

Examining Drug Compounding

**Testimony before the House Energy & Commerce Committee
Subcommittee on Health
Thursday May 23, 2013**

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Key Points:

1. There exists a practice of pharmacy. It was never intended that all compounding would create a new drug and be subject to Food and Drug Administration regulation but for the enforcement discretion of the FDA or for the willingness of Congress to provide explicit exemption to certain pharmacists and certain activities.
2. FDA has authority to target compounders that cross the line between the practice of pharmacy and engage in drug manufacturing under the guise of a pharmacy license. While legal precedents cited by other witnesses have created some ambiguity, what the FDA largely lacks is ease of administering its authority. FDA is generally not able to force firms to submit advance information to FDA (before the firm is suspected of any wrongdoing) so that the agency is able to more efficiently identify firms engaged in wrongdoing and target its oversight. In some cases, FDA doesn't know about these firms until a problem arises. In other instances, FDA is forced to make an affirmative case that a compounding pharmacy is violating the law before the agency is able to compel an inspection or take other measures.
3. FDA generally lacks tools and/or resources to regulate a new class of firms that the agency has dubbed "non traditional compounders". I would argue that the firms in question here are not compounders, and calling them such confuses different issues. These are firms that repackage sterile FDA approved products into new dosage forms to improve their administration and enable the drugs to be tailored to therapy - for example, breaking chemotherapy into pediatric volumes, mixing hyperalimentation, preparing IV fluids, and breaking hospital-volume anesthetics like propofol for use in appropriately supervised outpatient settings. These firms fall into a gray area right now where they are treated as compounders but are not engaging in traditional forms of compounding. Rather they are engaging in the bulk repacking and manufacturing sterile preparations of FDA approved drugs, in advance of (and often not in response to) prescriptions for individual patients. To the degree that these large-scale operations prepare sterile volumes of drugs in a bulk form and ship these units widely, they present some novel risks.

4. As we address issues of supply, we also must address the policy decisions that have increased demand for compounded products from large scale “non traditional” compounders. At times, FDA has exercised its authority unevenly, which has given more incentive to compounders to skirt the law. Also FDA’s actions against generic firms have driven the market for many drugs to compounders. In law and regulation, we need to take a risk-based approach that encourages sourcing of drugs from the most competent parts of the market, not its least competent elements.

5. This is going to be especially important if we create a new class of compounders that FDA has dubbed “non traditional compounding”. If FDA doesn’t exercise its authority evenly, which means not allowing firms to compound identical versions of FDA approved products, then FDA will give incentive for drug makers to re-mask themselves as “non traditional compounders” to skirt the new drug requirements.

6. Part of the reason why FDA’s oversight has been, at times, inconsistent is that the agency often had a product orientation -- not a facility-based orientation – to its enforcement activity. That needs to change. FDA often targeted products they believed were being inappropriately marketed for inappropriate uses, rather than firms that were not operating under sound conditions. Enforcement was often reactive as a result. The agency’s enforcement needs to take on both considerations.

7. Finally, the market for compounded drugs is evolving quickly. It’s consolidating, and other entities (distributors, generic manufacturers) could well start buying out the large compounders. To these ends, what we do today may be irrelevant to the market we see in the near future. It may pay to wait and see how things shake out, and also to see how FDA’s recent enforcement activity impacts these markets.

The views expressed in this testimony are those of the author alone and do not necessarily represent those of the American Enterprise Institute.

Introduction

Mr. Chairman Pitts, Mr. Ranking Member Pallone, and members of the House Energy and Commerce Committee, Subcommittee on Health:

Thank you for the opportunity to testify today before this Committee.

The tragic deaths of 55 Americans and sickening of more than 740¹, resulting from contaminated steroid injections (methylprednisolone acetate) that were shipped by a disreputable “compounding pharmacy” located in Massachusetts, have rightly focused public attention and the work of this Committee on a largely unfamiliar, but prominent part of our drug supply chain – the practice of pharmacy compounding.

¹ CDC Statistics: <http://www.cdc.gov/hai/outbreaks/meningitis.html>

Before this House Committee, as well as the Senate, are proposals to tighten federal regulatory oversight of these compounding pharmacies, and of the practice of pharmacy more generally. Observers are calling on Congress to give the Food and Drug Administration (FDA) expanded oversight of these establishments.

New laws merit consideration. We should articulate clear and bright lines between the legitimate practice of pharmacy compounding, and those firms operating illegally as large-scale drug manufacturers under the guise of a pharmacy license.

I don't believe that it should be left to FDA's discretion to establish these boundaries as the agency goes about its work, or allow a fuzzy standard to persist. I believe that this would only add to uncertainty in the marketplace and create an undue burden on FDA to interpret vague authority. Ultimately it would result in uneven enforcement that would risk repeating some of the past mistakes.

Nor do I believe any pharmacy practice where drugs are compounded necessarily creates a new drug. There is such a thing as the practice of pharmacy that was, in my view, a sphere of medical practice that was never intended to be subject to FDA oversight. There are pharmacies that clearly practice within the scope of their profession, and are subject to state and professional regulation. And there are pharmacy compounders that are clearly crossing the line between the practices of pharmacy and taking on all the characteristics of a drug manufacturers and, as such, already fall squarely within FDA's existing oversight and authority.

But it seems illogical, inconsistent with prior statute, and administratively burdensome to declare that all pharmacy compounding – even done locally, for individual patients, and in response to valid prescriptions – creates a new drug and could be subject to FDA oversight but for Congress' willingness to exempt certain activity from new drug requirements, or FDA's exercise of enforcement discretion.

Instead, we should establish a clear boundary and objective tests for when pharmacies are engaging in legitimate compounding – and are subject to state regulation; and when establishments have crossed the line and are operating as drug manufacturers under the facade of a pharmacy license. When these lines are crossed, FDA has clear authority to assert – at the least – its Good Manufacturing (GMPc) standards to ensure the safety and effectiveness of products. This basic principle exists today, and should be part of any further clarification of existing law.

The merit in considering these issues is made urgent by the tragedy in Massachusetts and the apparent malfeasance at the New England Compounding Center (NECC). But it's also made necessary by the changing face of this industry.

These changes in the way compounding pharmacies operate, along with policy decisions (some made by FDA) that have increased demand for these compounded products, have strained FDA's existing resources and its policies in this area.

These challenges may call for a greater role for both state and federal regulators. But we need to be mindful of the reasons why the practice of pharmacy has traditionally been left to state regulation. When proper oversight demands that regulators examine the relationship between a provider and a patient (as proper oversight of the practice of pharmacy entails) then these endeavors are best left to state and professional authorities who have more proximity to the actual provision of care. Not every regulatory endeavor benefits from federal involvement.

In addition, we also need to be mindful of the policy decisions that drive more widespread – and sometimes inappropriate – use of compounded products. Finally, we need to be aware of the authority that FDA currently has that – with proper attention and perhaps additional resources – could provide better protections.

We need to take measure of these things before we enact new laws.

The recent problems didn't arise from traditional compounding, which is a legitimate part of the practice of pharmacy and an important part of medical care.

The traditional practice of pharmacy compounding is generally regarded as the combining or altering of ingredients by a licensed pharmacist, in response to a licensed practitioner's prescription for an individual patient. This activity produces a medication tailored to a patient's special medical needs. Compounding pharmacies mix or alter drug ingredients to adapt a medicine based on a doctor's prescription—for example by changing a pill into a formula, changing dosage forms, tailoring chemotherapy, or adding cherry flavoring to a child's medicine.

The practice of pharmacy compounding lets physicians customize drugs to individual patients. Traditional pharmacy compounding typically is performed on a small scale and is always performed in response to a valid patient prescription.

The FDA normally doesn't get involved with such practices because it isn't tasked with regulating the legitimate practice of pharmacy. Like the practice of medicine, pharmacy is largely left to professional and state oversight. But once pharmacies begin manufacturing and shipping medicines on a wide scale, and do so in a way that isn't in response to a valid prescription, these firms often become "drug manufacturers" and fall squarely under the FDA's extensive authority.²

In recent years, we have seen much more widespread use of compounded pharmacy products. Along with this increased use, we have seen the simultaneous expansion in the scope of the industry, and the advent of very large compounding pharmacies that commercialize and distribute drugs on a wide scale, without a doctors' prompting, and outside the boundaries of an individual patient encounter.

² A compounding fracture at the FDA. Scott Gottlieb and Sheldon Bradshaw. The Wall Street Journal, November 14, 2012. A24.

These mega establishments stretch the traditional definition of what it means to be a compounding pharmacy. It's the intersection between the activities of these non-traditional establishments and existing state and federal regulation, that I believe bears closer scrutiny. With my testimony today I want to do three things:

First, I want to outline some policy decisions that I believe have increased demand and weakened oversight of compounding under FDA's existing authorities.

I believe these policy decisions merit scrutiny, and perhaps re-examination. The compounding industry has evolved significantly in recent years, in many cases magnifying old risks and creating new ones. Some of this evolution owes to changes in the market for these products. But in other cases, it stems from changes in regulation that have shifted the market away from traditional manufactures, and at times, emboldened compounders to expand production into gray areas.

All of these factors bear close scrutiny. Any solution to mitigate existing risks must address not only the supply of higher-risk products, but also the factors that create the demand for these products to be produced by lower-standard manufactures.

Moreover, if Congress does seek to give FDA clearer authority to regulate these so-called non-traditional compounders, who I believe already fall outside the traditional practice of pharmacy and are subject to FDA oversight today, there is an important consideration. This new authority has to go hand-in-hand with vigorous enforcement by FDA of rules that prohibit compounders from making copies of FDA-approved drugs. Otherwise, creating this third category of "compounding manufacturers" where the full brunt of FDA's requirements don't apply will create incentive for drug manufacturers to re-cast themselves as non-traditional compounders so that they can float into this new, regulatory-light category.

In recent years, FDA has been reluctant to stop compounders from copying FDA-approved drugs out of economic concerns that it would limit consumers to higher priced products. These economic concerns have to be addressed separately.

If the NDA process imposes costs that end up raising the price of finished goods, that has to be separately addressed, perhaps through thoughtful review of how the NDA process could be made more efficient when it comes to certain lower risk, better understood sterile products. But so long as FDA is going to create a new category of compounding manufactures, it needs to prevent traditional FDA approved products from moving into this new category and undermining the safety of products now being produced by reputable manufacturers to high standards. We also need to make sure that the intellectual property surrounding those NDA products is not deliberately undermined by a new category of FDA-sanctioned manufacturers.

Second, I want to outline where FDA has existing authority to regulate non-traditional pharmacy compounding, and try and give this committee a sense for

how, in my view, that authority has been exercised by FDA and why the agency has made certain choices in how it interpreted those rules. Much is made of FDA's concern that legal challenges to the existing statute and policies have left FDA's current authority muddled. While these complaints have merit, I believe that there are other considerations that also shape the strength of FDA's authority.

For example, FDA often targets specific products rather than troubled facilities. The FDA has also, at times, not enforced rules evenly out of concern that knocking certain violating products and firms out of the market might impose higher costs on consumers. All of these considerations and policy choices have merit. But they create a regulatory scheme that is at times reactive and can appear arbitrary.

Third and finally, I want to propose some ideas for how I believe that a clearer standard in policy and law could provide for more effective oversight in this area and create a clearer boundary between the legitimate practice of pharmacy compounding and those firms that are distorting that traditional custom.

FDA has noted that legal challenges to its existing policies have served to muddle its authority. We also need to consider the way that FDA's own actions have contributed to this haziness. The FDA's influence on stoking some of the challenges it now faces is instructive because as I will explain, it speaks to the need for FDA and Congress, to establish a clear line between the activities that fall within the FDA's scope and those that are traditional pharmacy left to state authority.

The Evolution of Large Scale Compounding

As FDA Commissioner Dr. Peggy Hamburg stated in recent testimony, the practice of pharmacy compounding has undergone an evolution in recent decades. We have seen the advent of very large scale compounding firms that operate with many of the characteristics of traditional drug manufacturers. In recent months, FDA has referred to this practice as "non traditional compounding."³

Part of this growth in compounding has been driven by greater sourcing of these products by hospitals. As Dr. Hamburg stated in recent testimony, to save costs, hospitals have outsourced compounding that they used to do in house.⁴

³ Pharmacy Compounding: Implications of the 2012 Meningitis Outbreak, Statement of Margaret A. Hamburg, M.D., Commissioner of Food and Drugs, Food and Drug Administration, Department of Health and Human Services, Before the Committee on Health, Education, Labor and Pensions United States Senate. November 15, 2012

⁴ Statement of Margaret A. Hamburg, MD Commissioner of Food and Drugs, Food and Drug Administration, Before the Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, U.S. House of Representatives. "A Continuing Investigation Into the Fungal Meningitis Outbreak and whether it Could have Been Prevented." April 16, 2013.

Let me elaborate on this point. While I agree with the FDA's general analysis, I would cast the different pieces of this broader industry into different slices.

What have evolved are essentially three types of outfits when it comes to the area generally referred to as compounding.

First is traditionally compounding, where a pharmacy works in consultation with a physician to tailor a product based on a valid prescription.

This practice of pharmacy falls within professional and state purview and has not been the source of recent concerns.

Next, there are firms that masquerade as pharmacies, but engage in large scale manufacturing, often of unique products or drugs designed to compete with FDA approved medicines. These firms develop these drugs in bulk, without valid prescriptions or in anticipation of prescriptions, and do not adhere to good, sterile manufacturing techniques. These firms seem to be violating current federal law. Many are manufacturing new and unapproved drugs. In so doing, they are already subject to FDA's current and extensive oversight.

There is a third category of manufacturers that FDA has dubbed "non traditional compounding" but which I would offer is not compounding in its traditionally form, but another new and vital manufacturing service that has evolved over time.

Firms in this third category typically produce sterile products in bulk, usually to supply large medical practices and hospitals. In its most common form, these outfits will break down large volumes of FDA approved products into smaller units, for example taking large units of an anesthetic and breaking it into syringes to be more easily administered, taking a large unit chemotherapeutic and breaking it into smaller units to be dosed for a pediatric indication, or producing hyperalimentation for supplemental nutrition delivered by parental or enteral means.

These outfits are really sterile repackaging and re-mixing firms – not compounders in the traditional, local sense. Hospitals used to do this sort compounding of work in house, in their own pharmacies. When it was a hospital-based pharmacist working on a small scale under a sterile hood, there was manageable risk and a lower likelihood of wide contamination. But to save costs and improve quality and efficiency (in part, as a response to the tightening of the hospital industry's regulations) the hospitals have outsourced this work to these new, large firms.

The firms now performing this role are doing it on a wide scale, and are not compounders in the traditional sense. FDA confuses the issues by referring to these firms as "non traditional compounders". I would call these firms sterile preparation manufacturers or sterile prep manufacturers. These firms are a new, and important category of drug suppliers. They are now a vital part of the drug supply chain for hospitals and large outpatient practices. And their work creates certain risks.

If generic drug firms were engaging in this activity, FDA would require separate drug applications for each dosage form. FDA would require the generic firms to do stability studies, container closure studies, and pay separate user fees, among other things. This is one of the reasons why the generic drug makers do not supply drugs in the full range of dosage forms and packaging – and why the hospitals have to turn to these “sterile prep manufacturers” (or non-traditional compounders).

This begs the question: Should these sterile prep manufacturers be subject to the same oversight as a generic drug firm engaging in the same activity?

It’s a relevant question, but I think the answer is no. Because these hospital preps and repackaged drugs have a shorter dating period, it might be reasonable to subject them to a lighter regulatory touch.

The firms doing this sort of “non traditional compounding” (to borrow FDA’s poorly suited lexicon) generally do a good job. But they have been the source of some problems, including some fatal contaminations in recent years. A review of FDA’s recent oversight work has found that these products are not uniformly produced under sterile techniques, and in some cases have some significant contaminations. To the degree these “sterile” products are being used in hospitalized patients, who often have a lot of co-morbid illness, this can create public health risks.

It is reasonable to consider whether these outfits should be subject to GMP requirements to make sure they adhere to sterile techniques.

I would offer that these firms should be the focus of the present discussion.

Traditionally compounding should continue to be the domain of state and professional oversight. And the compounders like NECC engaged in manufacturing new drugs already fall under FDA’s current scrutiny. As for the sterile prep manufacturers (or “non traditional compounders”) since the sterile preps and repackaged goods are often produced and shipped on a wide scale, an inadvertent contamination in one lot could have widely distributed risks before a product could be recalled by an overlapping patchwork of state and federal authority.

Policy Choices and the Rising Demand for Compounded Products

To exam why the industry has grown and evolved in recent years, also requires a closer examination of the policy measures that I believe have contributed to these circumstances. Some of these recent policy decisions have driven demand away from traditional manufacturers like generic drug firms, and to compounders.

In at least some cases, providers are turning to a small number of unreliable compounders because they cannot source these products elsewhere.

To begin, a recent tightening in FDA's oversight of generic drug firms that made nearly identical versions of the same sterile injectable drugs produced by many compounders (including NECC) has prompted providers to source more products from large scale compounders. This tightening was rooted in some legitimate concerns that FDA had about the reliability of the generic manufacturing facilities. But it has created a contradictory set of policies that at has had the effect of shifting purchases from more reliable sources to firms with more questionable practices.

A key question is this: Even assuming that the FDA's concerns around the generic drug makers were all proven correct, would the continued production of drugs from these facilities – under close FDA supervision – been preferable to the alternative outcome -- closing these generic facilities and driving some providers to source products that were in shortage from compounders. By driving the generic firms to close their facilities while they underwent remediation, it left the market to be supplied by the only outfits still capable of operating – the compounders. This fueled further growth of these compounded products. But one must also ask whether the overall risk to the public was increased as a result of the fact that so much of the utilization had shifted to these more lightly regulated outfits.

This question is important is because it gets to the heart of the kinds of considerations that a risk-based approach to regulating these products should take up, and to how we make sure clinical needs are met with the most reliable products available. This same challenge has played out in other contexts where the decisions that FDA took may have served to increase demand for compounded drugs.

For example, Congress intended for FDA's enforcement over compounding to take into consideration when drugs were being manufactured by compounders that competed directly with FDA approved medicines, and therefore didn't offer any unique tailoring or differentiation that was a key clinical characteristic of the practice of pharmacy and the traditional role of compounding.

To these ends, the FDA has historically asserted its authority when compounding pharmacies were supplying their own versions of drugs that were also available commercially -- as FDA-approved branded and generic products. In these circumstances, the FDA held that these compounding firms were guilty of distributing unapproved new drugs. Among other things the New England Compounding Center, the outfit behind the tainted steroid shots, was cited for this sort of activity in that 2006 warning letter that FDA sent to the troubled firm.

However, a policy change made in recent years curtailed some of the exercise of this authority. This policy change gave greater economic incentive and political license to compounders to engage in more widespread production of drugs that exist as FDA approved products and compete directly with FDA regulated medicines.

In particular, FDA changed a longstanding guidance document that stipulated that the agency would clear the market of compounded drugs once a drug went through the new drug approval process and earned FDA approval for the same indication.

The guidance was changed to read that FDA would use its discretion in such cases, and only take action to remove the compounded products in cases where it had specific public health concerns. While I understand the agency's economic concerns around the potential for drug costs to rise when compounders are forced to exit the market, these considerations should not factor into the consistency by which the agency applies its policy. There are other avenues to address these economic concerns. FDA could also give greater consideration to the cost of the NDA process and ways to make that more efficient, especially in the case of old, well-understood drugs seeking FDA approval to sell approved versions of compounded drugs.

But the policy of removing the older, unapproved drugs remains controversial, and expectations that FDA would enforce it were largely squashed after FDA said it would not step in when the company KV Pharma, sought and received FDA's nod for Makena, an approved form of a type of progesterone that's widely compounded.

The FDA decided not to take action out of a well-publicized concern about the high cost of Makena relative to the compounded formulations. This political decision undermines the incentive for other companies to run registration trials to get FDA approval for drugs that are widely compounded. It emboldened compounders. The company that got FDA approval for Makena, KV Pharma, went into bankruptcy.

What kind of incentive does that give to other firms to invest in the development of FDA-approved versions of drugs that are being widely compounded?

The intervention in the KV Pharma case sends a message to would-be violators that the pricing of products could factor into how the FDA can enforce its own safety rules. The New England Compounding Center was also among the compounding firms distributing an unapproved version of the KV Pharma product. Does this committee believe that it's a good outcome that the active ingredient in Makena is now being widely used in woman who are pregnant, and made by firms like NECC?

Or would an FDA approved version of that medicine be preferable?

It's hard to have it both ways when it comes to these matters. That's why it was important that FDA lay out clear lines and enforces them vigorously and consistently to reduce the incentive of firms to skirt the law by operating as new drug manufacturers under the guise of a pharmacy license.

This is especially true if Congress creates a third category of "non traditional compounders". If FDA doesn't vigorously and consistently enforce a clear boundary between drugs that must be compounded because of the way they are made, and those that have gone through the NDA process and exist in the market as FDA

approved new drugs, then the agency will create a clear and improper incentive for some drug manufacturers to re-cast themselves as “non traditional compounders” to skirt the new drug requirements of the Act. Congress should be aware that there are significant, competing tradeoffs as a result of this approach. For example, there’s the potential for new policies to drive compounders out of certain popular markets.

The Exercise of FDA’s Existing Authorities

Even while we consider new legislation, we should first look for avenues to help FDA make better use of its existing authority to regulate non-traditional pharmacy compounding. As FDA has shown with its recent, robust actions, the agency has some clear authority in this space and the ability to exert considerable oversight.

Indeed, by FDA’s account, it targeted 29 firms for inspections based on their sterile processing practices and took stern actions against some of those firms. In most cases FDA was able to exercise its oversight without interference. In a few instances FDA needed to seek a court’s backing to get access to the records. While this may have imposed some brief delays, the agency seems to have fulfilled its mission.

Much is made of FDA’s concern that legal challenges to the existing statute and to the agency’s policies have left FDA’s current authority muddled.

While these complaints have some merit, I believe there are other considerations that also shape the exercise of FDA’s authority. Considering these can provide a fuller understanding of the challenges that FDA faces, and potential policy solutions.

In particular, I believe that the FDA has historically taken a product approach to its enforcement of its compounding oversight, rather than a facility based approach. What I mean by this, more specifically, is that the enforcement actions were often taken in response to individual products that the FDA was concerned with – either because the products carried inappropriate claims, or were being used for circumstances where FDA didn’t believe that the benefits justified the risks.

For example, in 2006 FDA sent a series of warning letters to compounders who were formulating topical lidocaine for use as a pre-treatment in electrolysis, to help numb peoples’ legs before they had the sometimes-painful procedure.

FDA was rightly concerned that using large amounts of topical lidocaine in this way could cause systemic side effects, and was an inappropriate use of the drug.

I use this example to illustrate a simple point: That the enforcement activity often targeted the products rather than the facilities. This often made the agency’s enforcement a reactive process, rather than a pro-active assessment of risk. While products being used in inappropriate ways create risks, and deserve regulatory scrutiny, the FDA can probably get as much, if not more bang for its public health dollar by bringing equal or even greater focus on the facilities that are

inappropriately compounding products in ways that are unsterile and cross the line between traditional compounding and the wholesale manufacture of new drugs.

It's a difference of where the enforcement mindset emanates from – whether it flows from the drug reviewers in charge of reviewing products, or facility inspectors in charge of overseeing the quality of facilities, or some combination of each.

In the past, a lot of the enforcement activity emanated from the drug review divisions and the drug center's office of compliance. This led to an orientation that sometimes targeted products, rather than facilities. FDA would bring enforcement actions in cases where FDA found drugs that were being compounded for uses that the agency believed created risk, or misled consumers.

I believe an equal focus should be placed on targeting unsafe, unsanitary facilities whose business practices violate existing law. This requires a greater role for the FDA field in doing actual inspectional work that focuses on unsafe facilities as much as it requires a focus by drug review staff on the products themselves, and the indications they are used for.

Establishing Bright Regulatory Lines

Above all else, the inspectional activities must be targeted in a way that creates a clear delineation between the protected practice of pharmacy, and those firms that are creating new, unapproved drugs, or the sterile prep manufacturers I spoke of.

FDA has outlined a number of key factors that establish the boundary between traditional and “non traditional” compounding pharmacy. So it has historically articulated where a boundary could rest. These principles should guide policy.

It's these factors that have been the basis of FDA's recent vigorous and successful oversight efforts in this area. The agency's recent enforcement work demonstrates that the agency is able to enforce its supervision when firms fall outside of these boundaries. Moreover, some of these factors have already formed the basis of Congressional statute in section 503(A). These factors should form one basis of FDA's enforcement going forward and any re-articulation of that policy.

It's noteworthy that size, as well as shipping across state lines, alone, are not reliable criteria. There are good reasons why some products may be produced on a large scale even in response to physician prescriptions. For example, it may not be possible to develop a single dose from a bulk ingredient.

So a pharmacy producing a drug for a single physician in response to a single prescription may be forced to produce extra volumes of the same finished product.

There are equally good reasons why some pharmacies might ship products interstate. It could be as simple as a pharmacy that resides close to a state border. Proper criteria involve more than just one or several factors, but a multi-part test.

FDA has expressed some of the factors that would be part of a multi-part test in its prior guidance documents that addressed its enforcement. They include:

1. Compounding of drugs in anticipation of receiving prescriptions, except in very limited quantities that are done in close relation to the amounts of drugs that will need to be compounded after receiving valid prescriptions.
2. Compounding drugs that were already withdrawn by FDA or removed from the market for safety reasons.
3. Compounding finished drugs from bulk active ingredients that are not components of FDA approved drugs without an FDA sanctioned investigational new drug application (IND) in accordance with 21 U.S.C. § 355(i) and 21 CFR 312.
4. Receiving, storing, or using drug substances (for use in compounding) without first obtaining written assurance from the supplier that each lot of the drug substance has been made in an FDA-registered facility.
5. Receiving, storing, or using drug components not guaranteed or otherwise determined to meet official compendia requirements.
6. Using commercial scale manufacturing or testing equipment for compounding drug products.
7. Compounding drugs for third parties who resell to individual patients or offering compounded drug products at wholesale to other state licensed persons or commercial entities for resale.
8. Except in certain narrow circumstances, compounding drug products that are commercially available in the marketplace or that are essentially copies of commercially available FDA-approved drug products.
9. Failing to operate in conformance with applicable state law regulating the practice of pharmacy.

Conclusion

FDA has rightly noted that non-traditional compounding should, because of the higher risk presented, be subject to a greater degree of oversight. The large scale compounding we've seen in the marketplace, where firms manufacture large volumes of sterile products, and do so in advance of (and sometimes without) a proper physician prescription, and then ship these finished products across the country, should be subject to a higher level of manufacturing controls.

“Compounders” operating in this manner are not operating as pharmacies. Let's make no mistake. They are making new sterile dosage forms on a mass scale.

Other “compounding pharmacies” operating with these same characteristics, and making unapproved new drugs (like NECC) already fall outside the traditional practice of pharmacy and make themselves subject to FDA’s oversight.

FDA’s main complaint, in my opinion, isn’t that these entities aren’t subject to the agency’s regulation under the existing law. The FDA’s main complaint, when you boil it down, is that the existing legal framework puts too much burden on FDA (in the agency’s opinion) to have to make the affirmative case that these firms are operating in a way that places them under the agency’s jurisdiction. That’s a valid complaint, but it’s a different concern than the one commonly reported.

At its core, the issues we are talking about here aren’t issues of whether or not FDA has proper authority. They do. The issues are whether or not FDA has the legal and regulatory tools to make its role in these regulatory endeavors administratively easier, more consistent and anticipatory, and less resource intensive.

FDA’s traditional regulatory posture is to compel the submission of information to the agency that allows FDA to target its regulatory oversight. In the case of compounding pharmacies, FDA – at the margins – needs to often make the affirmative case that certain firms are not acting as pharmacies but as drug manufacturers and are therefore subject to the agency’s oversight.

What FDA wants, in my view, is the means to compel the submission of certain information that would enable FDA to more easily demonstrate when compounders are no longer acting as compounders. But we should be candid about this key fact. Legislation could be narrowly tailored to address the real problems here. I believe that some of the proposals address issues that are peripheral to the key challenge.

In closing, I wish to make one final point. The market for compounding is changing very rapidly, not only as a result of the tragedy in Massachusetts, but the stepped up oversight that FDA has exerted in recent months, as well as the activity on Capitol Hill. It’s also driven by issues in the marketplace itself, where certain lower margin businesses are looking to get into higher margin work in drug manufacturing.

To these ends, we’re seeing compounders consolidate, and get acquired by more reputable manufacturers. It’s my belief that this industry will undergo an evolution in the next few years, where many of the large-scale compounders will either consolidate or close because they can’t meet the current scrutiny, and reputable manufacturers and maybe drug distributors will acquire many others.

We may also benefit from seeing the culmination of FDA’s recent enforcement activity, and get a better sense of the contours of FDA’s existing influence.

As this process unfolds, it will leave behind a much different compounding industry. This should serve as a cautionary note to all of us. The rules that we might write today may no longer be applicable to the market that we see tomorrow.

The market forces that are transforming this industry may accomplish many of the public health goals that we seek to address through legislation.

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