July 29, 2013

Executive Summary of PCCA's Response to:

Frequently Asked Questions – S.959 – "Pharmaceutical Quality, Security and Accountability Act" – Published July 24, 2013 by Proponents of Senate Bill 959

Attached is PCCA's detailed response to an FAQ published by proponents of Senate Bill 959 (S.959). The FAQ attempts to clarify many issues raised by the bill but falls short of telling the whole story regarding unintended consequences that would occur if the bill were passed.

S.959 has strayed from its original intent to increase the quality and safety of compounded medications and to try to prevent another New England Compounding Center (NECC) tragedy from happening by inserting Federal oversight into the practice of pharmacy. PCCA and many others believe that this will severely restrict patient access to needed, sometime life-saving, compounded medications.

The Senate FAQ document tries to divert attention away from the reality of the consequences of what will really happen, so we've taken the FAQ document and added our perspective regarding the factual language of what's in the bill.

Summary of our response:

- If S.959 is passed as written, it will decrease patient access to compounded medications and negatively affect healthcare for hundreds of thousands, if not millions, of patients.
- S.959 addresses the false assumption that the FDA does not currently have oversight authority over compounding pharmacies acting as manufacturers when in fact, the Agency already has that authority. The FDA already has criteria for determining when an alleged pharmacy is manufacturing drugs, not compounding them.
- The bill inserts the FDA directly into the practice of medicine, removing the ability of the prescriber to decide what is best for their patient.
- Clarification on how S.959 will worsen the national problem of drug shortages, affecting scores of Americans.
- The bill currently offers many exemptions to certain types of pharmacies, including pharmacies located in health systems and those pharmacies administered by Pharmacy Benefit Managers. PCCA believes that, in order to be effective, any new regulations should be applicable to all practices of pharmacy.
- The bill will directly affect the free trade of compounded medications for pharmacies near state borders.

PCCA strongly objects to the current version of S.959 and believes it is unworkable and will tremendously alter the practice of pharmacy for the worse, negatively affecting access to compounded medication for potentially millions of patients.

We have made our best effort to work with the Senate HELP Committee, offering recommendations to draft proposals and repeatedly meeting with Senate staff. Our goal was to try to help construct a bill that would increase safety and quality of compounded medications while preserving patient access to these needed and sometimes lifesaving therapies. We believe S.959 falls far short of that goal and should not be passed.

PCCA response to:

"Frequently Asked Questions: S.959 – Pharmaceutical Quality, Security and Accountability Act" – Published July 24, 2013 by proponents of Senate Bill 959.

The FAQs are reproduced below in their entirety without alteration followed by PCCA's response. Text in *italics* is a verbatim copy from the proponents of S.959's FAQ.

Pharmaceutical Compounding Q & A – Title I of S.959

On May 22, 2013, the Committee on Health, Education, Labor and Pensions (HELP) approved S.959, the Pharmaceutical Quality, Security and Accountability Act, by voice vote. In Committee, S. 959 was joined with S.957, the pharmaceutical track and trace provisions. S.959 now contains two titles. Title I contains the pharmaceutical compounding provisions, and Title II is drug tracing. Title I clarifies the regulation of pharmacy compounding. Traditional pharmacy practice will continue to be regulated by the states, and compounding manufacturers, which compound sterile products without a prescription and ship them across state lines, will be overseen by the Food and Drug Administration (FDA). Compounding manufacturers will be required to register and be inspected by the FDA.

PCCA RESPONSE

While Title I of S.959 attempts to clarify the regulation of pharmacy compounding, we feel that the bill wanders greatly from its intended purpose. The statement "Traditional pharmacy practice will continue to be regulated by the states," is disingenuous as many new provisions and regulations will squarely increase FDA's role in the regulation of the "traditional" practice of pharmacy. Also, the promulgation of a new category, called "compounding manufacturers", muddies the regulatory waters and places pharmacy practices across the United States in impossible situations when trying to provide patient care. **In the end, S.959 as it stands will decrease patient access to compounded medications and negatively affect healthcare for hundreds of thousands, if not millions, of patients.**

How does the bill distinguish between pharmacy practice and manufacturing?

In current law, large-scale compounders operating under state pharmacy licenses – like the New England Compounding Center that was responsible for the fungal meningitis outbreak last fall – can essentially act as drug manufacturers while evading FDA oversight. Title I of S. 959 clearly distinguishes between traditional pharmacies, which will be primarily subject to state oversight, and compounding manufacturers, which will be regulated by the FDA.

PCCA RESPONSE

The opening paragraph of the FAQ document regarding S.959 states: "Traditional pharmacy practice will continue to be regulated by the states…." However, in the paragraph above, it instead states: "traditional pharmacies, which will be *primarily subject* to state oversight…." (Emphasis added). **The FAQ document itself confuses at the outset on who will be regulating which type of practice.** How then, can the bill "clearly distinguish" the two different types of practices?

In many instances, the Committee maintains that the legislation would not have an impact on traditional compounding. In making this argument, however, the Committee uses the term "traditional compounding" or "compounder" in the proposed (and too narrowly defined) statutory sense. It is true some of the most restrictive provisions do not affect "traditional compounding," as defined in the legislation. **However, the legislation will, in fact, heavily affect traditional pharmacy practices and patient access to compounded medications.** These issues will be covered later in this document.

We'd also like to point out that the statutory definition also does not address the root cause of the New England Compounding Center (NECC) matter – a drug manufacturer in all material respects that allegedly did not engage in appropriate aseptic practices. For the same reasons, PCCA also disagrees with the Committee's assertion that NECC was able to "essentially act as [a] drug manufacturer while evading FDA's oversight." The Congressional record concerning the investigation into the NECC meningitis outbreak, as well as FDA's multiple recent regulatory activities against pharmacies, demonstrate that FDA always had, and currently has, authority over compounding pharmacies acting as manufacturers – the Agency was actually aware of NECC's poor quality practices as far back as March 2002 (House Committee on Energy and Commerce Report: "FDA'S Oversight Of NECC And Ameridose: A History Of Missed Opportunities?"). **The legislation cannot be based on a purported lack of authority to regulate pharmacies like NECC, since FDA did take enforcement action against NECC.**

FDA already has criteria for determining when a putative pharmacy is manufacturing drugs, not compounding them. A pharmacy that distributes prescription drugs without orders from authorized practitioners, or that distributes drugs to wholesalers or middlemen, or that is proven to engage in any other activity prohibited by applicable state pharmacy law, is – and should be – subject to losing its state license, and is subject to FDA regulation as a drug manufacturer, even if existing federal laws are not changed.

Does the bill interfere with State regulation of pharmacy practice?

No, the intent of the bill is to preserve state regulation of traditional pharmacy practice. The bill clarifies that traditional pharmacy practice is regulated by state boards of pharmacy. States will continue to set quality and practice standards for traditional pharmacies, just as they do in current law.

PCCA RESPONSE

Yes, intrusive FDA oversight of the pharmacy profession will result if S.959 is enacted, with the unintended consequence of restricting access to compounded medications for hundreds of thousands, if not millions of patients each year. While the goal of the bill was to originally provide oversight of those compounding sterile products, dispensed interstate for non-patient specific situations, S.959 allows sweeping intrusions into compounding while excluding key areas of compounding, specifically hospitals. The legislation will impose federal requirements on many other aspects of pharmacy practice, including but not limited to: giving power to the FDA to determine what bulk and other ingredients, and dosage forms, may or may not be used in the practice of compounding; assigning arbitrary beyond use dates for preparations

compounded for office use, regardless of scientific studies or use of FDA-recognized best practices (USP regulations regarding compounding); limiting by a month percentage the amount of preparations that may be compounded for office use; requiring recordkeeping beyond what State Boards of Pharmacy require; and forcing traditional pharmacies to report to the FDA when the pharmacy compounds a preparation in response to a drug shortage.

While the bill does not directly give oversight power to the FDA over traditional pharmacies, it also does not directly forbid it. Given the new Federal provisions regarding traditional pharmacy practice, we are left to ask – who will oversee the implementation of these new provisions? We believe that the FDA will use the provisions to introduce new burdensome Federal oversight over traditional pharmacy practice, which has traditionally, and appropriately, been left to individual State Boards of Pharmacy.

Will traditional compounders be subject to current Good Manufacturing Practices (cGMPs) -- the quality standards that apply to pharmaceutical manufacturers?

Traditional compounders are exempt from cGMP requirements. The legislation exempts traditional compounders from the statutory cGMP requirements (section 50l(a)(2)(B)), adequate directions for use (section 502(f)(l)), and the new drug approval requirements (section 505). In contrast, compounding manufacturers will be subject to cGMP requirements, although they will be exempt from the new drug approval requirements and the adequate directions for use requirements.

PCCA RESPONSE

Yes, compounders could be subject to current Good Manufacturing Practices, or cGMPs, because the current language is clear when it comes to compounders who may just occasionally produce sterile compounds, ship over a state line and compound prior to a prescription. **The practice of compounding in advance of a prescription currently occurs regularly, based on the need to test sterile products which can take up to eighteen days to complete.** The only way to provide a compounded sterile preparation for an identified patient in a timely manner would be to compound the medication prior to receiving the prescription in order to allow enough time for the testing process to occur. Even if the pharmacy received a patient specific prescription before dispensing the medication, the simple act of preparing the medication before receipt of a prescription would place the compounding pharmacies into the compounding manufacturer world. Therefore, the FDA would have the right to apply onerous cGMP regulations that would outright prohibit smaller compounding pharmacies, especially those located near state borders who regularly compound for out-of-state patients, from providing needed medications.

The cGMP regulations (21 C.F.R. Parts 210 and 211), that apply to drug manufacturers would apply to the newly defined entity and the only significant difference between compounding manufacturers and regular FDA-registered drug manufacturers would be an exemption from new drug approval requirements for new drugs (Section 505 of the FDCA, 21 U.S.C. § 355, for human drugs, and Section 512 of the FDCA, 21 U.S.C. § 360b, for animal drugs), and from requirements of adequate directions for use (Section 502(f)(1) of the FDCA, 21 U.S.C. § 352(f)(1)). **With these slight differences, we wonder why there is a need for a "compounding**

manufacturer" designation in the first place. PCCA supports the House draft proposals circulated to date that identify a business as either a pharmacy or a manufacturer.

By categorizing all compounded drugs as new drugs, will the burden on traditional pharmacies be so great that it is impractical to compound even to fill a specific prescription?

No. The legislation exempts traditional compounders from the new drug approval requirements, cGMP standards, and adequate directions for use requirements, so they are not subject to the major requirements applicable to most new drugs. The FDA currently categorizes all compounded drugs as new drugs, and this legislation maintains that principle.

PCCA RESPONSE

PCCA believes that this provision would impair a patient's ability to seek reimbursement for compounded medications from insurance companies and potentially increase FDA enforcement actions against compounding pharmacies by allowing FDA to allege that the pharmacies did not file a New Drug Application for every compound they make.

Will the legislation limit or even eliminate doctors' options for prescribing the most beneficial treatment, in their medical opinion, for a patient?

No. The legislation protects the practice of medicine, which continues to be regulated by states. To ensure that patients get the safest possible products, the FDA is directed to work with stakeholders to create a list of products too complex to safely compound such that they are reasonably likely to lead to an adverse effect on safety or effectiveness taking into account risks and benefits to patients. Only after a transparent regulatory process, with a comment period for the public and doctors, can FDA add any product to that list.

PCCA RESPONSE

Yes, in many instances the legislation will either limit or eliminate doctors' options for prescribing the most beneficial treatments for patients. For example, the legislation would limit ingredients available for drug compounding that are currently used by physicians. Section 503A(e)(1). In addition, the Secretary may establish a list of bulk substances that may not be used in compounding, notwithstanding the fact that some prescribers may determine that such ingredients may be critical to a patient's medical care. See Section 503A(e)(6). FDA will substitute its judgment for that of physicians. HELP's focus on "the safest possible products" points to a fundamental flaw: **FDA will consider safety for the mass population, not the unique needs of individual patients as determined by medical practitioners exercising their learned judgment.**

PCCA also opposes any restrictions on compounded drugs based on an arbitrary finding by the FDA as to what is (and is not) a product that is "demonstrably difficult" to compound. Codifying a set of dosage forms as difficult to compound (as determined by the Secretary) does not address individual patient needs for certain dosage forms as determined by a physician, or

the rapid innovation that occurs in our industry. Also, the FDA could use this avenue to outlaw the compounding of certain classes of medications FDA deems as ineffective, in the exercise of its own discretion, notwithstanding a practitioner's contrary determination for an individual patient.

The FDA has shown that it cannot fulfill its commitments when it comes to working with stakeholders or in creating and maintaining lists. Here are just a few examples from the Food and Drug Administration Modernization Act (FDAMA) of 1997:

Example 1: FDAMA Section 503A – (b)(3)(A)

"...such drug product is not a drug product identified by the Secretary by regulation as a drug product that presents demonstrable difficulties for compounding that reasonably demonstrate an adverse effect on the safety or effectiveness of that drug product; and..."

FDA Failure:

Since the bill was passed in 1997, FDA failed to make any identification of drug products required by this Section.

Example 2: FDAMA Section 503A – (b)(3)(B)

"The Secretary shall, in consultation with the National Association of Boards of Pharmacy, develop a standard memorandum of understanding for use by the States in complying with subparagraph (B)(i)."

FDA Failure:

Since the bill was passed, FDA failed to develop the required standard memorandum of understanding.

Does the bill restrict health care decisions by prescribers and their ability to prescribe a variation of a manufactured drug to meet patient needs?

No, the bill does not interfere with prescribers' treatment decisions. If a prescriber determines that a compounded product--including a compounded variation of an FDA-approved product--is the best option to meet a patient's clinical need, the prescriber can write a prescription for that compounded variation and the product can be compounded from bulk. Compounded variations that are made starting with an FDA-approved product (such as adding a flavoring) do not require this determination of clinical need.

PCCA RESPONSE

Yes, the bill will significantly restrict health care decisions by prescribers in several respects. For example, the bill limits ingredients included in compounded medications and the types of products or dosage forms that can be compounded. Physicians often are presented with patient needs that in their medical judgment are best treated by dispensing a medication that is a variant of a manufactured product. Whether it is changing a component of the formulation for

patient intolerances, changing the dispensing device for patient compliance, modifying the strength of the active ingredient or combining it with other active ingredients because of variations in patient needs, a very large part of a compounding practice results from filling these types of prescriptions. **These variants of manufactured products, as well as other compounded products that physicians prescribe based on their medical judgment for patients that need them, are in jeopardy if S.959 becomes law.**

In dealing with "Exceptions Regarding Marketed Drugs" (Section §503A(d)(1)-(5)), PCCA believes that the text as it currently stands produces both an undue burden on the prescribing practitioner and also federalizes the practice of medicine, a profession that has historically been controlled by state Boards of Medicine. **Prescribing practitioners and pharmacists should be allowed to exercise professional judgment, as permitted by state law, to determine if a compounded preparation is the best option for a particular patient in their care, without their choices being subject to FDA review or second guessing.**

Currently, there are hundreds of thousands of patients who are receiving compounded drugs who will no longer be able to have those prescriptions filled because of the limits the proposed legislation places on active ingredients. If FDA bans certain compounding as "demonstrably difficult" – which the bill authorizes FDA to do – the numbers of individuals that cannot obtain needed medications will increase significantly. **It is difficult to understand how the inability to prescribe compounded drugs that are currently compounded "does not interfere with prescribers' treatment decisions."**

Does the bill prohibit compounding 17P?

Makena contains a preservative, and 17P generally does not. If a prescriber determines that a compounded variation of an FDA-approved product is the best option to meet a patient's clinical need, the prescriber can write a prescription for that compounded variation and the product can be compounded from bulk.

PCCA RESPONSE

The statements regarding 17P in the FAQ are untrue. The vast majority of compounded 17P in the United States DOES contain a preservative. In fact, the formula used by the drug manufacturer to produce Makena is an essential copy of the formula used by compounding pharmacies to provide this needed medication to pregnant women for almost twenty years before Makena was approved. The bill would absolutely prohibit the compounding of 17P as it would be an essential copy of a commercially available product. **However, this would go against the FDA's March 30, 2011 decision to exercise enforcement discretion with regard to compounded versions of 17P, which allowed compounding pharmacies to continue compounding the preparation.**

Will the legislation make drug shortages worse?

No. The legislation specifically allows for compounding copies of products on the FDA drug shortage list to help alleviate the impact of drug shortages.

PCCA RESPONSE

Yes, this bill would make drug shortages worse. Pharmacies currently compound when drugs are not commercially available. A drug may not be "available" even though it does not appear on FDA's drug shortage list.

S.959's drug shortage provisions permit copies of marketed FDA-approved drugs only under extremely limited circumstances. Under the legislation, in order to compound a copy of a marketed FDA-approved drug, the compounded product would have to be, at the time of compounding and its distribution, on FDA's drug shortage list for human or veterinary products maintained on FDA's website. The drug shortage list maintained by FDA does not accurately reflect all current drug shortages because drug manufacturers are only required to report drug shortages to FDA under certain circumstances. (Center for Drug Evaluation and Research, Food and Drug Administration, Guidance for Industry, Notification to FDA of Issues That May Result in a Prescription Drug or Biological Product Shortage; Draft Guidance (Feb. 2012))

We recently compared the FDA drug shortage list with the much more comprehensive drug shortage list maintained by the authoritative and reliable American Society of Health-System Pharmacists. **The FDA drug shortage list was missing 133 different drug entities that appear on the ASHP list**. The FDA's list also does not take into account regional shortages. While the bill gives FDA discretion to take this into account, it does not mandate that FDA do so. FDA officials have stated that they do not believe regional drug shortages exist. Thus, requiring compounders to rely solely on FDA's listing of a drug before they can compound the product does not alleviate the threat to the public health caused by immediate unavailability of an unlisted, yet needed, life-saving medication.

Also, on July 23, 2013, the DC Circuit Court of Appeals held that **FDA had acted unlawfully when it permitted the importation of unapproved drugs from an unregistered manufacturer.** *Cook v. Food and Drug Administration.* The court unanimously held that FDA did not have the discretion to allow this importation since the drugs in question clearly did not comply with the FDC Act.

The decision has a direct bearing on whether S.959 would exacerbate the drug shortage problem. In arguing that the drugs should be permitted to be imported, FDA asserted that it needed to be able to allow importation of unapproved drugs to address drug shortages. The court rejected that argument. Thus, importation of unapproved drugs cannot be used to remediate drug shortages.

Drug shortages have been a persistent and clinically critical issue. Despite various tactics used by FDA to address the inability of manufacturers to supply these drugs, there are many instances in which the manufactured versions are not available. As a result of the Cook decision, one of the approaches that FDA has been using may no longer be permitted. Compounded

drugs have helped to address the problem of drug shortages. **Limiting compounding to drugs which appear on FDA's drug shortage list means that many necessary drugs will not be available, particularly since one of the remedies that FDA relied upon has been found to be unlawful.**

Additionally, even though proponents of S.959 say that States will continue to have oversight of "traditional compounders," **the bill inserts Federal oversight of these same compounders by requiring them to notify** "the Secretary not later than 3 calendar days after beginning the compounding;" of drugs that are in short supply. Pharmacies will have other reporting obligations as well.

How can the definition of "compounding manufacturer" refer to "prescriptions" when pharmacies dispense prescriptions, while manufacturers sell drugs?

The definition of a "compounding manufacturer" refers to prescriptions only to say that an entity that compounds a sterile drug without a prescription for an identified individual patient and ships it interstate is a compounding manufacturer. If the pharmacy has a prescription for a compounded drug, it's a traditional pharmacy under the bill's language.

PCCA RESPONSE

Herein rests one of the biggest issues with the bill. Can a business exist as a compounding manufacturer and a traditional compounding pharmacy simultaneously? Parts of the bill indicate that they cannot. So, what would the scope of business be for the compounding manufacturer? Solely making sterile preparations that are compounded prior to receiving a drug order or prescription and shipped interstate? If so, wouldn't that be the definition of a drug manufacturer? We believe that this essential issue creates much more confusion for regulation of businesses engaging in compounding – when is the "magic time" that a pharmacy is no longer regulated by a Board of Pharmacy and is regulated by the FDA? Can a "compounding manufacturer" revert back to a "traditional compounder" if they agree to not conduct business as a "compounding manufacturer?" What happens then? In essence, if this bill is enacted, either one of two things will happen: traditional compounding pharmacies will decide to stop compounding sterile products that would be sold into another state OR traditional compounding pharmacies will be forced to become a compounding manufacturer. Under the bill's provisions, those entities would no longer be able to compound non-sterile drugs except under limited circumstances approved by the Secretary. **Either scenario directly decreases patient access to compounded preparations.**

How will the bill hold the FDA accountable and facilitate Congressional oversight?

By clearly demarcating accountability between FDA and the states, the bill will make it clear that FDA is solely accountable for oversight of compounding manufacturers, and will enhance Congressional oversight over FDA's regulation of manufacturer-like compounding. In addition, FDA is required to issue

annual reports to Congress regarding the agency's use of resources to inspect compounding manufacturers.

PCCA RESPONSE

We believe that FDA's appropriate regulatory role should remain where it has always been – the regulation of drug manufacturers, not pharmacies. FDA always had regulatory authority over drug manufacturers, including NECC. PCCA remains concerned that FDA's track record regarding drug manufacturers disguised as pharmacies at least since the introduction of the last major compounding regulation, the Food and Drug Administration Modernization Act (FDAMA) of 1997, demonstrates FDA's authority to regulate, but FDA's failure to exercise that authority. Here are a few examples:

Example 1: FDAMA Section 503A–(b)(1)(A)(i)(III):

"if such a monograph does not exist and the drug substance is not a component of a drug approved by the Secretary, that appear on a list developed by the Secretary through regulations issued by the Secretary under subsection (d);..."

FDA Failure: Since FDAMA passed sixteen years ago, FDA failed to promulgate any "positive list" of components.

Example 2: FDAMA Section 503A–(b)(1)(C)

"does not compound a drug product that appears on a list published by the Secretary in the Federal Register of drug products that have been withdrawn or removed from the market because such drug products or components of such drug products have been found to be unsafe or not effective...."

FDA Failure: Since FDAMA passed *sixteen years ago*, FDA only published one such list, which list FDA has failed to update has since that original publication.

Does the bill put the FDA in charge of determining if a pharmacy is acting within the scope of its pharmacy license rather than the State Board of Pharmacy?

No, the bill gives FDA no role in determining whether a pharmacy is complying with State law.

PCCA RESPONSE

The bill only addresses how the FDA will act when it receives notification from a State Board of Pharmacy that a pharmacy is acting a compounding manufacturer. It does not address how the FDA will act if it receives the same notification or complaint from other sources. Will the FDA assign the applicable Board of Pharmacy the task of inspecting the pharmacy to judge whether or not the pharmacy is engaging in compounding manufacturer activities? **Prior actions by the FDA suggest that the Agency would conduct their own investigations and inspections of pharmacies regulated by the State Boards of Pharmacy to determine the scope of the pharmacy's practice.**

There will be facilities that are deemed pharmacies under state law but a "compounding manufacturer" under the bill. These facilities will now be regulated by FDA and can no longer be pharmacies. **Presumably, FDA's decision that a facility is subject to its jurisdiction will trump any contrary view by the State Board of Pharmacy.**

Does the legislation create loopholes for pharmaceutical companies to manufacture new drugs without new drug applications (NDAs)?

Under current law, compounded drugs are considered new drugs. The legislation maintains current law in this respect, while clarifying that the new drug application requirements apply unless the criteria to be either a traditional compounder regulated by states or a compounding manufacturer regulated by FDA are met. Under the legislation, a traditional compounder, a compounding manufacturer, or a manufacturer may not make a product from a bulk unknown to United States Pharmacopeia (USP)or FDA and distribute it in interstate commerce without an Investigational New Drug Exemption, NDA, or Abbreviated New Drug Application (ANDA).

PCCA Response:

While the bill would not create a loophole in the NDA process, it could create a backdoor for generic manufacturers to introduce new generic products to the market based on bulk drug substances already known to USP or approved by the FDA.

Does the legislation create a loophole for hospital compounding pharmacies that will allow them to compound outside of industry best practices?

Hospital-based pharmacies are treated as traditional compounders under the legislation, and must meet the same criteria as other traditional compounders. Hospital-based compounding will continue under the exact same state pharmacy board, accreditation organization (e.g. Joint Commission), and Centers for Medicare and Medicaid Services standards that exist today. The legislation also requires the Government Accountability Office to examine compounding in hospitals and report to Congress.

PCCA RESPONSE

PCCA believes that all practices of pharmacy should be treated the same in regards to pharmacy compounding. Creating an exemption for "a pharmacy within a health system" creates regulatory confusion that compromises patient safety. In an OIG Report, 43.8% of hospitals surveyed do not have a USP <797> compliant Clean Room, meaning that over 40% of hospitals are not properly equipped to perform correct sterile compounding. The bill DOES create a loophole for these types of pharmacies, since they will be allowed to act as compounding manufacturers but will not be subject to regulations concerning compounding manufacturers. All pharmacies participating in sterile compounding should meet minimum pharmacy standards set forth by the State Board of Pharmacy in which the hospital is located. Allowing sterile compounds to be distributed within a hospital system from a central pharmacy does not address the safety of sterile preparations that are needed immediately, such as those for "crash carts."

Will the FDA be required to provide evidence of patient safety or impact on patient care when it prohibits categories of drugs deemed "difficult to compound"?

As is true in current 503A, the bill would allow FDA to work with stakeholders to determine that some products cannot be safely made outside of a traditional manufacturing environment. These include products that FDA, consulting with pharmacists and other stakeholders, would identify as too complex to be safely made in pharmacies and that are reasonably likely to have an impact on the safety and efficacy of the drug, taking into account risks and benefits to patients. To designate products that cannot be safely compounded, FDA will have to publish its rationale, consider comments, and go through the full rulemaking process.

PCCA RESPONSE

The draft legislation states that certain "demonstrably difficult" drugs may not be compounded except under limited circumstances. Those drugs could include complex dosage forms as designated by FDA pursuant to regulation. By permitting FDA to determine which drugs are "complex," **FDA would be authorized to undermine physicians' ability to determine what, in the exercise of their medical judgment, are the best medications to treat certain medical conditions.** This provision impedes physicians' practice of medicine, contrary to the interests of patient health and to important, long-standing policy that FDA will not interfere with the practice of medicine. *Washington Legal Found. v. Kessler*, 880 F. Supp. 26, 28 n.1 (D.D.C. 1995) (FDA recognizes "unapproved uses" of drugs may play "important role" in "practice of medicine"); FDCA Section 1006 (21 U.S.C. § 396) (FDA will not interfere with "authority of a health care practitioner to prescribe or administer any legally marketed device").

Will the legislation eliminate drug compounding for animals?

No. Animal drugs are not included in S.959.

Will the legislation prohibit the use of sterile liposomal or transdermal products?

The draft does not ban the compounding of any specific products. The legislation, similar to current law, does allow FDA to establish a list of products that are too complex to currently be compounded, but that list must be developed in consultation with stakeholders and through an open and transparent regulatory process.

PCCA RESPONSE

Permitting the FDA to determine which drugs are "complex," would allow the FDA to hinder physicians' ability to determine what are the best medications to treat patients' medical conditions. This provision thus impedes physicians' practice of medicine, contrary to the interests of patient health and to important, long-standing policy that FDA will not interfere with the practice of medicine. *Washington Legal Found. v. Kessler*, 880 F. Supp. 26, 28 n.1 (D.D.C. 1995) (FDA recognizes "unapproved uses" of drugs may play "important role" in "practice of

medicine"); FDCA § 1006 (21 U.S.C. § 396) (FDA will not interfere with "authority of a health care practitioner to prescribe or administer any legally marketed device").

Any drug that is to be included on a "do not compound" list should be added only after completion of a sufficient notice and comment period, and passage of an applicable regulation, without any predesignation by Congress or the Committee of specific types of drugs. Moreover, "demonstrable difficulties" is a vague term and could well result in applying prohibitions that affect all pharmacies, including ones with a demonstrated ability to compound the drug in question. While the law does not directly ban classes of compounded drugs, it gives the FDA the authority to do so.

In the end, the question should be: "demonstrably difficult" for whom? A drug product that may be difficult for a community pharmacy may be readily compounded by a pharmacy with the necessary equipment, skills, and training. **It would be equivalent to saying that "neurosurgery" is "demonstrably difficult" as a type of surgery even though neurosurgeons specializing in that discipline routinely perform those types of difficult procedures.**

How does the compounding bill affect dietary supplements?

Dietary supplements are not affected by the bill. FDA regulates dietary supplements under the Dietary Supplement Health and Education Act of 1994 (DSHEA).The bill does not amend or affect DSHEA.

How does the compounding bill affect homeopathic medicines?

The compounding bill will not affect FDA's regulation of homeopathic medicines. Currently, homeopathic drugs which lack an approved New Drug Application are marketed in accordance with the provisions in the FDA Compliance Policy Guide (CPG) Sec. 400.400. For over 20 years FDA has exercised a policy of enforcement discretion with regard to the importation of homeopathic drugs that meet the provisions of CPG Sec. 400.400.We have worked with FDA to ensure that the compounding bill will not affect the Agency's implementation of CPG 400.400.

How does the compounding bill affect bio-identical hormones?

Title I of the legislation maintains the model under which bio-identical hormone products are typically made and marketed. Bio-identical hormones are typically not sterile drugs, and thus could be made and shipped interstate by traditional compounders.

The compounding bill does not ban the compounding of bio-identical hormone products, such as estriol. As is true of current law, it sets standards for the ingredients that may be used in compounded products, to prevent unscrupulous actors from using the safe harbor for compounding to commit health fraud or market dangerous products.

Current law requires that any drug compounded from bulk must use bulk active pharmaceutical ingredient (API) that 1) either complies with an applicable USP or National Formulary (NF) monograph, is part of an FDA-approved drug, or appears on a list established by the Secretary; 2) is manufactured in a registered establishment; and 3) is accompanied by a valid certificate of analysis.

The revised section 503A in S. 959 would permit the Secretary to identify a bulk API that only has an applicable USP or NF monograph as not suitable for compounding due to public health concerns after taking into account historical use, peer-reviewed literature, or other criteria following the publication of the reasoning and consideration of comments submitted to a docket open for at least 60 days. The bill would thus only allow FDA to prohibit use of an ingredient for compounding if it establishes a public health concern with the ingredient and follows a transparent process.

PCCA RESPONSE

This bill will affect access to bio-identical hormones (BHRT). S.959 grants FDA the authority ban certain components of compounded BHRT if, in the opinion of the FDA, they pose "public health concerns." **In 2008, FDA took similar action against the female hormone estriol, a component contained in approximately 80 percent of all compounded estrogens.** FDA's action was in direct response to a request in a "Citizen Petition" filed by a drug company that sells synthetic hormones that competed with BHRT. FDA instituted import bans on estriol and sent warning letters to suppliers and pharmacies trying to prevent or limit women from obtaining BHRT with estriol. FDA was unable to enforce these actions. S.959 gives them that authority.

S.959 greatly expands the definition of a "copy" of a drug company product to include a "variation." FDA would be given expansive authority to determine the definition of variation, and would have the power to determine that compounded BHRT medications are copies of one-size-fits-all and synthetic hormones manufactured by drug companies. **This could turn compounded BHRT into an illegal copy of a manufactured drug product.**

While there is an exception that allows a provider to continue to write prescriptions for the now illegal BHRT, under S.959 he or she would have to determine that BHRT produces a "clinical difference" in a patient's treatment outcome as opposed to using the drug company product, before the prescription is even written or compounded. **While a doctor presumably would be able to make this determination, the bill would allow the FDA to determine compliance and impose criteria for how doctors must show that the drug does produce a clinical difference.**

How does the bill address "office use"?

The manager's amendment for Title I specifically allows traditional compounders to dispense compounded products to health care providers for use in their office. The traditional compounder must receive a practitioner order with an identified practitioner that indicates the drug may be compounded. There is a volume limit, similar to many state laws, such that only 10 percent of the total drugs dispensed by the pharmacy in any 30 day period may be drugs compounded for office use. The traditional compounder must receive the names of the patients that received the drug in the office within 14 days of dispensing; however, there is safe harbor for a traditional compounder that makes a reasonable effort to obtain the names and doesn't fill multiple orders for a practitioner who has previously failed to provide names. States will continue to enforce their own office use policies, which can be more restrictive.

PCCA RESPONSE

While the bill allows for compounds for office use, it is under unprecedented restrictions that would not only increase the cost of such medications used in a practitioner's office but also

would force some, if not all pharmacies to discontinue the practice. The FAQ does not mention that an artificial beyond use date of fourteen days (or less) must be applied to all compounds for office use, regardless of scientific studies or USP recommendations that could provide for much longer beyond use dates (up to 180 days).

PCCA also strongly disagrees with any volume limits in regards to office use compounding. **Volume limits reduce access and add regulatory complexity while doing nothing to increase quality of the compounded preparation or increase patient safety.**

The "safe harbor" provision that is mentioned, which may sound good on paper, could actually decrease patient safety in regards to compounded preparations. If a practitioner fails even once to provide patient names to the pharmacy for an office use compound, the pharmacy must no longer provide office use compounds to that practitioner to take advantage of the safe harbor provision. Because of what could be a simple clerical error, the practitioner would be forced then to "shop around" to find a pharmacy willing to sell to their office.

Will the legislation prohibit "traditional compounders" near state lines from shipping products interstate because of arbitrary boundaries?

Traditional compounders may ship sterile or non-sterile products interstate if they receive a prescription prior to compounding. Traditional compounders may ship non-sterile products across state lines without a prescription subject to the office use restrictions. In both bases, traditional compounders are required to follow all applicable state laws, which may be more restrictive.

PCCA REPONSE

This part of S.959 will negatively impact hundreds of thousands of patients and practitioners across the country. The important part of the paragraph above is "if they receive a prescription prior to compounding." **Waiting for a prescription to arrive at the pharmacy before commencing the compounding of a sterile product is simply unfeasible.** Proper testing of sterile compounded products, per USP regulations, requires up to eighteen days to complete. Because of this time frame, it would be impossible to provide a sterile compounded preparation to a patient living across a state line in a timely manner without the pharmacy subjecting itself to the regulations of a compounding manufacturer. Many patients and communities will be forced to find a pharmacy within their state (one that could be hundreds of miles away) rather than using a pharmacy that could be literally a couple of blocks away and has a history of successfully meeting patient and physician needs.

What is exempt from the legislation?

Medical gases, blood and blood products for transfusion, and human cells, tissues, or other cellular or tissue-based products are explicitly exempted from S.959.