July 24, 2013

Frequently Asked Questions

S. 959 -- Pharmaceutical Quality, Security and Accountability Act

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.

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.

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 affirms 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.

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 501(a)(2)(B)), adequate directions for use (section 502(f)(1)), drug tracing requirements (section 582, added by Title II), 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.

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.

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.

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.

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.

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.

How can the definition of "compounding manufacturer" refer to "prescriptions" when pharmacies dispense pursuant to prescriptions, unlike manufacturers that 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. Section 503A(b)(1)(C) of the bill clarifies that compounding manufacturers do not receive prescriptions.

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.

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.

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. This legislation does not give a traditional compounder, a compounding manufacturer, or a manufacturer the authority to make a product from a bulk substance 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).

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.

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 drugs cannot be safely made outside of a traditional manufacturing environment. These include drugs 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.

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 drugs 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. Products may only be added to the list if they are reasonably likely to lead to an adverse effect on safety or effectiveness taking into account risks and benefits to patients.

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 that 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. The Committee has 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.

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.

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.

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.