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From: Pharma & Biopharma Outsourcing Association
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To: Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
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RE: Comments from Pharma & Biopharma Outsourcing Association (PBOA) on Docket No. FDA-2021-D-1031 for "*Reporting Amount of Listed Drugs and Biological Products Under Section 510(j)(3) of the Federal Food, Drug, and Cosmetic Act; Draft Guidance for Industry*".

On behalf of the Pharma & Biopharma Outsourcing Association ("PBOA"), a trade association representing Contract Manufacturing Organizations and Contract Development & Manufacturing Organizations ("CDMOs"), I am pleased to offer feedback on the recent draft guidance, "*Reporting Amount of Listed Drugs and Biological Products under Section 510(j)(3) of the Federal Food, Drug, and Cosmetics Act*". PBOA's Quality Technical Group, composed of quality and operations leads from many of our member companies, has discussed this draft guidance and supports FDA in its efforts to gain better insight into the pharmaceutical pipeline.

We understand that FDA seeks to better understand the drug supply chain to the American public with the goal of identifying, preventing, and mitigating risks associated with possible drug shortages. Our members agree this is an important goal and want to help ensure that FDA can achieve this objective by gathering valuable data with meaningful contribution from industry. Our sector has a wealth of experience in managing the supply of drugs to global markets and we believe FDA should collaborate across industry to identify the most relevant dataset and reporting requirements. As such, we respectfully request that FDA consider extending the comment period and delay implementation and reporting timelines to allow for a clear picture to be assembled through collection of a single unambiguous dataset. We also ask that FDA reconsider the monthly reporting requirement, which will be unduly burdensome and of limited value. Instead FDA should continue with annual reporting and consider collecting information in stages, potentially studying a subset of products to assess the utility of the data.

PBOA also believes that reporting data for the 2020 calendar year will take a significant effort to assemble and may not provide value, due to the exceptional period this represents during the public health emergency. In any event, the reporting timeline for this data is too short. The timeline for 2020 reporting allows for only 6 weeks from the end of the comment period, which does not give adequate time for FDA to consider the feedback of stakeholders and issue a final guidance, nor for the data to be collected for submission. Similarly, FDA's comment in footnote 50 — "Contract facilities should consider outlining the reporting arrangements in a written

quality agreement or other written contract" — is not feasible within the timelines given for 2020 and 2021 reporting, given the large number of clients and products many CDMOs work with.

PBOA agrees with the collection of meaningful data and requests FDA take additional time to consider the reporting requirements to determine what data it actually needs and how it can most effectively be gathered. There is wide variation in the interpretation of roles and responsibilities under this guidance, which will likely result in conflicting duplicative data from different registrants. This will result in disparate data that is more likely to introduce confusion rather than affording clarity. How does FDA propose to deal with discrepancies, and what consequences will result from either reporting errors or more likely different interpretations of the reporting requirements by reporting entities? There is no information provided on enforcement or what actions FDA intends to take.

We feel this draft guidance brings to a light several issues that have been discussed by our members, who have differing interpretations of the regulations and the requirements that are placed on CDMOs. For this guidance and future guidance documents, we request the FDA be more specific in the definitions of "Manufacturer", "Trading Partners", or "Sponsors", specifically considering the role of CDMOs to avoid confusion. CDMOs are service providers and do not hold any business interests in the products they manufacture other than to meet the contractual obligations to their clients. As such, a CDMO does not have the legal right to share information about the products it manufactures, which creates significant conflicts when interpreted to be included in the definition of the terms "Manufacturer" or "Trading Partners" or "Sponsor".

According to the Public Law 113-54-NOV.27, 2013 127STAT.587 TITLE II -Drug Supply Chain Security, Section 581 DEFINITIONS:

- (10) MANUFACTURER.—"*The term 'manufacturer' means, with respect to a product—(A) a person that holds an application approved under section 505 or a license issued under section 351 of the Public Health Service Act for such product, or if such product is not the subject of an approved application or license, the person who manufactured the product; (B) a co-licensed partner of the person described in subparagraph (A) that obtains the product directly from a person described in this subparagraph or subparagraph (A) or (C); or (C) an affiliate of a person described in subparagraph (A) or (B) that receives the product directly from a person described in this subparagraph or subparagraph (A) or (B)*."

  and

- (23) TRADING PARTNER.—"*The term 'trading partner' means— (A) a manufacturer, repackager, wholesale distributor, or dispenser from whom a manufacturer, repackager, wholesale distributor, or dispenser accepts direct ownership of a product or to whom a manufacturer, repackager, wholesale distributor, or dispenser transfers direct ownership of a product; or (B) a third-party logistics provider from whom a manufacturer,*

repackager, wholesale distributor, or dispenser accepts direct possession of a product or to whom a manufacturer, repackager, wholesale distributor, or dispenser transfers direct possession of a product."

Both these definitions are focused on ownership rights and responsibilities, which a CDMO never obtains throughout performance of its services. And according to the Public Law 116-136-MAR.27, 2020 134STAT.286 TITLE – Coronavirus Aid, Relief, and Economic Security Act or the "CARES Act", Subtitle F – Over-the-Counter Drugs PART I-OTC DRUG REVIEW:

- introduces Sec 505G(q) Definitions: (2) *The term 'sponsor' refers to any person marketing, manufacturing, or processing a drug that— (A) is listed pursuant to section 510(j); and (B) is or will be subject to an administrative order under this section of the Food and Drug Administration*";

  and

- Further, the CARES Act stipulates in Subpart B – Mitigating Emergency Drug Shortages Sec. 3112(f) "CONFIDENTIALITY.—*Nothing in the amendments made by this section shall be construed as authorizing the Secretary to disclose any information that is a trade secret or confidential information subject to section 552(b)(4) of title 5, United States Code, or section 1905 of title 18, United States Code.*"

It remains the position of our membership that a CDMO does not qualify as a 'Manufacturer', 'Trading Partner', or 'Sponsor' under these laws, unless that CDMO is registered as an Outsourcing Facility under the provisions of Sec. 503B and manufacturing a product that is "*not the subject of an approved application or license*" and therefore subject to the Compounding Quality Act or the market authorization holder for the product in question under Sec. 503A. As such, our position is that CDMOs are not required to report under or meet the requirements placed on 'Manufacturers' or 'Trading Partners' under the Drug Supply Chain Security Act or on 'Sponsors' by the Coronavirus Aid, Relief, and Economic Security (CARES) Act.

PBOA recommends FDA consider referring to the definition given to 'Contract Manufacturing Organization Facility' under Public Law 115-52-AUG.18,2017-131STAT.1020 TITLE III-FEES RELATING TO GENERIC DRUGS SEC.302. DEFINITIONS that states:

- (5) The term 'contract manufacturing organization facility' means *a manufacturing facility of a finished dosage form of a drug approved pursuant to an abbreviated new drug application, where such manufacturing facility is not identified in an approved abbreviated new drug application held by the owner of such facility or an affiliate of such owner or facility*.''.

and Public Law 116-136-MAR.27,2020 134STAT.459 SEC. 3862. FEES RELATING TO OVER-THE-COUNTER DRUGS, which amends Subchapter C of chapter VII of the Federal Food, Drug, and Cosmetic Act (21 U.S.C 379f et seq.) by inserting the following definition in SEC. 744L. DEFINITIONS:

- ‘‘(2) The term ‘contract manufacturing organization facility’ means *an OTC monograph drug facility where neither the owner of such manufacturing facility nor any affiliate of such owner or facility sells the OTC monograph drug produced at such facility directly to wholesalers, retailers, or consumers in the United States*.

While we are aware that these definitions are part of discrete User Fee statutes, we feel that by using these definitions as reference, FDA can specify that the term ‘contract manufacturing organization facility’ means, for the purposes of this draft guidance, “*a manufacturing facility of a finished dosage form of a drug approved pursuant to a new drug application, abbreviated new drug application, or an OTC monograph where neither the owner of such manufacturing facility nor any affiliate of such owner or facility sells the drug product produced at such facility under such new drug application, abbreviated new drug application, or OTC monograph directly to wholesalers, retailers, or consumers in the United States.*”

With this definition of a CDMO, we believe that such a service provider is not required to file its own NDCs, since it neither has legal control of the materials it produces nor authority to determine where they are distributed. Under Section 510 of the Federal Food, Drug, and Cosmetic Act, 21 USC §360 – Registration of producers or drugs or devices, annual registration under Section (b)(1) is required for “*every person who owns or operates any establishment in any State engaged in the manufacture, preparation, propagation, compounding, or processing of a drug or drugs*” and under 21 USC §360(a)(1) “*the term ‘manufacture, preparation, propagation, compounding, or processing’ shall include repackaging or otherwise changing the container, wrapper, or labeling of any drug package or device packages in furtherance of the distribution of the drug or device from the original place of manufacture to the person who makes final delivery or sale to the ultimate consumer or user.*”

Our members do follow the regulation that their establishments register their facilities with the Secretary, under 21 USC §360(j)(1) “*Every person who registers with the Secretary under subsection (b), (c), (d), or (i) shall, at the time of registration under any such subsection, file with the Secretary a list of all drugs and a list of all devices which are being manufactured, prepared, propagated, compounded, or processed by him for commercial distribution*”. However, PBOA believes that since our members do not hold title to or ownership of the products that they produce, CDMOs should not be required to list these products, as they are not released by the CDMO for commercial distribution. We believe that it is FDA’s intent that the Market Authorization Holder (MAH) is the responsible party for releasing drugs to the market. Reporting requirements should be aligned with those parties having ownership and control of release and distribution to the market (exchange of ownership), the Market Authorization Holder (MAH).

Aligning reporting requirements in this way will provide a single set of useful data for FDA to meet its goals to gain insight into the American drug supply chain from the entities that actually own and distribute the products to the American public. In most instances, CDMOs are manufacturing products under regulatory filing documents such as an BLA, NDA or ANDA on behalf of MAHs who bear the responsibility and authority to distribute these products. As such,

except for very special circumstances, CDMOs should not be required to list the products they produce, nor file their own NDCs.

In addition to responsibilities of reporting under the CARES Act, PBOA recommends that FDA reconsider the data being collected to ensure that it is accurately meeting the goal of predicting drug shortages and understanding the drug supply chain in the United States. We believe the current reporting requirements will result in data that cannot easily be interpreted with this goal in mind. Specifically, our members are concerned that reporting requirements for produced active pharmaceutical ingredients (API) and drug product intermediates (DPI) not intended to be distributed in the US will result in greater confusion than clarity. In addition, API and DPI that are shipped for further processing may require unique package sizes or partial lots destined to different markets. In the absence of complete understanding of the supply chain and distribution plans, this data would be nearly impossible to interpret. Some of our members ship bulk capsules, tablets, or vails for downstream packaging and labeling specific to the markets they will be distributed in and the intermediate data will not add to understanding the US supply chain.

Furthermore, collecting this information from CDMOs along the supply chain will result in greater confusion about the US drug supply chain, particularly when most CDMOs do not make these decisions and, in many cases, may not know where the products they manufacture are distributed after leaving their loading docks. Collecting information from entities that have no authority over when and how much material they manufacture, nor what market that material is distributed to, will not help FDA to meet its goals.

Regardless of the final reporting requirements, PBOA recommends FDA explicitly state that all information reported under FDCA Section 510(j)(3) is considered 'Confidential Information'. Data collected on drug volumes and site of manufacture is highly sensitive confidential information, which is specifically protected under the CARES Act in Sec. 3112. As such, we feel FDA should add language to the draft guidance explicitly recognizing the data reported under FDCA Section 510(j)(3) is regarded as confidential information and subject to protection under applicable law. PBOA also requests FDA to specify how the confidentiality of reported information will be maintained.

As mentioned earlier, our members hold differing interpretation of the regulations regarding the need for CDMOs to file their own NDCs, and thus question the value of data collected from CDMOs under these reporting requirements. However, if FDA indicates that CDMOs are required to file their own NDCs for their customers' products, we note there will not be enough time in the current implementation timeline for CDMOs to establish and then report on new NDCs. This would create a significant burden in effort, cost and complexity at the CDMO level. We understand that any company responsible for manufacturing and distributing into the US market must list the drug by filing an NDC and, based upon this, that MAH is responsible for reporting to FDA. We do not believe that a CDMO falls into this category. In the event that FDA holds that CDMOs should register their own NDCs and report under this guidance, we note that FDA does not include "packaging" as an identifiable business operation in the Technical Conformance Guide as specified under 21 USC §360(a)(1). PBOA requests that FDA should

clarify whether a facility that performs only packaging should identify their facility as a manufacturer when submitting these reports.

The guidance document indicates that FDA is seeking to gain more visibility and understanding into the drug supply chain and further notes that the current reporting mechanisms result in reports arriving in different times throughout the year, which "makes it challenging for the Agency to identify, prevent, and mitigate drug shortages at any particular point in time." Our members believe the new annual and monthly reporting requirements will add burden to the industry without alleviating any of the current reporting requirements, and will result in additional and potentially confusing data reaching FDA.

It is also unclear how this additional data will be used to meet the objective of identifying, preventing, and mitigating drug shortages. FDA has numerous data- and reporting-driven initiatives currently in place to address shortage and supply chain issues, but has not demonstrated or clarified how this data will or can be used to meet the objective of minimizing shortages of drugs for the American public. Instead of requesting the industry report additional and potentially conflicting release data, PBOA recommends that FDA analyze the data it already has access to under its current initiatives and assess what gaps exist, to make new reporting requirements worthwhile for industry, the Agency, and patients.

PBOA appreciates the opportunity to review and provide comments pertaining to the draft guidance. We look forward to working with FDA on its continued efforts to ensure public access to high quality pharmaceutical products.

Thank you for considering our views.

Respectfully,

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PBOA

PBOA Member Companies

Ajinomoto Bio•Pharma Services
Alcami
ApiJect Systems Corp
Avid Bioservices
Afton Scientific
Baxter BioPharma Solutions
Bora Pharmaceuticals
Cambrex
Catalent Pharma Solutions
CMIC CMO USA, Inc.
Coating Place, Inc.
Cytovance Biologics
DPT, a Viatris Co.
Frontida
Grand River Aseptic Manufacturing
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Metrics Contract Services
Pace Analytical Life Sciences
Particle Sciences, a Lubrizol Co.
Patheon Inc., part of Thermo Fisher Scientific
PCI Pharma Services
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