PHARMA & BIOPHARMA OUTSOURCING ASSOCIATION

Advancing the regulatory, legislative, and general business interests of the pharmaceutical and biotech services community

The Honorable Lamar Alexander
Chairman
Health, Education, Labor & Pensions Committee
455 Dirksen SOB
U.S. Senate
Washington, D.C. 20510

The Honorable Patty Murray
Ranking Member
Health, Education, Labor & Pensions Committee
154 Russell SOB
U.S. Senate
Washington, D.C. 20510

Dear Senators Alexander and Murray,

As the President of the **Pharma & Biopharma Outsourcing Association (PBOA)**, I am writing on behalf of our members to comment on the discussion draft of the ***Opioid Crisis Response Act of 2018***. PBOA represents the regulatory, legislative and general business interests of pharmaceutical and biopharmaceutical contract manufacturing organizations and contract development and manufacturing organizations operating in, or selling into, the United States. PBOA members provide the technologies and services that enable the biopharmaceutical industry to develop, manufacture and package drugs, biologics, vaccines, and other treatments safely and cost-effectively. Our members represent more than 20,000 domestic manufacturing jobs, and manufacture more than 220 billion doses annually, including between 30 to 40% of all doses distributed annually in the U.S. We appreciate the efforts Congress and the federal government are taking to combat the opioid crisis in America, and offer our resources in that fight, given our understanding of drug manufacturing and packaging technologies.

At the same time, we recognize that the role of contract manufacturers and packagers is only one component of a much larger strategy that will involve changes in prescribing practices, enhanced treatment models, and new enforcement resources.

We have reviewed the recent discussion draft from the Senate HELP committee, and appreciate the opportunity to comment specifically on *Sec. 302. Clarifying FDA Packaging Authorities*, as well as *Sec. 501. Study on Prescribing Limits*. Sec. 302 gives HHS and FDA the authority to mandate "unit dose packaging or another packaging system" and "safe disposal packaging or a safe disposal system" for drugs covered under the REMS/ETASU program.

REMS/SCOPE

We recognize that new tools are required to help battle opioid abuse, but we are concerned with the use of REMS/ETASU as the classification to grant HHS and FDA new authority for packaging. We feel this authority is overly broad to be applied to all REMS/ETASU products. Instead, we believe such authority should be limited to REMS/ETASU Controlled Substances on Schedule II, or that another, narrow category be established for this authority.

UNIT-DOSE PACKAGING

In order for the shift from bottles to unit-dose packaging to have an impact on opioid abuse, we feel this initiative must be wedded to a change in prescribing practices. We are unaware of any evidence indicating that such packaging will reduce the misuse or abuse of products so packaged, and it is critical that the new mandates proposed in this bill have a firm foundation on science and data in order to benefit the public health without putting patients and the manufacturing portion of the supply chain at risk. Elsewhere in the discussion draft, Sec. 501 mandates a study on "the impact of Federal and State laws and regulations that limit the length, quantity, or dosage of opioid prescriptions." We would like to see the timing of a unit-dose mandate harmonized with the outcome of such a prescribing report.

Our members have concerns that a large-scale changeover from bottle-packaging of opioids to unit-dose blister-packaging may require significant length of time to implement. Validation, tooling, stability studies and,

in some cases, acquisition of new equipment will be required and could take a year or longer to complete. If the contract manufacturer and packager of an opioid product does not have unit-dose blister-packaging equipment, the license-holder may choose to ship the bulk product to a packaging facility for that step.

The discussion draft makes no mention of timelines to implement such a change. Other proposals we've reviewed do provide timelines -- 180 days "or such longer time period as determined to be appropriate" to file the supplement proposing changes, and 90 days "or such longer time period as determined to be appropriate" to implement it -- but we feel that those timelines are not realistic and will almost certainly have to default to the Secretary's discretion, leading to uncertainty among license-holders and contract manufacturers and packagers.

If a unit-dose mandate is large-scale and sweeping in terms of the drugs covered, it may cause packaging capacity constraints and shortages. If new packaging equipment must be purchased, this will require extended timelines for installation, qualification and validation. Some CMOs that possess blister-packaging capabilities currently employ it primarily for physician samples or clinical materials, and changing over to commercial production would require adding DSCSA-compliant hardware and software that could also cause delays. We recommend a phase-in process that will permit changeover without causing supply disruptions for currently-marketed products.

In practice, unit-dose blister-packaging is less efficient and more costly than bottle-packaging, resulting in greater costs. Generic products would experience the greatest price-sensitivity, as reimbursement rates are extremely low.

In addition, while certainly an unintended consequence, holders of original NDAs for these products may adopt proprietary packaging that would prohibit generics from complying with the law, potentially reducing the supply and raising prices further. We feel it is important the FDA engage in its standard guidance process for any such packaging mandate.

SAFE DISPOSAL

Regarding the second half of Sec. 302, mandating "safe disposal packaging or a safe disposal system", we are concerned that the technologies for such systems are nascent at best, and will require significant development before they can be deployed. We recommend commissioning a report on the status of such systems, and that any mandate authority permit the use of a broad range of such systems, rather than a "one-size-fits-all" technology.

This is also an area where NDA holders could potentially use a propriety packaging or disposal system that would "lock out" generics.

Perhaps legislation could include funding to fast-track the development of such systems. Such funding could come from FDA's Regulatory Science program.

STUDY ON PRESCRIBING LIMITS

As mentioned above, we feel that the study mandated in Sec. 501 should include several additional sections:

- evidence, if any, of the effectiveness of unit-dose packaging or other packaging configurations on altering physician prescribing behavior;
- evidence, if any, of the effectiveness of unit-dose packaging or other packaging configurations on reducing drug abuse or misuse;
- the costs associated with unit dose packaging or other packaging configurations;
- the costs associated with drug disposal systems, and an analysis of the success of such systems in reducing abuse.

We thank the Committee for the opportunity to comment on this discussion draft, and look forward to working with you to reduce opioid abuse and save lives.

Sincerely,

Gil Roth
President
Pharma & Biopharma Outsourcing Association