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Division of Dockets Management (HFA-304)
U.S. Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

CITIZEN PETITION

Crowell & Moring, LLP ("Crowell & Moring") respectfully submits this citizen petition pursuant to 21 C.F.R. § 10.30 to request that the Commissioner of Food and Drugs take the action set forth below in Section A with respect to a definition of the term "distribution"[1] that includes patient-specific dispensing for purposes of Section 503A(b)(3)(B) of the Federal Food, Drug, and Cosmetic Act ("FDCA").

A. Actions Requested

Through this petition, and for the reasons explained in more detail below, Crowell & Moring respectfully requests that the U.S. Food and Drug Administration ("FDA" or "the Agency") refrain from finalizing the memorandum of understanding ("MOU") under section 503A(b)(3)(B)(i) or taking any regulatory action[2] against compounders based on section 503A(b)(3)(B)(ii) that relies on a definition of "distribution" that includes "dispensing" unless and until FDA:

1) Promulgates a final regulation with such a definition consistent with the Administrative Procedure Act ("APA"), the Regulatory Flexibility Act ("RFA"), the Unfunded Mandates Reform Act ("UMRA"), the Congressional Review Act

[1] For purposes of this citizen petition, the term "distribution" refers not only to the term "distribution" as used in section 503A(b)(3)(B)(i), but also to the terms "distributes" and "distributed" as used throughout section 503A(b)(3)(B).

[2] For purposes of this citizen petition, "regulatory action" includes issuance of inspectional observations in a Form FDA 483, advisory actions (e.g., warning letters), and enforcement actions (e.g., injunctions).

("CRA"), the Paperwork Reduction Act ("PRA"), and Executive Orders ("EOs") 12866 and 13132; and

2) Issues a final guidance describing the conditions under which the Agency does not intend to take action against compounders, including specialty pharmacies, in states that have not signed the MOU, for distributing more than 5 percent of their compounded drug products interstate ("Five Percent Limit").

B. Statement of Grounds

I. Executive Summary

FDA cannot lawfully finalize the MOU with a definition of "distribution" that includes patient-specific dispensing without first promulgating that definition in a final rule consistent with the APA, CRA, RFA, UMRA, PRA, and EOs 12866 and 13132. Nor can FDA lawfully take regulatory action against compounders located in states that have not signed the MOU based on a definition of "distribution" that includes dispensing without such a rule in place. Yet, FDA appears to be on the verge of doing both after nearly 20 years of controversy surrounding this interpretation, employing procedures that fall far short of what is required for substantive significant rules and failing to institute measures to lessen the adverse impact on patient access to compounded drugs.

Substantive rulemaking under the APA is required for FDA's proposed definition of distribution for several reasons. First, the definition modifies federal and state legal norms that distribution and dispensing are distinct acts. The FDCA, the Controlled Substances Act, the National Association of Boards of Pharmacy ("NABP") Model State Pharmacy Act, and state laws define distribution to exclude dispensing and distinguish between the terms. Second, FDA's proposed definition imposes new, substantial, binding laws, rights, and duties on the states, industry, and itself. For example, it would require states that enter into the MOU to collect and review information about nearly all of the drugs that pharmacies in their state compound and dispense interstate to individual patients in the course of their traditional pharmacy practice. It also would require compounders located in states that do not enter into the MOU to observe the Five Percent Limit or be subject to civil and criminal penalties for dispensing drugs as they ordinarily would in traditional pharmacy practice. Third, section 503A requires rulemaking to implement its provisions on interstate distribution. Section 503A(c)(1) states that "[t]he Secretary **shall** issue regulations to implement this section."[3] Accordingly, FDA's proposed definition must undergo notice-and-comment rulemaking under the APA.

[3] FDCA § 503A(c)(1) (emphasis added).

Instead of promulgating a substantive rule, FDA proposed its definition of distribution in multiple drafts of the MOU and notices of availability ("NOAs") and described its intent to enforce the Five Percent Limit based on the definition in those NOAs. The public was consequently deprived of adequate notice and a meaningful opportunity to comment on the controversial definition of distribution and its potentially deleterious impact on states, compounders, healthcare providers, and patients nationwide. In addition to failing to comply with the notice-and-comment rulemaking procedures under the APA, the draft MOUs and NOAs did not include the analyses required for substantive rules under the RFA, UMRA, CRA, PRA, and EOs 12866 and 13132. There was no review of the impact of the definition on small businesses, no analysis of whether the definition produces an unfunded mandate, no assessment of whether legislative action is needed, no records burden estimate for the Five Percent Limit, no regulatory impact analysis with a cost-and-benefit assessment, and no federalism impact statement. These omissions are fatal to a proposed definition that could drastically limit interstate distribution of medically necessary compounded drugs. FDA must abandon its plan to finalize the MOU and set aside its enforcement intentions based on this definition unless and until the Agency promulgates a final rule in accordance with applicable federal statutes and EOs.

In addition, FDA must address the detrimental impact on access to compounded drugs that would ensue from a definition of distribution that includes dispensing. Should states decline to sign the MOU, pharmacies that currently specialize in compounding drugs regionally or nationally, or that are located near a state border, will no longer be able to meet the needs of their patients. For example, home infusion pharmacies prepare compounded therapies pursuant to patient-specific prescriptions that are highly tailored to the needs of individual patients. These specialty pharmacies provide compounded therapies along with home infusion services to patients and healthcare practitioners nationwide. If the boards of pharmacy in the states where home infusion pharmacies reside do not sign the MOU, compounded drugs supplied by these pharmacies would be subject to the Five Percent Limit. FDA should therefore collaborate with stakeholders to develop an enforcement discretion policy that appropriately balances the public health protections afforded by the interstate distribution conditions in section 503A and the need to preserve patient access to compounded drugs.

II. Legal and Regulatory Background

A. Compounding Under the FDCA

1. Section 503A of the FDCA

Section 503A, added to the FDCA by the Food and Drug Administration Modernization Act of 1997, describes the conditions that must be satisfied for drug products compounded by a licensed pharmacist or licensed physician to be exempt from certain provisions of the FDCA related to current good manufacturing practice ("CGMP"), labeling with adequate directions for use, and new drug approval. Section 503A contains conditions on interstate distribution, which

are the subject of this petition and are discussed more fully in section (B) below. Another applicable condition in section 503A is that compounding must be based on the receipt of a valid prescription for an individually identified patient.[4] FDA has interpreted this provision to mean that a 503A compounder cannot distribute a compounded drug product before receiving a patient-specific prescription, often referred to as "office stock."[5]

B. Conditions on Interstate Distribution in Section 503A

One of the conditions that must be satisfied for a drug product to qualify for the exemptions under section 503A is that the drug product is compounded by a licensed pharmacist or a licensed physician in a State

i. that has entered into a memorandum of understanding with the Secretary which addresses the **distribution** of inordinate amounts of compounded drug products interstate and provides for appropriate investigation by a State agency of complaints relating to compounded drug products **distributed** outside such State; or

ii. that has not entered into the memorandum of understanding described in clause (i) and the licensed pharmacist, licensed pharmacy, or licensed physician **distributes** (or causes to be **distributed**) compounded drug products out of the State in which they are compounded in quantities that do not exceed 5 percent of the total prescription orders **dispensed or distributed** by such pharmacy or physician.[6]

Put simply, a drug product may be eligible for the exemptions in section 503A if the compounder is either located (1) in a state that has signed the MOU, or (2) in a state that has not signed the MOU, but the compounder distributes compounded drug products interstate in quantities that do not exceed five percent of the total prescription orders dispensed or distributed by that compounder.

As indicated in bold above, the MOU described in section 503A(b)(3)(B)(i) and the Five Percent Limit described in section 503A(b)(3)(B)(ii) apply only to "distribution" of compounded

[4] FDCA § 503A(a).

[5] *See* FDA, *Guidance for Industry: Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act* (Dec. 2016), https://www.fda.gov/media/97347/download (interpreting § 503A to require a prescription prior to distribution).

[6] FDCA § 503A(b)(3)(B) (emphasis added).

drug products, and Congress distinguished between the terms "distribute" and dispense" in section 503A(b)(3)(B)(ii).

For two decades, FDA has been working to develop an MOU for the states' consideration.[7] FDA issued Federal Register notices to announce the availability of draft MOUs in 1999, 2015, and 2018. Within these draft MOUs and NOAs, FDA has consistently defined "distribution" to include patient-specific dispensing for purposes of both the MOU and the Five Percent Limit over the objections of commenters.

C. FDA's Controversial Interpretations of "Distribution"

In the 1999 draft, FDA proposed a draft standard MOU accompanied by an NOA that interpreted "distribution" to include patient-specific dispensing.[8] FDA received more than 6,000 comments in response to the 1999 draft MOU, including comments criticizing an interpretation of "distribution" that includes patient-specific dispensing.[9] FDA did not issue another draft standard MOU for 16 years.

In the 2015 draft MOU, FDA defined "distribution" as follows:

> Distribution means that a compounded human drug product has left the facility in which the drug was compounded. **Distribution includes** delivery or shipment to a physician's office, hospital, or other health care setting for administration and **dispensing** to an agent of a patient or to a patient for the patient's own use.[10]

In the NOA accompanying the MOU, FDA interpreted the language in section 503A(b)(3)(B)(ii) "total prescription orders **dispensed or distributed**" to encompass both compounded and non-

[7] FDCA § 503A(b)(3) ("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).").

[8] 64 Fed. Reg. 3,301 (Jan. 21, 1999).

[9] *See* 80 Fed. Reg. 8,874 at 8,875 (Feb. 19, 2015).

[10] FDA, *Draft Memorandum of Understanding Addressing Certain Distributors or Compounded Human Drugs Between the State of [insert State] and the U.S. Food and Drug Administration*, at 8 (2015) (emphasis added), available at: https://www.regulations.gov/document?D=FDA-2014-N-1459-0002.

compounded drugs.[11] To explain why Congress used the terms "dispense" and "distributed," FDA wrote that Congress sought to

> make clear that the Agency must not limit its calculation of total prescription orders to compounded drugs that the pharmacy or prescriber makes, but also include any other prescription orders, such as conventionally manufactured drugs, for which the pharmacist or prescriber serves solely as the dispenser.[12]

FDA received over 3,000 comments in response to the 2015 draft MOU, including comments criticizing the inclusion of "dispensing" within the definition of "distribution" and FDA's explanation for the reference to "dispensed or distributed."[13]

FDA took a different approach in the NOA accompanying the 2018 draft MOU. First, in response to comments on the MOU, FDA limited the phrase "total prescription orders **dispensed or distributed**" to compounded drugs.[14] Then, to give meaning to the use of the terms "dispensed or distributed," FDA's 2018 NOA described distribution as including dispensing, except that distribution would exclude in-person dispensing at a pharmacy.[15] FDA only slightly amended the definition of distribution, which appears on the Appendix to the revised draft MOU.[16] Instead, the substance of the definition and how FDA intends to use it for enforcement appears in the NOA:

> FDA proposes that in-person dispensing, where the transaction between the compounder and the patient is completed without the compounded drug leaving the facility in which it was compounded,

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[11] 80 Fed. Reg. at 8,878.

[12] *Id.*

[13] *See* Docket No. FDA-2014-N-1459.

[14] *See generally* 83 Fed. Reg. 45,631 (Sept. 10, 2018).

[15] *Id.* at 45,635-36.

[16] FDA made the following change, here highlighted in bold font: "*Distribution* means that a compounder **has sent** a drug product out of the facility in which the drug was compounded. Such distribution may include, but is not limited to, delivery or shipment to a physician's office, hospital, or other health care setting for administration, and dispensing the drug product by sending it to a patient for the patient's own use." FDA, *Draft Memorandum of Understanding Addressing Certain Distributions of Compounded Drug Products Between the State [insert State] and the U.S. Food and Drug Administration*, at 9 (Sept. 2018) (emphasis added), available at: https://www.fda.gov/media/91085/download.

> is appropriately overseen, primarily, by the State outside the context of the MOU, regardless of whether the compounded drug product subsequently leaves the State. Such an intrastate, local transaction generally indicates a close connection among the patient, compounder, and prescriber. By contrast, transactions by mail often have a less direct nexus among the patient, compounder, and prescriber than in-person pickups and would be considered "distributions."[17]

Only four months after the comment period on the 2018 draft MOU closed, FDA announced its intent to finalize the MOU and NOA in 2019.[18]

D. FDA Enforcement of Section 503A's Limitations on Interstate Distribution

In the 2015 and 2018 NOAs accompanying the draft MOUs, FDA announced that the proposed definitions of "distribution" would apply to the Five Percent Limit.[19] FDA further announced its intent to use the definition of "distribution" in the calculation and subsequent enforcement of the Five Percent Limit against compounders in states that have not signed the MOU after a proposed 180-day period following issuance of a final MOU.[20]

For several reasons, 180 days is far too short a time period. Multiple organizations have reported that no states are presently able to enter into the MOU. Several states do not have the necessary resources to fulfill obligations under the MOU, and others may need new authorities and new collaborations with other state bodies. Even in states that are interested in signing the MOU, 180 days is simply not enough time to enable them to do so.

E. Comments on FDA's Definition of Distribution Supplying Alternative Interpretations

The vast majority of the comments that FDA received in 2015 and 2018 on the definition of distribution strongly criticized the Agency's proposed inclusion of "dispensing" within the

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[17] 83 Fed. Reg. at 45,635-36.

[18] *See id.* at 45631; FDA, *Statement from FDA Commissioner Scott Gottlieb, M.D. and Deputy Commissioner Anna Abram on New 2019 Efforts to Improve the Quality of Compounded Drugs* (Apr. 3, 2019), available at: https://www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-and-deputy-commissioner-anna-abram-new-2019-efforts.

[19] 80 Fed. Reg. 8,874, 8,878 (Feb. 19, 2015); 83 Fed. Reg. at 45,636.

[20] 83 Fed. Reg. at 45,632, 45,637.

definition of distribution. Commenters asserted that FDA erred in defining distribution to include dispensing because federal and state laws expressly define distribution to exclude dispensing. Commenters proposed that FDA define "distribution" to exclude dispensing, consistent with federal and state laws. Under this alternative definition, the MOU and Five Percent Limit would apply exclusively to interstate shipments of compounded drug products before receipt of prescriptions for individually identified patients, or "office stock."[21] FDA has repeatedly responded to these comments in the NOAs by asserting that section 503A does not provide for office stock and that the definition of "distribution" must include patient-specific dispensing.

III. FDA Must Engage in Notice-and-Comment Rulemaking To Define Distribution to Include Patient-Specific Dispensing.

If FDA insists on defining "distribution" to include dispensing, it must do so through substantive rulemaking under the APA for two reasons. First, in contrast to an interpretive rule, which "only reminds affected parties of existing duties,"[22] the definition of "distribution" invokes the Agency's statutory authority to modify a legal norm.[23] Second, in contrast to a general statement of policy, which advises the public prospectively on the exercise of a discretionary power,"[24] the definition of "distribution" creates new law, rights, and duties with a substantial, binding impact on the Agency, states, and compounders.[25] In addition, section 503A requires substantive rulemaking to implement section 503A(b)(3)(B).

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[21] *See e.g.*, Reed Smith, Comments to Draft MOU, Dkt. No. FDA-2018-N-3065 (Dec. 10, 2018); National Community Pharmacists Association, Comments to Draft MOU, Dkt. No. FDA-2018-N-3065 (Dec. 10, 2018); New Hampshire Board of Pharmacy, Comments to Draft MOU, Dkt. No. FDA-2018-N-3065 (Nov. 14, 2018); Professional Compounding Centers of America, Comments to Draft MOU, Dkt. No. FDA-2018-N-3065 (Dec. 10, 2018); Arizona State Board of Pharmacy, Comments to Draft MOU, Dkt. No. FDA-2018-N-3065 (posted Dec. 14, 2018).

[22] Congressional Research Service ("CRS"), *A Brief Overview of Rulemaking and Judicial Review* 7, (Mar. 27, 2017), https://crsreports.congress.gov/product/pdf/R/R41546 (citation and quotation marks omitted).

[23] *Syncor Int'l Corp. v. Shalala*, 127 F.3d 90, 95 (D.C. Cir. 1997).

[24] CRS, *A Brief Overview of Rulemaking and Judicial Review* 7-8 (Mar. 27, 2017), https://crsreports.congress.gov/product/pdf/R/R41546.

[25] *United States ex rel. Shakopee Mdewakanton Sioux Cmty. v. Pan American Mgmt. Co.*, 616 F. Supp. 1200, 1212 (D. Minn. 1985); *see also Gen. Motors Corp. v. Ruckelshaus*, 742 F.2d 1561, 1565 (D.C. Cir. 1984). Of note, the agency's own label, while relevant, is not dispositive. *Gen. Motors Corp.*, 742 F.2d at 1565; *see also Neighborhood TV Co. v. FCC*, 742 F.2d 629, (Continued…)

A. FDA's Proposed Definition Modifies the Federal and State Legal Norm that Distribution and Dispensing are Distinct Acts.

FDA's proposed definition does not merely remind regulated entities of existing requirements; instead it *modifies* federal and state legal norms. Federal law has established a legal norm that distribution and dispensing are distinct activities by (1) separating the two terms with an "or" to signify a disjunctive list, (2) separating the terms as discrete elements of a list, and (3) affirmatively defining distribution to exclude dispensing.

First, the very text of section 503A(b)(3)(B) is clear that distribution and dispensing are separate activities. In the phrase "dispensed or distributed," the word "or" to separate "distributed" from "dispensed" indicates that the terms have distinct, non-overlapping meanings.[26] Second, section 503B, which was added to the FDCA by Title I of the Drug Quality and Security Act ("DQSA"), lists dispensing and distribution as separate items. In two subsections, section 503B applies certain conditions to drugs that appear on FDA's drug shortage list "at the time of compounding, **distribution, and dispensing**."[27] Dispensing and distribution must have distinct meanings if the drug needs to appear on the shortage list when each of these activities takes place.[28]

Third, the FDCA and the United States Code more broadly affirmatively define distribution to exclude dispensing. In Title II of the DQSA, Congress defined "distribute" to exclude "dispensing of a product pursuant to a prescription."[29] Congress similarly defined "distribute" in the Controlled Substances Act, also part of Title 21 of the U.S. Code, to "mean[ ] to deliver (other than by administering or dispensing) a controlled substance or a listed chemical."[30] Applying fundamental principles of statutory construction, the term "distribution" in section 503A is presumed to have a consistent meaning throughout the FDCA and Title 21.[31]

637–38 (D.C. Cir. 1984) (quoting *Pickus v. United States Bd. of Parole*, 507 F.2d 1107 (D.C. Cir. 1974) (parole board guidelines were substantive because they "were the kind calculated to have a substantial effect on the ultimate parole decisions")).

[26] FDCA § 503A(b)(3)(B).

[27] *See* FDCA §§ 503B(a)(2) & 503B(d)(2)(A) (emphasis added).

[28] *See id.*

[29] FDCA § 581(5).

[30] 21 U.S.C. § 802.

[31] When construing a statute, "[a] word or phrase is presumed to bear the same meaning throughout." Antonin Scalia and Bryan A. Garner, *Reading Law: The Interpretation of Legal Texts* 170 (Thomson/West 1st. ed. 2012).

Also establishing this legal norm are the state laws that consistently and nearly universally define distribution to exclude dispensing. For example, the NABP Model State Pharmacy Act, which many states have incorporated into their own statutes or regulations, states that "'[d]istribute" or "[d]istribution" "means to sell, offer to sell, deliver, offer to deliver, broker, give away, or transfer a Drug, whether by passage of title, physical movement, or both" and that "[t]he term does not include … To Dispense or Administer."[32] Similarly, more than half of the states' define "distribution," and the vast majority of those definitions explicitly exclude dispensing."[33] To adopt a definition of "distribution" that substantively deviates from its legal meaning within the very industry that the change affects, FDA must promulgate a substantive rule.

B. Through Its Proposed Definition, the Agency Creates New Law, Rights, and Duties on Itself, Industry, and the States, with Substantial and Binding Impact on Each.

1. FDA's proposed definition would create new and substantial law, rights, and duties for itself, the states, and compounders.

By drastically expanding the reach of the MOU and the Five Percent Limit from office stock to nearly all compounded drugs, FDA's proposed definition of "distribution" would create new and substantial law, rights, and duties for the Agency, the states, and compounders who seek to operate under section 503A.

As discussed in Section IV.A., the legal norm is for distribution to exclude dispensing and the MOU and Five Percent Limit to apply exclusively to office stock. The majority of states do not allow office stock, and those states that do permit office stock limit its amount, typically

[32] National Association of Boards of Pharmacy Model State Pharmacy Act, Art. 1, sec. 105 (s2) (Aug. 2019).

[33] Ariz. Rev. Stat. § 32-1901(29); Ark. Code § 17-92-1003(3); Cal. Health & Safety Code § 10-11012 (referring to controlled substances); Colo. Rev. Stat. § 12-280-103(15); Conn. Gen. Stat. § 21a-240(15) (referring to controlled substances); Del. Code § 24-25-2502(37) (defining "wholesale distribution"); Ga. Code Ann. § 26-4-5(11); Idaho Code § 54-1705(8); Ind. Code § 25-26-14-4.7; Kan. Stat. § 65-1626(q); La. Stat. § 37:1164(13); Me. Stat. § 32-117-13702-A-10; Mich. Comp. Laws § 333.17703(5); Miss. Code Ann. § 73-21-73(i); Neb. Rev. Stat. § 28-401(9); Nev. Rev. Stat. § 639.0155 (defining "wholesale distribution"); N.D. Cent. Code Ann. § 43-15-01.9; R.I. Gen. Laws § 5-19.1-2(j); S.C. Code § 40-43-30(26); S.D. Codified Laws § 36-11-2(9); Tenn. Code Ann. § 63-10-204(15); Tex. Occ. Code § 551.003(17); Utah Code § 58-17b-102(25); Va. Code § 54.1-3401 (referring to controlled substances); W. Va. Code R. § 15-1-2-2.1.15; Wis. Stat. § 450.01; Wyo. Code R. 059.0001.2 §4(q).

to five percent or less.[34] If FDA were to adhere to the legal norm that distribution excludes dispensing, then few compounders would have to adjust their interstate distribution practices to comply with the Five Percent Limit. Without a substantial adverse impact on resident businesses, few states likely would enter into the MOU. Even for those states that do enter into an MOU, their reporting obligations would be minimal because few compounders would reach the threshold percentage of interstate distribution triggering those obligations, and they would only need to adequately investigate complaints about office stock. FDA's responsibilities would be extremely limited due to the low number of states that would enter into the MOU and the limited impact of the Five Percent Limit.

Also as discussed in Section IV.A., the new legal norm proposed by FDA is for distribution to include dispensing and the MOU and Five Percent Limit to apply to dispensed drugs. All compounders dispense drugs, and states do not place limits on the amount of drugs that a compounder can dispense. If FDA were to adopt the new legal norm that distribution includes dispensing, then many compounders would have to adjust their interstate distribution practices to comply with the Five Percent Limit. With a substantial adverse impact on resident businesses, more states likely would enter into the MOU. Such states would be subject to burdensome, resource-intensive data collection and reporting obligations regarding the numerous compounders who would reach the threshold percentage interstate distribution. In addition, states would be required to investigate and report to FDA complaints about nearly any drug a compounder dispenses interstate.

FDA's responsibilities would be greatly expanded due to the higher number of states that would enter into the MOU and the substantial impact of the Five Percent Limit. In addition to entering into MOUs and reviewing the MOU submissions, FDA stated in the 2018 NOA that the Agency intends to use the information in the MOU submissions to inform its risk-based inspection priorities,[35] which could mean an increase in surveillance inspections of those that the Agency deems high risk based on the submissions received under the MOUs. Similarly, to give effect to the Five Percent Limit, FDA likely would inspect pharmacies that are located in states that do not enter into the MOU and enforce against pharmacies that distribute more than five percent of their compounded drugs interstate.[36] To accomplish these new and substantial

[34] The Pew Charitable Trusts, *State Oversight of Drug Compounding* 2 (Feb. 2018), https://www.pewtrusts.org/-/media/assets/2018/02/drug_safety_assesment_web.pdf ("39 states and the District of Columbia prohibit traditional pharmacies from compounding for sterile officestock for human use—through their laws, regulations, or state guidance, or by advising compounders to follow the DQSA.").

[35] 83 Fed. Reg. at 45,635.

responsibilities, FDA would need to significantly increase its inspection and enforcement resources well beyond those it presently devotes to compounding.

2. The new law, rights, and duties imposed on FDA, compounders, and the states by the definition of distribution would have binding effect.

Not only would the Agency's proposed definition create new and substantive duties for FDA, industry, and the states, but the definition would have binding effect. Section 503A(b)(3)(B) requires each state to decide whether to enter into the MOU, a legally binding agreement, with FDA. Pursuant to that agreement, the definition of "distribution" contained in the MOU will be binding on both FDA and states that chose to enter into it. States that enter into the MOU also will likely impose legal obligations on compounders in their states to supply the information specified in the MOU. Because FDA intends to apply the definition of "distribution" in the MOU to the calculation of the Five Percent Limit, the definition of distribution would also be binding on compounders that are located in states that do not enter into the MOU.[37] Compounders would need to remain below five percent interstate distribution or risk civil and criminal enforcement under the FDCA. FDA's clear intention to treat the definition of distribution with force and effect of law shows that substantive rulemaking is required.[38]

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[36] FDA, *Guidance: Pharmacy Compounding of Human Drug Products Under Section 503A of the Federal Food, Drug, and Cosmetic Act* 7 (Rev. 2 June 2016), https://www.fda.gov/media/94393/download ("If FDA determines that an individual or firm compounds a drug product that does not meet the conditions of section 503A, then … the individual or firm that compounds the drug product may also be subject to a warning letter, seizure of product, injunction, and/or criminal prosecution for violations of sections 501(a)(2)(B), 502(f)(1), and 505 of the FD&C Act.").

[37] *Id.* at 6 ("The *Federal Register* notice that will announce the availability of the draft MOU will specify a time period during which the MOU will be made available to the states to sign. After this time period expires, FDA intends to begin enforcing the 5% limit in states that have not signed the MOU.").

[38] *See, e.g., Gen. Elec. Co. v. EPA*, 290 F.3d 377, 382 (D.C. Cir. 2002) (ruling that a guidance document issued by the Environmental Protection Agency ("EPA") that advised the public of how to engage in risk assessments in order to comply with EPA regulations imposed binding obligations upon applicants, had the force of law, and thus qualified as a legislative rule).

C. Congress Contemplated Rulemaking to Implement Section 503A's Provisions on Interstate Distribution.

Section 503A(c)(1), titled "In General," states that "The Secretary **shall** issue regulations to implement this section."[39] The phrase "this section" directly follows the provision concerning the MOU and the Five Percent Limit. A plain reading of this section shows that Congress intended FDA to, "in general," issue regulations to implement section 503A. This requirement applies to section 503A's provisions on interstate distribution.

Where Congress had particular thoughts on how those regulations should be developed, it drafted the statute to make that clear. For example, section 503A(c)(1) provides specific instructions regarding the regulations implementing subsections (b)(1)(A)(i)(III), (b)(1)(C), and (b)(3)(A): the Secretary shall convene and consult an advisory committee before issuing regulations pursuant to those subsections.[40] Similarly, section 503A(c)(2) provides additional specific instructions regarding the regulations implementing subsection (b)(1)(A)(i)(III): the Secretary shall consult with the United States Pharmacopoeia Convention and include criteria for bulk drug substances, including historical use, reports in peer-reviewed medical literature, or other criteria the Secretary may identify.[41]

The provisions of a statute should be interpreted in a way that renders them compatible, not contradictory. A compatible reading of sections 503A(c)(1) and (2) is just the one described above: that Congress intended FDA to promulgate regulations to implement this section, generally, and provided guidance to the Agency about the method of promulgation for certain particular subsections. This is consistent with the fundamental tenet of statutory construction "that effect must be given, if possible, to every word, clause, and sentence of a statute."[42] "Courts construe a statute . . . so that no part is inoperative or superfluous, [and] [c]ourts assume that every word, phrase, and clause in a legislative enactment is intended.[43] Applying that elementary rule of construction here means giving meaning to the opening sentence in section 503A(c)(1), which instructs the Secretary to "issue regulations to implement this section," including section 503A's interstate distribution provisions.

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[39] FDCA § 503A(c)(1) (emphasis added).

[40] *Id.*

[41] FDCA § 503A(c)(2).

[42] 2A Sutherland Statutory Construction § 46:6 (7th ed.).

[43] *Id.*

IV. FDA's Proposed Definition of Distribution Must Be Promulgated as a Substantive Rule that Comports with the APA, RFA, UMRA, CRA, PRA, and Executive Orders 12866 and 131332.

In section III of this Petition, we established that FDA's definition of distribution requires substantive rulemaking. Rather than proposing a substantive rule, the Agency set forth the definition in an MOU and further interpreted the term in a mere Federal Register notice announcing the availability of the MOU. The MOU and NOA failed to provide interested persons adequate notice and a meaningful opportunity to comment as required by the APA for substantive rules. They also failed to comport with the RFA, the UMRA, the CRA, the PRA, and Executive Orders 12866 and 131332, thereby depriving small businesses, the states, Congress, the Office of Management and Budget ("OMB"), and the public more generally of the opportunity to fully evaluate the damaging impact of the proposed definition and suggest less detrimental alternatives.

A. FDA's Definition of Distribution Requires Compliance with the APA's Notice-and-Comment Rulemaking Procedures.

The APA sets forth the practices that an agency must follow to promulgate regulations.[44] Of particular relevance here, an agency must provide notice that it intends to promulgate a rule, typically by publishing a notice of proposed rulemaking ("NPRM") in the Federal Register.[45] The notice must state, among other things, the nature of the rulemaking proceedings, and it must permit "interested persons an opportunity" to comment on the proposed rule.[46] Then the agency must review the public comments and respond to any "significant" comments received.[47] To comply with the APA, the notice must be adequate for the public to understand the substantive proposals that the Agency is considering and for the opportunity to comment to be meaningful.[48]

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[44] CRS, *An Overview of Federal Regulations and the Rulemaking Process* (Jan. 7, 2019), https://crsreports.congress.gov/product/pdf/IF/IF10003.

[45] 5 U.S.C. § 553.

[46] *Id.*

[47] CRS, *An Overview of Federal Regulations and the Rulemaking Process*, *supra* n.44.

[48] *See CSX Transp., Inc. v. Surface Transp. Bd.*, 584 F.3d 1076, 1082 (D.C. Cir. 2009) (concluding that the public lacked adequate notice under the APA where the court "s[aw] no way that commenters here could have anticipated which particular aspects of the [Surface Transportation] Board's proposal [were] open for consideration." (third alteration in original) (citation and internal quotation marks omitted)); *see also Sherley v. Sebelius*, 689 F.3d 776, 784 (D.C. Cir. 2012) ("[T]he opportunity to comment is meaningless unless the agency responds to significant points raised by the public." (citation and internal quotation marks omitted)); (Continued…)

The agency publishes the final rule in the Federal Register. The final rule explains the regulatory requirements and the impact of these requirements on industry or the public, and also responds to the comments on the proposed rule. The regulatory requirements also are published in the Code of Federal Regulations ("C.F.R."), which is a permanent codification of agency regulations.[49]

FDA's MOU and NOA proposing the definition of distribution failed to meet the APA's requirements for notice and an opportunity for public comment. First, the Agency provided no notice that the NOA discusses the Five Percent Limit. For example, in 2015, FDA issued a NOA titled "Memorandum of Understanding Addressing Certain Distributions of Compounded Human Drug Products Between the States and the Food and Drug Administration; New Proposed Draft; Availability."[50] In 2018, FDA issued another NOA titled "Memorandum of Understanding Addressing Certain Distributions of Compounded Human Drug Products Between the States and the Food and Drug Administration; Revised Draft; Availability."[51] The summary section of the 2018 NOA states that FDA

> is announcing the availability for public comment of a revised draft standard [MOU] entitled "Memorandum of Understanding Addressing Certain Distributions of Compounded Drug Products Between the State of [insert State] and the U.S. Food and Drug Administration" (revised draft standard MOU). The revised draft standard MOU describes the responsibilities of a State that chooses to sign the MOU in investigating and responding to complaints related to compounded drug products compounded in the State and

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Chamber of Commerce of the United States v. OSHA, 636 F.2d 464, 470 (D.C. Cir. 1980) ("Prior notice and opportunity to comment permit [impacted parties] to voice their objections before the agency takes final action. Congress enacted 5 U.S.C. [Section] 553 in part to afford adequate safeguards to private interests. Given the lack of supervision over agency decision-making that can result from judicial deference and congressional inattention, this protection, as a practical matter, may constitute an affected party's only defense mechanism. … Most important of all, highhanded agency rulemaking is more than just offensive to our basic notions of democratic government; a failure to seek at least the acquiescence of the governed eliminates a vital ingredient for effective administrative action." (internal citations and quotation marks omitted)).

[49] 44 U.S.C. § 1510; *see also* FDA, *FDA Rules and Regulations*, https://www.fda.gov/regulatory-information/fda-rules-and-regulations (last visited Jan. 8, 2020).

[50] 80 Fed. Reg. at 8,874.

[51] 88 Fed. Reg. 45,631 (Sept. 10, 2018).

> distributed outside the State and in addressing the interstate distribution of inordinate amounts of compounded drug products.[52]

Based on the titles and summary, the most logical conclusion is that the NOAs announce the availability of the draft MOUs, not that they address the Five Percent Limit. Yet, the draft MOU and NOAs confer legally binding obligations on entities that are not even subject to the MOU, without affording clear notice to them. The NOAs state how the Five Percent Limit will be calculated, apply the definition of distribution to compounders operating under that limit, and announce FDA's intent to enforce the Five Percent Limit after a proposed time period.

Second, interested stakeholders did not have adequate notice that FDA's proposed definition of distribution in the MOU could only be fully understood by reviewing the NOA. FDA published the draft MOUs on its website with the definitions of distribution in the Appendix and the NOAs interpreting distribution in the Federal Register. The MOU appeared as a stand-alone document that was not published in the Federal Register, and NOAs (including the notice published for the MOU) typically do no more than announce the availability of documents. The MOU and its accompanying NOA are not consistently presented together on the FDA website. As a result, interested stakeholders who access the MOU through FDA's website may review the draft MOU alone. Indeed, in view of the dozens of NOAs that FDA's human drug compounding program has issued since 2013 without substantive content, stakeholders are likely accustomed to NOAs that merely announce the availability of a policy documents. Stakeholders reviewing the MOU in isolation could not fully understand the definition of distribution being proposed. For example, only the 2018 NOA, and not the 2018 MOU, states that the 2018 proposed definition of distribution excludes in-person dispensing. If stakeholders reviewed the definition of "distribution" in the MOU Appendix without the benefit of FDA's substantive explanation in the NOA, they may not have understood the types of transfers included within this definition for purposes of reaching the Five Percent Limit.

Persons who did not have adequate notice of FDA's definition of distribution and its application to the MOU and Five Percent Limit have not had a meaningful opportunity to comment. With regard to the Five Percent Limit, FDA opened dockets to comment on the MOU, not the Federal Register notices. Some stakeholders submitted comments concerning the NOAs through the docket to the MOU, but as noted above, many entities potentially impacted by the Five Percent Limit may not have known to comment. Stakeholders cannot meaningfully comment on FDA's definition of "distribution" unless they understand its relevance to the Five Percent Calculation and how FDA intends to interpret and apply it. Such notice should be provided through issuance of an NPRM clearly setting forth in its title and summary the application of the definition of distribution to the MOU and Five Percent Limit and the proposed regulatory requirements for codification in the C.F.R.

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[52] *Id.*

B. FDA's Definition of Distribution Requires Compliance with the Regulatory Flexibility Act.

According to the Regulatory Flexibility Act, agencies must publish in the Federal Register, among other things, "a description of the reasons why action by the agency is being considered; … a description of and, where feasible, an estimate of the number of small entities to which the proposed rule will apply; … a description of the projected reporting, recordkeeping and other compliance requirements of the proposed rule, including an estimate of the classes of small entities which will be subject to the requirement."[53] The agency's analysis must also "contain a description of any significant alternatives to the proposed rule which accomplish the stated objectives of applicable statutes and which minimize any significant economic impact of the proposed rule on small entities."[54] Agencies must "transmit a copy of the initial regulatory flexibility analysis to the Chief Counsel for Advocacy of the Small Business Administration."[55] Those comments should inform the content of the final rule, as well as its implementation.

FDA is required to analyze regulatory options that would minimize any significant impact of a rule with the definition of distribution on small entities. FDA's proposed definition of distribution will affect thousands of small entities, including small pharmacies and local pharmacists and physicians, nationwide. Those entities and other interested stakeholders must have an opportunity to comment on how FDA's proposed definition will affect their small businesses and to suggest less burdensome alternatives or an implementation date that exceeds FDA's current proposal of 180 days.

C. FDA's Definition of Distribution Requires Compliance with the Unfunded Mandates Reform Act of 1995.

Unfunded Mandates Reform Act of 1995 requires agencies to prepare a written assessment of costs and benefits prior to proposing a rule that "includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of $100,000,000 or more (adjusted annually for inflation) in any 1 year."[56] Among other things, UMRA requires agencies to "develop a plan in which agencies provide notice of regulatory requirements to potentially affected small governments" and to "develop an effective process to permit elected officers of state, local, and tribal governments (or their

[53] 5 U.S.C. § 603(b).

[54] 5 U.S.C. § 603(c).

[55] 5 U.S.C. § 603(a).

[56] UMRA § 202(a), 2 U.S.C. § 1532.

designees) to provide input in the development of regulatory proposals containing significant intergovernmental mandates."[57]

FDA must perform the UMRA analysis prior to promulgating its proposed definition of distribution. As noted above, many have characterized the state obligations under the MOU as extremely burdensome and resource-intensive. For example, to supply the information that FDA is requesting, states will need to collect and review information from compounders in their states. They also may need to hire more pharmacy inspectors and devote substantially more time reviewing records during each inspection. Although FDA and NABP are developing a system to try to alleviate the burden on states, not all states may have the authority to require pharmacies to submit information into that system, particularly within the first 180 days of issuance of the final MOU. Obtaining the information required under the MOU could be very expensive, and FDA must consider that potential cost, and states' comments about that cost, when defining distribution.

D. FDA's Definition of Distribution Requires Compliance with the Congressional Review Act.

The CRA requires that "major" rules have a delayed effective date of at least 60 days after the rule is submitted to Congress or published in the Federal Register, and that the issuing agency must submit the rule to both houses of Congress and the Government Accountability Office before the rule can take effect.[58] The statute defines a "major" rule as one that the OMB Office of Information and Regulatory Affairs ("OIRA") administrator determines has resulted in or is likely to result in:

- An annual effect on the economy of $100 million or more;
- A major increase in costs or prices for consumers, individual industries, Federal, State, or local government agencies, or geographic regions; or

[57] CRS, *Federal Rulemaking: An Overview* 17 (June 17, 2013), https://fas.org/sgp/crs/misc/RL32240.pdf; *see also* UMRA §§ 203 & 204, 2 U.S.C. §§ 1533 & 1534.

[58] 5 U.S.C. §§ 801-808; CRS, *Counting Regulations: An Overview of Rulemaking, Types of Federal Regulations, and Pages in the* Federal Register 3 (Sept. 3, 2019), https://crsreports.congress.gov/product/pdf/R/R43056.

- Significant adverse effects on competition, employment, investment, productivity, innovation, or on the ability of United States-based enterprises to compete with foreign-based enterprises in domestic and export markets.[59]

FDA's definition of "distribution" would likely constitute a "major rule" because it affects state-licensed pharmacists, pharmacies, and physicians, as well as state governments, nationwide. It may have an annual effect on the economy of $100 million or more, but even if it does not, it likely will result in a major increase in costs or prices for consumers, industries, and government agencies and will certainly have significant adverse effect on productivity if compounders throughout the nation cannot distribute more than five percent of their compounded drugs interstate. Avoiding rulemaking would constitute an evasion of this important process for Congressional review and eliminate an opportunity for Congress to decide whether to take action, such as posing questions to agency heads, enacting new legislation, or imposing funding restrictions.

E. FDA's Definition of Distribution Requires Compliance with the Paperwork Reduction Act.

Under the PRA, agencies must justify any collection of information from the public by establishing the need and intended use of the information, estimating the burden that the collection will impose on respondents, and showing that the collection is the least burdensome way to gather the information.[60] Agencies must receive OIRA approval for each collection request before it is implemented; failure to obtain OIRA approval for an active collection represents a violation of the PRA, and no one can be penalized for failing to comply with a violative collection.[61] Agencies do not receive approval until the public has an opportunity to comment on the proposed collection of information.[62]

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[59] 5 U.S.C. § 804(2); CRS, Counting *Regulations: An Overview of Rulemaking, Types of Federal Regulations, and Pages in the* Federal Register, *supra* n.58, at 8.

[60] 44 U.S.C. §§ 3501-3520; Maeve P. Carey, CRS, *Cost-Benefit and Other Analysis Requirements in the Rulemaking Process* 15 (Dec. 9, 2014), https://crsreports.congress.gov/product/pdf/R/R41974. A "collection of information" is generally defined as the obtaining or disclosure of facts or opinions by or for an agency by ten or more nonfederal persons. 44 U.S.C. § 3502; Maeve P. Carey, CRS, *Cost-Benefit and Other Analysis Requirements in the Rulemaking Process*, *supra* n.60, at 14-15.

[61] 44 U.S.C. § 3512; Maeve P. Carey, CRS, *Cost-Benefit and Other Analysis Requirements in the Rulemaking Process*, *supra* n.60, at 15.

[62] 5 C.F.R. § 1320.8(d) ("Before an agency submits a collection of information to OMB for approval, … the agency shall provide 60-day notice in the Federal Register, and otherwise (Continued…)

FDA did not conduct a PRA analysis for the distribution of compounded drugs in the context of the five percent calculation. Compounders located in states that have not entered into the MOU will have to maintain records that will enable the compounders and FDA investigators to calculate whether the compounders have distributed more than five percent of their compounded drug products out of state. This type of recordkeeping is exactly the kind of public information collection that must be assessed under the PRA to ensure the collection request is implemented in the least burdensome manner possible.

F. FDA's Definition Requires a Regulatory Impact Analysis ("RIA") and Executive Branch Review under Executive Order 12866.

Under Executive Order 12866, agencies must submit "significant" rules to OIRA for review prior to publication.[63] A "significant" regulatory action is one likely to result in a rule that may:

1) Have an annual impact on the economy of $100 million or more,[64] or adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, or tribal governments or communities;

2) Create a serious inconsistency or otherwise interfere with an action taken or planned by another agency;

3) Materially alter the budgetary impact of entitlements, grants, user fees, or loan programs or the rights and obligations of recipients thereof, or;

4) Raise novel legal or policy issues arising out of legal mandates, the President's priorities, or the principles set forth in [Executive Order 12866].

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consult with members of the public and affected agencies concerning each proposed collection of information, to solicit comment.").

[63] Exec. Order No. 12866, 58 Fed. Reg. 51,735 (Oct. 4, 1993); *see also* CRS, *An Overview of Federal Regulations and the Rulemaking Process*, *supra* n.43.

[64] Executive Order 13563 requires agencies "to use the best available techniques to quantify anticipated present and future benefits and costs as accurately as possible." Exec. Order No. 13563, 76 Fed. Reg. 3,821 (Jan. 21, 2011).

Rules meeting the first condition are often referred to as "economically significant" or "major" regulatory actions.[65] Agencies must provide to both the public and OIRA "a careful and transparent analysis of the anticipated consequences of economically significant regulatory actions," including an assessment of the benefits and costs that the agency anticipates will result from the proposed action, as well as from alternative actions.

Two options that must be considered are not promulgating the regulation and designing the regulation in a manner that is more cost-effective. According to OIRA, "[a]gencies should select the alternative that maximizes net benefits, while also taking into consideration distributive impacts and qualitative benefits and costs, unless a statute requires another approach."[66] OIRA reviews RIAs to ensure that the "rulemaking is necessary to ensure that regulations are consistent with applicable law, the President's priorities, and the principles set forth in . . . Executive order [12866], and that decisions made by one agency do not conflict with the policies or actions taken or planned by another agency."[67]

With regard to FDA's proposed definition of distribution, it is important that stakeholders have the opportunity to comment on the potential significant economic impact. Businesses, including compounders engaged in traditional pharmacy practice and ingredient suppliers, must have the opportunity to comment on the impact of the definition on their ability to thrive and survive if they are no longer able to dispense interstate more than five percent of their total prescription orders in a patient-specific manner.

States need to have the opportunity to consider the impact on their local economy if compounders in their state cannot distribute more than five percent of their total prescription orders out of state. In some states, large compounding pharmacies that only engage in patient-specific distribution may represent a significant sector of the state economy. Further, some states are home to suppliers of ingredients used in compounding, and those suppliers' sales could be affected if compounding in their state is drastically reduced.

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[65] Maeve P. Carey, CRS, *Cost-Benefit and Other Analysis Requirements in the Rulemaking Process*, *supra* n.60, at 4. OMB has published a document entitled *Regulatory Impact Analysis: Frequently Asked Questions (FAQs)* (Feb. 7, 2011), which notes that a rule may be considered "economically significant" even if it does not cause $100 million in costs, benefits or transfers in any one year, if the rule could adversely affect a small sector of the economy and would threaten to create significant job loss.

[66] OIRA, OMB, *Regulatory Impact Analysis: A Primer* 2 (Aug. 15, 2011), https://reginfo.gov/public/jsp/Utilities/circular-a-4_regulatory-impact-analysis-a-primer.pdf.

[67] Exec. Order No. 12866, *supra* n.63, at 51737.

Further, healthcare providers and patients who have a medical need for compounded drugs also must have an adequate opportunity to comment on potential access and cost considerations associated with the definition of distribution. Patients and their healthcare providers need to understand that the pharmacies with whom they have a longstanding relationship, whom they trust to provide high quality compounded drugs, may no longer be able to supply those drugs if the compounder is limited to five percent interstate distribution of patient-specific compounded drugs. They also need to be notified that the transaction costs associated with the MOU and Five Percent Limit may result in increased prices of their needed compounded medications.

Government assessment of an FDA-proposed regulation also entails review and clearance by more than just OMB—the review includes consideration by the Department of Health and Human Services and relevant agencies within it, as well as other Executive Branch entities.[68] For example, the Department of Defense, National Institutes of Health, and Indian Health Service may have an interest in the MOU and Five Percent Limit to the extent that those entities obtain compounded drugs for their patients. Additionally, the Centers for Disease Control and Prevention may express concern about a policy that so substantially limits the ability of pharmacists to compound drugs that it has the unintended effect of increasing compounding by physicians, whose compounding activities are largely unregulated and whose largescale compounding could create drug quality concerns. Undergoing the rulemaking process in conformance with Executive Order 12866 would help to ensure that FDA has taken into account all potential concerns and perspectives from these stakeholders.

G. FDA's Definition Requires a Federalism Assessment under Executive Order 13132.

Under Executive Order 13132, agencies must "have an accountable process to ensure meaningful and timely input by State and local officials in the development of regulatory policies that have federalism implications."[69] An agency may not promulgate any regulation with unfunded federalism implications unless the agency has "(1) consulted with state and local officials early in the development of the proposed rule, and (2) prepared a 'federalism summary impact statement' consisting of a description of the prior consultation with state and local officials, a summary of their concerns and the agency's position regarding the need to issue the

[68] *See* FDA, *Staff Manual Guide* 1410.10, Delegations of Authority to the Commissioner of Food and Drugs, at 10 (Aug. 26, 2016), https://www.fda.gov/media/81983/download (HHS reserving its rights to approve regulations that FDA intends to promulgate); Exec. Order No. 12866, *supra* n.63, at 51737 (assigning OIRA responsibility to coordinate review of a regulation among executive branch agencies).

[69] Exec. Order No. 13132, 64 Fed. Reg. 43,255, 43,257 (Aug. 10, 1999).

rule, and a statement of the extent to which the officials' concerns have been met." Here, although FDA has consulted with the NABP and the state boards of pharmacy during the MOU preparation process and considered their comments, it has not prepared a summary impact statement on which the states and other interested stakeholders can comment.

The federalism requirement is particularly important in the context of the definition of distribution. While states typically have day-to-day oversight responsibility over pharmacies in their state, FDA routinely exerts regulatory authority over pharmacies that fail to meet the conditions of section 503A. If FDA subjects dispensed drugs to the Five Percent Limit and pharmacies exceed it, the Agency may substantially increase its regulatory responsibility over pharmacies throughout the United States. This has significant federalism implications that must be addressed in the rulemaking.

V. FDA's Enforcement Policy

Three types of compounders could be significantly impacted if they are subject to the Five Percent Limit: (1) pharmacies that specialize in compounding certain drugs or treating certain conditions for patients nationally or regionally ("specialty pharmacies"), (2) health systems' pharmacies, and (3) pharmacies located near a state border whose customers are primarily in the other state. Enforcing the Five Percent Limit with regard to such pharmacies could result in a harmful effect on patient access to critically needed compounded drugs. With regard to (1), there may be few specialty pharmacies in the country or in a region that have the competencies to produce a particular drug product or treat a particular condition. With regard to (2), centralized pharmacies in health systems compound patient-specific drugs for hospitals and clinics throughout an interstate region. With regard to (3), a pharmacy located just over a state border services customers on the other side of that border. If these pharmacies can only ship five percent of their drugs interstate, patients will not be able to receive the drugs that they need.

In addition, with regard to the limited number of states that we know to have expressed an interest in considering entering into the MOU, they will need time to promulgate new laws or regulations to require pharmacies to supply the information being requested. Enforcing the Five Percent Limit against pharmacies in such states would be counterproductive when the state is actively working to adopt the necessary authorities to sign the MOU.

To address these concerns, we request that FDA adopt an enforcement discretion policy that balances enforcement of important protections in section 503A on the requirement for prescriptions and limitations on interstate distribution with the equally important need to preserve patient access to medically necessary compounded drugs. We have enclosed a proposed guidance document that we feel would address these important objectives, and we look forward to collaborating with the Agency on finalizing such a policy before it begins enforcing the Five Percent Limit.

VI. Conclusion

For the reasons explained above, to include dispensing within the term "distribution," FDA must promulgate a rule through notice-and-comment rulemaking in a manner consistent with federal laws and executive orders governing rulemaking. The Agency's present failure to do so is greatly to the detriment of FDA, states, businesses, healthcare providers, and, ultimately, patients. We urge FDA to engage in substantive rulemaking consistent with these requirements before finalizing the draft MOU and engaging in any regulatory action under section 503A using a definition of "distribution" that includes dispensing, and to develop a policy that will protect patients from losing access to critical compounded drugs if their pharmacies are located in a state that does not sign the MOU.

C. Environmental Impact

Petitioners claim a categorical exclusion under 21 C.F.R. § 25.30(h).

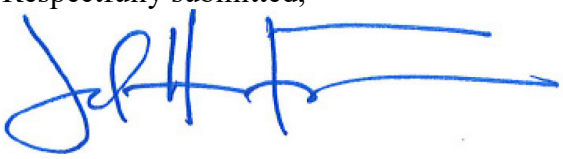
D. Economic Impact

Information on the economic impact of this petition will be provided on request.

E. Certification

Pursuant to 21 C.F.R. § 10.30(b), the undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petitioner relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Respectfully submitted,



John H. Fuson

Enclosure

cc: Alex M. Azar, Secretary of Health and Human Services
Robert P. Charrow, General Counsel of Health and Human Services
Brenda Aguilar, Branch Chief of Food, Health, and Labor, Office of Information and Regulatory Affairs of the Office of Management and Budget