PHARMA & BIOPHARMA OUTSOURCING ASSOCIATION

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

May 3, 2018

The Honorable Richard Hudson
House Committee on Energy & Commerce
United States House of Representatives
429 Cannon House Office Building
Washington, DC 20515

Dear Representative Hudson,

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 have reviewed the recent discussion draft you have submitted as part of the opioid-related bills under consideration by the Energy & Commerce Committee. 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.

EXPANSION OF AUTHORITY

We are concerned about the expansion of authority granted to HHS and FDA under this new discussion draft. Where the previous version explicitly addressed "unit-dose packaging or another packaging consideration," the current one appears to more broadly grant powers requiring implementation of "packaging or disposal" license-holders of affected drugs (Schedule II/III drugs that are or contain opioids).

We appreciate that any such order will require consultation with relevant stakeholders, but are concerned that such consultation may simply be pro forma and that such consultations will not weigh into the Secretary's decision-making process.

PACKAGING CHANGES

We remain concerned that a shift in packaging (from bottles to unit-dose, for example) may have no impact on opioid abuse, without being 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.

Our members have concerns that a large-scale changeover in packaging modes 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 timelines provided in the draft are not realistic and will almost certainly have to default to the Secretary's discretion and/or a license-holder's request, leading to uncertainty among license-holders and contract manufacturers and packagers. The draft bill should take these implementation issues into account, and permit a manufacturer up to one year after the order is issued, or a longer time period as determined appropriate by the Secretary, to respond to the order; and 180 days after a supplement is approved, or longer time period as determined appropriate by the Secretary, to implement such changes.

If a packaging 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. In other cases the CMOs may have the requisite equipment, but it may need to be commissioned for commercial use. Some CMOs that possess blister-packaging capabilities, for example, currently employ it primarily for physician samples or clinical materials; 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.

Depending on the mandated packaging, significantly greater manufacturing costs may be incurred. For example, unit-dose blister-packaging is less efficient and more costly than bottle-packaging, and some CMOs estimate the cost would be three times higher to package those drugs. Generic products would experience the greatest price-sensitivity, as reimbursement rates are extremely low.

We appreciate the inclusion of alternative measures, as we were concerned that holders of original NDAs for these products could otherwise 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 provisions for the safe disposal of these drugs, we are concerned that the patient-facing technologies for such systems are nascent at best, and will require significant development before they can be deployed. We commend inclusion of a GAO report on this class of packaging technology, but are concerned that the bill would give HHS and FDA authority to mandate such packaging prior to that report's completion. This would provide authority to mandate packaging in an area where the scientific, technical, implementation, and outcomes data is missing. We would recommend that any authority to mandate disposal packaging or technology be postponed until such a report is complete and demonstrates the feasibility and usefulness of disposal packaging systems, based on sound science. As mentioned above, it is critical to understand both the benefits and risks of such a program.

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

We would also like to note that disposal should not simply be a task for the makers and license-holders of these drugs. There are many other steps in the chain from manufacturing to the patient -- wholesalers, distributors, hospitals and pharmacies -- that should bear responsibility for safe disposal and share in the cost.

STUDY ON PRESCRIBING LIMITS

We feel that a second GAO study be added, to report on several on topics:

- 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 you for the opportunity to comment on this discussion draft, and look forward to working with you and the Energy & Commerce Committee to reduce opioid abuse and save lives.

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Sincerely,

Gil Roth
President
Pharma & Biopharma Outsourcing Association

Cc: Representative Greg Walden, Chairman, House Committee on Energy and Commerce
Representative Frank Pallone, Ranking Member, House Committee on Energy and Commerce