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October 27, 2023

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: Docket No. FDA-2023-N-3575-0001
Reauthorization of the Over-the-Counter Monograph Drug User Fee Program; Public Meeting; Request for Comments. 88 Fed. Reg. 60688 (September 5, 2023)

Dear Sir or Madam:

The Consumer Healthcare Products Association (CHPA) welcomes the opportunity to comment on the above captioned request for comments on the reauthorization of the over-the-counter (OTC) Monograph Drug User Fee Program (OMUFA). For more than 142 years, CHPA has served as a vital advocate for the consumer healthcare products industry. A member-based trade association, CHPA represents the leading manufacturers and marketers of OTC medicines, consumer medical devices, and dietary supplements. Our members provide millions of Americans with safe, effective, and affordable therapies to treat and prevent many common ailments and diseases.

Accomplishments to date. CHPA and its members are committed to working with FDA to ensure prompt and effective implementation of OTC monograph reform, as enacted under the CARES Act, March 2020. CHPA and its members also recognize that the OMUFA program is part of the success of OTC monograph reform. We believe that a thoughtfully crafted OMUFA program should provide FDA with ample resources to implement the OTC monograph review program, while also assuring that the industry and other stakeholders receive the essential guidance, feedback, and other support necessary to advance key innovations in the OTC drug market.

We commend the FDA for the steps it has taken to implement monograph reform and to carry out its OMUFA I commitments. For instance, we appreciate that FDA has issued draft guidance on key topics, including:

- OTC Monograph Formal Meetings;
- Formal Dispute Resolution and Administrative Hearings on Final Administrative Orders;
- OTC Monograph Order Request Format and Content; and
- OTC Submissions in Electronic Format

We look forward to FDA's finalization of these guidance documents and the issuance of additional draft guidances, including guidance on minor changes in solid oral dosage drugs and future guidances that will eventually extend minor change concepts to other dosage forms. The guidance provided by the FDA on these critical matters will serve as essential tools for industry as it navigates through the OTC Monograph Order Request (OMOR) process.

CHPA acknowledges the FDA's fulfillment of its statutory obligation to issue deemed final orders for all drugs that were previously classified as Generally Recognized as Safe and Effective (GRAS/E) drugs under final monographs and tentative final monographs. This marks a significant initial first step that will enable the FDA to focus its resources on label changes and reviewing new OMOR submissions in the coming years. We also commend the FDA's initiative in implementing new OTC IT infrastructure and achieving its OMUFA hiring goals.

Points for Alignment During OMUFA II Reauthorization. As we embark on the OMUFA reauthorization process, it is important that we recognize the important progress achieved during the first OMUFA cycle and reflect upon areas for improvement that should be addressed during the OMUFA II cycle. This approach will allow us to advance our shared goal of unlocking key innovations in the OTC drug market while upholding current statutory-based standards for general recognition of safety and effectiveness. In this spirit, CHPA would like to underscore five key points that we believe will play a central role in building upon accomplishments to date and ensuring the success of OTC monograph reform as we move into the OMUFA II cycle.

1. The GRAS/E standard has not changed. OTC monograph reform did not change the substantive standard FDA must apply when making GRAS/E determinations. Under this standard, GRAS/E determinations should be based principally on reports of the relevant studies in the published literature. The relevant regulations, set out in 21 CFR 330.10, state that GRAS/E determinations "shall ordinarily be based on published studies," which may be corroborated by unpublished studies and other data, and reports of significant human experience in the market. Those regulations are consistent with the GRAS/E concept as applied by FDA and the courts over many decades.

In adding section 505G to the Federal Food Drug & Cosmetic Act, Congress made clear that its intent was to maintain the substantive standards in 21 CFR 330.10 for GRAS/E determinations. This is reflected in statements by the principal sponsor of the legislation in the House of Representatives on the day section 505G was enacted:

> *"[These regulations] recognize that results of clinical studies supporting general recognition of safety and effectiveness will in most instances be*

> *contained in the published scientific literature. Such publications seldom, if ever, contain the same level of detail as the clinical study reports and data tabulations submitted in support of new drug applications, but it has long been understood that they may form the basis for determinations of general recognition of safety and effectiveness under the OTC monograph system. … It is our intent that the FDA should continue to apply these standards in making determinations of general recognition of safety and effectiveness under the monograph reform legislation." Congressional Record* H1864 (March 27, 2020) (statement of Mr. Latta).

FDA acknowledged this in its June 2023 draft guidance on Formal Dispute Resolution and Administrative Hearings of Final Administrative Orders Under Section 505G, where it confirmed that "'general recogni[tion]' of safety and effectiveness . . . requires, among other things, the information demonstrating that a drug is safe and effective for its intended use to be published so that such information is generally available to qualified experts." Although section 505G requires FDA to withdraw certain regulations governing the ***procedures*** for OTC Drug Review, it does not require the Agency to withdraw or modify the ***substantive requirements*** for GRAS/E determinations. FDA therefore remains bound by those substantive requirements and must continue to apply them unless it engages in notice and comment rulemaking to change these regulations.

As we move into the OMUFA II cycle, it is essential that FDA ground its review — and the advice it provides during the review process — in the long-established GRAS/E standard. In particular, it is essential that FDA reaffirm that GRAS/E determinations shall be based principally on reports of the relevant studies in the published literature. It will also be important for FDA to recognize the valuable role real world evidence can play in supporting GRAS/E conclusions including, for example, evidence showing a lack of safety signals for drugs with a long marketing history. This too was referenced by Congressman Latta in his statement of intent: "*These regulations clearly recognize the importance of what is now termed 'real world evidence,' including experience from marketing, in determining general recognition of safety and effectiveness." Congressional Record* H1863 (March 27, 2020) (statement of Mr. Latta).

2. GRAS/E determinations are distinct from NDA-style submissions. It is well established that GRAS/E determinations in the nonprescription drug context assess the safety and efficacy of the *active ingredients* to be authorized under the applicable monograph. The list of information to be submitted to support general recognition in 21 CFR 330.10 makes this clear. This does not involve a review of inactive ingredients, which can vary between products authorized under a single monograph, as long as those inactive ingredients meet the applicable regulatory standard for safety and suitability.

Similarly, while OTC medicines must be produced in compliance with FDA's current good manufacturing practices (CGMPs), **GRAS/E determinations do not involve a review of the manufacturing process for each drug marketed under a monograph**. Thus, requestors or sponsors are not required to submit the same chemistry and manufacturing controls data to support an OTC GRAS/E determination that they would be expected to submit under an NDA.

Finally, when evaluating OMOR submissions for drugs that were previously evaluated by an advisory panel under the OTC Drug Review, including, for example, drugs that were classified as Category III under a TFM or Category I under an ANPR, FDA should refrain from undertaking a redundant review of the data already assessed by the panel. Instead, **the statute specifies that the FDA must outline the general categories of data it deems necessary for establishing general recognition, as outlined in section 505G(b)(2)(B)**. In other words, FDA should flag gaps that need to be filled that build on previous preliminary findings by the agency, not start a de novo review process. This will allow FDA to uphold rigorous substantive standards while allowing for needed efficiencies in either the OMOR process or in FDA-initiated GRAS/E determinations on Category III ingredient uses.

3. CHPA encourages FDA to initiate orders on its own initiative where the Agency is well-positioned to do so. Section 505G established pathways for both FDA and industry to initiate the administrative order process. This choice enables either FDA or companies to efficiently leverage available information, promoting progress in the OTC monograph process. While industry is committed to submitting certain GRAS/E finalization OMORs and innovation and safety OMORs it is worth noting that in many instances, the FDA already possesses sufficient data to support GRAS/E determinations or to amend existing monographs. We encourage the FDA to take the lead in initiating orders when it has sufficient information/data to do so. For example, safety OMORs in cases where a Sponsor submits a safety related supplement to an NDA for an ingredient that is also subject to a Monograph. Once FDA has approved the NDA supplement, FDA should initiate the safety OMORs to update the relevant Monograph, as opposed to expecting the NDA Sponsor to duplicate the submission.

This approach will allow industry to focus on concurrently developing key OMORs with FDA's efforts, ultimately heightening the overall efficiency of the OTC monograph process.

4. Prompt, high-quality advice through OMUFA meetings will be necessary to ensure the success of monograph reform. For industry stakeholders participating in the OMOR process, it is essential to have access to timely and comprehensive guidance from the FDA, especially regarding the specific types of data FDA expects

for OMOR submissions. This feedback is of utmost importance given the unique nature of this process, which lacks established guidance or precedent.

CHPA has concerns about how FDA has approached OMUFA meetings to date. For example, we are aware that some stakeholders have faced delays in scheduling OMUFA meetings with FDA and that, in some cases, FDA has been hesitant to offer in-person meetings, or any meetings at all. We acknowledge that there have been positive developments in addressing meeting delays and in providing in-person options, and we are optimistic that this positive trajectory will continue in the remaining duration of OMUFA I. We also recognize that some of these delays were due to the necessary onboarding and training of new OMUFA program staff. However, we strongly encourage the FDA to explore avenues for streamlining these processes in preparation for the OMUFA II cycle. In particular, it is crucial that the FDA maximize opportunities for in-person/video/tele-con interactions and ensures that all meeting guidance is both comprehensive and firmly rooted in statutory principles, as well as a thorough review of the full record, including any relevant OTC panel reviews.

5. CHPA requests that FDA prioritize the development of the administrative orders required to permit minor changes in dosage forms without the need for submission and approval of OMORs. Section 505G(c) establishes a process where sponsors can implement minor changes in dosage forms without necessity of submitting an OMOR. This is contingent upon the sponsor maintaining records that demonstrate that the minor change will not affect the safety or efficacy of the drug, nor materially affect the absorption or other exposure to an active ingredient in the drug when compared to a suitable reference product. Sponsors will be required to provide FDA with such records upon request. This pathway will enable industry to advance key innovations in the OTC drug market efficiently, addressing a significant hurdle to innovation within the pre-CARES[1] Act OTC monograph system. The ultimate goal is to provide consumers with access to convenient and enhanced dosage forms of products that are both safe and effective.

This pathway will not become available, however, until FDA fulfills its statutory mandate to issue one or more administrative orders specifying requirements for determining whether a minor change qualifies for this pathway. The legislative record makes clear that implementation of this provision was a priority for Congress, as reflected in statements by the principal sponsor of the legislation in the House of Representatives on the day section 505G was enacted. We are aware this remains a goal under OMUFA I with a target of spring 2025.

[1] Coronavirus Aid, Relief, and Economic Security Act https://home.treasury.gov/policy-issues/coronavirus/about-the-cares-act

Conclusion. We look forward to working closely with FDA and other key stakeholders throughout the OMUFA reauthorization process, including in development of a goals letter, as we work together to ensure the continued success of FDA's OTC monograph program.

Submitted,

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