



A VOICE FOR WOMEN, A NETWORK FOR CHANGE

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October 31, 2005

Dockets Management Branch  
Food & Drug Administration  
5630 Fishers Lane  
Room 1061 (HFA-305)  
Rockville, MD 20852

Re: Comments in Support of Petition filed by the Consumer Health Alliance for Safe Medication (CHASM);  
Docket No. 05P-0116

Dear Sir or Madam:

On behalf of the National Women's Health Network, we are writing in support of the Consumer Health Alliance for Safe Medication (CHASM) petition asking FDA to exercise its authority over compounding pharmacies to ensure that the drugs they dispense are safe and effective products, and to require honest marketing practices in product promotion to the public. While the CHASM petition specifically addresses FDA regulation of aqueous-based drugs for inhalation that have been compounded by pharmacy operations, the NWHN respectfully requests that the FDA also consider the recommended actions with regard to hormones dispensed by compounding pharmacies. Accordingly, the NWHN requests that the Commissioner:

1. Ensure that all compounding pharmacies, health care professionals or businesses that dispense or promote pharmacy-compounded hormones to the public are compliant with the regulations in the Food, Drug & Cosmetic Act (FDCA) and adhere to the FDA Compliance Policy Guide.<sup>1</sup> Specifically, that there is compliance in providing material facts in all labeling and advertisements provided to patients and to health care professionals, including the following:
  - a. The product is not approved by the FDA.
  - b. The product is/was compounded [or prepared] in a pharmacy and therefore is not subject to FDA standards for good manufacturing practices.
  - c. The product has not been demonstrated as safe or effective in clinical trials.
2. Promulgate regulations to govern specific wording and appropriate labeling based on the above information.
3. Promulgate regulations to govern marketing and advertising campaigns of compounding pharmacies.
4. Appropriately inform the public of these actions in order to:
  - a. Ensure compounding pharmacies are aware of their obligations.
  - b. Ensure patients and allied health care professionals are aware of their rights to information and appropriate product labeling.
  - c. Specifically advise patients who have concerns about taking these products to inform the prescribing health care professional.

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5. Establish enforcement procedures to ensure that when a compounding pharmacy does not comply with the requirements set forth in the FDCA, and is issued an FDA warning, the health care providers and patients who have patronized the offending pharmacy will be notified of the warning and supplied the appropriate information.

## **I. Consumers Want, Expect, and Need FDA Regulation of Hormone Therapies**

FDA regulation is not unwarranted or burdensome in this case; in fact, it is preferred by the vast majority of women in the United States. In a survey conducted in February 2005 and sponsored by Solvay Pharmaceuticals, 86% of women over age 45 reported they were unaware that compounded hormones were not FDA approved (see attachment # 1). Further, 75% of the same respondents stated that FDA approval was very important in making a decision about hormone therapy as an option. Although this survey was not independently conducted, its findings are consistent with other surveys demonstrating the significant importance the public accords to FDA approval.

FDA enforcement of standards in medication labeling and marketing of compounded pharmacies is not only desired by the public, but necessary to ensure that consumers can make informed choices about their health care.

## **II. Consumers Are Being Misled about Important Health Issues**

### ***Promotion of Compounded Hormones as Natural or Bioidentical***

The term 'bioidentical' indicates that the hormone product is chemically identical to the hormones found in a woman's body and this is used to convey the idea that these are a 'natural' alternative to conventional hormone therapy. Yet, describing bioidentical hormones as 'natural' relative to conventional hormone therapy is misleading. In fact, some of the hormones produced by large pharmaceutical companies can also be called bioidentical under this definition. These synthesized hormones are chemically identical to hormones in our bodies, but there is nothing natural about their manufacture. Further, what manufacturers of compounded hormones do not tell women is that they purchase many of the hormones for their products from pharmaceutical companies, some of which use the same hormones in their own conventional hormone therapy.

This confusion around terminology is significant from a regulatory perspective because women who purchase compounded hormones to avoid "synthetic" or "pharmaceutical" hormones are in fact often using exactly the same synthetic pharmaceutical hormones.

### ***Claims that Compounded Formulations Are Safer***

Based on the purported distinction between compounded hormones and conventional hormone therapy, compounding pharmacies have been promoting their unapproved products as being safer than the FDA-approved products without any studies directly comparing products or research evidence to support those claims. There are serious health risks associated with the use of compounded hormones and the lack of federal oversight of these product promotions poses a threat to women's health.

First, all hormones, including those that humans create within their bodies, have adverse health effects. None are safe in an absolute sense and no responsible pharmacist or health care provider should be promoting a hormone product based on an unqualified safety claim.

In fact, there is no evidence to support any safety claim whatsoever for compounded hormone products. Unlike FDA-approved conventional hormone therapy, there is no regulation that compounded hormones be studied for safety or effectiveness and none have never been demonstrated to be safe in the sense that their proven benefits have not been found to outweigh their risks. Compounding pharmacies have not established the risk profiles of their products; therefore, patients are getting products of unknown risk and are not even aware of the lack of safety evidence. Claims by compounding pharmacies that so-called bioidentical, natural, or naturally-occurring hormones are safer than FDA-approved conventional hormone therapy are also inappropriate (see attachments # 2, 3, 4, 5). These claims are not backed by comparative clinical trials to prove that compounded hormones are safer than conventional hormone therapy.

Unfounded safety claims are especially troubling when one considers that multiple studies<sup>2</sup> have demonstrated that post-menopausal women who have naturally higher levels of estradiol, estrone, testosterone, DHEA, and other sex hormones are at greater risk for breast cancer when taking hormone therapy. In addition, well-conducted clinical trials of women taking conventional hormone therapy manufactured by pharmaceutical companies indicate an increased risk for heart attack, stroke, breast cancer, blood clots, and dementia. Until proven otherwise, the most reasonable course of action is to assume that these risks are associated with both FDA-approved hormones and compounded hormones. Without testing of compounded hormones, we do not know the true level of risk associated with such products.

The FDA has previously issued guidance on labeling standards to manufacturers of conventional hormone products;<sup>3</sup> this same standard should apply to untested compounded hormones:

*The FDA is asking all manufacturers of estrogen and estrogen-progestin products for postmenopausal use to make similar changes to their product labeling because it is believed these products have risks similar to those of Prempro, the drug used in the WHI study. "We don't want women to think these other products don't have any risk or are less risky—we simply don't have the data yet because we haven't studied them in the manner Prempro was studied," says Florence Houn, M.D., director of the FDA office that reviews reproductive drugs. "However, from what limited information we do have, we know that blood clots, heart attacks, and other side effects may also happen with other estrogen and estrogen-progestin products."*

### **Claims that Compounded Hormones Are Effective in Prevention of Disease**

Unsubstantiated claims of protective benefits against heart disease, stroke, and cancer have been made by providers of compounded hormones, without clinical efficacy studies or any credible scientific evidence to support these assertions (attachments # 2, 3, 4, 5). These very claims were evaluated in studies of conventional hormone therapy; the Women's Health Initiative actually found that not only was hormone therapy not protective for these indications, but it actually put women at greater risk for these diseases. Consumers of compounded hormones must be made aware that claims of protective effects are unsubstantiated, have not been evaluated by the FDA, and that use of similar products has been proven to put women at greater risk for the very diseases they are seeking to prevent.

### **III. The Comments of the International Academy of Compounding Pharmacies (IACP) Are Misguided**

Contrary to the assertions made by the International Academy of Compounding Pharmacies (IACP) in comments submitted to the docket of the CHASM Petition on August 15, 2005, the CHASM petition does not ignore the benefits that compounding pharmacies offer. Rather, the petition asserts that the public deserves to be fully informed of the benefits and risks associated with compounded drugs, and that FDA approval and manufacturing requirements need to be mandated and enforced in order to ensure that safe compounded products are provided to consumers. Our request, like that of the CHASM petitioners, is not to eliminate compounding pharmacies, but rather to hold these pharmacies accountable to public health standards that will protect consumers.

Moreover, misleading claims are not made by “a handful” of compounding pharmacists as IACP claims, but by nearly all advertisements for hormones dispensed by compounding pharmacies that we have seen. It should be noted that these materials violate the IACP’s own standards for promotional materials (see attachment # 6).

#### **IV. There Are Many Examples of Misleading Promotion of Compounded Hormones**

The IACP comments also state that CHASM does not offer evidence to establish that the dissemination of misleading promotional materials is widespread (p.3, IACP letter to FDA). We have attached to our comments evidence of misleading promotional materials for compounded hormone preparations which are widely available to all consumers (see attachments # 2, 3, 4, 5).

One need only look at Steven Hotze’s website to see multiple examples of these misleading claims (attachment # 3). Other examples of misleading advertising of hormones by compounding pharmacies abound. The Women’s International Pharmacy (WIP) sends informational material to interested clients upon request<sup>1</sup>. The WIP packet contains no articles describing the findings of the Women’s Health Initiative, the largest scientific study of hormone therapy ever conducted based on over 16,000 women, but rather only provides articles that state support for hormone treatment based on study samples as small as 15 women (attachment # 5). Of perhaps greater concern, WIP purports to provide scientific support for its claims, but it uses articles that have been scientifically disproved. For example, a chapter on estrogen replacement therapy published in 1994 that WIP sends to potential customers states:

*As mentioned previously, the greatest concern about estrogen therapy is that it might cause cancer. Whether or not this concern is well founded (and we do not yet know, for sure), some women will not take estrogen and some doctors will not prescribe it, because of their fear of promoting cancer. Fortunately, there is a way to take estrogen that does not appear to increase the risk of cancer. In fact, this ‘alternative’ method of estrogen replacement therapy could actually prevent cancer. (see attachment # 5 insert, “Estrogen Replacement Therapy”, by Alan R. Gaby, page 2, 3<sup>rd</sup> column)*

The ‘alternative’ method that the author was referring to in 1994 is combination estrogen & progestin, which has since been shown to actually increase the risk of breast cancer, not reduce the risk as this dated article would lead a consumer to believe. Sending out-of-date scientific articles to consumers is not misleading and dangerous to women – especially those at high risk for breast or endometrial cancer. The Women’s Health Initiative showed that estrogen & progestin combination hormone therapy significantly increases the risk of breast cancer in women over age 50 but there is no mention of this potential danger in WIP’s packet. Sending these dated, scientifically inaccurate materials to consumers who request information about hormone treatment is misleading and confusing to women and may even suggest intentional deception.

#### **V. The Impact of Partial and Inaccurate Health Information**

The practice of providing partial, and often inaccurate, information to American women about the efficacy and safety of compounded hormones has far-reaching consequences; policymakers have begun to repeat the misleading claims potentially giving them additional credibility. In the summer of 2004, Congressional hearings were held entitled, “Balancing Act: The Health Advantages of Naturally-Occurring Hormones in Hormone Replacement Therapy.” During these hearings, U.S. Representative Dan Burton (R-TX) made several scientifically incorrect remarks regarding the use of bidentical hormone therapy.<sup>5</sup> These inaccurate statements include:

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<sup>1</sup> The attached information was obtained from The Women’s International Pharmacy in August, 2005.

*It not only balances the hormone level within a patient, but it also serves as a preventative measure to ward off potential health risks associated with imbalanced hormone levels such as: osteoporosis, and the #1 cause of death in the United States – heart disease.*

The Women's Health Initiative demonstrated the exact opposite is true for conventional hormone therapy: it increases the risk of stroke and heart disease. The naturally-occurring hormones that Representative Burton was discussing have not been adequately studied to demonstrate that they are different in this regard.

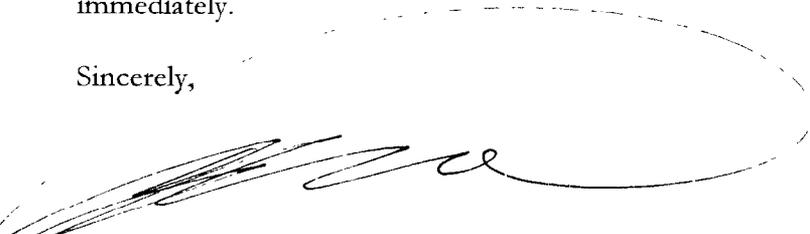
*Because these biologically identical hormones are the same chemical structure as the hormones created in the body, the body does not have the same harmful reactions as it does when the synthetic hormones are administered.*

These types of conclusions, often heard in promotion of compounded hormones, are based on assumptions and guess work; there is no scientific evidence comparing natural and synthetic hormones to support such assertions. Again, there is no scientific evidence to suggest that natural hormones are any less dangerous or offer any less risk than synthetic hormones. Representative Burton's statements echo misleading claims of the manufacturers who promote and profit from the natural hormone market, and are a threat to the public's health in that they may lead women to unknowingly expose themselves to serious health risks. The purpose of highlighting the Representative's statements in this letter is to demonstrate the insidious nature of permitting unsubstantiated health information that is often included in advertisements for compounded hormones to be disseminated without oversight or regulation.

These unsubstantiated assertions are dangerous to the health of women. When government officials begin repeating misleading and potentially harmful promotional claims, it is time to consider the effects of such promotion and what action needs to be taken to protect the public's health. American women deserve no less than complete, accurate, and scientifically substantiated health information.

The National Women's Health Network is committed to promoting informed consumer decision-making; we do not accept funding from any medical device or pharmaceutical company. Clearly, given the misleading promotional practices by compounding pharmacies in marketing so-called natural and bioidentical hormones, and the safety concerns surrounding the formulation of these products, greater FDA oversight and regulation are absolutely essential. We respectfully request that these concerns and those of the petition submitted by CHASM be addressed immediately.

Sincerely,



Cynthia A. Pearson  
Executive Director

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<sup>1</sup> See FDA Press Release, Compliance Policy Guide Addresses Prescription Drug Compounding (Apr. 14, 1992) <http://www.fda.gov/bbs/topics/ANSWERS/ANS00394.html>.

<sup>2</sup> Writing Group for the Women's Health Initiative Investigators, "Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women," *Journal of the American Medical Association* 288, no. 3 (July 2002): 321-333.

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<sup>3</sup> United States Food & Drug Administration. Estrogen and Estrogen with Progestin Therapies for Postmenopausal Women, created January 8, 2003. Accessed October 28, 2005 at: [http://www.fda.gov/cder/drug/infopage/estrogens\\_progestins/default.htm](http://www.fda.gov/cder/drug/infopage/estrogens_progestins/default.htm).

<sup>4</sup> Bren, Linda. *The New Estrogen and Progestin Dilemma: New Advice, Labeling Guidelines*. FDA Consumer Magazine, March-April 2003. Accessed September 26, 2005 at: [http://www.fda.gov/fdac/features/2003/203\\_estrogen.html](http://www.fda.gov/fdac/features/2003/203_estrogen.html).

<sup>5</sup> Opening Statement of the Honorable Dan Burton. Government Reform Committee, Subcommittee on Human Rights & Wellness Hearing: "Balancing Act: The Health Advantages of Naturally-Occurring Hormones in Hormone Replacement Therapy." July 22, 2004.