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Pharmacy compounding is the preparation of a customized medicine that has been prescribed by a doctor and is prepared by a state-licensed pharmacist. It has been recognized by the Food and Drug Administration (FDA), the U.S. Supreme Court, Congress and virtually every major health professional organization as a vital part of healthcare.

Millions of Americans have unique health needs that off-the-shelf prescription medicines cannot meet. For many of them a customized, compounded medication prescribed by licensed physicians or veterinarians and mixed by trained, licensed compounding pharmacists are the only way to better health. If customized medicines were not available, some of our most at-risk patients would needlessly suffer and some would die.

Compounded medicines can only be prescribed by physicians, veterinarians and other licensed health professionals as allowed under state law. They alone can assess their patients' conditions and determine when a compounded medicine is the most effective treatment. The basis of the profession of pharmacy has always been the triad – the patient-physician-pharmacist relationship. Through this relationship, patient needs are determined by a physician, who chooses an appropriate treatment regimen. Because every patient is different and has different needs, customized, compounded medications are a vital part of quality medical care.

<u>Patients Who Rely on Compounded Medicines</u>

Examples of those who rely on compounded medicines include:

- Infants and children: Compounding pharmacists can transform medicines from hard-to-swallow pills intended for adults into syrups, elixirs, suspensions, and emulsions for children, at the request of physicians. Flavors offered by compounding pharmacists can make drugs more palatable to children. In addition, premature infants often rely on lifesaving and life-sustaining drugs made only in compounding pharmacies.

- Hospital patients: Many, if not most, of the lifesaving intravenous drugs given in hospitals and clinics are compounded. Because hospital patients are often on multiple medications, compounding them into one treatment saves the hospital personnel time and the patient multiple injections or administrations.

- Cancer patients: Cancer treatment often involves special mixtures of cancer drugs that are compounded pursuant to a doctor's prescription. Pharmacists can combine multiple drugs into one treatment, leading to shorter administration times for cancer patients.

- Senior citizens: Elderly patients often have difficulty with traditional dosage forms, such as pills taken orally. Compounding pharmacists create alternate methods of delivery, like transdermal gels, to make it easier for the elderly to take their medicine.

- Pets: Animals come in all shapes and sizes, so one-size-fits-all pharmaceuticals do not always meet their needs. In many cases, a compounded medication may be necessary for a non-food animal to be satisfactorily treated.

- Patients with allergies: Patients who are allergic to a preservative, dye, flavor or other ingredient in commercial products can have their doctor write a prescription for a compounding pharmacist to customize the same medication without the offending ingredient.

- Menopausal women: Many women experience significant pain and discomfort as their bodies' progress through menopause. Doctors prescribe bioidentical hormones for patients for whom synthetic hormone treatments may be ineffective or produce undesired side effects. Several bioidentical hormone products are available in FDA-approved, one-size-fits-all formulations from pharmaceutical companies. However, physicians may determine that their patients have unique needs that warrant prescribing a different compounded hormone treatment. This often allows patients to take the smallest amount of a given hormone preparation to treat their symptoms, in conjunction with the recommendation provided by the Women's Health Initiative study.

- Patients who require non-traditional dosage forms: Many patients are unable to take medications orally or as injections – the traditional dosage forms for manufactured drugs. Compounding pharmacists can create alternate methods of delivery, like ointments, solutions or suppositories, to fit these patients' unique health needs. The pharmaceutical industry supplies only limited strengths of drugs, which some patients cannot tolerate. It is often necessary for a doctor to request a different strength of a drug for a patient through compounding.

- Patients who rely on discontinued drugs: Pharmaceutical manufacturers have discontinued thousands of drug products over the years, due to low profitability. For certain groups of patients, these were very effective, important, and sometimes life-saving medications. Such medications are now only available if a doctor prescribes them to be compounded.

- Hospice patients: End-of-life therapy involves the compounding of many different and unique dosage forms to allow patients to live out their lives free of pain and discomfort. Many combinations of drugs are prescribed by doctors and used for these patients who cannot swallow medications and who don't have the muscle mass that is required to receive multiple injections each day. Compounding pharmacists can provide alternate delivery methods such as oral inhalation, nasal administration, topical, transdermal or rectal use.

State and Federal Regulation of Pharmacy Compounding

State boards of pharmacy, state medical boards, the Food and Drug Administration, the Federal Trade Commission, the Drug Enforcement Agency, and other federal and state agencies each have some degree of oversight over compounding practice. The U.S. Pharmacopeia and the Pharmacy Compounding Accreditation Board also play critical roles. Together, they have constructed a web of regulations and standards that protect patients.

States boards of pharmacy license pharmacists and pharmacies. State pharmacy laws, enforced by state pharmacy boards, govern the processes and equipment pharmacists use to prepare those medicines. States also have requirements that mandate record keeping, labeling, and proper procedures for sterile compounding, among other aspects of pharmacy practice.

The FDA, which primarily regulates manufacturers, still has an important role to play in regulating compounding. Compounded medicines, including compounded hormones, are prepared using ingredients that must come from FDA-registered facilities – ultimately, the same facilities that supply manufacturers. The FDA also has authority to inspect any pharmacy's facilities, equipment, and ingredients. In addition, the FDA and the Federal Trade Commission have authority over false and misleading marketing practices by pharmacies.

In addition to state boards and federal agencies, compounding pharmacists follow national standards and guidelines set by the U.S. Pharmacopeia (USP). Since 1820, USP has been the official national standards-setter for pharmaceutical ingredients, recognized by Congress as such. It has strong standards for compounding of both sterile and non-sterile medications. USP's compounding committee, of which I am a member, is continually improving and strengthening its standards.

The increase in activity of the USP since the 1980s and 1990s has resulted in revision of chapters related to compounding, both nonsterile and sterile. The revisions resulted in USP Chapter <795> Nonsterile Compounding and USP Chapter <797> Sterile Compounding, both of which have many new and rigorous standards. Since 1995, most state boards of pharmacy have developed comprehensive regulations for pharmacy compounding and now many are beginning to adopt the USP standards as well. In fact, this May at their annual meeting, the National Association of Boards of Pharmacy is conducting special training for state board inspectors with regards to the USP standards for pharmacy compounding.

As an example, for sterile compounding, the process must be done in an ISO Class 5 environment using specialized equipment and documented procedures. By incorporating standards that adopt or mirror USP standards, state boards require much more detail regarding the environment in which both nonsterile and sterile compounding must be done and the documentation that is required. Also, standard operating procedures are required as well as additional continuing education, testing of compounded preparations, record-keeping, quality assurance and patient education.

In 2004, the pharmacy profession joined together to form the Pharmacy Compounding Accreditation Board (PCAB), a voluntary accreditation body whose mission is to assure the quality of compounded medications that patients are prescribed. PCAB's founders include the American Pharmacists Association, the National Association of Boards of Pharmacy, USP, and five other organizations.

To become PCAB-accredited, compounding pharmacies are tested against ten stringent standards, most with detailed sub-standards. These standards encompass regulatory compliance; personnel; facilities and equipment for both sterile and non-sterile compounding; chemicals and the compounding process; beyond-use dating and stability; packaging, labeling, delivery for administration and dispensing; practitioner and patient education; quality assurance and self-assessment.

PCAB-accredited pharmacies must adhere to the following set of principles:

- **Compounding is the preparation of components into a drug product** either as the result of a practitioner's prescription drug order based on a valid **practitioner/patient/pharmacist relationship** in the course of professional practice, or for the purpose of, or as an incident to, research, teaching, or chemical analysis that are not for sale or dispensing. Compounding is a part of the practice of pharmacy subject to regulation and oversight from the state boards of pharmacy.

- **Compounded medication may be dispensed to prescribers for office use**, where applicable state law permits. Office use does not include prescribers reselling compounded medications.

- **Compounding may be conducted in anticipation** of receiving prescription orders when based on routine, regularly observed prescribing patterns. Anticipatory compounding is limited to reasonable quantities, based on such patterns.

- **Compounding does not include** the preparation of copies of commercially available drug products. Compounded preparations that produce, for the patient, a **significant difference** between the compounded drug and the comparable commercially available drug product or are determined, by the prescriber, as necessary for the medical best interest of the patient are not copies of commercially available products. "Significant" differences may include, for example, the removal of a dye for a medical reason (such as an allergic reaction), changes in strength, and changes in dosage form or delivery mechanism. Price differences are not a "significant" difference to justify compounding.

- **Both the prescriber** (via the prescription) **and the patient** (via the label) should be aware that a compounded preparation is dispensed.

- **The pharmacy may advertise** or otherwise promote that it provides prescription drug compounding services. Such advertising should include only those claims, assertions, or inference of professional superiority in the compounding of drug products that can be independently and scientifically substantiated.

An extensive Accreditation Summary is publicly available for every accredited pharmacy, and contains information on compounding pharmacy, the pharmacy's scope of compounding at the time the pharmacy was last inspected; the date of the last and next Review and Survey (inspection), and the results of the inspection.

With 13 pharmacies already accredited, and nearly 100 others pending, PCAB is already giving patients and prescribers a way to select a pharmacy that meets high quality standards.

Additionally, the association representing compounding pharmacists – the International Academy of Compounding Pharmacists (IACP) – has issued guidelines for the labeling of compounded medications. These are designed to help pharmacists communicate to their patients that the compounded medications they've been prescribed are different from off-the-shelf, one-size-fits-all pharmaceuticals and offer a unique value – a medication customized to meet the individual patient's unique needs.

Pharmacists and physicians communicate much of this information to patients already, but the labeling guidelines provide an extra measure to ensure patients understand (1) that their medicine was compounded in a pharmacy, (2) how to use and care for the medication, and (3) that their doctor or pharmacist can provide additional information.

IACP's guidelines are meant to encourage pharmacists to go beyond what the laws require to ensure patients understand the unique value of compounded medicines. For the first time, the guidelines will provide a standardized labeling model for compounded medicines across all 50 states.

Compounded Medicines are not Subject to the FDA New Drug Approval Process

Despite the fact that state boards of pharmacy primarily oversee pharmacy compounding, the FDA has stated: "A new drug -- including a compounded new drug -- may not be legally manufactured or sold in the United States unless it has been pre-approved by FDA as safe and effective for its intended uses. … In virtually every instance, the drugs that pharmacists compound have not been so approved." *(emphasis added)*

While the FDA approval process is well suited for mass-produced pharmaceuticals, inserting the FDA into the approval process for each of the individual compounded medications, which number in the millions, is simply unworkable. Patients' access to these needed medications would be cut off. Already, many practitioners are discouraged from prescribing and administering the most appropriate medications to patients because of the misconception that compounding is illegal.

There is legal precedent for exempting compounded medicines from the FDA new drug approval process. As federal district court Judge Robert Junell ruled in *Medical Center Pharmacy v. Gonzales* in 2006, "Public policy supports exempting compounded drugs from the new drug definitions. If compounded drugs were required to undergo the new drug approval process, the result would be that patients needing individually tailored prescriptions would not be able to receive the necessary medication due to the cost and time associated with obtaining approval. When a licensed practitioner writes a prescription for a compounded drug for a patient, the medication is normally needed soon thereafter. It is not feasible, economically or time-wise for the needed medications to be subjected to the FDA approval process. It is in the best interest of public health to recognize an exemption for compounded drugs that are created based on a prescription written for an individual patient by a licensed practitioner. […] Compounded drugs, when created for an individual patient pursuant to a prescription from a licensed practitioner, are implicitly exempt from the new drug definitions."

In *Tommy G. Thompson, Secretary of Health and Human Services, et al., Petitioners v. Western States Medical Center et al.* in 2002, the United States Supreme Court ruled that "The Government argues that eliminating the practice of compounding drugs for individuals would be undesirable because compounding is sometimes critical to the care of patients with drug allergies, patients who cannot tolerate particular drug delivery systems, and patients requiring special drug dosages. Preserving the effectiveness and integrity of the FDCA's new drug approval process is clearly an important governmental interest, and the Government has every reason to want as many drugs as possible to be subject to that approval process. The Government also has an important interest, however, in permitting the continuation of the practice of compounding so that patients with particular needs may obtain medications suited to those needs. And it would not make sense to require compounded drugs created to meet the unique needs of individual patients to undergo the testing required for the new drug approval process. Pharmacists do not make enough money from small-scale compounding to make safety and efficacy testing of their compounded drugs economically feasible, so requiring such testing would force pharmacists to stop providing compounded drugs."

<u>Bioidentical Hormone Replacement Therapy (BHRT)</u>

All medications, including all compounded medications containing any form of estrogen, require a valid prescription from a licensed prescriber. Physicians work with their patients to determine when bioidentical hormones are appropriate and, if they are, they work with pharmacists to design individualized treatments to meet their patients' individual needs – needs that are unmet by off-the-shelf, one-size-fits-all, mass-produced pharmaceuticals. Doctors often prescribe manufactured synthetic hormone products such as Premarin and Prempro. When they determine those products are inappropriate, doctors sometimes prescribe bioidentical hormones tailored to meet each patient's unique needs. Also, there are manufactured bioidentical hormones on the market – Prometrium and Estragel are two examples.

For many patients, manufactured synthetic products are effective, but for some they are not.

- That may be because the manufactured drugs simply don't relieve the symptoms of menopause. It may also be because doctors determine that their patients need a lower dose than what is available commercially.
- Some patients experience adverse side effects from the manufactured synthetic products. In those cases a compounded medication may be prescribed in the attempt to lessen the bad effects while achieving intended therapeutic effect.
- Other times, doctors find that changing combinations of hormones – progesterone, estradiol, estriol and estrone – in ways that are not commercially available alleviate their patients' symptoms.
- Or doctors find that different delivery forms – creams, liquids, capsules, troches – are more effective for an individual patient.
- One manufactured bioidentical medication, Prometrium is made with peanut oil, a common allergen. Many patients are allergic to peanut oil and need progesterone – the active ingredient in Prometrium – to be compounded without it.
- When compounded hormones are prescribed, it is because doctors determine that their patients have needs for medications that are significantly different from what is manufactured.

Existing laws enforced by the FDA and the Federal Trade Commission prohibit the making of unsubstantiated claims of safety and efficacy in pharmacists marketing practices. It is important to remember that compounded hormones are prescribed by doctors and no amount of marketing is going to allow a patient to obtain compounded hormones without a doctor's prescription. Also, compounded hormones are always prepared pursuant to a doctor's prescription and dispensed directly to patients at retail.

Because compounded medications are regulated by state pharmacy boards and are not subject to federal laws designed to regulate mass-produced drugs, bioidentical hormones are not subject to FDA approval. While the pharmacy profession supports and is funding studies to determine the risk profile of BHRT, there are risks with all pharmaceuticals. It is up to a physician to weigh the risks and rewards of any prescription drug.

Millions of women have been prescribed manufactured hormone products. Many of them have found relief from torturous symptoms of menopause. Some have not and, instead, have been prescribed compounded hormones by their physicians. They have found relief and I would respectfully urge the Members of this Committee and Congress overall to consider the impact any new policies would have on these patients.