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Division of Compliance Policy
Office of Enforcement
Food and Drug Administration
12420 Parklawn Dr., Room 4025
Rockville, MD 20857

Comments of Members of the Patient, Consumer, and Public Health Coalition
on the Food and Drug Administration's Draft Guidance
"Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act"
[Docket No. FDA-2013-D-1444]

As members of the Patient, Consumer, and Public Health Coalition, we conditionally support the draft guidance "Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act" (FD&C) because it clarifies FDA enforcement actions that can be taken against individuals or firms that illegally make drugs under the banner of traditional compounding.

The guidance makes clear that while Section 503A exempts traditional compounding pharmacies from the FD&C Act's regulations on current good manufacturing practices, labeling of drugs, and new drug applications, the pharmacies are not exempt from other provisions of the FD&C Act. The guidance lists specific (but not all-inclusive) examples such as "the drug's strength must not differ from and its quality or purity must not fall below, that which it purports to have." As for enforcement, FDA can issue individual traditional compounding firms warning letters, or seize their products, or criminally prosecute them, if they violate other requirements of the FD&C Act.

However the draft guidance needs to clearly define three terms: "limited quantities," "inordinate amounts," and "valid certificate of analysis," and FDA should clarify registration requirements for pharmacies.

Limited quantities & inordinate amounts

The draft guidance states a drug can be compounded by "a licensed pharmacist or licensed physician in limited quantities before the receipt of a valid prescription" but it never defines "limited quantities." The draft guidance also states that a pharmacist or physician should "not compound regularly or in inordinate amounts any drug products that are essentially copies of commercially available drug product." The terms "limited quantities" and "inordinate amounts" are key to distinguishing between individually tailored compounded drugs that meet unique clinical needs of a patient (traditional compounding), and mass-produced manufactured drugs. FDA needs to modify the draft guidance to explicitly define "limited quantities," and when compounding copies of commercially available drugs is considered to be occurring in "inordinate amounts." Lack of precise definitions may open the door to abuse of Section 503A as has happened in the past with the New England Compounding Center (NECC). Nearly 14,000 patients in 23 states received tainted injectable steroid drugs manufactured by NECC, which led to 751 infections and 64 deaths.[1] Such a large outbreak is less likely to happen in the future if the law specifically defines these two terms.

Valid certificate of analysis

Under the "Conditions of Section 503A" of the draft guidance, it states that drugs compounded using bulk drug substances must be accompanied by "valid certificates of analysis." [2] But there is no regulatory definition that describes what should be included in the certificate of analysis. The certificates should certainly contain the name and contact information of the original manufacturer of the bulk product and any middlemen who handled the substance, a description of any repackaging, the identity of the quality assurance officer of the manufacturer, and the dates and results of sterility, potency and other tests that demonstrate compliance with United States Pharmacopeia standards. FDA should publish guidance indicating what needs to be included in "valid certificate of analysis."

Clarification of Registration Requirements

The FDA needs to clarify whether Section 503A compounders are required to register under Section 510 of the FD&C Act. Section 510 requires entities engaged in the "manufacture, preparation, propagation, compounding, or process"[3] of drugs to annually register with the FDA. Confusion over registration could increase after the implementation of Section 503B, which requests outsourcing facilities to register with the FDA.

Section 503A traditional compounders could register under Section 510 and then promote themselves as "FDA-registered," giving their customers a false sense of security about the quality of their drugs. Customers may think that these traditional compounders are complying with current Good Manufacturing Practices, or are making FDA-approved products, neither of which is true. To prevent this, FDA should thoroughly inspect all entities that register under Section 510.

Drug Quality and Security Act

We opposed the Drug Quality and Security Act of 2013 (DQSA) because it created Section 503B, which allows nontraditional compounders (called outsourcing facilities) to mass produce drugs without the same stringent requirements that the FDA rightfully demands of drug manufacturers (such as clinical trials and labeling standards).

Despite major flaws in the DQSA, FDA could save lives if the agency develops and finalizes guidance to industry and consumers explaining how it intends to distinguish between traditional compounding (503A) and outsourcing compounding (503B). If FDA fails to provide clear guidance, it will encourage companies to manufacturer and sell drugs illegally under the guise of traditional compounding. This would lead to more NECC-like disasters, which is clearly unacceptable.

FDA enforcement of section 503A will also affect the success of section 503B. If traditional compounders are allowed to continue to produce large volumes of drugs because 'limited quantities" and "inordinate amounts" are poorly defined or not defined at all, then compounders will be discouraged from participating in the voluntary registration under 503B. An industry trade publication, PharmTechTalk, reported last month that only a handful (14) of outsourcing compounding companies have voluntarily registered with the FDA.

Conclusion

We would support this draft guidance only if the FDA clearly defines the terms "limited quantities," "inordinate amounts," and "valid certificate of analysis," and if FDA clarifies registration requirements.

We remain concerned about the relationship between the States and the FDA, because enforcement efforts could fall through the cracks. The draft guidance states the "FDA expects State boards of pharmacy to continue their oversight and regulation of the practice of pharmacy, including traditional pharmacy compounding" and FDA will continue to cooperate with State authorities to address violations of the FD&C Act, "including section 503A." As part of that cooperation, the FDA should send copies of the final guidance document to all State boards of pharmacy and suggest that the board of pharmacies pass the guidance along (or make it accessible on their Web sites) to the traditional compounders in their states. This is will help to ensure that all parties understand the FDA's rules regarding "traditional compounders."

Community Catalyst
National Consumers League
National Physicians Alliance
National Research Center for Women & Families
National Women's Health Network
U.S. PIRG

For more information, contact Paul Brown at (202) 223-4000 or pb@center4research.org

[1] Centers for Disease Control and Prevention. Multistate Outbreak of Fungal Meningitis and Other Infections – Case Count. October 23, 2013. http://www.cdc.gov/hai/outbreaks/meningitis-map-large.html#casecount_table. Accessed January 31, 2014.

[2] 21 U.S.C. § 353a(b)(1)(A)(iii). Accessed February 3, 2014. http://www.gpo.gov/fdsys/pkg/USCODE-2010-title21/html/USCODE-2010-title21-chap9-subchapV-partA-sec353a.htm.

[3] 21 U.S.C. § 360(b). Accessed February 3, 2014. http://www.gpo.gov/fdsys/pkg/USCODE-2010-title21/html/USCODE-2010-title21-chap9-subchapV-partA-sec360.htm.