Alliance for Pharmacy Compounding

Compounding the Joy of Living®

June 18, 2024

Submitted electronically via regulations.gov

Documents Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2023-N-0061

To Whom It May Concern:

I write on behalf of the Alliance for Pharmacy Compounding to comment on the U.S. Food and Drug Administration's (FDA or the Agency) proposed rule that would add initial categories to the 503A and 503B demonstrably difficult to compound (DDC) lists.

APC is the voice for pharmacy compounding, representing more than 500 compounding small businesses – including compounding pharmacists and technicians in both 503A and 503B settings – as well as prescribers, educators, researchers, and suppliers.

We provide the following comments:

1. **No Authority for 'Categories' in 503A**

We question FDA's authority to issue rulemaking that addresses both the 503A and 503B DDC lists in the same rule.

The Agency's proposed rule aims to include "categories" of drug products on both the 503A and 503B DDC lists without regard to a critical statutory distinction in the respective enabling legislation that must be considered. The language in section 503B of the Federal Food, Drug, and Cosmetic Act (FD&C Act) indeed permits the inclusion of "drugs or categories of drugs" on the 503B DDC list. However, section 503A specifies "a drug product," and does not authorize the addition of *categories* to the 503A DDC list. Therefore, FDA's intention to introduce categories to the 503A DDC list is not authorized by Congress. FDA does not have the statutory authority to add *categories of products* to the 503A DDC list.

2. **No Current Compounding of Proposed Categories**

Additionally, we question why the Agency proposes to add items to the 503A and 503B DDC lists without any evidence of those items being compounded by either 503A or 503B facilities.

3. **Proposed Evaluation Criteria are Unbounded**

The Agency has failed to articulate a meaningful definition for the terms "complex" and "complexity" used in the six evaluation criteria listed in Section V.A. of the proposed rule. The criteria are subjective and unbounded in scope. We are concerned about how these evaluation criteria will be interpreted and applied in the future. Furthermore, both DDC provisions in 503A and 503B require a nexus between "demonstrable difficulties" for compounding "that are reasonably likely to lead to an adverse effect"; the terminology used in the Section V.A. criteria omit the core concern – adverse events – articulated in the statute. We are concerned that the imprecise terminology in the proposed new 21 CFR §215.25 will allow for FDA additions to the DDC list without an appropriately justified concern for adverse events.

Compounding is not a simple endeavor. Compounders are required to undertake rigorous training and meet stringent standards in compounding drug products for the patient population. Many formulations require significant skill and involve some level of difficulty. However, the fact remains that some patients *require* drug products that are not available unless compounded. The process by which the availability of such compounded drug products is limited must therefore be appropriately confined. We ask that the Agency include specific limitations to define "complex" and "complexity" as used in the evaluation criteria and delineate exactly what level of complexity and evidence of potential adverse events would exceed the acceptable threshold. While APC acknowledges the Agency's important role in protecting the public health, we have a significant concern that the evaluation criteria as currently drafted could encompass compounded drug products that are not truly difficult to compound – and in fact have been compounded for decades – and leave way for overzealous and arbitrary rulemaking in the future that would significantly impact medication access and patient care.

4. **No Process for Public Participation**

While the federal register notice mentioned that the Agency intends to continue using PCAC meetings for discussing further inclusions on the list, it remains unclear if the Agency will follow notice and comment rulemaking when making changes to the evaluation criteria or the categories of drug products on the DDC lists in the future. Precluding the public's ability to comment on the Agency's decisions regarding the availability of compounded drug products is not appropriate. As such, we ask that the Agency clearly outline the procedure it intends to implement for the review of the DDC lists and their evaluation criteria, and clarify whether it intends to follow the notice and comment rulemaking procedure each time modifications to the DDC lists or their processes are made.

5. **No Process for Removing Items from the DDC Lists**

We are concerned that there is no established process for removing items from the 503A or 503B DDC lists once they have been added. This is another significant procedural deficiency in the proposed rule. While the comment period during rulemaking allows for public input, there is no mechanism to reverse a decision if (and when) circumstances change. As technology advances and production capabilities improve, it is crucial to have a defined process for removing items from these lists to reflect the evolving landscape of compounding practices. We would urge the Agency to address that issue in any final rule.

6. **Inclusion of Analytical Testing**

Lastly, we are concerned about the inclusion of Criterion #6: Analytical Testing Complexity in the DDC evaluation criteria. Compounders typically do not conduct analytical testing on their own products. Instead, they rely on third-party analytical laboratories with specialized expertise. The complexity of testing, such as cell-based assays and mass spectrometry, is managed by these expert laboratories and has been a common practice in the testing of compounded drugs for the past two decades. Thus, the complexity of the testing process should not be a criterion for determining whether a drug or category of drugs is demonstrably difficult to compound by pharmacies. In addition, the ability of labs to conduct testing of compounded formulations continues to advance and evolve. What may be complex to test today may not be complex to test in the future. This adds to the need for the evaluation of items on the DDC list to be able to be reevaluated as new technologies and processes for testing become available.

We urge FDA to consider these points in the final rulemaking process and to ensure that the FD&C Act is adhered to and the practical implications for patients are thoroughly considered.

Thank you for your attention to our concerns. We look forward to a constructive dialogue and stand ready to provide any additional information if needed.

Sincerely,

Scott Brunner, CAE
Chief Executive Officer
scott@a4pc.org