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Senate Bill 2388 Over the Counter Ivermectin
Senate Human Services Committee
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Madam Chair Lee, and members of the Senate Human Services Committee, for the record I am Mark Hardy, Executive Director of the North Dakota State Board of Pharmacy. I appreciate the opportunity to be here today to discuss Senate Bill 2388.

It appears the language of this bill is attempting to make the human formulation of the prescription product, Ivermectin, available as an over-the-counter drug instead of the current approval as a prescription drug. I've attached some documents related to the approval of over-the-counter items as well as the process for switching a prescription product to an over-the-counter product published by the Food and Drug Administration (FDA) for the committee's information.

Whether we like it or not, the process for drug approval is a responsibility reserved to the federal government, specifically the FDA, under federal law. I do not see a legal pathway where a state could change the designation of a prescription product like this bill attempts to do. Furthermore, the FDA approved manufacturers of the product would need to market the product with the appropriate labeling, which would need to be approved by the FDA, to sell products over the counter.

I hope this testimony provides some details that would be helpful in your decision making on SB 2388. I would be happy to answer any questions I can for the Committee.

Small Business Assistance: Frequently Asked Questions on the Regulatory Process of Over-the-Counter (OTC) Drugs

Introduction

1. What is an Over-the-Counter (OTC) Drug Product?

An OTC drug product is a drug product marketed for use by the consumer without the intervention of a health care professional in order to obtain the product. Two regulatory pathways exist for the legal marketing of such products:

- marketing in compliance with an OTC drug monograph
- marketing under the authority of an approved product-specific new drug application (NDA), abbreviated new drug application (ANDA), or biologics license application (BLA).

2. What is a prescription drug product?

A prescription drug product is a drug product approved for marketing that can only be obtained with a prescription from an appropriate health care practitioner.

3. What is an OTC monograph drug?

An OTC monograph drug is a nonprescription or OTC drug that may be marketed without an approved drug application under section 505 of the FD&C Act if it meets the requirements of section 505G of the FD&C Act, as well as other applicable requirements.

Drug Product Applications

4. What is a human drug application?

The term *human drug application* means an application for:

- approval of a new drug submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (/federal-food-drug-and-cosmetic-act-fdc-act) (FD&C Act)
- approval of a new drug submitted under section 505(b)(2) of the FD&C Act
- approval of an abbreviated new drug application under section 505(j) of the FD&C Act
- licensure of certain biological products under section 351 of the Public Health Service Act

5. What is a 505(b)(1) application?

A 505(b)(1) application is an application that contains full reports of investigations of safety and effectiveness.

The investigations the applicant relied on for approval were conducted by, or for the applicant, or the applicant has obtained a right of reference or use for the investigations.

6. What is a 505(b)(2) application?

A 505(b)(2) application is one described under section 505(b)(2) of the FD&C Act as an application for which one or more of the investigations relied upon by the applicant for approval "were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted" (21 U.S.C. 355(b)(2)). This provision permits FDA to rely on a previous finding of safety and effectiveness that led to approval of an NDA or on data not developed by the applicant such as published literature.

505(b)(2) applications are submitted under section 505(b) of the Act and are therefore subject to the same statutory provisions that govern 505(b)(1) applications that require among other things, "full reports" of safety and effectiveness.

7. What is an Abbreviated New Drug Application (505)(j)?

An abbreviated new drug application is described under section 505(j) of the Act as an application that contains information to show that the proposed product is identical in active ingredient, dosage form, strength, route of administration, labeling, quality, performance characteristics and intended use, among other things to a previously approved application (the reference listed drug (RLD)). ANDAs do not contain clinical studies as required in NDAs but are required to contain information establishing bioequivalence to the RLD. In general, the bioequivalence determination allows the ANDA to rely on the Agency's finding of safety and efficacy for the RLD.

8. What is a supplement to an approved application?

The Federal Food, Drug, and Cosmetic Act says, "The term *supplement* means a request to the Secretary to approve a change in a human drug application which has been approved." Each indication or claim is considered a separate change for which a separate supplement should be submitted. This policy allows FDA to approve each indication or claim when it is ready for approval rather than delaying approval until the last of a group of indications or claims is ready to be approved.

OTC Drug Product Monographs

9. What is an OTC monograph?

The OTC monographs represent regulatory standards for the marketing of non-prescription drug products not covered by new drug applications. These standards provide the marketing conditions for some OTC drug products including the active ingredients, labeling, and other general requirements.

10. The OTC drug monograph and the CARES Act

The On March 27, 2020, the Coronavirus Aid, Relief, and Economic Security Act (CARES Act; P.L. 116-136) was signed into law. The CARES Act added section 505G to the Federal Food, Drug and Cosmetic (FD&C) Act. Section 505G reforms and modernizes the framework for the regulation of OTC monograph drugs.

OTC monograph drugs may be marketed without an approved drug application under section 505 of the FD&C Act if they meet the requirements of section 505G of the FD&C Act, including the OTC drug monograph (OTC monograph) and other applicable requirements.

Under the process set forth in section 505G(b) of the FD&C Act, FDA has the authority to issue an administrative order (proposed and final) that adds, removes, or changes generally recognized as safe and effective (GRASE) conditions for an OTC drug monograph. Either FDA or a requestor can initiate the administrative order process.

11. Is pre-clearance necessary if the standards of the OTC monograph are met?

No. Marketing pre-clearance of OTC drug products by the FDA is not required if the standards of the applicable monograph are met. Additional requirements for the marketing of human drug products may be found in Title 21 of the *Code of Federal Regulations*.

12. Are there other options for marketing an OTC drug products besides the OTC monograph?

Yes. A new drug application, abbreviated new drug application, or biologics license applicationcan be submitted.

13. What is the appropriate process to request amendment or repeal of conditions covered by exiting OTC monographs?

A request to amend or repeal a condition or conditions in the OTC monograph can be performed by submission of an OTC monograph order request (OMOR).

The term "OTC monograph order request" (or OMOR) is defined in section 744L(7) of the FD&C Act and refers to a request for FDA to issue an administrative order under section 505G of the FD&C Act.

There are two types of OMORs: Tier 1 and Tier 2.

As described in section 744L(8) of the FD&C Act, a Tier 1 OMOR is any request not determined to be a Tier 2 OMOR.

Examples of Tier 1 OMORs include additions of:

- A new ingredient to a monograph that already has one or more ingredients that have been found to be GRASE.
- A new indication to a monograph that already has one or more ingredients that have been found to be GRASE, and the new indication applies to one or more of the GRASE ingredients.
- New monograph therapeutic category (each ingredient proposed for the new therapeutic category will be a separate OMOR).

As described in section 744L(9) of the FD&C Act, a Tier 2 OMOR is a request for:

- Reordering of existing information in the drug facts label of an OTC monograph drug;
- Addition of information to the "Other Information" section of the drug facts label of an OTC monograph drug (subject to certain limitations);
- Modification to the "Directions for Use" section of the drug facts label of an OTC monograph drug, consistent with a minor dosage form change;
- Standardization of the concentration or dose of a specific finalized ingredient within a particular finalized monograph;
- Change to ingredient nomenclature to align with nomenclature of a standards-setting organization; or
- Addition of an interchangeable term in accordance with section 330.1 of title 21, Code of Federal Regulations (or any successor regulations).

Based on program implementation experience or other factors found appropriate by FDA, FDA may also characterize any OMOR as a Tier 2 OMOR (including recharacterizing a request from Tier 1 to Tier 2) and publish such determination in a proposed order issued pursuant to section 505G of the FD&C Act.

Prescription to OTC Switch

14. What is prescription to OTC switch?

Prescription to OTC switch refers to over-the-counter marketing of a product that was once a prescription drug product, for the same dosage form, population, and route of administration.

15. How is a prescription to OTC switch accomplished?

An efficacy supplement should be submitted to an approved NDA for a prescription product if the sponsor plans to switch the drug product covered under the NDA to OTC marketing status in its entirety without a change in the previously approved conditions of use (e.g., indication, dosage form, route of administration, target population, etc.). An NDA should be submitted if the sponsor is proposing to convert some but not all of the approved prescription conditions of use to OTC marketing status. An original NDA needs to be submitted if the sponsor plans to market either a new product OTC whose active ingredient, indication, dosage form, etc. has never previously been marketed OTC.

Standardizing the OTC Labeling

16. What is standardizing OTC labeling?

In the *Federal Register* of March 17, 1999 (PDF - 1MB) (http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=1999_register&docid=fr17mr99-24.pdf), FDA published a final regulation (21 CFR 201.66 (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?FR=201.66)), establishing standardized content and format for the labeling of OTC drug products. Standardized labeling for OTC drug products is intended to make it easier for consumers to understand and use OTC drug products safely and effectively. The labeling regulations in 21 CFR 201.66 (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?FR=201.66) cover all OTC drug and drug-cosmetic products, whether marketed under a 505(b)(1) application, a 505(b)(2) application, abbreviated new drug application ,or an OTC drug monograph.

Professional Labeling

17. What is professional labeling?

Some OTC monographs contain professional labeling that provides specific information to health professionals for uses not included in OTC drug labeling.

18. What monographs contain professional labeling?

OTC drug monographs with professional labeling include those in the following drug categories:

- Antacid
- Antiflatulent
- Topical Antifungal
- Antiemetic
- Cough and cold
- Internal analgesics
- Ophthalmic
- Anticaries
- Anthelmintic
- Cholecystokinetic

Additional Information

19. Where can I find additional information about the Office of Nonprescription Drugs and nonprescription drug products?

Helpful Web Sites:

- Office of Nonprescription Drugs (/about-fda/about-center-drug-evaluation-and-research/division-nonprescription-drugs-dndp)
- OTC Monographs @ FDA (https://dps.fda.gov/omuf)
- Small Business Assistance (/cder-small-business-and-industry-assistance)
- Drug Application Approval Process (http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/default.htm)

20. Whom should I contact if I still have questions about the Office of Nonprescription Drugs and nonprescription drug products?

- Consumer Questions: Division of Drug Information at (301) 796-3400 or by email at druginfo@fda.hhs.gov (mailto:druginfo@fda.hhs.gov)
- Industry Questions: The Office of Nonprescription Drugs on the web (Office of Nonprescription Drugs (/about-fda/about-center-drug-evaluation-and-research/division-nonprescription-drugs-dndp))

Prescription-to-Nonprescription (Rx-to-OTC) Switches

A sponsor of a nonprescription drug product may seek to market a prescription drug product as nonprescription. A sponsor of a prescription drug product may initiate this change in marketing status through the NDA process. This change in the marketing status is commonly referred to as a Prescription-to-Nonprescription (RX-to-OTC) switch.

Types of Rx-to-OTC Switches

There are two types of Rx-to-OTC switches: full switch or partial switch.

1. Full switch: A sponsor switches the drug product covered under the NDA to nonprescription marketing status in its entirety. To initiate a full switch, a sponsor submits an efficacy supplement to an approved NDA or a 505(b)(2) application. After a full switch, the drug is only available as a nonprescription drug.
2. Partial switch: A sponsor partially switches some of the conditions of use (e.g. indications) to nonprescription marketing status, while retaining others within a prescription status. To initiate a partial switch, a sponsor submits a new NDA. After a partial switch, the drug is available as a prescription drug for certain conditions of use and a nonprescription drug for other conditions of use.

Data Supporting an Rx-to-OTC Switch

An application or efficacy supplement to an application for an Rx-to-OTC switch should contain both efficacy and safety data demonstrating that the drug product is safe to use in the nonprescription setting. Efficacy and safety data to support an Rx-to-OTC switch may include data from randomized, controlled clinical trials submitted in the original NDA for the prescription drug; and new randomized, controlled clinical trials. Additionally, the applicant must provide data that demonstrate consumers can understand how to use the drug safely and effectively without the supervision of a healthcare professional. The applicant must also provide post-marketing safety surveillance data.

Approval of an Rx-to-OTC Switch

FDA will approve an Rx-to-OTC switch application when FDA determines that the previous prescription status is "not necessary for the protection of the public health by reason of the drug's toxicity or other potentiality for harmful effect, or the method of its use, or the collateral measures necessary to its use, and . . . the drug is safe and effective for use in self-medication as directed in proposed labeling." See 21 CFR 310.200(b).

Additional Information

- New Drug Application (NDA) (/drugs/types-applications/new-drug-application-nda)
- Abbreviated New Drug Application (ANDA) (/drugs/types-applications/abbreviated-new-drug-application-anda)
- FAQs on the Regulatory Process of Over-the-Counter (OTC) Drugs (/drugs/cder-small-business-industry-assistance-sbia/small-business-assistance-frequently-asked-questions-regulatory-process-over-counter-otc-drugs)
- Label Comprehension Studies for Nonprescription Drug Products (/media/75626/download?attachment) guidance document
- Self-Selection Studies for Nonprescription Drug Products (/media/81141/download) guidance document
- Prescription to Over-the-Counter (OTC) Switch List (/about-fda/center-drug-evaluation-and-research-cder/prescription-nonprescription-switch-list)