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Over-the-Counter Monograph Reform in the CARES Act

March 27, 2020

Pharma and Biotech

On March 27, 2020, Congress passed H.R. 748, the **Coronavirus Aid, Relief, and Economic Security Act** (the "CARES Act"). Subtitle F of the CARES Act would significantly change FDA's regulations of over-the-counter (OTC) monograph drugs subject to OTC Drug Review. Congress had introduced earlier versions of the bill, with the latest bill, S. 2740 – Over-the-Counter Monograph Safety, Innovation, and Reform Act of 2019, introduced in October 2019. This client alert provides a summary of Subtitle F.

Part I – OTC Drug Review

A. Regulation of OTC Monograph Drugs

Section 3851 of the Cares Act would add section 505G to the Federal Food, Drug, and Cosmetic Act (FDCA). Section 505G would make several important changes to how FDA regulates drugs marketed under an OTC monograph. H.R. 748 makes clear that homeopathic drugs are excluded from OTC Drug Review, in accordance with paragraph 25 in 37 Fed. Reg. 9466.

A nonprescription drug that is not subject to a section 505 application and that does not comply with section 505G would be "misbranded." A drug would also be misbranded if it was "manufactured, prepared, propagated, compounded, or processed in a facility" that does not pay the user fees described in Part I of Subtitle F, if applicable.

Section 505G(a) of the FDCA Would Outline the Regulatory Status of Drugs Currently Marketed under the OTC Monograph System.

- Drugs Deemed GRASE: A drug that is in category I in a final monograph or a tentative final monograph (TFM) and that complies with the relevant monograph and general rules governing OTC drugs will be deemed to be generally recognized as safe and effective (GRASE) and exempt from the requirement for an approved new drug application (NDA). There are special provisions for sunscreen drugs, which will be GRASE if they comply with the applicable requirements of 21 C.F.R. Part 352, except that the requirements governing effectiveness and labeling will be those in 21 C.F.R. § 201.327.
- Drugs Permitted to Remain on the Market: Drugs that are in category III under a TFM or category I in an advance notice of proposed rulemaking (ANPRM) and that comply with applicable provisions of such monographs and the general provisions governing OTC

drugs will be permitted to remain on the market without approved NDAs unless and until FDA issues a final administrative order determining that they are not GRASE.

- Drugs to Be Removed from the Market: Drugs that are in category II in TFMs (or classified in category II in preambles to proposed regulations) must be removed from the market within 180 days of the enactment of the CARES Act unless FDA takes action to permit their continued marketing.
- New Drugs: Drugs that FDA has deemed not to be generally recognized as safe and effective, as well as non-prescription drugs not in the categories discussed above, unless exempt, will be deemed "new drugs" and subject to the requirement for an approved new drug application under section 505.

Administrative Orders Establish Requirements Relating to Active Ingredients and Conditions for Use for OTC Monograph Drugs.

The administrative order process would replace notice-and-comment rulemaking and would establish the conditions of use for OTC monograph drugs. There are three procedures for issuing administrative orders:

- FDA-Initiated Orders: Orders proposed by FDA under the ordinary procedure will entail public notice, opportunity for comment, a dispute resolution procedure, an opportunity for an administrative hearing, and an opportunity for judicial review. In certain circumstances, FDA will be permitted to deny a hearing.
- Expedited Orders: Expedited orders are permitted only when drugs are deemed to present an imminent hazard to public health or when FDA requires safety statements in labeling that "[are] reasonably expected to mitigate a significant or unreasonable risk of a serious adverse event associated with use of the drug." Expedited orders can be issued in final form by FDA before an opportunity for comment, dispute resolution, and a hearing.
- Industry-Initiated Orders: Industry-initiated proceedings will be based on submissions by sponsors seeking approval of new active ingredients, new dosage forms of existing acting ingredients, or other changes in currently marketed products. As with FDA-initiated orders, there would be an opportunity for public comment, dispute resolution, an administrative hearing, and judicial review. Sponsors could receive an 18-month period of market exclusivity for industry-initiated orders in certain circumstances (e.g., where an active ingredient has never previously been permitted in a monograph drug or where FDA approves a change in an existing monograph drug for which certain types of new human clinical data – as defined by the law – are essential to approval). Exclusivity would begin "following the effective date of such final order and beginning on the date the requestor may lawfully market such drugs pursuant to the order."

Procedure for Minor Changes for Drugs Under OTC Drug Review.

Subsection 505G(c) establishes a procedure under which minor changes in dosage forms could be implemented without approval of administrative orders, provided that manufacturers carried out specified studies, which would be available to FDA on request, and notify the Agency when changes are implemented. This procedure will only apply after FDA has adopted an administrative order establishing data requirements for a specific type of dosage form. As is true today, a manufacturer could continue to make small changes to a drug if those changes fall within the confines of the administrative order governing the drug.

Subsections 505G(d)-(q) Include Other Provisions to Implement Section 505G.

Subsection	Description
505G(d)	Section 505G(d) governs the confidentiality of information submitted to FDA. Proposed section 505G(d) reiterates that information will remain exempt from public disclosure by FDA under the Freedom of Information Act (FOIA) if it is a trade secret or confidential commercial information, unless the requestor consents to disclosure.
505G(e)	Section 505G(e) requires sponsors to submit updated drug listing information to FDA within 30 days after the date a drug is first commercially marketed, except a sponsor who is the requestor of an industry-initiated order should submit updated drug listing information on or before the date that the drug is first commercially marketed.
505G(f)	Section 505G(f) specifies that an OTC drug that is GRASE can be relied upon as part of a section 505(b)(2) application.
505G(g)	Section 505G(g) requires FDA to establish, maintain, update, and make publicly available administrative orders issued under this section, including a list of all FDA-initiated orders proposed and under development.
505G(h)	Section 505G(h) establishes procedures where sponsors or requestors may meet with FDA to support submissions under the section or discuss other matters relevant to the regulation of OTC monograph drugs.
505G(i)	Section 505G(i) requires FDA to establish procedures to allow multiple sponsors or requestors to participate in joint meetings with FDA.
505G(j)	Section 505G(j) mandates all submissions under the section be in electronic format.
505G(k)	Section 505G(k) makes implementing changes to FDA's regulations related to OTC monograph drugs.
505G(l)	Section 505G(l) specifies certain guidance documents that FDA will need to issue to implement the provisions of this section.
505G(m)	Section 505G(m) states that the section will not affect an OTC drug that is marketed without a section 505 application and does not fall within the first five categories under subsection (a). For example, drugs that are currently marketed under enforcement discretion would remain on the market under enforcement discretion after the enactment of this section.
505G(n)	Section 505G(n) states that a drug subject to an investigational new drug application (IND) is not subject to section 505G.
505G(o)	Section 505G(o) exempts information collected under this section from the requirements of the Paperwork Reduction Act.

505G(p)	Section 505G(p) states that the administrative order procedures outlined in this section will apply instead of the notice-and-comment rulemaking requirements in the Administrative Procedure Act (APA).
505G(q)	Section 505G(q) provides definitions for key terms used in section 505G.

B. Treatment of the Sunscreen Innovation Act (SIA)

Section 3854 of the CARES Act would sunset the SIA on September 30, 2022. Until then, a sponsor of a nonprescription sunscreen active ingredient that is the subject of a proposed sunscreen order may choose to continue review under the SIA provisions or may choose review under the new administrative order process for monograph drugs. If a sponsor chooses review under the administrative order process, the proposed sunscreen order will turn into a request for an administrative order that has been accepted for filing.

The section would also make changes to harmonize the procedures under the SIA with those under OTC Drug Review. A final sunscreen order will no longer be incorporated into the final sunscreen monograph. Instead, a final sunscreen order will automatically be deemed to be a final administrative order. Further, sponsors can request confidential meetings with respect to a proposed sunscreen order. A final sunscreen order will provide the requestor exclusivity for a period of 18 months, beginning on the date the requestor may lawfully market the sunscreen ingredient, if the sunscreen order permits a sunscreen active ingredient not previously marketed as a sunscreen monograph ingredient.

FDA must issue a proposed administrative order concerning nonprescription sunscreens no later than 18 months after the date of enactment of the Act. The final administrative order must be issued at least one year prior to the effective date of the order.

Part II – User Fees

The bill establishes a user fee system to fund activities related to OTC Drug Review. Section 3862 establishes two types of user fees.

Facility Fees	▪ Paid by entities that manufacture or process finished OTC drug products. ▪ Facility fees for FY 2021 will be due the later of July 1, 2020 or 45 days after FDA publishes the OTC monograph drug facility fees for FY 2021 in the Federal Register.
OTC Monograph Order Request Fees	▪ Paid by entities submitting industry-initiated administrative orders (except for certain changes in safety labeling). ▪ Two types of OTC Monograph Order Request Fees: ● Tier 1 – Any request that is not Tier 2. Will be $500,000, adjusted for inflation. ● Tier 2 – Request for certain, minor modifications of a monograph. Will be $100,000 adjusted for inflation.

	• Due on date of submission of an OTC monograph order request.

FDA has agreed to timeframes for reviewing and acting on industry-initiated submissions, response times for industry-requested meetings, and other administrative actions in a goals letter, the Over-the-Counter Monograph User Fee Program Performance Goals and Procedures –Fiscal Years 2018-2022.

If you have any questions concerning the material discussed in this client alert, please contact the following members of our Pharma and Biotech practice:

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