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The Honourable Tony Clement, PC, MP
Minister of Health
Brooke Claxton Building, Tunney's Pasture
Postal Locator: 0906C
Ottawa, Ontario K1A 0K9

Black Cohosh

Re: Require packages of all products containing black cohosh--an herb widely used for menopausal symptoms--to bear: (1) warnings of potential liver toxicity that have required liver transplant; (2) information on how to recognize liver toxicity and steps to take if such symptoms develop; and (3) a notice that the preponderance of scientific evidence shows that black cohosh is no more effective than placebos in alleviating menopausal symptoms.

Dear Minister Clement:

We are writing on behalf of the Centre for Science in the Public Interest* to urge that labels for all natural health products sold in Canada containing the herb *cimicifuga racemosa* (black cohosh) be required to carry a prominent warning about the potential risk of liver toxicity. According to the Health Canada web site, as of April 17, 2007, there are 18 licensed products containing black cohosh but, as you know, unlicensed products may also be available for sale as the Natural Health Product Directorate continues to process license applications. The labelling for products containing black cohosh should also inform consumers of the signs and symptoms of liver toxicity and what steps to take should these symptoms develop. Health Canada must also issue a stop sale order for all black cohosh containing products that do not carry such warnings.

Furthermore, a recent large double-blind clinical trial funded by the U.S. government found that women taking black cohosh were no less likely to experience hot flashes than women taking a placebo.¹ This research casts considerable doubt on

* The Centre for Science in the Public Interest (CSPI) is an independent health advocacy organization, focusing on nutrition and food safety, with offices in Ottawa, Canada and Washington, D.C. CSPI's Canadian advocacy efforts are supported by more than 100,000 subscribers to the Canadian edition of its *Nutrition Action Healthletter*. CSPI does not accept funding from either industry or government.

the efficacy of black cohosh to deliver the health benefits Health Canada has approved for all products licensed pursuant to its product monograph/compendium.

Evidence of Human Health Risk

The black cohosh monograph adopted by Health Canada's Natural Health Products Directorate (NHPD), dated May 1, 2004 and updated April 2, 2007, makes no mention of the possibility of liver toxicity from the use of this herb² except that users should consult a physician if the user has or develops a liver disorder while using it (i.e., without suggesting the causal link). In fact, despite ample evidence to the contrary, the monograph misleadingly states that there are "No reports known" of adverse reactions.

On August 18, 2006, Health Canada acknowledged a health risk from this herb by issuing a public advisory³ about the possible link between black cohosh and liver toxicity. The government advised the following:

- Consumers should exercise caution in the use of products containing black cohosh, and consult a health care practitioner if they have concerns about its use.
- Consumers should discontinue the use of products containing black cohosh and consult a physician if they have unusual fatigue, weakness, loss of appetite, or if they develop symptoms suggestive of liver injury such as yellowing of the skin or whites of the eyes, dark urine or abdominal pain.

Health Canada had previously warned of potential liver toxicity in the July 2005 issue of the *Canadian Adverse Drug Reaction Newsletter* where it alerted its readers (industry and health sector subscribers) to international reports of liver toxicity associated with the use of black cohosh outside Canada.⁴

Health Canada's advisories alone, however, are woefully inadequate to protect the public. This particular public advisory received only little, and predictably fleeting, media coverage. For this vital information to be useful to consumers, it must appear on the label of every product containing black cohosh sold in Canada.

Drug regulatory authorities in other countries have already taken steps to protect their citizens' health by requiring liver toxicity warnings on the labels of black cohosh containing products.

Label Warnings Required in Other Countries

On July 19, 2006, the United Kingdom's Medicines and Healthcare Products Regulatory Agency (MHRA) and the European Medicines Agency (EMA) issued public statements about the risk of liver toxicity with the use of black cohosh.^{5,6} The MHRA reported that as of May 31, 2006, 31 reports of suspected adverse reactions

associated with black cohosh had been received by the agency. Of these, 22 were reports of liver reactions that ranged in severity from abnormal liver function (15 cases) to various forms of hepatitis (six cases) including one case of liver failure. Accordingly, warnings are being added to the labels for all black cohosh products sold in the U.K. and the MHRA is working with the relevant marketing authorization holders and the herbal sector to ensure people are fully informed about this potential risk.⁵

The EMEA and the Committee on Herbal Medicinal Products (HMPC) reviewed 42 available case reports of liver reactions with black cohosh and advised there is a potential connection between the use of black cohosh and liver toxicity.⁶ The MHRA found sufficient evidence to support a causal association between black cohosh and the risk of liver toxicity.⁵

On February 9, 2006, Australia's Therapeutic Goods Administration (TGA) announced that all black cohosh containing products would be required to carry the following warning on their labels:

"Warning: Black cohosh may harm the liver in some individuals. Use under the supervision of a healthcare professional."⁷

At the time of its review, the Australian TGA identified 47 cases of liver reactions worldwide, including nine Australian cases. In Australia, four patients required hospitalization, including two who required liver transplants. Although some reports were confounded by multiple ingredients, by more than one medication, or by other medical conditions, there is sufficient evidence of a causal association between black cohosh and serious hepatitis (liver inflammation).⁷

The Swedish government has reportedly been requiring a liver toxicity warning in the product leaflets for black cohosh products for several years, albeit not on the outside packaging. Swedish authorities are currently considering the possibility of strengthening the language used in the leaflets and requiring companies to describe the symptoms of liver damage to consumers.⁸

Inadequate Evidence of Efficacy for Black Cohosh

The menopause-related health claims approved by Health Canada in its Compendium of Monographs are based on nine cited sources, four of which were published more than 70 years ago.² In contrast, the strongest type of scientific evidence, randomized controlled clinical trials, have failed to consistently demonstrate a therapeutic benefit for black cohosh in relieving the symptoms of menopause.⁹⁻¹¹ A recent randomized clinical trial published in June 2006 was unable to provide any evidence that black cohosh reduced hot flashes more than an inactive placebo.¹²

A large double-blind clinical trial sponsored by the U.S. government published in December 2006 in the *Annals of Internal Medicine*¹ that found no

benefit for black cohosh use was conspicuously absent from mention in the black cohosh monograph that was updated by Health Canada on April 2, 2007.² This study showed that women taking black cohosh daily for one year were as likely as women taking daily placebos to report hot flashes.¹

The available evidence puts into serious question the “traditional” evidence that underpins the Health Canada black cohosh monograph, namely that this herb helps to relieve menopausal symptoms.

Suggested Required Label Warnings in Canada for Black Cohosh

We recommend that Health Canada require the following warning and information to be prominently displayed on all products containing black cohosh sold in Canada:

“The use of black cohosh has been linked to severe liver damage including liver failure that has resulted in the need for liver transplant.

If you develop any of the symptoms of potential liver toxicity while taking black cohosh, you should seek medical attention immediately. These symptoms are:

- *Pruritus (itchy skin)*
- *Jaundice (yellowing of the skin or whites of the eyes)*
- *Dark urine*
- *Upper right-sided abdominal tenderness (location of the liver)*
- *Unexplained “flu-like” symptoms*

High quality independent research has found that the use of black cohosh was no more effective than an inactive placebo in managing menopausal symptoms.”

Furthermore, we urge that Health Canada issue a stop sale order for any product containing black cohosh that does not display these warnings and information.

Conclusion

Currently, Health Canada’s generic product monograph for black cohosh can be used as the basis for fast-tracking product license applications for black cohosh – i.e., a product license conforming to the monograph will be obtained in as little as 60 calendar days unless Health Canada objects. Yet, the monograph updated April 2, 2007 failed to include information from important studies raising considerable doubts about the usefulness of black cohosh as a treatment for the symptoms of menopause. This monograph fails to reflect precautions taken earlier by Health Canada and other national regulatory authorities. Finally, the monograph incorrectly denies the existence of numerous adverse reaction reports recorded world-wide.

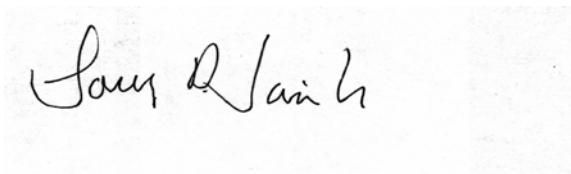
Health Canada must revise the product monograph for black cohosh to require that product label warnings inform Canadians about the risk of liver toxicity that have come to light in recent years and how to identify and avoid that risk. Health Canada should also ensure that labels and advertisements convey the dismal prospects for relieving the symptoms of menopause. Finally, the Minister should carefully consider issuing a stop sale order for products containing this herb – as was done to remove the herb kava kava from the market on August 21, 2002 because of liver toxicity¹³ – at least until unresolved concerns about the safety and effectiveness of black cohosh can be resolved.

Canadians are entitled to a supply of safe and effective natural health products. However, ineffective substances that also pose health risks should certainly not be sold with Health Canada's imprimatur of therapeutic benefit and, depending on the extent of the safety risk, should either be the subject of a clear label warning or should be removed from the market altogether.

Sincerely,

[original signed by BJ]

Bill Jeffery, LL.B.
National Coordinator,
Centre for Science and the Public Interest

A handwritten signature in black ink, appearing to read "Larry D. Sasich". The signature is written in a cursive style and is positioned above a light grey rectangular background.

Larry D. Sasich, Pharm.D., MPH
Consultant Pharmacist to
Centre for Science and the Public Interest

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