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Department of Health and Human Services
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Janet Woodcock, M.D.
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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
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Re: Compounded Drug Products That Are Essentially Copies of Approved Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act: Draft Guidance for Industry (Docket No. FDA–2016–D–1267)

Dear Drs. Califf and Woodcock:

Public Citizen, a consumer advocacy organization with more than 400,000 members and supporters nationwide, submits these comments regarding the Food and Drug Administration's (FDA's) draft guidance document on compounded drug products that are essentially copies of approved drug products under section 503B of the Federal Food, Drug, and Cosmetic Act (FDCA).

The draft guidance document explains the FDA's policies regarding the requirement under section 503B(a)(5) that drug products made by outsourcing facilities not be essentially copies of one or more approved drugs.

In general, we support the policies expressed in the draft guidance document. In particular, the proposed guidance appropriately seeks to tightly limit, under section 503B, pharmacy

compounding of drug products that are essentially copies of approved drug products. Stringent limits on such pharmacy compounding under section 503B are critically important to protecting public health for the following reasons, highlighted by the FDA in its draft guidance:

- [Compounded drugs] pose a higher risk to patients than FDA-approved drugs. Drug products compounded by outsourcing facilities in accordance with the conditions of section 503B are exempt from FDA drug approval requirements and the requirement to be labeled with adequate directions for use. Because they are not FDA-approved, they have not undergone FDA premarket review for safety, effectiveness, and quality. Although outsourcing facilities must comply with CGMP [current good manufacturing practice] requirements and are inspected by FDA according to a risk-based schedule, their drugs also lack a premarket inspection and finding of manufacturing quality that is part of the drug approval process. Because they are subject to a lower regulatory standard, drugs compounded by outsourcing facilities should only be distributed to health care facilities or dispensed to patients to fulfill the needs of patients whose medical needs cannot be met by an FDA-approved drug.[1]

- The restrictions on compounding drugs that are essentially copies of approved products ensure that outsourcing facilities do not compound drug products under the exemptions in section 503B for use in patients who could use an approved product. Compounding copies of these products would unnecessarily expose patients to drug products that have not been shown to be safe and effective.[2]

- In addition to these immediate public health risks, section 503B's prohibition on producing a drug product that is essentially a copy of an approved drug product protects the integrity and effectiveness of the new drug and abbreviated new drug approval processes. Sponsors would be less likely to invest in and seek approval of innovative, life-saving medications if an outsourcing facility could, after a drug is approved, compound "substitutes" that may be less expensive because they have not gone through the drug approval process.[3]

Public Citizen strongly agrees with all these reasons.

Public Citizen offers the following comments regarding specific provisions of the proposed guidance document:

A. Defining "essentially a copy of an approved drug"

Section 503B(d)(2) defines "essentially a copy of an approved drug" as meaning:

[1] Food and Drug Administration. Compounded drug products that are essentially copies of approved drug products under Section 503B of the Federal Food, Drug, and Cosmetic Act: Draft guidance for industry. July 2016. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM510153.pdf. Accessed October 5, 2016.
[2] *Ibid.*
[3] *Ibid.*

> (a) a drug that is identical or nearly identical to an approved drug, or a marketed drug not subject to section 353(b) of this title and not subject to approval in an application submitted under section 355 of this title, unless, in the case of an approved drug, the drug appears on the drug shortage list in effect under section 356e of this title at the time of compounding, distribution, and dispensing; or
>
> (b) a drug, a component of which is a bulk drug substance that is a component of an approved drug or a marketed drug that is not subject to section 353(b) of this title and not subject to approval in an application submitted under section 355 of this title, unless there is a change that produces for an individual patient a clinical difference, as determined by the prescribing practitioner, between the compounded drug and the comparable approved drug.

1. Defining "identical or nearly identical"

The draft guidance document states that the FDA intends to consider a compounded drug product to be identical or nearly identical to an approved drug if the compounded drug product and the FDA-approved drug have the same active ingredients, route of administration, dosage form, dosage strength, and excipients. Public Citizen agrees with this proposed policy for defining "identical or nearly identical."

2. Compounded drugs that are identical or nearly identical to an approved drug on FDA's drug shortage list after the shortage is resolved

Under section 503B(d)(2)(A), a compounded drug is not essentially a copy of an approved drug if the approved drug appears on the FDA's drug shortage list at the time of compounding, distribution, and dispensing. The FDA proposes to allow outsourcing facilities to fill orders for compounded drugs that are identical or nearly identical to an approved drug that was on the FDA's drug shortage list at the time that the outsourcing facility received the order, provided the drug also had appeared on the FDA drug shortage list within 60 days of the outsourcing facility distributing or dispensing the drug.

Public Citizen strongly opposes this provision of the guidance. As the FDA noted in the draft guidance document, compounded drugs pose a higher risk to patients than FDA-approved drugs. Allowing outsourcing facilities to dispense compounded drugs that are identical or nearly identical to an approved drug for up to 60 days after the approved drug has been removed from the FDA drug shortage list would unnecessarily expose patients to drug products that have not been shown to be safe and effective. Such a policy would place the business interests of outsourcing facilities above the interests of patients and public health. We urge the agency to eliminate this provision from the guidance and instead take enforcement action against pharmacies that continue to distribute or dispense compounded drugs that are essentially copies of approved drugs after those drugs have been removed from the drug shortage list.

3. Compounded drugs that contain a bulk drug substance that is a component of an approved drug

We support the policy positions outlined in the draft guidance document for implementing the following provision under section 503B(d)(2)(B):

> A compounded drug product is essentially a copy of an approved drug if a component of the compounded drug product is a bulk drug substance that is also a component of an approved drug, unless there is a change that produces for an individual patient a clinical difference, as determined by the prescribing practitioner, between the compounded drug and the comparable approved drug.

We particularly endorse the FDA's proposals to (a) consider this provision as applying to a compounded drug whether it was compounded from bulk drug substances or from drugs in finished form; and (b) require documentation of a prescriber's determination that there is a change that produces for an individual patient a clinical difference between the compounded drug and the comparable approved drug.

We also strongly agree that a lower price is not sufficient to establish that a compounded drug product made by an outsourcing facility is not essentially a copy of an approved drug product.

4. Essentially a copy of one or more approved drug products

Public Citizen supports the proposed policy for applying section 503B(d)(2)(B) to a compounded drug product that has bulk drug substances that are components of more than one approved drug.

B. Recordkeeping

We agree with the FDA's proposed policy that outsourcing facilities compounding drug products under section 503B should maintain records to demonstrate compliance with section 503B(a)(5) and that such records should include:

(a) for a drug compounded under section 503B(d)(2)(B) where a component of the compounded drug is a bulk drug substance that is a component of an approved drug, the prescription or order records of a prescriber's determination that there is a change that produces for an individual patient a clinical difference between the compounded drug and the comparable approved drug; and

(b) for compounding of an approved drug product that appears on the FDA's drug shortage list, documentation regarding the status of the drug on the FDA's drug shortage list at the time of compounding, distribution, and dispensing.

In closing, the guidance document, when finalized after appropriate revisions are made, should place, under section 503B, appropriately stringent limits on pharmacy compounding of drug products that are essentially copies of approved drug products. Public Citizen encourages the FDA to promptly issue final guidance on this topic.

Thank you for the opportunity to comment on these important public health matters.

Sincerely,

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