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June 12, 2023

Submitted via www.regulations.gov

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

Re: Over-the-Counter Monograph Order Request (OMORs): Format and Content; Draft Guidance for Industry: 88 *Fed. Reg.* 22451-3. Docket No. FDA-2023-D-1188.

Dear Sir or Madam:

The Consumer Healthcare Products Association[1] ("CHPA") submits these comments in response to the U.S. Food and Drug Administration's ("FDA's" or the "Agency's") request for stakeholder input on its draft guidance, "Over-the-Counter Monograph Order Requests (OMORs): Format and Content". 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 medical products. CHPA members provide millions of Americans with safe, effective, and affordable therapies to treat and prevent many common ailments and diseases.

CHPA members appreciate the Agency releasing the draft guidance which provides recommendations for submitting OMOR requests for OTC drug programs regulated under OMUFA. Industry appreciates that individual meetings between FDA and requestors will be necessary to discuss specific data, studies and related information for the OMOR. Our comments are divided into general comments followed by comments that reference specific lines in the guidance document.

General Comments

Industry appreciates that it is difficult to write one guidance document that applies to the many types of OMORs envisioned under OMUFA. Hence, this guidance seems highly inclusive, and in some ways, even more broad in scope and potentially burdensome than a submission for a New Drug Application (NDA). We note that in no way was it envisioned that the OMUFA innovation pathway would be equivalent to the NDA pathway in terms of data requirements and resources. For certain types of OMORs, certain sections referenced in the guidance will not be included in the submission. For OMORs related to safety updates or test methods, we assume the majority of the sections included in the guidance will not be needed; however, the content for different types of OMORs remains unclear. Therefore, one of our recommendations is for FDA to include several examples of the type of content FDA might

[1] The Consumer Healthcare Products Association (CHPA), founded in 1881, is the national trade association representing the leading manufacturers and marketers of consumer healthcare products, including over-the-counter (OTC) medicines, dietary supplements, and consumer medical devices. CHPA is committed to empowering self-care by ensuring that Americans have access to products they can count on to be reliable, affordable, and convenient, while also delivering new and better ways to get and stay healthy. Visit www.chpa.org.

expect to see for various types of OMORs. This will enable industry to better understand expectations, have productive pre-OMOR meetings with FDA and file a suitable OMOR. At a minimum, FDA could include examples of Tier 1, Tier 2 and safety labeling OMORs.

Another general comment is that the requests for extensive data in the various modules should only apply to very specific situations, such as those OMORs requesting new ingredient GRASE determinations for inclusion in a monograph. For ingredients deemed GRASE in an existing final order (formerly known as Category 1), complete data summaries (e.g., literature and postmarketing experience summaries) are unnecessary and burdensome. Additionally, for Category 3 ingredients in a former TFM or Category 1 in an ANPR, similarly, a requestor should not be expected to re-submit data supporting GRASE status if this has already been determined for the ingredient or combination of ingredients. Pre-submission meetings with FDA could highlight any new or additional data that may be required to satisfy GRASE in a proposed or final order.

Industry commends the Agency for the recent publication of the draft guidance, "Generally Accepted Scientific Knowledge in Applications for Drug and Biological Products: Nonclinical Information (May 2023)" ("Draft GASK Guidance"). When finalized, the GASK guidance should be applicable to 505G submissions in addition to the other drug applications within scope. As described in the draft GASK guidance, "the term GASK is used to refer to medical or scientific information that is generally accepted by experts qualified by scientific training and experience in the relevant field, including FDA experts.". We believe the Expert Panels and Advisory Committees that reviewed nonclinical and clinical safety of ingredients during the OTC Drug Reviews would be included in this description and applicability of the concept would extend to 505G drug applications. This is reinforced in the draft GASK guidance with the idea that "GASK is based on widely accepted scientific principles that are typically long-standing." Many of these expert reviews of the time (1972 and beyond) support multiple categories of safe and effective use of monograph ingredients. If a sponsor submits a 505g application with evidence of a nonclinical review performed as part of Advisory Review Panel proceedings this should be considered GASK and potentially sufficient evidence of nonclinical safety.

<u>Specific Line Comments</u>
Line 63: Industry understands that OMORs must be submitted in electronic format and should follow the organizational structure and format outlined in the Common Technical Document. Footnote 11 states that at this time, OMORs should not be submitted through the electronic CTD. FDA should state where OMOR submissions should be filed, for example, the NextGen portal.

Line 108: Industry requests that one table of contents for the OMOR be required and no tables of contents be expected for individual modules. This is similar to the format and content requirements for ANDAs, where only one table of contents is expected/permitted. This can be clarified by deleting lines 228, 365, 395 and 436.

Line 138: The requested certification for all evidence related to GRASE status should be requested only under certain circumstances, for example, where the ingredient or condition of use is currently not GRASE. A complete summary of all evidence should not be requested when the ingredient is GRASE.

Line 214: Proposed labeling should be characterized more specifically to reference the format used in Deemed Final Orders, where bullets precede key text that the OMOR references. It should be stated in the guidance that representative labeling, including full Drug Facts labeling, is not required.

Line 257 and 375: Chemistry and/or manufacturing characteristics of drug substances or drug products have not historically been included in OTC monographs. Monographs include conditions under which a drug is GRASE. The drug product must be manufactured according to cGMPs. Manufacturing information is typically included in manufacturing records, including specifications and standards for making drug products that meet cGMPs. This chemistry and manufacturing information is generally confidential business information owned by the requestor. Under OMUFA, this information is available to FDA on request or during an inspection. It would never be made public.

FDA should expect the focus of the OMOR to be on the active ingredient, not the drug product - only as necessitated by the type of OMOR. The monographs (now orders) do not include how to formulate or manufacture finished products and do not include or mandate specific excipients. Manufacturers have the flexibility to use a range of excipients as long as they have data to support their safety. The OMOR review should be focused on active ingredients unless an excipient plays a critical role in the safety or efficacy of the active ingredient. This is especially important as the OMOR applicant should not have an excessively high bar for generation of data on excipients when after inclusion in a monograph, other sponsors will have broad flexibility in selection and use of excipients. This is codified in 21 CFR 330.1(e).

Industry suggests FDA reference the 2016 format and content of data submissions for nonprescription sunscreen drug products guidance document. Suggested language below has been paraphrased from that document:

Chemical and/or Manufacturing Characteristics: Should include any known chemical and/or manufacturing characteristics of the active ingredient that may be relevant to FDA's GRASE evaluation. Such characteristics should include both known interactions with other active ingredients of commonly used formulation components. Requestors should also include any aspects of formulation needed to ensure stability or any other characteristics needed to establish conditions under which the active ingredient is GRASE for use as proposed.

Line 320: Nonclinical summaries should only be requested for ingredients not deemed GRASE in a final order or for OMORs that rely on nonclinical studies as supporting evidence. FDA should add a statement referencing its support for alternatives to animal testing.

Line 381: Industry supports the inclusion of the current compendial status of the active ingredient(s) in the OMOR. If there is no USP-NF monograph for the active ingredient, the requestor should provide an update on any proposed USP-NF monograph. Detailed information should be provided to USP as part of the established process to create USP monographs for active ingredient(s). This timeline should not in any way interfere with the OMOR review timeline. Once the USP monograph is established, sufficient time should be allotted for active ingredient suppliers to comply.

Line 388: Nonclinical reports should be expected and provided only as necessary for FDA to determine GRASE status. Full study reports will only likely be available from requestors if they conducted the studies. Data from published peer-reviewed literature should also be acceptable for the determination of GRASE status.

Line 423: FDA states that data from studies provided only in summary form will generally not be sufficiently informative to support a determination that the condition of use is GRASE. Data from the published peer-reviewed literature has always been considered acceptable for the determination of GRASE status. These reports will seldom, if ever, contain the level of detail expected for reports of nonclinical tests and clinical trials submitted in support of NDAs. FDA should thus not disregard data from the published literature simple because case level detail is not included nor should data from other, "older" studies be excluded due to their being performed according to standards of quality which have since been revised.

Line 447: The content of Module 5 should be agreed upon between FDA and the requestor at a pre-submission meeting. As in other cases, full reports may not be available for older ingredients. This should not prevent a GRASE determination. The description of requested data for Module 5 appears to go far beyond what is anticipated for most OMORs and reads like that required for an NDA submission. For example, what does FDA mean by use of the term "all" when referencing clinical studies, consumer studies and literature studies? What does FDA mean by postmarketing experience? These may be necessary for a GRASE determination, but for any other type of OMOR, it is confusing and unclear as to intent. When postmarketing data are required, FDA should clarify the parameters expected, such as years of data, US-only, etc. FDA should also state that they will search their own database, FAERS, for such information.

In conclusion, industry appreciates this guidance to enable the assembly of suitable and successful OMORs. We reiterate that FDA must adopt standards and expectations consistent with the intent of OMUFA, rather than the NDA paradigm, with which it is very familiar. The OMUFA innovation pathway will be successful when industry and FDA align on requirements for GRASE status of ingredients and data requirements for an OMOR submission.

Respectfully submitted,

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