



Bioidentical Hormones: Facts, Women's Rights, and Choices

By Elizabeth Lee Vliet, M.D. © 2006

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Hormone therapy in the United States is in a state of chaos and confusion that is devastating to women seeking options to relieve symptoms that disrupt quality of life and cause untold suffering and increased health risks. We must change this.

Although not a "citizen," pharmaceutical giant Wyeth has filed a "Citizen's Petition" with the FDA to restrict compounding of bioidentical hormones for women. Their focus is on "women's hormones," competitors for their products Premarin, Prempro, and Premphase. Clearly, this attempt to limit access to choices for hormone options grossly discriminates against women. *This is no longer acceptable.*

We must not let the financial interest of one major drug company restrict the rights of women to choose hormone options that may be more suited to their needs than the "cookbook" approach of Premarin and Prempro.

Women, and the families who love them, need sound facts NOW. A voice of balance must be heard. We must retain individual's right to choose from a variety of health options—commercial products and individually compounded ones.

Who am I to speak on this issue?

I am a practicing physician who has spent 20 years working in this field listening to women and their health needs and finding ways to effectively treat complex hormonally-triggered problems for women of all ages. I have treated thousands of patients over the last 25 years, many with tragic stories of lost years of health and productivity, lost marriages, and lost careers because these health problems were not addressed timely or appropriately.

I am the sole author of six consumer books on hormones and women's health problems, all carefully referenced from medical research. I have authored published papers for peer-reviewed medical journals. I have been an invited speaker for several hundred CME programs for physicians and other health professionals all over the country and overseas, including a Congressional Briefing in May 2004. I have also presented hundreds of keynote speeches and women's health talks across the United States. Every year, I attend a World Congress of one or more international organizations at which cutting-edge hormone research is presented.

I am an *independent* physician in private practice and I have no financial ties to any pharmaceutical company, compounding pharmacy, or other commercial entity involved with products either directly or indirectly referenced in this material to follow.

I speak as a physician hearing women's tragic stories day in and day out, and working to help them regain their health.

I speak as a woman who has experienced these life events and health problems. I speak as a doctor and as a patient, one who has been through many difficult surgeries and diagnostic dilemmas.

I speak as a scientist who has taught biology and chemistry, and who has practiced the science *and the art* of medicine. I know the value of *evidence...* both that from scientific studies *and from patients.*

I know this field of science and medicine at many levels and the issues facing us are crucial to the health and well-being of millions of Americans.

Millions of patients—men, women, and children, across the United States are potentially adversely affected by Wyeth's Citizens Petition to restrict compounded medicines.

We must take action now to stop this petition.

The *extremes* occurring nationally today are harmful to patients. Some examples of the problems that need to be addressed:

- Physicians who simply give up prescribing hormones altogether based on *one* study (WHI) of *one* type of hormone therapy, Premarin, Wyeth's conjugated equine estrogens (CEE) and Prempro, a potent synthetic progestin, medroxyprogesterone acetate (MPA) with estrogen.
- Wyeth's Citizen's Petition seeking to restrict patient access to individually-compounded hormone medicines appears aimed to preserve their own economic and financial interests.
- Some compounding pharmacies marketing and selling inappropriate doses, products, saliva tests, and "hormone consults" for their own commercial interests.
- Widespread marketing by many companies of unproven OTC "menopause" herbal remedies with no regulatory oversight for quality control or scientific studies to show effectiveness.
- Multi-level marketing and health food store sales of progesterone creams, many of which

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contain higher levels of USP progesterone than found in FDA-approved commercial products, a clear violation of prescription regulations.

We need a balanced, medically-sound approach to address all of these issues. And, ***we need enforcement of existing regulations to curb abuses. We do not need further restriction.***

Further restricting the compounding pharmacies will put them out of business. Is that what we really want?

Overview of the Issues Facing Us:

- Wyeth, maker of Premarin, the estrogen mixture derived from **pregnant mares' urine**, and Prempro (horse estrogens plus a potent synthetic progestin), filed a "Citizens Petition" with the FDA to restrict compounding and dispensing of bioidentical hormones (i.e., estradiol, progesterone, and testosterone) for women needing hormone therapy.
- A number of national women's health organizations, **with long-standing research and other supportive financial ties to Wyeth**, have filed statements with the FDA in support of Wyeth's petition.
- The International Academy of Compounding Pharmacists filed comments rebutting Wyeth's claims. Thousands of consumers have filed letters in opposition to Wyeth's petition.
- Much of the furor arose following the July 2002 press release of adverse results from The Women's Health Initiative (WHI), using horse-derived estrogen and synthetic progestin (Wyeth's product Prempro): more blood clots, heart attacks, strokes and breast cancer in the Prempro group.
- In 2004, the estrogen-only arm of the study, using Premarin (Wyeth's product), was stopped a year early due to increased risk of stroke. But there was no increased risk of breast cancer or heart attack in the estrogen-only group.
- Press coverage of the Women's Health Initiative (WHI) caused panic and fear in women everywhere. Women in droves abruptly stopped hormones.
- Wyeth lost almost *two-thirds* of its annual sales of Premarin, Prempro, Premphase. Sales dropped from over \$2 billion in 2001 (prior to release of WHI outcomes) to 880 million in 2004.
- After the WHI, doctors advised women to stop hormones or not start hormone therapy for menopausal symptoms. Women suffering return of symptoms besieged physicians with phone calls asking "What do I do now?"
- Popular consumer books gained media attention, and described "*bioidentical hormones*," supposedly only made by compounding pharmacies. Compounding pharmacies began increased marketing of these options for patients who were understandably concerned about taking Premarin or Prempro after the reported WHI risks.
- Many consumer-oriented publications, and physicians, **ignored FDA-approved bioidentical hormone products**

available in the United States since 1975. In fact, a review article in a respected US medical journal *also* ignored the FDA-approved products that have been subject to safety and efficacy studies, and have been available for over 30 years with lower risks and better side effect profiles.

- The International Menopause Society (IMS) and International Society of Gynecological Endocrinology (ISGE) issued position papers and expert editorials explaining flaws in the WHI study and rebutting the media's exaggerated risks of hormones. This balanced presentation has not generally been seen in U.S. medical journals that derive advertising revenues from companies like Wyeth, and whose editors have research and consulting financial ties with many pharmaceutical companies.
- Most consumers, and the majority of U.S. physicians, have not seen these thoughtful, balanced analyses from IMS and ISGE.
- Physicians and consumers need medically-sound, balanced information from worldwide research that address these issues.

It's not just "Women's Issues"

The issue is not just about hormones for women, as important as that is. The issue is about:

- **Maintaining individual options in health care.**
- **Having freedom of choice to seek individually compounded hormones by prescription from a physician prepared by a licensed pharmacist.**
- **Getting away from "cookbook medicine" in a day when we are learning the genetic underpinnings of individual medication response, and even considering testing people for such mutations. We need more options, not fewer.**
- **Maintaining the ability to individually compound appropriate, safe medication options when patients need it and choose this approach.**

Make no mistake—

While Wyeth's petition focuses on *women's hormones*, the restrictions they seek in their detailed petition are so draconian that no small pharmacy could meet them, and it would effectively *eliminate compounding of all medicines*—pain medications for cancer patients, asthma medications without dyes, lower doses of many medicines for all types of clinical problems, to name a few examples.

Patients across the country *still* need options for individually compounded medications in many areas of medicine to meet special needs, such as allergies to dyes, binders and preservatives in commercial products, medication sensitivities that need lower doses than commercially-available, individually-compounded pain medication for cancer patients and hospice palliative care. The list is long. It isn't just hormones for menopause!

The FDA has a responsibility to *enforce existing regulations*. We do not need the FDA to bow to one drug company's

efforts to protect market share by further restricting patient options to choose crucial individually-tailored medications.

Although we need better enforcement of current regulations to uphold safety standards for patients, we do not need more restrictions that end compounding altogether.

Background:

Bioidentical hormones are not new. “Bioidentical” simply means those hormones that are *exact molecular copies* of the human form of the hormone.

Ovarian hormones were identified and synthesized by major pharmaceutical researchers as early as the 1930s. FDA-approved commercial versions of “bioidentical hormones” have been available in the United States since the 1960s for the primary human endocrine systems—thyroid, adrenal, ovary, testes, pancreas, and pituitary, to name a few.

All bioidentical hormones used for prescription menopausal therapies, including the FDA-approved commercial products, are made in the laboratory by synthesis from chemical building blocks (*sterols*) found in various plants, commonly Mexican yams and soybeans. These plant compounds cannot be turned into hormones by the human body because we lack the necessary enzymes for this to occur.

The WHI used only one type of hormone product: a mixture of *conjugated equine estrogens* (CEE) derived from the urine of pregnant mares (Premarin) alone or in combination with the synthetic progestin, *medroxyprogesterone acetate* (MPA), brand name Provera.

Both CEE and MPA are markedly different in chemical makeup from *estradiol and progesterone* made by the human body.

Consumers and many physicians do not recognize the difference between the Wyeth products used in the WHI and the bioidentical hormones, either compounded or the commercial ones already approved by the FDA. In fact, this distinction appears to be deliberately blurred as a strategy to prevent greater product liability fallout from the WHI.

Further confusion was generated for the public and for physicians when most media stories used the word “estrogen” when referring to results of the WHI—they did not label the type of estrogen used as Premarin, *nor did most stories correctly attribute risks to the Prempto group.*

Following intensive lobbying efforts, the FDA gave a “black box” warning to *all* estrogens and *all* progestins, even though the WHI only used *one* product with pharmacologic properties quite different from those seen with non-oral estradiol or bioidentical progesterone.

As a result, we are struggling with the aftermath of this generalized warning on all hormones, when only one type of product was studied.

Not once during my career in medicine have I seen a situation in which *all products* in a field have been tarred with the same brush when problems arose with *one* medication in a class.

The FDA did not generalize to all antihistamines, statins, or diabetes medicines when serious side effects came to light with Seldane, Baychol, and Rezulin. *Yet that is what has been allowed to occur with menopausal hormone products for women.*

Table I lists the brands of FDA-approved bioidentical estradiol and progesterone currently available in the United States.

Media reports, many women’s health organizations, and nationally-known physicians have said we have no studies on bioidentical hormones. *This is false.*

There are many studies showing safety and effectiveness of these FDA-approved bioidentical products. *How else could they have gained FDA approval?*

Despite documented benefits of bioidentical hormones, many physicians are still not aware that there are many FDA-approved options they can be using for their patients, in addition to individually compounded ones currently the focus of Wyeth’s petition.

Wyeth’s Citizens Petition implies that the WHI clinical

Table 1: Examples of FDA-Approved Bioidentical Hormone Products

<u>Human form of Hormone</u>	<u>FDA-approved Bioidentical Products</u>
17-beta estradiol:	<p>Tablets: Estrace, Gynodiol, generic estradiol, Activella (with non-bioidentical progestin), Vagifem (topical vaginal product)</p> <p>Patches: Climara, Vivelle DOT, Estraderm, Menostar, Climara PRO (with non-bioidentical progestin), several generic estradiol patches</p> <p>Rings: Femring (systemic), Estring (vaginal)</p> <p>Gel: Estrogel</p> <p>Lotion: Estrasorb</p> <p>Cream: (vaginal): Estrace</p>
progesterone:	<p>Tablets: Prometrium</p> <p>Gel/cream: Prochieve (formerly Crinone)</p>
testosterone:	<p>none currently FDA approved, several in Phase II or III trials</p> <p>Androsorb cream by Novavax</p> <p>LibiGel (gel) by BioSante</p> <p>Intrinsa patch by Procter and Gamble</p> <p>Tostrelle (gel) by Cellegy</p> <p>Vivus’ nasal spray (unnamed)</p>
levothyroxine (T4)	Synthroid, Unithroid, Levoxyl, many generics
triiodothyronine (T3)	Cytomel
growth hormone	Humatrop, Genotropin, Nutropin, Norditropin
insulin	Humulin, Novalin

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studies evaluated bioidentical hormones. *This is false.* The WHI did not include *any* bioidentical hormone products in the clinical trial. The *only* products used in the WHI were Wyeth's Premarin and Prempro.

Wyeth's Citizens Petition to the FDA attempting to restrict compounding of bioidentical hormones asserts that compounded bioidentical hormone products have the same risk profile as Wyeth's Premarin and Prempro. *This is also false.*

Respected British researchers Campbell and Whitehead showed back in the 1970s that oral Premarin had a more potent effect to *increase* blood pressure than did oral human 17-beta estradiol.

The NIH-sponsored Progestin-Estrogen Postmenopausal Intervention (PEPI), a large randomized, placebo-controlled clinical trial published in the mid 1990s, showed that oral progesterone did not have the same adverse effects on cardiovascular markers and cholesterol as was caused by Provera (medroxyprogesterone acetate), the synthetic progestin in Prempro.

The risks that occurred in the WHI were *already known* to international menopause researchers. So why did such a large, expensive trial even go forward using the same products, Premarin and Prempro, that had already been shown to have more problems than bioidentical estradiol and progesterone?

There have been numerous clinical studies published in peer-reviewed national and international medical journals over the last 30 years showing significant differences in risk profile between horse-derived estrogens with synthetic progestins compared to bioidentical estradiol and progesterone. Risks have repeatedly been found to be *lower* with bioidentical estradiol and progesterone, particularly when these bioidenti-

cal hormones are delivered in a non-oral form. Some examples from clinical studies published in peer-reviewed national and international medical journals are shown in Table 2.

The only major limitation in the clinical research at present is that we don't yet have a randomized clinical trial (RCT) the size of the WHI to do a head-to-head comparison of bioidentical hormones with the horse-derived estrogens and synthetic progestins that were used in the WHI.

One such RCT is now underway, the privately funded KEEPS trial using bioidentical estradiol and progesterone compared with Premarin, and starting hormone therapy in younger menopausal women, unlike the elderly women in the WHI.

Misperceptions and Misunderstandings About Compounding and Bioidentical Hormones

The following are some of the most common misunderstandings about the use of bioidentical hormones.

Misperception #1: "Pharmaceutical companies don't make bioidentical hormones, they can only be obtained from compounding pharmacies."

Some consumer books, pharmacists, and some physicians claim that *only* compounding pharmacists can make "bioidentical" hormones. Others claim that big drug companies don't make bioidentical hormones because they can't patent the natural molecule and make money on them. *Both claims are completely false.*

Comments such as these are designed to promote "natural hormone therapy" in consumer marketing and exploit consumer fear about pharmaceutical products fueled by sensationalized reporting and accentuated risks after the first group of the WHI was stopped in 2002.

The truth is that we have a wide variety of FDA-approved bioidentical hormone products, shown in Table 1, some available for more than 30 years. Most are covered under major health plans. Patients can obtain them by prescription from a local drugstore pharmacy or mail-in prescription plan. As a result, patients tend to spend less money out-of-pocket since FDA-approved products are usually covered by insurance.

Many medical organizations supporting Wyeth's petition have made it sound as if "bioidentical hormones" are somehow inferior to Wyeth's Premarin and Prempro, or have not been subject to the appropriate clinical studies. *This is false.*

The commercial, FDA-approved bioidentical hormones have been subjected to rigorous safety and efficacy studies before they could even gain FDA approval, and these products are also subject to post-marketing surveillance. In addition, there is regulatory oversight of major pharmaceutical companies to insure standardization of dosing and quality control. For these reasons, I prefer using standardized, FDA-approved forms of bioidentical hormones when possible.

But we must keep open the option to have individually-compounded estradiol, progesterone, testosterone, and thy-

Table 2: Route of Delivery Affects Risks and Benefits

Bioidentical and foreign hormone products offer different benefits. The route of delivery for hormones can also change the response, side effects and risks. Consider the following examples (see references):

- (a) transdermal 17-beta estradiol has been shown to have a lower risk of gallstone formation than oral estrogens, particularly CEE and ethinyl estradiol.
- (b) Vaginal progesterone has fewer sedative and depressive side effects than either oral micronized progesterone or oral MPA.
- (c) Oral micronized estradiol has less potential to stimulate formation of renin substrate and raise blood pressure than does oral CEE, and estradiol used non-orally can lower blood pressure significantly.
- (d) Non-oral bioidentical testosterone has a lower risk of adverse lipid effects (i.e. decrease in HDL cholesterol) than does oral methyl testosterone

Using these differences allows individualized therapy regimens for patients with different risk profiles or who may be having adverse side effects with one method of delivery.

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roid medications for those patients who have adverse reactions with ingredients in commercial products such as dyes, binders and preservatives.

Compounding pharmacists are important members of the health care team and can be very helpful in making up individually tailored hormone preparations in special circumstances: (1) allergies or reactions to commercial products, such as preservatives, dyes, binders and adhesives, (2) commercial products are not available in low enough doses for medication-sensitive patients, or (3) the bioidentical hormone is not yet available as an FDA-approved product, as currently is the case for testosterone for women.

We must preserve this option for patients who need it.

Examples from my medical practice over the years treating men, women and children, where individually compounded medicines have been critically necessary for treating individual patients include:

- Women allergic to peanuts cannot use Prometrium, the FDA-approved brand of progesterone and need a compounded form of progesterone using a different oil or delivery method.
- Men who cannot tolerate commercial doses of testosterone
- Men and women with asthma who have asthmatic reactions to some of the dyes and preservatives in commercial products.
- Children with allergies who can't take medicines with colorings, certain binders, peanut oil, etc.
- Cancer patients who need individually compounded pain medicines.
- Women who need alternative routes of delivery than are available in commercial products can have individually compounded options.
- Many of my patients in all age groups are medication-sensitive and need lower doses than are commercially available.
- Women who cannot tolerate the side effects of synthetic progestins need individually-compounded progesterone.
- Many women experience stinging and burning from preservatives that have to be present in all commercial vaginal estrogen products in order to extend shelf life. For these patients, I prescribe compounded vaginal hormones that are made without these preservatives.
- We have no commercially available testosterone-only product for women who have had their ovaries removed. They suffer loss of ovarian androgens and need testosterone to maintain energy, bone and muscle mass, normal sexual response, and sense of well-being.

The only FDA-approved commercial product for combined estrogen-testosterone menopausal therapy is Estratest. This product contains *methyl* testosterone and a mixture of *esterified* estrogens that delivers primarily estrone (E1) rather than 17-beta estradiol (E2).

Methyl testosterone has been known for decades to cause hepatic toxicity. In the 1980s, the German Endocrine Society recommended against its use in humans. Due to its higher

potency, methyl testosterone has the potential to cause unwanted androgenic effects (acne, oily skin, irritability, restless sleep) at the dose used in commercial products. Menopausal women typically need lower doses of testosterone than are available commercially.

At this time, compounding pharmacies are the only source for bioidentical testosterone, or for testosterone in lower doses than available in commercial products. A number of such products are in clinical trials, but women (unlike men) do not have FDA-approved commercial products using the bioidentical testosterone.

Individually-compounded hormones are made from United States Pharmacopeia (USP) grade, standardized, pure estradiol, progesterone and testosterone, unlike herbs, which have no regulatory oversight at all!

If individually-compounded hormone medications are no longer available, and commercial products are too limited in dose and type to meet individual women's needs, then women desperate for relief of symptoms are left with only the option of unproven OTC herbs and supplements that are even less well-studied.

OTC herbal or soy menopausal products are widely marketed today to women to use instead of prescription hormones. Plant/herbal sources contain compounds foreign to the human body, lack quality control, have no standardization of active ingredients, and even lack accurate information on product contents. Most double-blind placebo-controlled clinical studies of these products show them to be no better than placebo, so they are often a waste of consumer's health care dollars.

But a greater concern is that published medical studies have found contaminants from heavy metals to banned drugs in Chinese herbal products and various supplements. Chemicals in plants also contribute to adverse drug-herb interactions that lead to potentially serious complications and adverse reactions.

New studies also show serious long-term adverse effects of plant sterols, including potential increase in growth of breast cancer cells, abnormal growth of the uterine lining, bleeding problems, and interference with thyroid function due to components in OTC products. We have only scratched the surface of understanding these problems.

Misperception #2: "Bioidentical hormones from compounding pharmacies are safer than commercial hormones."

Marketing materials from some compounding pharmacies imply or directly state that compounded bioidentical hormones are safer or more effective than FDA-approved bioidentical hormones or standard non-bioidentical menopausal products.

In fact, the converse may be true in certain situations when there is misuse of such products.

Examples I have encountered in my own medical practice:

- Patients given excessively high doses of progesterone and testosterone in compounded creams when physicians and pharmacists have not correctly lowered the doses to reflect better absorption with non-oral delivery.
- Women who had male blood levels of testosterone from the 1% (10 mg/gm) and 2% (20 mg/gm) testosterone cream that was recommended by a compounding pharmacist and prescribed by a physician not experienced in hormone dosing.
- One-quarter teaspoon (one gram) of a 1% or 2% testosterone cream can equal approximately 100 mgs to 200 mgs oral dose, which is a *male* dose.
- Compare this with the testosterone patch for women that is currently in clinical trials and not yet approved by the FDA: this patch delivers 300 mcg (0.03 mg) of testosterone, or the equivalent of 3 mg oral dose. This brings testosterone levels into the ideal 1 to 4 mg daily dose for women.

Misuse by pharmacists or physicians is not a problem that requires new restrictive regulations on *all* compounding.

- It is an *education* issue to teach correct dosing.
- It is an *enforcement* issue when physicians prescribe or pharmacists dispense in violation of existing regulations.

The goal is to keep hormone levels in the normal physiological range for women. Doses need to be kept low to avoid unwanted side effects while achieving desired benefits. This is an education issue, and does not need restriction of all compounded medicines!

Misperception #3: "Synthetic hormones are dangerous."

Clearly, this is not the case. Premarin, Provera, birth control pills, and many other chemically different formulations of hormones have been used safely worldwide for many years. On the other hand, these chemically different molecules do have different effects in the body from the effects triggered by our own body hormone molecules. For many patients, these differences can be quite significant and can lead to unwanted side effects.

For example, new studies by U.S. researcher, Dr. Roberta Diaz-Brinton has shown that MPA causes accelerated clumping of abnormal proteins in the CNS that lead to Alzheimer's disease. Dr. Diaz-Brinton proposes that this is one mechanism by which MPA caused increased risk of Alzheimer's in older women in the WHI.

MPA's damaging effect on the brain was *not found with either bioidentical progesterone or the progestin norethisterone* (in the U.S., norethindrone). Such profound differences have a significant impact on long term risks for hormone therapy.

Patients often confuse the word "synthetic" to mean "foreign" or "artificial." Synthetic simply means putting together various molecule building blocks to create a new compound, a process called synthesis. This process can occur in a biological organism (human, plant, or animal), or in a laboratory.

Even though such bioidentical hormones are "synthetic" because they have to be made in a laboratory rather than in a biological organism, it does not mean they are any less effective than the ones our own body makes. An analogy is going to a locksmith to have a spare key made. If the copy is a correct duplicate, it opens the lock just as effectively as the original master key.

All bioidentical hormones, whether commercial products or obtained from compounding pharmacies, are "synthetic" because they are made in the laboratory. The resulting estradiol, progesterone and testosterone are then sold in bulk as USP grade powder for commercial pharmaceutical companies or compounding pharmacies to make their hormone tablets, creams, gels and patches.

Both large pharmaceutical companies and small compounding pharmacies use the same USP grade raw materials.

Why restrict compounded hormone options that use the same USP estradiol and progesterone supplies already used in FDA-approved bioidentical commercial products? ***This makes no sense at all!***

Misperception #4: "Natural hormones are bioidentical, and therefore better."

The myth here is that all "natural" hormones are also "bioidentical." This is not the case. The estrogens found in Premarin are "natural" because they are made by a biological organism (horse), and phytoestrogens in soy are "natural" because they are also made by a biological organism (plant). But neither of these mixtures of estrogenic compounds are natural to the human body, so they are not "bioidentical" to 17-beta estradiol produced by the human ovary.

The foreign estrogens in Premarin and soy have some effects that are similar to human estradiol but also have effects in the human body that are quite different and potentially detrimental to women. Genistein in soy at higher concentrations *stimulates* the growth of breast cancer cells.

Bioidentical estradiol produced by pharmaceutical companies is "natural" because it is exactly the same molecule a woman's body has always made. As a result, it is generally better tolerated, more effective, with fewer side effects than the mixture of horse-derived estrogens in Premarin.

For example, studies have found that Premarin can *increase* risk of deep venous thrombosis (DVT) and oral Premarin increases C-reactive protein (CRP), a risk marker for heart disease.

Published medical studies, on the other hand, show that non-oral, transdermal bioidentical estradiol lowers risk of DVT and decreases CRP. There are several FDA-approved brands of non-oral estradiol, as shown in Table 1.

Pig-derived thyroid, sold as the brand Armour and marketed as "natural thyroid," actually is not "natural" for humans: the pig thyroid has a higher ratio of T4 to T3 at 4:1, which is quite different from the 10:1 ratio in humans.

Commercial FDA-approved thyroid products are bioiden-

tical T4 compounds, and natural to the human, even though synthesized in the laboratory. FDA-approved bioidentical T4 products made in the laboratory also help eliminate the allergic responses that can occur with pig-derived thyroid products.

We still need the bioidentical individually-compounded T3 and T4 to provide patients with lower doses than are available commercially or to make tablets that do not have allergy-causing dyes.

Synthetic bioidentical human insulin is another example: use of a laboratory-synthesized medicine eliminated the problem of allergic reactions seen when natural pig or cow-derived insulins were the only available forms for clinical use.

The primary issue is whether a particular product provides hormones that are identical to human ones or hormones that are chemically different. Physicians prescribing any hormones, whether bioidentical or not, need to assess the individual patient and develop a prescription tailored to her medical needs and personal preferences. One product, such as Premarin, in limited doses, *does not fit all women*.

Misperception #5: "It's always better to use bioidentical hormones."

This is not correct. There are many situations when a patient's particular therapeutic needs are met more effectively with a chemically different, more potent type of hormone therapy, such as medroxyprogesterone acetate (MPA), ethinyl estradiol (used in birth control pills worldwide), and other progestins in birth control and menopause products.

For example, women requiring contraceptive benefits need the higher potency of chemically different estrogens and progestins, even if these are "synthetic hormones," because these compounds have the ability to reliably suppress ovulation to provide effective contraception. Bioidentical 17-beta estradiol and progesterone do not suppress ovulation enough to provide reliable contraception. In fact, bioidentical estradiol and progesterone are used in fertility treatment for cycle management to *enhance* fertility.

Endometriosis is another example. "Synthetic" progestins are more potent than progesterone and better suppress pelvic pain from bleeding of endometrial tissue in the pelvis. Such progestins also suppress growth of endometriosis and help prevent further pain and pelvic damage from endometriosis.

Menopausal women, on the other hand, often do not need the potency of MPA to oppose estrogen. The WHI demonstrated that prescribing the more potent MPA progestin had many adverse metabolic effects and health risks in older women. Studies have also shown that many women feel better, have fewer adverse mood side effects, fewer adverse effects on cholesterol, and less problem with weight gain when using micronized progesterone or low-dose norethindrone instead of MPA.

Summary

I feel it is critically important to keep open the option of individually compounded bioidentical hormones for the women who need them.

We do NOT need more restrictions on compounding. Women in the United States need more variety of hormone therapy options, not fewer. We need better education and enforcement, not more restrictive regulations.

Make no mistake. Women are not taking compounded prescriptions because they are cheaper or easier. Most have to pay out of pocket for these compounded prescriptions since few insurance plans cover them. It is often difficult for patients to find physicians who know how to use them. *If compounded Rx were less effective, or caused more side effects, obviously patients would not continue to seek them!*

Restricting compounded hormone options would seriously reduce the flexibility for physicians to individually tailor hormone therapy prescriptions *at a time when this is the very standard of care being promoted by the FDA and national women's health organizations.*

Even though we still lack the degree of Level I evidence for bioidentical hormones as was obtained from the WHI on CEE and MPA, women still need hormone therapy for relief of symptoms and improved quality of life. Women need medical professionals who will help them explore these bioidentical hormone options in an appropriate risk-benefit discussion between physician and patient.

Increased concerns about potential risks of horse-derived and other non-bioidentical estrogens and potent synthetic progestins mean that physicians and consumers need to learn more about bioidentical hormone options. Both those that are already FDA-approved and commercially available, and those that can be individually compounded are useful for appropriate patients.

Compounded prescriptions play a vital role in other health care areas such as pain management, cancer treatment, hospice palliative care, thyroid disease management, blood pressure management, to name a few.

We must keep this option open.

Tailoring hormone approaches for the individual woman results in better medical treatment for patients. We must have medication options to achieve this goal. It would be tragic to lose this flexibility.

It would be deplorable if men, women, and children who need individually-compounded medicines for special health needs are denied their right to chose this option.

We can't let one drug company's focus on profits prevent our having options for individualized health care for millions of Americans. We must act now to prevent a blow to individualized health care by government giving in to Big Pharma.

Table 3: Saliva vs Blood (Serum) Hormone Tests

Consumer marketers and some pharmacies have recently pushed saliva testing to measure ovarian and other hormones. Saliva test kit makers claim that a measurement of the free hormone in saliva gives a more reliable result than the combined fractions measured in serum.

These claims have not been proven in menopause research settings as a reliable tool for assessing adequacy of clinical response and/or therapeutic effect.

A number of problems exist with saliva tests. They only measure the free, unbound portion of the hormone molecule in serum and don't give a complete picture of the available potentially active, or bioavailable, hormone.

Previously, researchers believe that only the free form hormone was biologically active at hormone receptors. But we know that sex steroid hormones are carried in the bloodstream three ways: strongly bound to sex-hormone binding globulin (SHBG), weakly bound to albumin (ALB), and in the free form (not bound to carrier protein). The most recent research has shown that many tissues actively utilize both ALB and free forms of these hormones at the steroid receptors.

Serum assays reflect the total levels of protein bound and free fractions to provide a complete picture of the biologically active steroid hormones. Serum hormone measures, in conjunction with a physician's evaluation, should be the approach when monitoring response to hormone therapy and making assessments of hormone effects on complex problems involving multiple organ systems.

Saliva tests were initially thought to have some promise because they're easy to use and convenient for patients. But most specialists stopped using these tests because they simply weren't reliable; they didn't correlate with women's symptom descriptions, nor did they correlate with tissues samples (such as endometrial biopsy) or the more useful results of serum hormone assays that are widely used in fertility centers throughout the world.

Many variables affect the amount of saliva produced, the excretion of hormones from serum into saliva, and the amount of hormone in serum in the bound vs. free state. For example, medications that affect protein-binding may drastically alter the amount of bound vs. free ovarian hormone in serum. Concurrent use of anticholinergic or antihistamine medications decreases saliva production, which alters the amount of free hormone in saliva.

Urine hormone measures assess the metabolic breakdown products of the various forms of estrogens and other hormones. They're indirect measures of circulating levels of the active forms of these hormones. As such, they are not clinically useful in helping make treatment decisions about ovarian hormone therapy anymore than a urine glucose serves as the assay for determining insulin therapy dose in diabetics.

Serum measures remain the worldwide gold standard in fertility and menopause research settings, and should be the test methods used to guide clinical decision making as well.

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Disclosure Statement:

Dr. Vliet is an independent physician in private practice who has no financial ties to any pharmaceutical company, compounding pharmacy, or other commercial entity involved with products either directly or indirectly referenced in this article.

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Interested readers should also refer to the position statements by the Expert Panel of the International Menopause Society, and other world leaders in climacteric medicine and menopause, available on line at the website of the International Menopause Society, www.imsociety.org

- Guidelines for the hormone treatment of women in the menopausal transition and beyond. Position Statement by the Executive Committee of the International Menopause Society Revised August 28, 2004.
- Original Statement, February 13, 2004 *Climacteric* 2004;7:8-11
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- The View of the International Menopause Society on the Women's Health Initiative, *Climacteric* 2002;5:211-16