without cleft palate in infants from 564 first trimester lamotrigine monotherapy exposures giving a rate of 8.9 per 1,000, as compared to 0.37 per 1000 in the reference population for that registry. The prevalence of oral clefts noted in the NAAED registry is also higher than the background prevalence of non-syndromic oral clefts reported in the literature, including studies from the United States, Australia and Europe. While different studies have differing results due to geographic and case ascertainment variations, the reported range is 0.50 to 2.16/1000 3-17. To assist with the assessment of risk, analysis of data from additional pregnancy registries, with approximately 2200 additional lamotrigine monotherapy first trimester exposures has been conducted, and 4 additional non-syndromic cases of oral cleft have been identified. http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/2006/lamictal_2_hpc-cps_e.html

Health Canada Jan/10 is advising consumers not to use any unauthorized health products sold under **Natural Choice Lithium Orotate**.

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Sept/05 Nice:Depression in children & young people http://www.nice.org.uk/pdf/CG028NICEguideline.pdf ; (Simon GE, Savarino J, Operskalski B, Wang PS. **Suicide risk during antidepressant treatment**. Am J Psychiatry. 2006 Jan;163(1):41-7. CONCLUSIONS: The risk of suicide during acute-phase antidepressant treatment is approximately one in 3,000 treatment episodes, and risk of serious suicide attempt is approximately one in 1,000. Available data do not indicate a significant increase in risk of suicide or serious suicide attempt after starting treatment with newer antidepressant drugs.)(Cheung AH, et al. The use of antidepressants to treat depression in children and adolescents. CMAJ. 2006 Jan 17;174(2):193-200.) & (Hammad TA, et al. Suicidality in pediatric patients treated with antidepressant drugs. Arch Gen Psychiatry. 2006 Mar;63(3):332-9. CONCLUSION: Use of antidepressant drugs in pediatric patients is associated with a modestly increased risk of suicidality. InfoPOEMs: The use of antidepressant medications in children is associated with an increased risk of suicidal ideation and suicide-related behaviors. It is uncertain what overall effect antidepressant medications have on the morbidity and mortality of treated children. Close monitoring of patients using these medications regarding the risk of suicidality is recommended. (LOE = 1a-)) (Glaxo May/06 Meta analysis: 8958 paroxetine & 5953 placebo pts; suicidal behavior aged 18-24yrs (2.19 vs 0.92%); all ages (0.32 vs 0.05%); all were nonfatal suicide attempts; 8 of 11 attempts were in aged 18-30yrs) Emslie GJ, et al. Paroxetine Treatment in Children and Adolescents With Major Depressive Disorder: A Randomized, Multicenter, Double-Blind, Placebo-Controlled Trial. J Am Acad Child Adolesc Psychiatry. 2006 Jun;45(6):709-719. Paroxetine was not shown to be more efficacious than placebo for treating pediatric major depressive disorder. (Misri S, et al. Internalizing behaviors in 4-year-old children exposed in utero to psychotropic medications. Am J Psychiatry. 2006 Jun;163(6):1026-32.) (Dubicka B, Hadley S, Roberts C. Suicidal behaviour in youths with depression treated with new-generation antidepressants: meta-analysis. Br J Psychiatry. 2006 Nov;189:393-8. Self-harm or suicide-related events occurred in 71 of 1487 (4.8%) of depressed youths treated with antidepressants v. 38 of 1254 (3.0%) of those given placebo (fixed effects odds ratio 1.70, 95% CI 1.13-2.54, P=0.01).) (Gibbons RD, Hur K, Bhaumik DK, Mann JJ. The relationship between antidepressant prescription rates and rate of early adolescent suicide. Am J Psychiatry. 2006 Nov;163(11):1898-904. The aggregate nature of these observational data precludes a direct causal interpretation of the results. More SSRI prescriptions are associated with lower suicide rates in children and may reflect antidepressant efficacy, treatment compliance, better quality mental health care, and low toxicity in the event of a suicide attempt by overdose.) (Juurlink DN, et al. The risk of suicide with selective serotonin reuptake inhibitors in the elderly. Am J Psychiatry. 2006 May;163(5):813-21. Initiation of SSRI therapy is associated with an increased risk of suicide during the first month of therapy compared with other antidepressants. The absolute risk is low, suggesting that an idiosyncratic response to these agents may provoke suicide in a vulnerable subgroup of

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(Bhatia SK, Bhatia SC. Childhood and adolescent depression. Am Fam Physician. 2007 Jan 1;75(1):73-80.) (Bridge JA, et al. Clinical response and risk for reported suicidal ideation and suicide attempts in pediatric antidepressant treatment: a meta-analysis of randomized controlled trials. JAMA. 2007 Apr 18;297(15):1683-96. Relative to placebo, antidepressants are efficacious for pediatric MDD, OCD, and non-OCD anxiety disorders, although the effects are strongest in non-OCD anxiety disorders, intermediate in OCD, and more modest in MDD. Benefits of antidepressants appear to be much greater than risks from suicidal ideation/suicide attempt across indications, although comparison of benefit to risk varies as a function of indication, age, chronicity, and study conditions.) (Gibbons RD, Brown CH, Hur K, Marcus SM, Bhaumik DK, Mann JJ. Relationship between antidepressants and suicide attempts: an analysis of the veterans health administration data sets. Am J Psychiatry. 2007 Jul;164(7):1044-9. These findings suggest that SSRI treatment has a protective effect in all adult age groups. They do not support the hypothesis that SSRI treatment places patients at greater risk of suicide.)

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Hetrick S, Merry S, McKenzie J, Sindahl P, Proctor M. Selective serotonin reuptake inhibitors (SSRIs) for depressive disorders in children and adolescents. Cochrane Database Syst Rev. 2007 Jul 18;(3):CD004851. There was also evidence of an increased risk of suicidal ideation and behaviour for those prescribed SSRIs (RR 1.80, 95% CI 1.19 to 2.72). Fluoxetine was the only SSRI where there was consistent evidence from three trials that it was effective in reducing depression symptoms in both children and adolescents (CDRS-R treatment effect -5.63, 95% CI -7.38 to -3.88), and 'response' to treatment (RR 1.86, 95% CI 1.49 to 2.32). Where rates of adverse events were reported, this was higher for those prescribed SSRIs. While untreated depression is associated with the risk of completed suicide and impacts on functioning, it is unclear whether SSRIs would modify this risk in a clinically meaningful way. (Cheung AH, Zuckerbrot RA, Jensen PS, Ghalib K, Laraque D, Stein RE; GLAD-PC Steering Group. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): II. Treatment and ongoing management. Pediatrics. 2007 Nov;120(5):e1313-26.)

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Biddle L, Brock A, Brookes ST, Gunnell D. Suicide rates in young men in England and Wales in the 21st century: time trend study. BMJ. 2008 Mar 8;336(7643):539-42. Epub 2008 Feb 14. Suicide rates in young men have declined markedly in the past 10 years in England and Wales. Reductions in key risk factors for suicide, such as unemployment, might be contributing to lower rates.

Barbui C, Esposito E, Cipriani A. Selective serotonin reuptake inhibitors and risk of suicide: a systematic review of observational studies. CMAJ. 2009 Feb 3;180(3):291-7. Based on data from observational studies, use of SSRIs may be associated with a reduced risk of suicide in adults with depression. Among adolescents, use of SSRIs may increase suicidality.

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FDA: Oct/06 Letter regarding venlafaxine overdose concern http://www.fda.gov/medwatch/safety/2006/effexor_DHCPletter.pdf
FDA: Aug/11 Antidepressant citalopram (Celexa, Forest Laboratories) should not be used in doses higher than 40 mg per day because of concerns that it can cause potentially fatal changes in heart rhythm.
FDA: Dec/11 Selective Serotonin Reuptake Inhibitor Antidepressants: Use During Pregnancy & Potential Risk of Persistent Pulmonary Hypertension of the Newborn http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm283696.htm
FDA Aug/13 Health and Beyond LLC is voluntarily recalling quantity lots of product **Tranquility**. The products have been found to contain a trace of Doxepin which is a pharmaceutical for sleep and Chlorpormazine for psychotic disorders.
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Health Canada Oct/08 Venlafaxine overdose warning http://www.hc-sc.gc.ca/dhp-mps/medeff/advisories-avis/prof/_2008/venlaflaxine_hpc-cps-eng.php

Health Canada Feb/11 **Methylene blue injectable** in combination with serotonin reuptake inhibitors - Association with serotonin toxicity Cases of serotonin toxicity have been reported and published in association with the use of methylene blue injectable in patients exposed to drugs with serotonin reuptake inhibition properties.

Health Canada Jan/12: Lundbeck Canada, in collaboration with Health Canada, would like to inform you that the antidepressant **Celexa® (citalopram** hydrobromide; also marketed as generics), should no longer be used at doses greater than **40 mg per day** due to study results indicating a dose-dependent potential for QT prolongation.

Health Canada May/12 is informing Canadians of a labelling update for the prescription drug **Cipralex** (the brand name of the drug **escitalopram**) regarding a dose-related risk of abnormal heart rhythms. Cipralex is used to treat depression and belongs to a family of drugs known as Selective Serotonin Reuptake Inhibitors (SSRIs). 10 mg per day is the maximum recommended dose for patients who: are 65 years of age or older, or have liver problems, or are taking the heartburn drugs omeprazole or cimetidine which can increase the blood level of Cipralex. 20 mg per day is still the maximum recommended dose for most other patients.

Health Canada Mar/14: REMERON / **REMERON RD (mirtazapine)** – Abnormal Heart Rhythm - Merck Canada Inc. Cases of abnormal heart rhythm (eg. **QT** prolongation) have been reported with the antidepressant REMERON / REMERON RD (mirtazapine) mainly with drug overdose or when taking other drugs known to cause heart rhythm problems. The product information has been updated.

Health Canada June/14: **Adipotrim XT** contains fluoxetine.

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nefazodone[3A4] SERZONE	carbamazepine ⑨⑥ cisapride ⑥②$_{cv}$ lovastatin ⑥$_{(rhabdo)}$ MAOI's ③ sibutramine ③ simvastatin ⑥$_{(rhabdo)}$ sumatriptan ③	alprazolam ⑥ atorvastatin ⑥ cyclosporin ⑥	digoxin ⑥, fentanyl ⑧ fluvastatin ⑥ grapefruit juice ⑧ haloperidol ⑥	indinavir/ritonavir ⑧ L-tryptophan ③ midazolam ⑥ paroxetine ③	phenytoin ⑨⑥ **pimozide** ⑥ cv pravastatin ⑥ quinidine ⑥②, ritonavir ⑧	**sedatives** ① tacrolimus ⑥② triazolam ⑥

CV=cardiovascular **HTN**=hypertension

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SEDATIVE COMPARISON CHART

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FDA Jan/13 The recommendation applies to **zolpidem** products approved for bedtime use, marketed as generics and under the brand names *Ambien*, *Ambien CR*, *Edluar*, and *Zolpimist*. Data show the risk for morning impairment is highest with extended-release forms of these drugs, and **women** appear to be more susceptible to this effect because they eliminate zolpidem more slowly than men, a statement from the FDA notes.

FDA May/14 has notified health professionals and their medical care organizations of a new warning that the insomnia drug Lunesta (**eszopiclone**) can cause next-day impairment of driving and other activities that require alertness. FDA recommends a decreased starting dose of Lunesta to 1 mg at bedtime. Women and men are equally susceptible to impairment from **Lunesta**, so the recommended starting dose of 1 mg is the same for both.

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Health Canada April/07is advising consumers not to use a product called **Eden Herbal Formulations Serenity Pills II** because it contains the undeclared drug **estazolam**.

Health Canada Dec/11 **Sublinox** is the first formulation of **zolpidem** in Canada. Internationally, it has been reported in association with **complex sleep behaviours**.

Health Canada May/12 **[Chung Lien Kulin Brand] Anshen Bunai Pian.** Hong Kong Department of Health warned that this traditional Chinese health product, used for insomnia, contains excessive levels of the heavy metal mercury.

Health Canada Jan/14 **Sublinox (zolpidem** tartrate) - New Dosage Recommendations to Minimize Risk of Next-Day Impairment in Both **Women and Men** - Valeant Canada. The recommended initial dose has been lowered to 5 mg for women and either 5 or 10 mg for men, taken only once per night immediately before bedtime with at least 7-8 hours remaining before awakening.

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National Heart Lung and Blood Institute http://www.nhlbi.nih.gov/health/dci/Diseases/inso/inso_whatis.html
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Online extras :

Mast cell stabilizers	♦efficacy highly variable from pt to pt; not for acute attacks; may taper to BID over several weeks after effect achieved; role in pediatric, cold air induced asthma & EIB					
Sodium Cromoglycate (*Cromolyn* nebs 20mg/2ml) PL	MDI 1mg/puff 20mg Spincap for inhal'n	*INTAL Inhaler* →**D/C** product *INTAL* Spincaps →**D/C** product	2-8mg 40-160mg	ii puff QID (Up to 16puffs/day) 1 cap for inhal'n QID	$ 64 ✘▼ $ 73	♦~4week trial needed to evaluate effect; safe in children
Nedocromil PL	MDI 2mg/puff	*TILADE*→**D/C** product	4-16mg	ii puffs QID	$ 73	♦taste may limit compliance

ASTHMA & COPD PHARMACOTHERAPY: Comparison Chart

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Castro-Rodriguez JA, Rodrigo GJ. Efficacy of **inhaled corticosteroids in infants and preschoolers** with recurrent wheezing and asthma: a systematic review with meta-analysis. Pediatrics. 2009 Mar;123(3):e519-25. Infants and preschoolers with recurrent wheezing or asthma had less wheezing/asthma exacerbations and improve their symptoms and lung function during treatment with inhaled corticosteroids.

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Cates CJ, Cates MJ, Lasserson TJ. Regular treatment with **formoterol** for chronic asthma: serious adverse events. Cochrane Database Syst Rev. 2008 Oct 8;(4):CD006923.

Cates CJ, Lasserson TJ. Combination **formoterol and inhaled steroid** versus beta(2)-agonist as relief medication for chronic asthma in adults and children. Cochrane Database Syst Rev. 2009 Jan 21;(1):CD007085. In mild asthma it is not yet known whether patients who use a budesonide/formoterol inhaler for relief of asthma symptoms derive any clinically important benefits. In more severe asthma, one study that enrolled patients who were not controlled on quite high doses of inhaled corticosteroids, and had suffered an exacerbation in the previous year, demonstrated a reduction in the risk of exacerbations that require oral corticosteroids with budesonide/formoterol for maintenance and relief in comparison with budesonide/formoterol for maintenance and terbutaline or formoterol for relief. The incidence of serious adverse events in children was also less using budesonide/formoterol for maintenance and relief in one study, which similarly enrolled children who were not controlled on medium to high doses of inhaled corticosteroids, and compared to terbutaline relief with an explorative maintenance dose of budesonide/formoterol that is not approved for treatment.

Cates CJ, Lasserson TJ, Jaeschke R. Regular treatment with **formoterol** and inhaled steroids for chronic asthma: serious adverse events. Cochrane Database Syst Rev. 2009 Apr 15;(2):CD006924. It is not possible, from the data in this review, to reassure people with asthma that inhaled corticosteroids with regular formoterol carries no risk of increasing mortality in comparison to inhaled corticosteroids alone as all four deaths occurred among 6,594 people using inhaled corticosteroids with formoterol. On the other hand, we have found no conclusive evidence of harm and there was only one asthma related death registered during over 3,000 patient year observation on formoterol.

Cates CJ, Lasserson TJ, Jaeschke R. Regular treatment with **salmeterol and inhaled steroids** for chronic asthma: serious adverse events. Cochrane Database Syst Rev. 2009 Jul 8;(3):CD006922. No significant differences have been found in fatal or non-fatal serious adverse events in trials in which regular salmeterol has been randomly allocated with inhaled corticosteroids, in comparison to inhaled corticosteroids at the same dose.

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Cates CJ, Rowe BH. Vaccines for preventing **influenza in people with asthma**. Cochrane Database Syst Rev. 2013 Feb 28;2:CD000364. doi: 10.1002/14651858.CD000364.pub4. Uncertainty remains about the degree of protection that vaccination affords against asthma exacerbations that are related to influenza infection. Evidence from more recently published randomised trials of inactivated split-virus influenza vaccination indicates that there is no significant increase in asthma exacerbations immediately after vaccination in adults or children over three years of age.

Cates CJ, Jaeschke R, Schmidt S, et al. Regular treatment with **salmeterol and inhaled steroids for chronic asthma: serious adverse events**. Cochrane Database Syst Rev. 2013 Mar 28;3:CD006922. doi: 10.1002/14651858.CD006922.pub3. We found no statistically significant differences in fatal or non-fatal serious adverse events in trials in which regular salmeterol was randomly allocated with ICS, in comparison to ICS alone at the same dose. Although 13,447 adults and 1862 children have now been included in trials, the frequency of adverse events is too low and the results are too imprecise to confidently rule out a relative increase in all cause mortality or non-fatal adverse events with salmeterol used in conjunction with ICS.

Cates CJ, Karner C. **Combination formoterol and budesonide** as maintenance and reliever therapy versus current best practice (including inhaled steroid maintenance), for chronic asthma in adults and children. Cochrane Database Syst Rev. 2013 Apr 30;4:CD007313. doi: 10.1002/14651858.CD007313.pub3. Single inhaler therapy has now been demonstrated to reduce exacerbations requiring oral corticosteroids against current best practice strategies and against a fixed higher dose of inhaled steroids. The strength of evidence that SiT reduces hospitalisation against these same treatments is weak. There were more discontinuations due to adverse events on SiT compared to current best practice, but no significant differences in serious adverse events.

Cates CJ, Jaeschke R, Schmidt S, et al. Regular treatment with **formoterol and inhaled steroids** for chronic asthma: serious adverse events. Cochrane Database Syst Rev. 2013 Jun 7;6:CD006924. doi: 10.1002/14651858.CD006924.pub3. From the evidence in this review, it is not possible to reassure people with asthma that regular use of inhaled corticosteroids with formoterol carries no risk of increasing mortality in comparison with use of inhaled corticosteroids alone. On the other hand, we have found no conclusive evidence of serious harm, and only one asthma-related death was registered during more than 4200 patient-years of observation with formoterol. In adults, no significant difference in all-cause non-fatal serious adverse events was noted with regular formoterol with inhaled corticosteroids, but a significant reduction in asthma-related serious adverse events was observed in comparison with inhaled corticosteroids alone. In children the number of events was too small, and consequently the results too imprecise, to allow determination of whether the increased risk of all-cause non-fatal serious adverse events found in a previous meta-analysis on regular formoterol alone is abolished by the additional use of inhaled corticosteroids.

Cates CJ, Welsh EJ, Rowe BH. **Holding chambers (spacers) versus nebulisers** for beta-agonist treatment of acute asthma.Cochrane Database Syst Rev. 2013 Sep 13;9:CD000052. Nebuliser delivery produced outcomes that were not significantly better than metered-dose inhalers delivered by spacer in adults or children, in trials where treatments were repeated and titrated to the response of the participant. Spacers may have some advantages compared to nebulisers for children with acute asthma.

Cates CJ, Wieland LS, Oleszczuk M, Kew KM. **Safety of regular formoterol or salmeterol** in adults with asthma: an overview of Cochrane reviews. Cochrane Database of Systematic Reviews 2014, Issue 2. Art. No.: CD010314. DOI: 10.1002/14651858.CD010314.pub2. Available evidence from the reviews of randomised trials cannot definitively rule out an increased risk of fatal serious adverse events when regular formoterol or salmeterol was added to an inhaled corticosteroid (as background or as randomly assigned treatment) in adults or adolescents with asthma.An increase in non-fatal serious adverse events of any cause was found with salmeterol monotherapy, and the same increase cannot be ruled out when formoterol or salmeterol was used in combination with an inhaled corticosteroid, although possible increases are small in absolute terms.However, if the addition of formoterol or salmeterol to an inhaled corticosteroid is found to improve symptomatic control, it is safer to give formoterol or salmeterol in the form of a combination inhaler (recommended by the US Food & Drug Administration (FDA)). This prevents the substitution of LABA for an inhaled corticosteroid if symptom control is improved on LABA.

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Chan Walter W.; Chiou Eric; Obstein Keith L.; et al. The Efficacy of **Proton Pump Inhibitors** for the **Treatment of Asthma** in Adults: A Meta-analysis. *Arch Intern Med*. 2011;171(7):620-629.

Chandra A, Shim C, Cohen HW, et al. Regular vs **ad-lib albuterol** for patients hospitalized with acute asthma. Chest. 2005 Sep;128(3):1115-20. CONCLUSIONS: In the management of asthma exacerbation, ad-lib administration of albuterol is therapeutically as effective as regular, scheduled administration. This method of drug administration also reduces the total dose of beta-agonists received by the hospitalized patient.

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Chandratilleke MG, Carson KV, Picot J,et al. **Physical training for asthma**. Cochrane Database of Systematic Reviews 2012, Issue 5. Art. No.: CD001116. DOI: 10.1002/14651858.CD001116.pub3. This review demonstrated that physical training can improve cardiopulmonary fitness and was well tolerated among people with asthma in the included studies. As such, people with stable asthma should be encouraged to partake in regular exercise training, without fear of symptom exacerbation.

Chang A, Halstead R, Petsky H. **Methylxanthines** for prolonged non-specific cough in children. Cochrane Database Syst Rev. 2005 Jul 20;(3):CD005310.

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Chauhan BF, Ducharme FM. **Anti-leukotriene agents** compared to inhaled corticosteroids in the management of recurrent and/or chronic asthma in adults and children. Cochrane Database Syst Rev. 2012 May 16;5:CD002314. As monotherapy, inhaled corticosteroids display superior efficacy to anti-leukotrienes in adults and children with persistent asthma; the superiority is particularly marked in patients with moderate airway obstruction. On the basis of efficacy, the results support the current guidelines` recommendation that inhaled corticosteroids remain the preferred monotherapy.

Chauhan BF, Chartrand C, Ducharme FM. **Intermittent versus daily inhaled corticosteroids** for persistent asthma in children and adults. Cochrane Database Syst Rev. 2013 Feb 28;2:CD009611. doi: 10.1002/14651858.CD009611.pub3. In children and adults with persistent asthma and in preschool children suspected of persistent asthma, there was low quality evidence that intermittent and daily ICS strategies were similarly effective in the use of rescue oral corticosteroids and the rate of severe adverse health events. The strength of the evidence means that we cannot currently assume equivalence between the two options.. Daily ICS was superior to intermittent ICS in several indicators of lung function, airway inflammation, asthma control and reliever use. Both treatments appeared safe, but a modest growth suppression was associated with daily, compared to intermittent, inhaled budesonide and beclomethasone. Clinicians should carefully weigh the potential benefits and harm of each treatment option, taking into account the unknown long-term (> one year) impact of intermittent therapy on lung growth and lung function decline.

Chauhan BF, Ben Salah R, Ducharme FM. **Addition of anti-leukotriene agents to inhaled corticosteroids** in children with persistent asthma. *Cochrane Database of Systematic Reviews* 2013, Issue 10. Art. No.: CD009585. DOI: 10.1002/14651858.CD009585.pub2. The addition of anti-leukotrienes to ICS is not associatedwith a statistically significant reduction in the need for rescue oral corticosteroids or hospital admission compared to the same or an increased dose of ICS in children and adolescents with mild to moderate asthma.

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Cheyne L, Irvin-Sellers MJ, White J. **Tiotropium versus ipratropium** bromide for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2013 Sep 16;9:CD009552. This review shows that tiotropium treatment, when compared with ipratropium bromide, was associated with improved lung function, fewer hospital admissions (including those for exacerbations of COPD), fewer exacerbations of COPD and improved quality of life. There were both fewer serious adverse events and disease specific events in the tiotropium group, but no significant difference in deaths with ipratropium bromide when compared to tiotropium. Thus, tiotropium appears to be a reasonable choice (instead of ipratropium bromide) for patients with stable COPD, as proposed in guidelines. We would advise some caution with tiotropium via the Respimat inhaler and suggest waiting for further information from an ongoing head-to-head trial comparing mortality in relation to tiotropium delivery devices and doses.

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Chong J, Poole P, Leung B, Black PN. **Phosphodiesterase 4 inhibitors** for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2011, Issue 5. Art. No.: CD002309. DOI: 10.1002/14651858.CD002309.pub3. In people with COPD, PDE4 inhibitors offered benefit over placebo in improving lung function and reducing likelihood of exacerbations, however, they had little impact on quality of life or symptoms. Gastrointestinal adverse effects and weight loss were common, and safety data submitted to the US Food and Drug Administration (FDA) have raised concerns over psychiatric adverse events with roflumilast.

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De Coster DA, Jones M, Thakrar N. **Beclometasone for chronic obstructive pulmonary disease**. Cochrane Database Syst Rev. 2013 Oct 9;10:CD009769. We found little evidence to suggest that beclometasone is a safer or more effective treatment option for people with COPD when compared with placebo or when used in combination with LABA; when statistically significant differences were found, they mostly were not clinically meaningful or were based on data from only one study. The review was limited by an inability to obtain data from one study and likely publication bias for BDP versus placebo, and by the inclusion of one study only for BDP/LABA versus LABA.
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Health Canada Aug/09 is informing health care professionals and Canadians that it is conducting a safety review of the potential association between the asthma drug **Xolair** (the brand name for the drug omalizumab) and an increased risk of cardiovascular problems. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_2009/2009_129-eng.php

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Jeppesen E, Brurberg KG, Vist GE, et al. **Hospital at home for acute exacerbations of chronic obstructive pulmonary disease**. Cochrane Database of Systematic Reviews 2012, Issue 5. Art. No.: CD003573. Selected patients presenting to hospital emergency departments with acute exacerbations of COPD can be safely and successfully treated at home with support from respiratory nurses. We found evidence of moderate quality that hospital at home may be advantageous with respect to readmission rates in these patients. Treatment of acute exacerbation of COPD in hospital at home also show a trend towards reduced mortality rate when compared with conventional inpatient treatment, but these results did not reach statistical significance (moderate quality evidence).

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Johnston SL, et al. TELICAST Investigators. The effect of **telithromycin** in acute exacerbations of asthma. N Engl J Med. 2006 Apr 13;354(15):1589-600.(InfoPOEMs: Telithromycin may add a small benefit of questionable clinical significance for adult patients with acute asthma. This comes at the price of high drug cost, increased nausea and diarrhea, and a theoretical increased risk of drug resistance in the community. Given this balance of benefits and harms, as well as recent reports of catastrophic liver failure in a small number of patients taking telithromycin, physicians should resist the temptation to prescribe this drug for asthma. (LOE = 1b))

Johnstone KJ, Chang AB, Fong KM, et al. **Inhaled corticosteroids for subacute and chronic cough** in adults. Cochrane Database Syst Rev. 2013 Mar 28;3:CD009305. doi: 10.1002/14651858.CD009305.pub2. The studies were highly heterogeneous and results were inconsistent. Heterogeneity in study design needs to be addressed in future research in order to test the efficacy of this intervention.

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Kaplan AG, Balter MS, Bell AD, Kim H, McIvor RA. **Diagnosis of asthma** in adults. CMAJ. 2009 Sep 29. [Epub ahead of print]

Karaca-Mandic P, Jena AB, Joyce GF, Goldman DP. **Out-of-pocket medication costs** and use of medications and health care services among children with asthma. JAMA. 2012;307(12):1284-1291.

Karner C, Cates CJ. The effect of **adding inhaled corticosteroids to tiotropium and long-acting beta(2)-agonists for chronic obstructive pulmonary disease**. Cochrane Database Syst Rev. 2011 Sep 7;9:CD009039. The relative efficacy and safety of adding inhaled corticosteroid to tiotropium and a long-acting beta(2)-agonist for chronic obstructive pulmonary disease patients remains uncertain and additional trials are required to answer this question.

Karner C, Cates CJ. **Long-acting beta(2)-agonist in addition to tiotropium** versus either tiotropium or long-acting beta(2)-agonist alone for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2012 Apr 18;4:CD008989. The results from this review indicate a small mean improvement in health-related quality of life for patients on a combination of tiotropium and long-acting beta(2)-agonist compared to tiotropium alone, but it is not clear how clinically important this mean difference may be. Hospital admission and mortality have not been shown to be altered by adding long-acting beta(2)-agonists to tiotropium. There were not enough data to determine the relative efficacy and safety of tiotropium plus long-acting beta(2)-agonist compared to long-acting beta(2)-agonist alone. There were insufficient data to make comparisons between the different long-acting beta(2)-agonists when used in addition to tiotropium.

Karner C, Cates CJ. Combination inhaled steroid and long-acting beta(2)-agonist in addition to **tiotropium versus tiotropium or combination** alone for chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2011 Mar 16;(3):CD008532.

Karner C, Chong J, Poole P. **Tiotropium versus placebo for chronic obstructive pulmonary disease.** Cochrane Database Syst Rev. 2012 Jul 11;7:CD009285. This review shows that tiotropium treatment was associated with a significant improvement in patients` quality of life and it reduced the risk of exacerbations, with a number needed to treat to benefit (NNTB) of 16 to prevent one exacerbation. Tiotropium also reduced exacerbations leading to hospitalisation but no significant difference was found for hospitalisation of any cause or mortality. Thus, tiotropium appears to be a reasonable choice for the management of patients with stable COPD, as proposed in guidelines. The review however, shows that tiotropium delivered via the Respimat soft mist inhaler was associated with a significantly increased risk of mortality compared with placebo, which calls for caution with this device whilst awaiting the results of an ongoing head-to-head trial comparing tiotropium delivery devices and doses.

Kawasumi Y, et al. **Comparative Effectiveness of Tiotropium and Ipratropium** in Prevention of Hospital Readmission for COPD: Population-Based Cohort Study. Clin Ther. 2013 Mar 12.

Keeney GE, Gray MP, Morrison AK, et al. **Dexamethasone for Acute Asthma** Exacerbations in Children: A Meta-analysis. Pediatrics. 2014 Feb 10.

Kelly HW, Van Natta ML, Covar RA, Tonascia J, Green RP, Strunk RC; CAMP Research Group. Effect of long-term corticosteroid use on **bone mineral** density in children: a prospective longitudinal assessment in the childhood Asthma Management Program (CAMP) study. Pediatrics. 2008 Jul;122(1):e53-61. Multiple oral corticosteroid bursts over a period of years can produce a dosage-dependent reduction in bone mineral accretion and increased risk for osteopenia in children with asthma. Inhaled corticosteroid use has the potential for reducing bone mineral accretion in male children progressing through puberty, but this risk is likely to be outweighed by the ability to reduce the amount of oral corticosteroids used in these children.

Kelly HW, Sternberg AL, Lescher R, et al; the **CAMP** Research Group. Effect of Inhaled Glucocorticoids in **Childhood on Adult Height**. N Engl J Med. 2012 Sep 3.

Kempsford R, Allen A, Bal J, et al. The effect of **ketoconazole** on the pharmacokinetics and pharmacodynamics of inhaled **fluticasone** furoate and **vilanterol** trifenatate in healthy subjects. Br J Clin Pharmacol. 2012 Nov 1.

Kenyon CC, Melvin PR, Chiang VW, et al. **Rehospitalization for Childhood Asthma**: Timing, Variation, and Opportunities for Intervention. J Pediatr. 2013 Nov 14.

Kerstjens HA, Bantje TA, Luursema PB, Sinninghe Damste HE, de Jong JW, Lee A, Wijker SP, Cornelissen PJ. Effects of short-acting bronchodilators added to maintenance tiotropium therapy. Chest. 2007 Nov;132(5):1493-9. Epub 2007 Sep 21. In conclusion, both short-acting bronchodilator classes were effective when added to maintenance treatment with tiotropium. The addition of the beta2-adrenergic fenoterol provided greater additional bronchodilatation than the short-acting anticholinergic ipratropium.

Kerstjens HA, Disse B, Schroder-Babo W, et al. **Tiotropium** improves lung function in patients with severe uncontrolled **asthma**: a randomized controlled trial. J Allergy Clin Immunol. 2011 Aug;128(2):308-14.

Kerstjens HA, Engel M, Dahl R, et al. **Tiotropium in Asthma** Poorly Controlled with Standard Combination Therapy. N Engl J Med. 2012 Sep 2.

Kew KM, Mavergames C, Walters JAE. **Long-acting beta2-agonists for chronic obstructive pulmonary disease**. Cochrane Database of Systematic Reviews 2013, Issue 10. Art. No.: CD010177. Moderate-quality evidence from 26 studies showed that inhaled long-acting beta2-agonists are effective over the medium and long term for patients with moderate to severe COPD. Their use is associated with improved quality of life and reduced exacerbations, including those requiring hospitalisation. Overall, findings showed that inhaled LABAs did not significantly reduce mortality or serious adverse events.

Kew KM, Karner C, Mindus SM, Ferrara G. **Combination formoterol and budesonide** as maintenance and reliever therapy versus combination inhaler maintenance for chronic asthma in adults and children. Cochrane Database of Systematic Reviews 2013, Issue 12. Art. No.: CD009019. DOI: 10.1002/14651858.CD009019.pub2. SiT reduces the number of people having asthma exacerbations requiring oral steroids and the number requiring hospitalisation or an ER visit compared with fixed-dose combination inhalers. Evidence for serious adverse events was unclear. The mean daily dose of inhaled corticosteroids (ICS) in SiT, including the total dose administered with reliever use, was always lower than that of the other combination groups. This suggests that the flexibility in steroid administration that is possible with SiT might be more effective than a standard fixed-dose combination by increasing the dose only when needed and keeping it low during stable stages of the disease. Data for hospitalisations alone could not be obtained, and no studies have yet addressed this question in children younger than age 12.

Kew KM, Seniukovich A. **Inhaled steroids and risk of pneumonia** for chronic obstructive pulmonary disease. Cochrane Database of Systematic Reviews 2014, Issue 3. Art. No.: CD010115. DOI: 10.1002/14651858.CD010115.pub2. Budesonide and fluticasone, delivered alone or in combination with a LABA, are associated with increased risk of serious adverse pneumonia events, but neither significantly affected mortality compared with controls. The safety concerns highlighted in this review should be balanced with recent cohort data and established randomised evidence of efficacy regarding exacerbations and quality of life. Comparison of the two drugs revealed no statistically significant difference in serious pneumonias, mortality or serious adverse events. Fluticasone was associated with higher risk of any pneumonia when compared with budesonide (i.e. less serious cases dealt with in the community), but variation in the definitions used by the respectivemanufacturers is a potential confounding factor in their comparison.

Kew KM, Dias S, Cates CJ. **Long-acting inhaled therapy** (beta-agonists, anticholinergics and steroids) for **COPD**: a network meta-analysis.CochraneDatabase of SystematicReviews 2014,

Issue 3.Art.No.:CD010844.DOI: 10.1002/14651858.CD010844.pub2. This network meta-analysis compares four different classes of long-acting inhalers for people with COPD who need more than shortacting bronchodilators. Quality of life and lung function were improved most on combination inhalers (LABA and ICS) and least on ICS alone at 6 and at 12 months. Overall LAMA and LABA inhalers had similar effects, particularly at 12 months. The network has demonstrated the benefit of ICS when added to LABA for these outcomes in participants who largely had an FEV1 that was less than 50% predicted, but the additional expense of combination inhalers and any potential for increased adverse events (which has been established by other reviews) require consideration. Our findings are in keeping with current National Institute for Health and Care Excellence (NICE) guidelines.

Khorfan FM, Smith P, Watt S, Barber KR. Effects of **nebulized bronchodilator** therapy on heart rate and arrhythmias in critically ill adult patients. Chest. 2011 Dec;140(6):1466-72. In critically ill adult patients, nebulized albuterol and ipratropium does not cause significant tachycardia or tachyarrhythmias. Substitution of levalbuterol for albuterol (salbutamol) to avoid tachycardia and tachyarrhythmias is unwarranted.

Kiljander TO, et al. Effects of **esomeprazole** 40 mg twice daily on asthma: a randomized placebo-controlled trial. Am J Respir Crit Care Med. 2006 May 15;173(10):1091-7. Epub 2005 Dec 15. n=770 16weeks Esomeprazole improved PEF in subjects with asthma who presented with both GERD and NOC. In subjects without both GERD and NOC, no improvement could be detected. (InfoPOEMs: In this study, esomeprazole (Nexium) was no better than placebo in improving peak expiratory flow, asthma symptoms, or quality of life in patients with stable asthma. Furthermore, esomeprazole was no better than placebo in pts with reflux, either. (LOE = 2b-))

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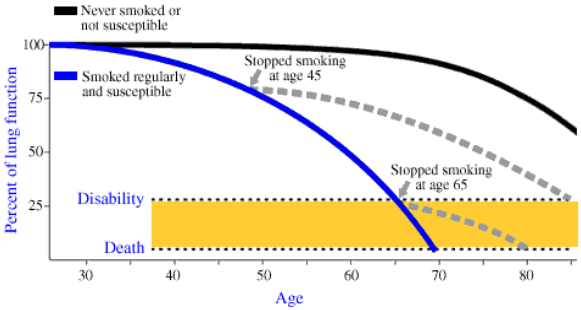

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Extras: **Rimonabant ACOMPLIA** –(not in Canada) cannabinoid receptor 1 blocker; 36% complete smoking cessation in final 4 wks of a 10 wk trial Dose: 20mg/d SE: nausea, **depression**, anxiety & ↓ weight. [xlvi,xlvii,xlviii] ??Clonidine use
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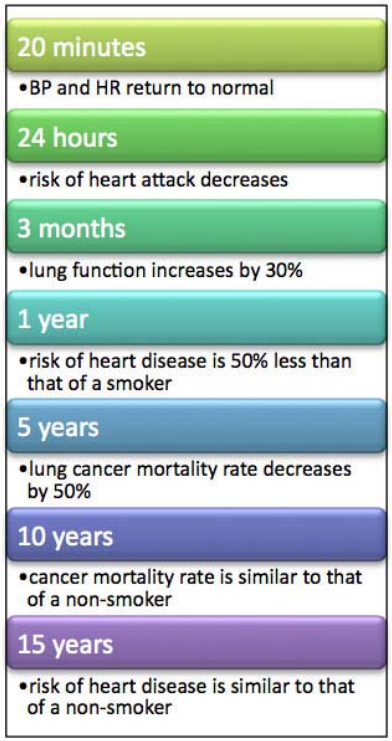
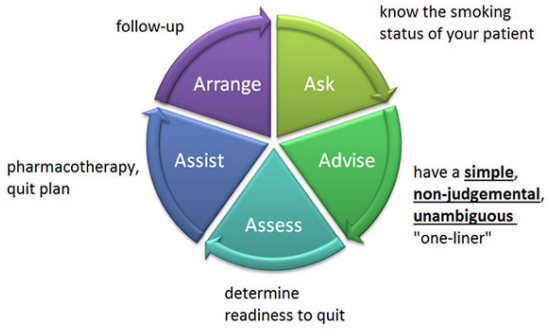
e-Cigaretes: 1) nicotine containing electronic cigarettes (misnomer as aerosolizing delivery device + cartridge). They are illegal in Canada. Current controversies with regulation in the USA. Counsel patients to avoid; alternate products/approaches available for smoking cessation.
2) Concerns: a) risk becoming starter product & skirt smoke free laws, b) potential toxicities, c) lack evidence for benefit as smoking cessation aid & strong potential to ↑ addiction, d) diversion of devices for use in delivering alternate drugs of abuse. e) short term use found to have adverse physiological effects, increased flow resistance and decreased FeNO. f.) toxic and carcinogenic compounds still delivered in e-cigarettes but in lower concentration than traditional cigarettes (Medical Letter Nov 2012.)

Cytisine: Derived from an extract of golden rain acacia seeds; (1.5 mg oral tablets) in 740 adults who smoked ≥ 10 cigarettes/day and were willing to attempt to stop smoking permanently. Patients were randomized to cytisine vs. placebo for 25 days. The dose was 6 tablets for the first 3 days, followed by 5 tablets/day on days 4-12, 4 tablets/day on days 13-16, 3 tablets/day on days 17-20, and finally 2 tablets/day on days 21-25. All patients received minimal counseling during 4 clinical visits and 3 telephone calls over 12 months. Cytisine is currently available in Russia and Poland (at the equivalent of $6 to $15 per course). [West 2011]

Benefits from stopping smoking:





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Modified Fagerström Test for Nicotine Dependence

1. How soon after you wake up do you smoke your first cigarette?
Within 5 minutes (3 points)
5 to 30 minutes (2 points)
31 to 60 minutes (1 point)
After 60 minutes (0 points)

2. Do you find it difficult not to smoke in places where you shouldn't, such as in church or school, in a movie, at the library, on a bus, in court or in a hospital?
Yes (1 point)
No (0 points)

3. Which cigarette would you most hate to give up; which cigarette do you treasure the most?
The first one in the morning (1 point)
Any other one (0 points)

4. How many cigarettes do you smoke each day?
10 or fewer (0 points)
11 to 20 (1 point)
21 to 30 (2 points)
31 or more (3 points)

5. Do you smoke more during the first few hours after waking up than during the rest of the day?
Yes (1 point)
No (0 points)

6. Do you still smoke if you are so sick that you are in bed most of the day, or if you have a cold or the flu and have trouble breathing?
Yes (1 point)
No (0 points)

Scoring: 7 to 10 points = highly dependent; 4 to 6 points = moderately dependent; less than 4 points = minimally dependent.

FIGURE 1. Modified Fagerström test for evaluating intensity of physical dependence on nicotine.
Adapted with permission from Heatherton TF, Kozlowski LT, Frecker RC, Fagerström KO. The Fagerström test for nicotine dependence: a revision of the Fagerström Tolerance Questionnaire. Br J Addict 1991;86:1119-27.

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FDA Chantix/**Champix** Warning Feb/2008: 491 **suicide** reports; **39 completed**. **Canada**: **46 psychiatric** adverse reactions reported from April 1-Nov23/07

FDA and Public Health Experts Warn About **Electronic Cigarettes** July,2009 Laboratory analysis of electronic cigarette samples has found that they contain carcinogens and toxic chemicals such as diethylene glycol, an ingredient used in antifreeze. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm173222.htm

FDA Aug, 2009 — Announced the launch of a new division, the **Center for Tobacco Products**, "in an historic effort to curb the hundreds of thousands of deaths caused by those products each year." The new center will oversee the Family Smoking Prevention and Tobacco Control Act, signed into law by President Barack Obama in June 2009.

FDA May/11 has decided to oversee **electronic cigarettes** the same way it does tobacco products.

FDA June/11 drug safety communication: **Chantix (varenicline) may increase the risk of certain cardiovascular adverse events** in patients with cardiovascular disease.

FDA Quit Smoking package **images** 2011 http://www.fda.gov/downloads/TobaccoProducts/Labeling/UCM259401.pdf

FDA July/11 has approved an updated drug label for the smoking cessation aid Chantix (**varenicline**) to include information about the efficacy and safety of the drug in two patient populations who may benefit greatly from giving up smoking—those with cardiovascular disease and those with chronic obstructive pulmonary disease (COPD).

FDAOct/11 has reviewed the results from two FDA-sponsored epidemiological studies that evaluated the risk of **neuropsychiatric adverse** events associated with the smoking cessation drug **Chantix (varenicline).** Neither study found a difference in risk of neuropsychiatric hospitalizations between Chantix and nicotine replacement therapy (NRT; e.g., NicoDerm patches). However, both studies had a number of study design limitations, including only assessing neuropsychiatric events that resulted in hospitalization, and not having a large enough sample size to detect rare adverse events (see 10/24/2011 Drug Safety Communication below for more information). Healthcare professionals and patients should continue to follow the recommendations in the physician label and the patient Medication Guide, and to monitor for neuropsychiatric symptoms when prescribing or using Chantix. The drug manufacturer is conducting a large safety clinical trial of Chantix to assess neuropsychiatric adverse events, and results from this study are expected in 2017.

FDA Dec/12 is informing the public about the results of a large, combined analysis (called a meta-analysis) of clinical trials that compared patients who received the smoking cessation drug **Chantix (varenicline)** to patients who received a placebo (an inactive treatment). A higher occurrence of major adverse cardiovascular events (a combined outcome of cardiovascular-related death, nonfatal heart attack, and nonfatal stroke) was observed in patients using Chantix compared to placebo. These events were uncommon in both the Chantix and placebo groups, and the increased risk was not statistically significant, which means it is uncertain whether the excess risk for the Chantix group was due to the drug or due to chance.

FDA Apr/13 is allowing makers of **nicotine-replacement products to change their labeling "to allow some flexibility on how they are used and for how long**," the agency announced. Almost 30 years' experience with the products shows that they "do not appear to have significant potential for abuse or dependence," according to the FDA. Nor are there safety concerns about people using the products even while continuing to smoke or using two products simultaneously. In addition, the agency says if smokers believe they need to use a product longer than the recommended 2 to 3 months in order to quit, "it is safe to do so in most cases."

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Health Canada July/07 Unauthorized Smoking Cessation Product **Resolve** May Pose Health Risk - Consumer Information. The product contains an unacceptable amount of an ingredient labelled as "CESTEMENOL-350." Consuming excessive amounts of this ingredient might result in damage to the kidney, liver or red blood cells.

Health Canada June/08 Pfizer Canada in collaboration with Health Canada would like to notify healthcare professionals of important safety information regarding **CHAMPIX**, and post-marketing reports of serious **neuropsychiatric adverse events**, including depressed mood, agitation, hostility, changes in behaviour, suicidal ideation and suicide, as well as worsening of pre-existing psychiatric illness (previously diagnosed or not). Since introduction of CHAMPIX in Canada, in April 2007 through April 30, 2008, a total of **226 Canadian cases** of neuropsychiatric adverse events have been reported. For the same time period, there have been **708 534 prescriptions filled** for CHAMPIX in Canada1. All patients attempting to quit smoking with CHAMPIX, their families & caregivers should be alerted about the need to monitor for symptoms of neuropsychiatric adverse events. Patients should be instructed to stop taking CHAMPIX and contact their healthcare provider immediately if they have or if their families or caregivers observe depressed mood, agitation, hostility or changes in behavior, that are not typical for the patient, or if the patient has suicidal ideation or suicidal behavior. Patients with concomitant psychiatric conditions, even if well controlled, or with a history of psychiatric symptoms, should be diligently monitored.

Health Canada Mar/09 is advising Canadians not to purchase or use **electronic smoking products**, as these products may pose health risks and have not been fully evaluated for safety, quality and efficacy by Health Canada. http://www.hc-sc.gc.ca/ahc-asc/media/advisories-avis/_2009/2009_53-eng.php (FDA and Public Health Experts Warn About Electronic Cigarettes http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm173222.htm)

Health Canada June/10 **CHAMPIX** (varenicline tartrate) - Changes to the Canadian Product Monograph - Pfizer Canada Inc. Changes include: 1- a boxed warning highlighting recommendations about neuropsychiatric adverse events, 2- a warning about rare reports of serious

allergic and skin reactions, 3- a guidance for prescribers about information to be shared with their patients prior to and during treatment, and 4- an additional dosing option for CHAMPIX.

Health Canada Jan/12 is informing Canadians that our **review of Champix** is now complete and the label has been updated with new information with respect to cardiovascular safety. Champix (brand name for varenicline tartrate) is a prescription drug used to help patients quit smoking in combination with supportive counselling. Health Canada evaluated data from a quit-smoking clinical trial involving 700 smokers with cardiovascular disease (approximately 350 who received Champix and 350 who received a placebo or "sugar pills"). Cardiovascular disease is a broad term for any condition that affects the heart and/or blood vessels, including heart attack and stroke. Although a slightly increased number of patients experienced serious heart-related events in the group treated with Champix compared to the group treated with placebo, the study was not adequately designed to be able to test the cardiovascular safety of Champix. The small study size combined with other study design weaknesses make it impossible to draw conclusions based on these data. The possibility of an increased risk of heart attack or stroke in patients with cardiovascular disease can neither be confirmed nor ruled out at this time.

Health Canada May/13 CHAMPIX (**varenicline** tartrate) and ZYBAN (**buproprion** hydrochloride) - Revision to the Consumer Information of Non-Nicotine Smoking Cessation Aids - Pfizer Canada Inc. and Valeant Canada LP. The revised product monographs indicate that thorough consideration should be given to the option of **nicotine replacement therapy**, prior to a decision to prescribe a non-nicotine treatment.

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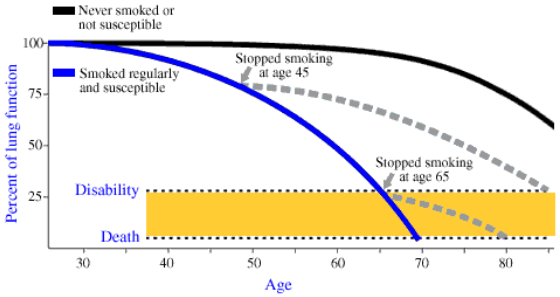

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Addional information about Mircera (Web-only)

Methoxy polyethylene glycol-epoetin beta **MIRCERA** [13] Single-dose **vials** (solution): 50, 100, 200, 300, 400, 600, 1000 µg/mL Single-dose **pre-filled syringes:** 50µg/0.3mL, 75µg/0.3mL, 100µg/0.3mL, 150µg/0.3mL, 200µg/0.3mL, 250µg/0.3mL, 400µg/0.6mL, 600µg/0.6mL	✓ **Tx of anemia with CKD** Pre-filled syringes: sterile & do not contain preservatives. Store in fridge at 2-8°. (Do not freeze) Keep in original package to protect from light. Stable at room temperature ≤ 25° C for up to 1 month Allow to reach room temp. before inj.		SC in ND-CKD & PD-CKD; **IV** or SC in HD-CKD Not currently on ESA tx: 0.6 mcg/kg every 2 weeks as a single IV or SQ inj Pts on ESA: can convert to MIRCERA given once a month as a single IV or SQ inj. Monthly Mircera starting IV or SQ dose mcg/monthly: 120 if <40 Aranesp or <8,000 Eprex; 200 if <40-80 Aranesp or 8-16,000 Eprex; 360 if >80 Aranesp or >16,000 Eprex (Aranesp in mcg/week, Eprex in IU/week) Equivalent with IV or SQ. If Hgb target is reached, may give once monthly using a dose equal to twice the previous every two week dose.	✗ ⊗ Not on formulary. Not yet avail. in Canada, but NOC received Mar 2008

Erythropoiesis Stimulating Agents (ESA) in Anemia of Chronic Kidney Disease (CKD): Therapeutic Alternatives

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FDA Feb/10 and Amgen notified healthcare professionals and patients that all ESAs must be used under a REMS risk management program. As part of the risk management program, a Medication Guide explaining the risks and benefits of ESAs must be provided to all patients receiving an ESA. Under the ESA APPRISE Oncology program, Amgen will ensure that only those hospitals and healthcare professionals who have enrolled and completed training in the program will prescribe and dispense ESAs to patients with cancer. Amgen is also required to oversee and monitor the program to ensure that hospitals and healthcare professionals are fully compliant with all aspects of the program. FDA is requiring a REMS because studies show that ESAs can increase the risk of tumor growth and shorten survival in patients with cancer who use these products. Studies also show that ESAs can increase the risk of heart attack, heart failure, stroke or blood clots in patients who use these drugs for other conditions.

FDA June/11 notified healthcare professionals that new, modified recommendations for more conservative dosing of Erythropoiesis-Stimulating Agents (ESAs) in patients with chronic kidney disease (CKD) have been approved to improve the safe use of these drugs. FDA has made these recommendations because of data showing increased risks of cardiovascular events with ESAs in this patient population. The new dosing recommendations are based on clinical trials showing that using **ESAs to target a hemoglobin level of greater than 11 g/dL in patients with CKD provides no additional benefit** than lower target levels, and increases the risk of experiencing serious adverse cardiovascular events, such as heart attack or stroke. http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm260641.htm

FDA: Feb/13 All lots of **peginesatide (Omontys)** — an anemia drug approved less than a year ago for adults on dialysis — are being recalled due to reports of serious and sometimes **fatal adverse hypersensitivity reactions**, including anaphylaxis. Approximately 0.02% of patients had a fatal reaction within 30 minutes of receiving a peginesatide injection, according to postmarketing data. About 0.2% of patients overall had reactions; about a third of these were serious (i.e., requiring immediate medical attention). Some 25,000 patients have received the drug since it was launched, the FDA says.

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Extras:

New FDA: Ferric carboxymaltose Injectafer for IDA if poor response to oral/ND-CKD, 750mg/15ml IV x 2 doses 1 week apart;. SE: nausea, dizzy, hypertension hypophosphatemia, anaphylaxis.

Oct/11 The FDA has granted accelerated approval for **deferiprone (Ferriprox)** to treat transfusion-related iron overload in patients with thalassemia who do not respond to prior chelation therapy. The drug, an oral iron chelator, is the first new treatment approved for this disorder since 2005, according to the agency. Agranulocytosis was noted in about 2% of patients in clinical studies. Other adverse effects included nausea, arthralgia, vomiting, neutropenia, and increased alanine aminotransferase levels.

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conversely, it may give false reassurance because hypersensitivity reactions have been reported in patients that had a negative initial test dose. Therefore, an **initial test dose on first use of an IV iron product for a patient is no longer** recommended. A Europe-wide review of intravenous iron products for iron deficiency and anaemia has recommended strengthened measures are taken to manage and minimise the risk of hypersensitivity reactions, which may be life-threatening or fatal as outlined in this article.

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Red Flags for calciphylaxis?

Natural Products Database Search on phosphate-containing products:

Enemol Sodium Phosphate Enema (Dominion Pharmacal): Each 60 ml serving contains: Sodium Phosphate dibasic, heptahydrate 6 g. • Sodium Phosphate monobasic, anhydrous 16 g. Other Ingredients: Benzalkonium Chloride, Edetate Disodium, Purified Water. NPN 02096900.

Enema (HJ Sutton): Each 30 mL serving contains: Dibasic Sodium Phosphate 7 g (118 mL) • Monobasic Sodium Phosphate 19 g (118 mL). Other Ingredients: Benzalkonium Chloride, Disodium EDTA, Purified Water. NPN 02231170.

Kali Phosphoricum 6x (Thompson's Homeopathic Supplies Ltd): For 'stress and tension'. Potassium Phosphate 6X. Other Ingredients: Ground Corn Starch, Lactose. DIN-HM 00190101
Magnesia Phosphorica 6x tabs (Thompson's Homeopathic Supplies Ltd): Oral Laxative. Magnesium Phosphate 6X. Other Ingredients: Ground Corn Starch, Lactose. DIN-HM 00189995.

Natrum Phosphoricum 6x tabs (Thompson's Homeopathic Supplies Ltd.): Oral laxative. Each tablet contains: Sodium Phosphate 6X. Other Ingredients: Corn Starch, Lactose. DIN-HM 00190160

Naturally Sourced Calcium from Milk with Vit D and Magnesium (Immunotec Inc): Oral Laxative. Two tablets contain: Calcium Phosphate 250 mg • Magnesium 15 mg • Vitamin D (D3) 100 IU. Other Ingredients: Acacia Gum, Carnauba Wax, Croscarmellose Sodium, Hypromellose, Magnesium Stearate, Microcrystalline Cellulose, Polyethylene Glycol, Purified Water. NPN 02243453
New Era Biochemic Tissue Salt 10, 2, 6, 8 (Seven Seas Limited): Each tablet contains: Sodium Phosphate 6x 0.07 mcg. Other Ingredients: Acacia Gum, Lactose Monohydrate. DIN-HM 0016935.

New Era Combination F Biochemic Tissue Salts (Seven Seas Limited): Each tablet contains: Magnesium Phosphate 6x 0.0175 mcg • Potassium Phosphate 6x 0.0175 mcg • Silicon Dioxide 6x 0.0175 mcg • Sodium Chloride 6x 0.0175 mcg. Other Ingredients: Acacia Gum, Lactose Monohydrate. DIN-HM 00147028

New Era Combination G Biochemic Tissue Salts (Seven Seas Limited): Each tablet contains: Calcium Fluoride 6x 0.0175 mcg • Calcium Phosphate 6x 0.0175 mcg • Potassium Phosphate 6x 0.0175 mcg • Sodium Chloride 6x 0.0175 mcg. Other Ingredients: Acacia Gum, Lactose Monohydrate. DIN-HM 00147036

New Era Combination N Biochemic Tissue Salts (Seven Seas Limited): Oral Laxative. Each tablet contains: Calcium Phosphate 6x 0.0175 mcg • Magnesium Phosphate 6x 0.0175 mcg • Potassium Chloride 6x 0.0175 mcg • Potassium Phosphate 6x 0.0175 mcg. Other Ingredients: Acacia Gum, Lactose Monohydrate. DIN-HM 00534862
Oral Laxative (HJ Sutton Industries): Each 1 tsp serving contains: Dibasic Sodium Phosphate 0.9 g. Other Ingredients: Glycerin, Sodium Saccharin, Sodium Benzoate, Purified Water. NPN 80003212

Phoslax: Oral Laxative (Odan Laboratories Ltd): Each one tsp serving contains: Dibasic Sodium Phosphate 0.9 g. • Monobasic Sodium Phosphate 2.4 g. Other Ingredients: Glycerin, Natural Ginger Flavour, Natural Lemon Flavour, Sodium Benzoate, Purified Water. NPN 80000689

Schuessler Tissue Salts General Debility Comb B (Martin & Pleasance): Oral Laxative. Each tablet contains: Calcium Phosphate 6.0 X • Ferrum Phosphoricum 6.0 X • Kali Phosphoricum 6.0 X. Other Ingredients: Anhydrous Calcium Hydrogen Phosphate, Lactose, Magnesium Stearate. DIN-HM 80003543

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- **BC CDUP: http://www.cdup.org/**
- **Dalhousie: http://cme.medicine.dal.ca/ADS.htm**

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Health Canada Mar/11 Salvia divinorum (S. divinorum) is a species of sage belonging to the mint family. Some street names for S. divinorum include: Sally D, Lady Sally, Maria pastora, ska Maria pastora, ska pastora, diviner's sage, magic mint, puff, incense special, and salvia. Canadians are cautioned against the use of products containing S. divinorum and/or salvinorin A because these products are known to cause hallucinations and little is known about the long-term effects of these substances on the brain and body.
Health Canada May/13 has been made aware of three products ("Rochefort", "Rush" and "Amsterdam Special"), commonly known as "poppers", labelled to contain alkyl nitrites . These products, labelled as leather cleaners and/or liquid incense, are known to be used by consumers to get "high" and may pose serious risks to health if they are inhaled or swallowed.
Health Canada Jun/13 Eight products labelled as leather cleaners or liquid incense contain, or allege to contain, alkyl nitrites were being sold by Saints N Sinners Ltd, 1715 Centre Street N.W., Calgary, Alberta. These products, commonly known as "poppers" are used by consumers to get "high" and may pose serious risks to health if they are inhaled or swallowed
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Organ Transplant Facts:

Canada: There were 2,083 solid organ transplants in Canada, as compared with 2,188 in 2007, according to Canadian Organ Replacement Register statistics (http://cihi.ca /cihiweb/dispPage.jsp?cw_page=AR3230_E&cw_topic=3230). The total number of organ donors also decreased, to 1038 from 1046 in 2007.
Roughly 4380 Canadians were on waiting lists for transplants as of Dec. 31, 2008. — Sabrina Doyle, Ottawa, Ont. http://secure.cihi.ca/cihiweb/dispPage.jsp?cw_page=media_20091222_e

Organ Donor Activity in Canada, 1999 to 2008 http://secure.cihi.ca/cihiweb/products/CORR_AiB_EN_20091222_rev20100106.pdf
During the past decade, the number of organ donors in Canada increased from 812 to 1,038 per year; living donors accounted for 69% of this increase. While there were increases in organ donation during the past decade, the demand for organs also grew. For example, in the case of kidneys, the incidence rate of end-stage renal disease increased from 149 to 168 per million population. The availability of donated organs in Canada rose by more than one-quarter (28%) over the past decade, but this increase is not keeping pace with demand. More than 1,000 Canadians donated organs in 2008, up from 812 in 1999, according to a new study released today by the Canadian Institute for Health Information (CIHI). With an increase in the number of Canadians with organ failure, combined with medical advancements that are keeping these patients alive longer, the results show an increase in the demand for organs. Last year, about 215 Canadians died while waiting for an organ transplant. A national paired exchange program has been launched for donor and recipient pairs who do not match as an initiatives to maximize the number of live-donor organs available at http://www.ccdt.ca/english/ldpe/index.htm called the Living Donor Paired Exchange Registry (LDPE).
According to the Canadian Organ Replacement Registry's 2008 annual report, there were an estimated 33,832 people with end-stage renal disease in Canada at the end of 2006, an increase of 69.7% since 1997. Of these, 20,465 were on dialysis and 13,367 were living with a functioning kidney transplant.

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