

March 4, 2004

The Honorable Mark B. McClellan, M.D., Ph.D. Commissioner
Food and Drug Administration
Room 14-71
Parklawn Building
5600 Fishers Lane
Rockville, MD 20857

## Dear Commissioner McClellan:

On behalf of our 750,000 American members, we write to urge you to take immediate action to protect consumers from the serious potential health risks of the dietary supplement black cohosh – which is marketed for the relief of menopausal symptoms. Labels on black cohosh do not reflect recent research indicating possibly increased risks of breast cancer metastasis and of acute liver failure in women taking black cohosh.

The lack of warnings on black cohosh may be especially significant in light of the FDA's warnings last year of the health risks associated with menopausal hormone therapy drugs. While such drugs can only be purchased with a physician's prescription, dietary supplements are readily available for purchase directly by those consumers who feel it may have some benefits.<sup>2</sup>

A study (enclosed) presented at a scientific meeting last summer by Vicki Davis of Duquesne University showed that mammary cancer was significantly more likely to spread to the lungs in mice given black cohosh (in an amount equivalent to what women take) than in mice

<sup>&</sup>lt;sup>1</sup> Last year the FDA advised women and health care professionals that menopausal hormone therapy – estrogen and estrogen with progestin – is associated with an increased risk of heart disease, heart attacks, strokes, and breast cancer. The FDA said these drugs should be used only when the benefits clearly outweigh the risks. See, for example, FDA press release of September 9, 2003.

<sup>&</sup>lt;sup>2</sup> The scientific evidence is unclear on its benefits. The National Institutes of Health ("NIH") says "Although preliminary evidence is encouraging, the currently available data are not sufficient to support a recommendation on the use of black cohosh for menopausal symptoms....Although some study results suggest that black cohosh may help relieve menopausal symptoms, other study results do not." <a href="http://ods.od.nih.gov/factsheets/blackcohosh.htm">http://ods.od.nih.gov/factsheets/blackcohosh.htm</a> (visited March 3, 2004). NIH is funding five human trials of black cohosh in women, including three on menopausal symptoms. <a href="http://ods.od.nih.gov/factsheets/blackcohosh.htm">www.clinicaltrials.gov</a> (visited March 3, 2004). The only harmful effects mentioned by NIH are a low incidence of gastric complaints, headaches, heaviness in the legs, and weight problems among women taking black cohosh for less than six months. <a href="http://ods.od.nih.gov/factsheets/blackcohosh.htm">http://ods.od.nih.gov/factsheets/blackcohosh.htm</a> visited March 3, 2004).

that did not receive the herb.<sup>3</sup> As <u>www.breastcancer.org</u> advises women, "based on these conclusions, researchers may consider it potentially unsafe for women with breast cancer to even try black cohosh....[I]t suggests that you may want to think twice before taking black cohosh supplements to relieve your hot flashes or other symptoms. This herbal remedy may NOT be a safer alternative to HRT [hormone replacement therapy], especially if you have already had breast cancer."<sup>4</sup>

Three cases of liver toxicity in women taking herbal preparations that included black cohosh have been reported. A 47-year-old woman in Australia who took black cohosh for one week developed fulminant hepatic failure and required an urgent liver transplantation.<sup>5</sup> A 52-year-old woman in Australia developed acute liver failure after three months of taking an herbal mixture containing black cohosh, and she required a liver transplantation.<sup>6</sup> A 57-year-old woman in the United States developed autoimmune hepatitis three weeks after starting to take black cohosh. Her symptoms resolved completely two weeks after discontinuing the herb.<sup>7</sup> The authors of the article reporting the second Australian case concluded "It is important for the medical and broader community to be aware of the potential toxicity of these preparations." The physician who reported the United States case was quoted as saying "Patients on black cohosh should be monitored for evidence of hepatic dysfunction. If physicians look for this, we'll be seeing more cases."

Current black cohosh labels do not warn women of those possible health risks:

• A Rite Aid brand of black cohosh says "women's herbal support for estrogen balance." The only warning on the label says "Do not use this product if you are pregnant or nursing a baby."

<sup>&</sup>lt;sup>3</sup> Vicki L. Davis *et al.*, American Association for Cancer Research annual meeting, July 11-14, 2003, Washington, D.C., abstract #R910.

<sup>&</sup>lt;sup>4</sup> www.breastcancer.org/resarch\_alternative\_cohosh.htm (visited March 3, 2004).

<sup>&</sup>lt;sup>5</sup> Med J Aust. 2002; 177(8): 440-443 (enclosed).

<sup>&</sup>lt;sup>6</sup> Med J Aust. 2003; 179(7): 390-391 (enclosed).

<sup>&</sup>lt;sup>7</sup> This case report is now in press and was presented by Stanley M. Cohen, M.D., now of Rush University Medical Center in Chicago, at a poster session of the American College of Gastroenterology's annual scientific meeting in 2003. It is described in an enclosed Medscape article at <a href="http://www.medscape.com/viewarticle463059">http://www.medscape.com/viewarticle463059</a> (visited March 2, 2004).

<sup>&</sup>lt;sup>8</sup> Med J Aust. 2003; 179(7): 390-391.

<sup>&</sup>lt;sup>9</sup> http://www.medscape.com/viewarticle463059 (visited March 2, 2004).

- Nature Resource black cohosh says it "may help alleviate menopausal discomforts....Black Cohosh has been used worldwide for centuries. It has been taken for its benefits during menstrual periods and menopause. Black Cohosh may have a beneficial effect on hormone levels." Its only warning is "Excessive use may cause upset stomach in certain people. If you are pregnant or nursing, consult a health professional before taking this product."
- Safeway Select Black Cohosh says "Black Cohosh may offset the decline in estrogen and help balance hormone levels in women. It may also help normalize menstrual cycles of women in childbearing years. Clinical studies have shown that black cohosh can help relieve menopausal symptoms such as hot flashes and night sweats." Its only warning is "If pregnant or nursing, consult your doctor before taking this product. Consult your doctor for continuous use over six months. If taking any medications, consult your healthcare professional before taking this product."

Nor do websites selling black cohosh warn women who are neither pregnant nor nursing about the possible health risks of black cohosh. See, for example:

- Medwing's website says black cohosh "delivers relief from menopausal symptoms including hot flashes, night sweats, and mood swings....Caution: Women who are pregnant or nursing should not use this product." 10
- Remifemin's website says "Historically, the use of black cohosh was based on observations that it successfully relieved menstrual symptoms and the discomfort associated with menopause....When used properly following the package directions, Remifemin Menopause has few side effects, if any. In clinical research, there was a small percentage of gastric discomfort complaints....Warnings: This products should not be used by women who are pregnant or considering becoming pregnant or are nursing."
- MotherNature's website says "some studies have shown black cohosh to be
  effective for easing symptoms of menopause...Do not use if pregnant or nursing.
  Occasional side effects may include gastro-intestinal disturbances. The German
  Commission E recommends the duration of treatment not to exceed six months."

<sup>&</sup>lt;sup>10</sup> http://www.medwing.com/ipp/phytopharmica/black-cohosh-phytopharmica.shtml (visited March 3, 2004).

<sup>&</sup>lt;sup>11</sup> http://www.remifemin.com/5 1.asp (visited March 3, 2004).

<sup>12</sup> http://www.mothernature.com/shop/detail.cfm/sku/49970 (visited March 3, 2004).

• GNC's website for black cohosh says "Warning: Keep out of reach of children. Contains black cohosh which is not to be used while pregnant or nursing." 13

We urge the FDA to use its current legal authority to take immediate steps to protect consumers. Such steps could include: (1) notifying all physicians of the possible risks of black cohosh and asking them to submit to the FDA any data on liver toxicity, cancer metastasis, or other health problems from patients using black cohosh; (2) asking the National Institutes of Health to be alert for adverse effects during its current studies of the effectiveness of black cohosh and to notify immediately those now participating in these studies, especially the women in the NIH breast cancer study; (3) issuing a consumer advisory about the possible risks of black cohosh; and (4) considering requiring warning labels on black cohosh.<sup>14</sup>

Thank you for your prompt attention to this important public health matter.

Sincerely,

Benjamin Cohen Senior Staff Attorney

David Schardt Senior Nutritionist

<sup>&</sup>lt;sup>13</sup> http://gnc.mondosearch.com/cgi-bin/MsmFind.exe?QUERY=black+cohosh (visited March 3, 2004).

<sup>&</sup>lt;sup>14</sup> Congress clearly contemplated that dietary supplements labels might contain warnings, for section 403(s) of the Federal Food, Drug, and Cosmetic Act ("FFDCA") provides, in pertinent part, that a dietary supplement is not misbranded "solely because its label ...contains...warnings." In 1997, when the FDA asked for comments on its proposed rule to require a warning statement on the label of dietary supplements containing ephedrine alkaloids, it said that "FDA's authority to require label warning statements on dietary supplement products derives from sections 201(n), 403(a)(1), and 701(a) of the" FFDCA. 62 Fed. Reg. 30678 (June 4, 1997) at 30700. Section 201(n) of the FFDCA provides, in pertinent part, that in determining whether an article is misbranded, the FDA shall consider "the extent to which the labeling or advertising fails to reveal facts material in the light of such representations or material with respect to consequences which may result from the use of article to which the labeling or advertising relates under the conditions of use prescribed in the labeling or advertising thereof or under such conditions of use as are customary or usual." Section 403(a)(1) says that a food is misbranded if "its labeling is false or misleading in any particular." Section 701(a) authorizes the FDA to promulgate regulations "for the efficient enforcement" of the FFDCA. (Section 201(ff) says that "a dietary supplement shall be deemed to be a food within the meaning of this Act.")

enclosures: Vicki L. Davis et al., American Association for Cancer Research annual meeting, July 11-14, 2003, Washington, D.C. abstract #R910

Med J Aust. 2002; 177(8): 440-443

Med J. Aust. 2003; 179(7): 390-391

Medscape Medical News "Black Cohosh Linked to Autoimmune Hepatitis"

cc: Robert E. Brackett, Ph.D.
Director
Center for Food Safety and Applied Nutrition

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