CARES ACT: OTC PATHWAY FOR NOVEL DRUG DOSAGE FORM TECHNOLOGIES

Ann Begley
Rebecca Dandeker
May 28, 2020

Before we begin…

- If you are experiencing technical difficulties, please contact WebEx Tech Support at +1.866.779.3239.
- The Q&A tab is located near the bottom right hand side of your screen; choose "All Panelists" before clicking "Send."
- We will mention a code at some point during the presentation for attendees who requested CLE. Please make note of that code, and insert it in the pop-up survey that will appear in a new browser tab after you exit out of this webinar. You will receive a Certificate of Attendance from our CLE team in approximately 30 to 45 days.
- The audio will remain quiet until we begin at 2:00.
- You will hear sound through your computer speakers/headphones automatically. Make sure your speakers are ON and UNMUTED.
- If you would prefer to access the audio for today's presentation by telephone, please click the "phone" icon below your name on the Participants Panel for teleconference information.

Morgan Lewis and Global Technology

Be sure to follow us at our website and on social media:

Web: **www.morganlewis.com/sectors/technology**

Twitter: **@MLGlobalTech**

LinkedIn Group: **ML Global Tech**

Check back to our Technology May-rathon page frequently for updates and events covering the following timely topics:

21st Century Workplace	**Cybersecurity, Privacy and Big Data**	**Medtech, Digital Health and Science**
Artificial Intelligence and Automation	**Fintech**	**Mobile Tech**
COVID-19	**Global Commerce**	**Regulating Tech**

CLE Credit Information

For ALL attorneys seeking CLE credit for attending this webinar, please write down the following alphanumeric code:

MYHT881

Kindly insert this code in the **pop-up survey** that will appear in a new browser tab after you exit out of this webinar.

Morgan Lewis Coronavirus/COVID-19 Resources

We have formed a multidisciplinary **Coronavirus/COVID-19 Task Force** to help guide clients through the broad scope of legal issues brought on by this public health challenge.

To help keep you on top of developments as they unfold, we also have launched a resource page on our website at

www.morganlewis.com/topics/coronavirus-covid-19

If you would like to receive a daily digest of all new updates to the page, please visit the resource page to subscribe using the purple "Stay Up to Date" button.

Presentation Topics

1. How the CARES Act changed the OTC Drug Monograph Review Process

2. Administrative Order process for drugs created by the CARES Act

3. Opportunities and pathways for development of novel technologies, including new OTC drug dosage forms

4. COVID-19 Connection

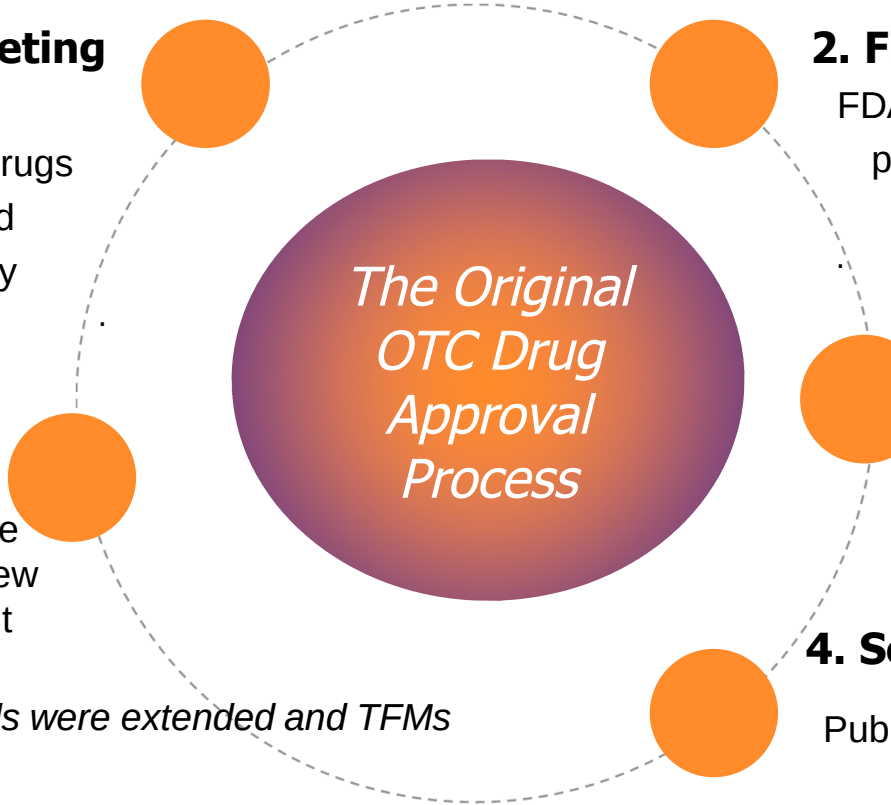
SECTION 01

HOW THE CARES ACT CHANGED THE OTC DRUG MONOGRAPH REVIEW PROCESS

Just How Significant is the New Administrative Order Process?

- Prior OTC Drug Monograph Process: Drugs can be marketed without FDA approval, if they meet the conditions of an OTC Monograph
- Active Ingredients and strengths were specified
  - Divided into 26 therapeutic categories (*e.g.*, antihistamines, laxatives, sunscreens)
  - Subcategories within each category
  - *E.g.*, within Oral Healthcare: toothache relief, antigingivitis/antiplaque
- Routes of Administration were specified (e.g., Cough-Cold: oral; Acne: topical)
- Dosage Forms were usually unspecified
  - E.g., Oral = tablet, capsule, liquid, lozenge; Topical = lotion, cream, ointment
  - FDA refers to being in the US market on or before inception of OTC Drug Review (1972)
- Categorized for legal authority to be marketed
  - Cat I – GRASE (Generally recognized as safe and effective); Cat II – not GRASE; Cat III – insufficient data available to determine if safe and effective

Just How Significant is the New Administrative Order Process? (Contd.)



1. Review Panel Meeting

Panel meets to categorize OTC drugs based on type and safety and efficacy

2. First Comment Period

FDA issues ANPRM; Opens period for public comment and FDA Review

3. Temporary Rule

FDA issues proposed rule (TFM) based on review and public comment

4. Second Comment Period

Public Comment Period and FDA Review

5. Final Rule

FDA issues final rule (FM) based on review and public comment

Often the comment periods were extended and TFMs were amended . . .

Now, FDA can allow changes to OTC monograph drugs by issuing administrative orders . . .

Process

- *FDA issues administrative order at FDA's own initiative or at the request of industry*
- *No full Notice and Comment rulemaking*

Intended Implications

- *Less time, money, and resources are required to make changes to OTC monograph drugs →*
- *OTC monograph drugs marketed faster*

But is the Administrative Order Process Actually Faster?

The CARES Act Reforms the OTC Monograph System in Several Other Key Ways . . .

Exclusivity Period

User Fees

Regulatory Status Impact

Exclusivity Period

PRE-CARES ACT

- No market exclusivity for OTC Monograph drugs

CARES ACT

- Possible 18-month period of exclusivity for:
  - New active ingredients
  - Changes in conditions for use, when new human data studies were essential to the issuance of the Order
- No exclusivity for Tier 2 changes, safety updates, safety/efficacy testing methods, minor changes (such as the reordering of existing information)

User Fee Program

PRE-CARES ACT

- User fees not required to market OTC Monograph products

CARES ACT

- OTC industry required to pay annual facility fees and one-time user fee for OMORs, beginning fiscal year 2021
- Will fund FDA's continued review of OTC drug ingredients
- Consequences for failure to pay fees: public listing; OMOR considered incomplete; ineligible for closed meetings; product is misbranded

Regulatory Status Impact: Changes to Monograph Categories

Category I	Category II	Category III	OTC drugs on the market that do not fall within the Categories or are not subject to an Administrative Order
Considered GRASE and not a "new drug," so long as all applicable conditions are met.	Automatically deemed a new drug.	Allowed to continue marketing pending further FDA Order in accord with the Act (assuming compliance with Act provisions)	Deemed a "new drug" subject to FDA's new drug approval process Considered misbranded and subject to enforcement if marketed.

How does the CARES Act Administrative Order provision affect pending monographs?

Existing Monographs	Tentative Final Monographs (TFM)	TFM Ingredients with more data needed ("Category III")	Ingredients in a most-recent ANPR	Ingredients found not GRASE in a TFM or ANPR	Sunscreen Monograph
Converted to Administrative Orders	Considered final Administrative Orders	Remain pending	Cat. I remain pending Cat. III treated as unapproved new drugs	Have 6 months from enactment before they are unapproved new drugs	Reverts to stayed 1999 final monograph + 2011 testing and labeling rule

SECTION 02

ADMINISTRATIVE ORDER PROCESS FOR OTC MONOGRAPH DRUGS

A Pathway for a Streamlined Approach For Introducing Innovations in the Marketing of Over the Counter Drugs

Administrative Order Application and Review Process

The CARES act outlines two methods for the Administrative Order Process:

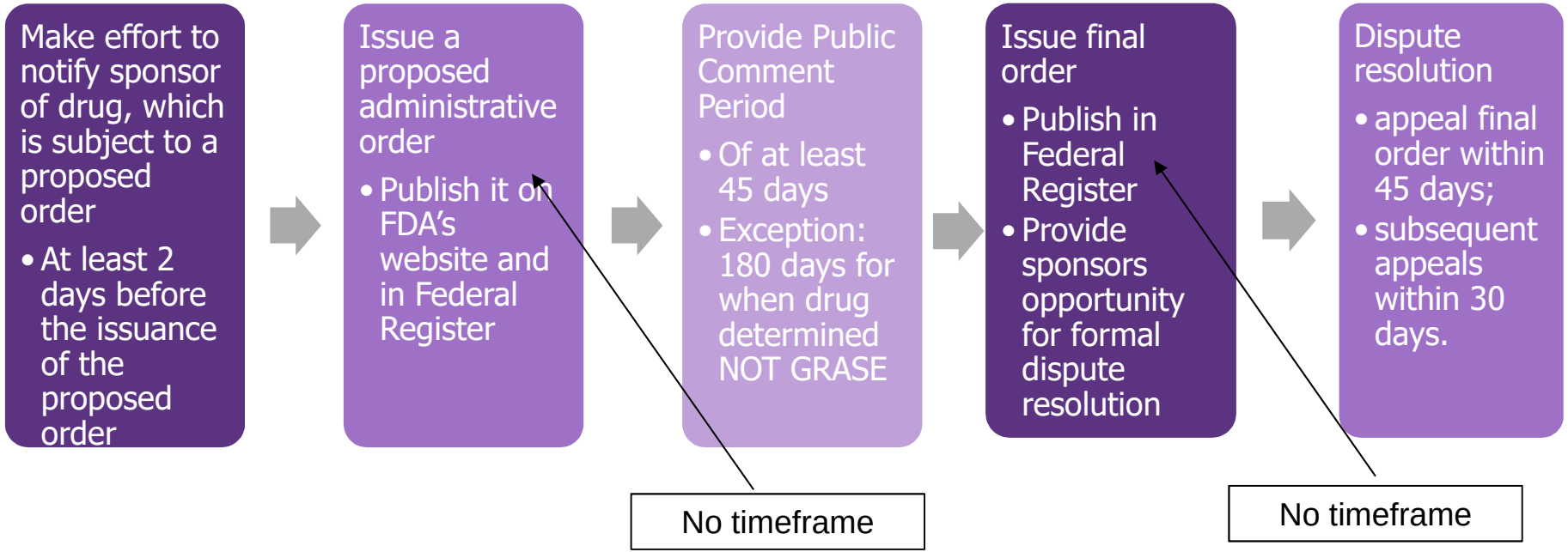
1. FDA-initiated

2. Requestor-initiated (also called OTC Monograph Order Request or "OMOR")

There are many unanswered questions on how this process will be implemented, but FDA's 2017 document, ***OTC Monograph User Fee Program Performance Goals and Procedures- 2018-2022***, gives us clues on what to expect.

FDA-Initiated Administrative Order Process

Upon FDA's decision to initiate an administrative order, FDA shall:



FDA-Initiated Administrative Order Process (Contd.)

And the Administrative Order process continues . . .

Hearings; Judicial Review

Requesting a Hearing

- *Only* sponsors/requestors who participated in final stage of dispute resolution may request a hearing, and must do so within 30 days of receiving final notice of dispute resolution decision
- FDA may deny hearing for sponsors who did not submit human or non-human data studies relevant to their drug's safety or effectiveness

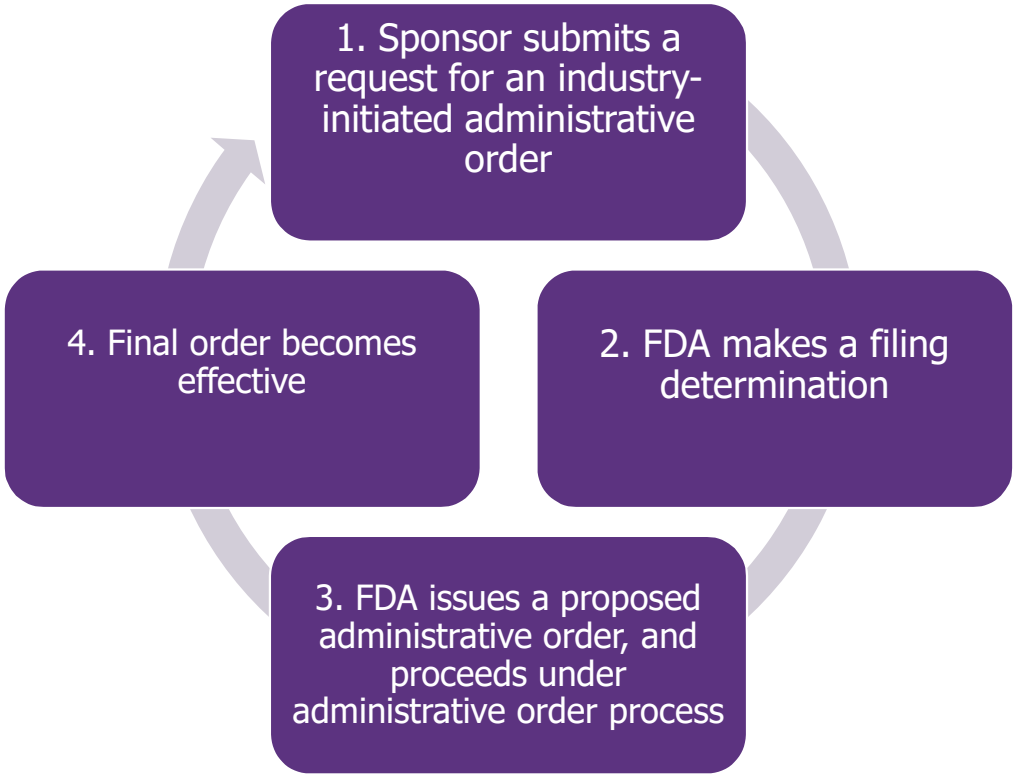
Final Decision

- Decision is final, but does not take effect until period for submitting a request for judicial review of decision expires

Judicial Review

- File within appropriate U.S. district court
- Within 60 days of final order; hearing denial; or hearing decision rendered (whichever is later)

OMAR Submission Process



Requestor-Initiated Administrative Order Process: *OTC Monograph Order Request (OMOR)*

Upon receiving a requestor's administrative order request, FDA shall determine whether the request is sufficiently complete:

Sufficient→ FDA files request and initiates order

↓

Proceeds with administrative order process as if FDA-initiated (*i.e.*, timeframes for comment period and appeals; dispute resolution; judicial hearing process)

Insufficient → requestor may demand request be filed and FDA shall initiate review proceedings

↓

Review Proceedings – A requestor may request issuance of administrative order determining:

↓

Whether a drug or change to a condition of use of a drug is GRASE

<u>Other Possible Outcomes:</u>

- Requestor withdraws request
- Secretary denies request for review due to inadequate basis for GRASE determination

Key Takeaway

Process is in Place

- But without specific timeframes to issue proposed and final orders, dispute resolution, judicial hearings

Efficiency & Timing is Unclear

- Hard to say whether Administrative Order process will be a "faster" way for new OTC drugs to get to market

Much is dependent on FDA's willingness and priorities – To Be Determined.

Is the new process actually faster?: Comparing the OMOR Process to the TEA and NDA Processes

OMOR	Time and Extent Application (TEA)	New Drug Application (NDA)
• Requestor submits OMOR • FDA makes a filing determination (**no definitive timeline**) • FDA issues a proposed administrative order (**no definitive timeline**) • FDA proceeds under administrative order process • Before final order becomes effective, there is a public comment period, as well as opportunity for dispute resolution and judicial hearing proceedings	• Must meet eligibility requirement – must market sufficient quantity of product for five continuous years. • Must demonstrate product is GRASE – involves same process as old OTC monograph system	• Pre-clinical Lab Tests • File Investigational New Drug (IND) with FDA's CDER • Significant clinical trials (animal then human testing), demonstrating safety and efficacy • File NDA with CDER for approval (10 month review period)

Timeframe of OMOR process under Goals letter and CARES Act

	Performance Goals Document	CARES Act
Time to decide to file OMOR	60 days	No timeframe provided
Time to issue proposed order	12 months to issue proposed order for Tier 1 (10 months for Tier 2)	No timeframe provided
Length of Comment Period	• 45-day comment period, which can be extended	• 45-day comment period (generally) that cannot be extended
Assessment of volume and substance of comments	• Begins one calendar day after the end of the comment period, and lasts 60 calendar days.	No timeframe provided
Issuance of final order	• 17.5 months after receipt of OMOR for Tier 1 (15.5 months for Tier 2)	• No timeframe provided

Note:
Both provide opportunity for dispute resolution and hearing proceedings and describe timeframes

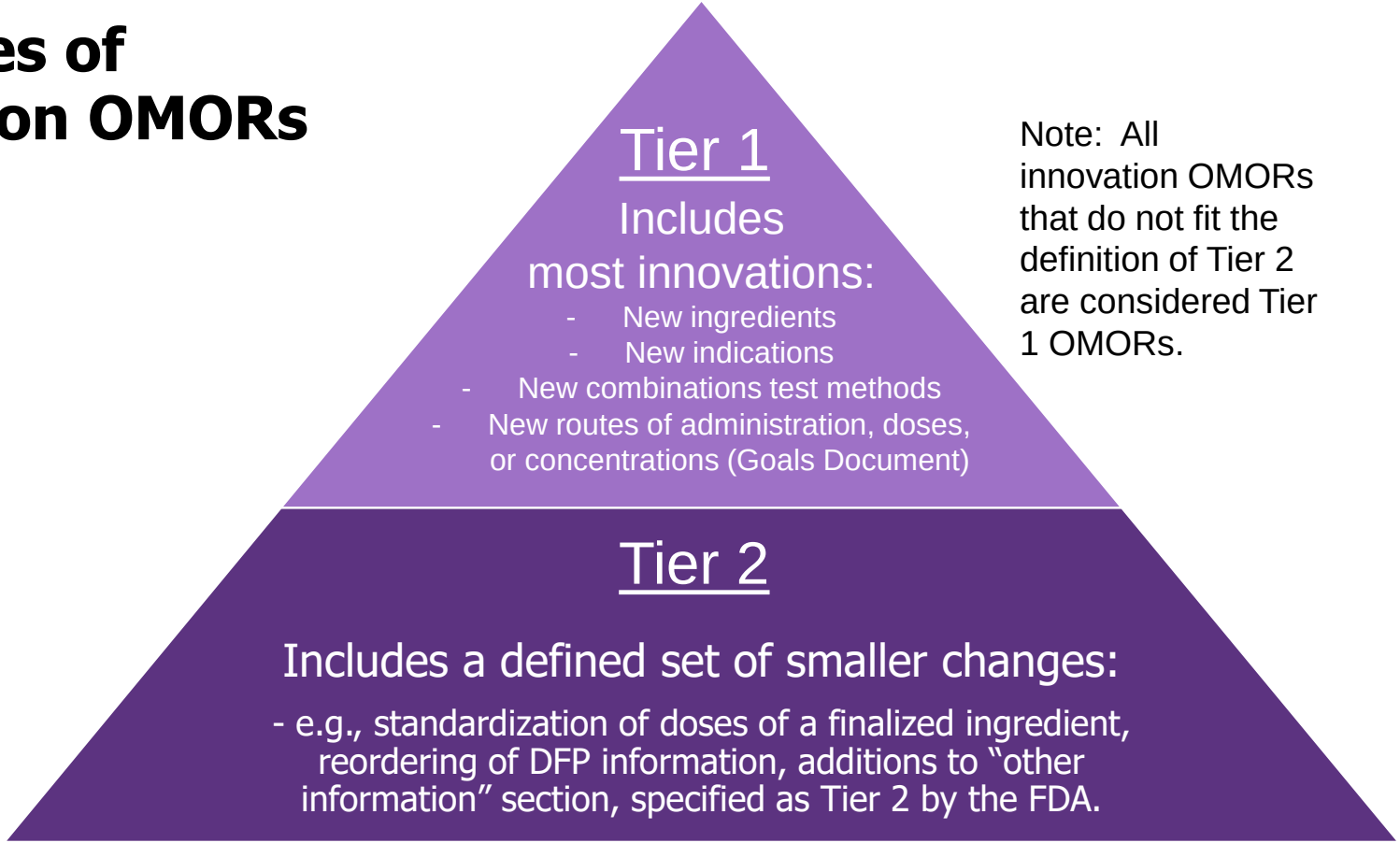
Information Required for GRASE Determination by Administrative Order - TBD

The CARES Act does not explicitly describe the content and format requirements for an OMOR

- Directs FDA to issue guidance on this topic

- FDA's **Performance Goals Document** recommends that requestors follow the FDA Guidance, *Nonprescription Sunscreen Drug Products – Format and Content of Data Submissions (2016),* in the interim.
  - Common Technical Document (CTD) format
  - Nonclinical and Clinical study reports, data and published studies
  - Quality data, relevant chemistry and manufacturing information

Two types of Innovation OMORs



Note: All innovation OMORs that do not fit the definition of Tier 2 are considered Tier 1 OMORs.

Pathways for New Ingredients *Without* Clinical Data
Safe Nonprescription Marketing and Use

FDA can accept OMORs for new active ingredients if it:

- ✓ Has a verifiable history of being marketed, and safely used, by consumers in the United States as a nonprescription drug under comparable conditions of use; or
- ✓ Was marketed, and safely used, under comparable conditions of marketing and use in a "listed country" or another country designated by the Secretary and
  - ✓ for a period of time necessary to provide assurance of safe use as a nonprescription drug
  - ✓ subject to adequate monitoring by a regulatory body deemed acceptable, including adverse event monitoring

Minor Changes: Guidance for Development Innovation (Minor Dosage Form Changes)

Goals Letter

- It *may be possible* for a "few types" of changes, including minor dosage form changes, to be accomplished without going through the OMOR Process
- By April 1, 2022, FDA will issue a proposed administrative order and draft guidance clarifying which types of minor changes to solid oral dosage forms might be possible without an OMOR (an "order/guidance pair")

CARES Act

- Minor dosage form changes *can be* made without the issuance of an order if consistent with an FDA order that sets forth the conditions under which a dosage form change:
  1. Will not affect the safety or effectiveness of the drug; and
  2. Will not materially affect the extent of absorption or other exposure to the active ingredient.

Does the Administrative Order Process under the CARES Act Protect Confidentiality of Data?

Generally, FDA must publicly release the requestor information no later than at the time the proposed order is issued, but there are limitations:

Limitations on Public Availability – Information will be not be publicized when:			
It pertains to pharmaceutical quality, unless such information is necessary for GRASE determination	The submitter withdraws the request	Information submitted in connection with a minor change not subject to the OMOR requirement	Raw Data Sets

Performance Goals Document: Building Necessary Infrastructure

- Extensive hiring over 5 years (2018-2022)
- Robust Training and Growth Program
  - Begin teaching scientific review skills right after onboarding, but take at least two years to develop
  - Increase reviewer work as skills develop
- Leadership Development
- Develop IT platform
- Develop nonbinding list of forecasted monograph activities
- User fee collection system

Note: At the time FDA published this letter, it believed it would be "net-negative" in terms of review capacity; expects to complete all goals by FY 4 and 5 (2021 and 2022)

SECTION 03

OPPORTUNITIES AND PATHWAYS FOR INTRODUCING NOVEL TECHNOLOGIES, INCLUDING NEW OTC DRUG DOSAGE FORMS

OTC Monograph Order Request (OMOR)

- A requestor can submit an OMOR to:
  - Add a New ingredient
  - Add a New indication for existing ingredient
  - Add a New combination of existing ingredients
  - Finalize a Category III TFM/ Category I ANPR ingredient if FDA does not initiate
  - Add a Novel dosage form?*

*It seems that if the dosage form is not a "minor change", it may be subject to the NDA process under 505G(c)(2)(C).
Yet, all non-Tier 2 conditions of use are automatically Tier 1 innovations, eligible for OMOR.

Novel/New Dosage Forms – What Are They?

Not Defined in the CARES Act

Dosage forms that have been marketed in the last 20 years, and have been, or may have been, considered novel by FDA:

- *e.g.*, oral beads, oral films, Analgesic Patches

New forms that may be acceptable as a minor dosage form change

- Continued consumer focus – improving taste and convenience
  - *e.g.*, gummies, fast dissolving tablets, non-spill liquids

Future: nano-droplets, buccal troche, oral inhalation?

Possible Dosage Form Pathways

- Included in OTC Monograph Orders
  - Dosage Forms that existed for "a material time and a material extent" at the time of enactment (March 2020)
    - No longer directly tied to 1972 inception of OTC Drug Review
- Minor Change
  - Will not affect safety, effectiveness or absorption of ingredient
- OMOR
  - Is FDA's Guidance needed first? How much data will support it?
- NDA
  - How novel is too novel?
  - This has always been FDA's "default" when supporting scientific data is needed

2 Steps for Minor Dosage Form Changes to Ingredients Subject to Final Administrative Orders

1. To market a new dosage form without FDA approval, Manufactures must:	Show change will not affect safety, effectiveness of the drug, and	Will not materially affect absorption of, or exposure to, the active ingredient; and
2. FDA must issue:	Administrative order specifying requirements for determining minor dosage form changes in comparison to suitable reference product	Guidances will consider public standards and standard practices for evaluating quality of drugs.
Manufacturers may also:	Continue to make changes that fall within an administrative or monograph separate from the minor dosage form process.	

SECTION 4

COVID-19 CONNECTION

Congressional Recognition of OTC Drug Treatment of COVID-19 symptoms

Some congressional leaders suggest that OTC drug monograph reform could be a necessary medical medium for treating COVID-19 symptoms, hence the addition to the CARES Act

Congressman Latta stated in a press release :

"*The CARES Act also includes a bill that I've long championed that will make it easier for Americans to protect themselves against COVID-19 by reforming and modernizing the way over-the-counter (OTC) products are approved by the U.S. Food and Drug Administration (FDA).*

Enforcement – Warning letters

FDA and FTC have issued several warning letters for product claims related to preventing, treating, and curing COVID-19, *i.e.*,

"HEPA air purifier . . . can greatly help to reduce the spread AND capture the Covid virus in your home or workplace"

"Chinese Medicine is a Highly Beneficial Treatment for COVID-19"

"Vitamin C, is not only a broad antiviral, but it is also an anti-oxidant, so it will reduce the effect a virus like Coronavirus can have on your body"

Warning Letter

The CARES Act has not changed FDA's authority for issuing warning letters for products marketed outside of Monograph conditions.

However, under the CARES Act, OTC drugs classified as category III in a TFM can be marketed without approval, if they meet the requirements set forth in the Act

Recently, FDA issued a warning letter to a hand sanitizer seller because its category III product did not meet the statutory requirements in the CARES Act

(The warning letter based its justification on the specific language of the CARES Act)

FDA Statement: The OTC product does "not meet the conditions under section 505G(a)(3) of the FD&C Act, as added by the CARES Act, for marketing without an approved application under section 505"

Enforcement - Protecting Against Price Gouging During COVID-19

Businesses selling disinfectants and other products that might be considered essential to the fight against COVID-19 should expect to face pricing scrutiny

- Federal and State Governments demonstrate intolerance for price gouging
  - **FTC Commissioner:** *"FTC will not tolerate businesses seeking to take advantage of consumers' concerns and fears regarding coronavirus disease, exigent circumstances, or financial distress."*
  - **Congress:** introduced *The Price Gouging Act*, which bans price-gouging practices that have led sellers to jack up the prices on items such as masks and **hand sanitizer** during the COVID-19 outbreak.

    Senator Warren: *"We can't let American families … be squeezed even further by companies out to make a quick buck."*
  - **NY State Bill:** *"The price gouging threshold outlined in the bill would apply to a variety of consumer medical items, such as **hand sanitizer, rubbing alcohol, tissues, antibiotic ointment and over-the-counter medications**."*

Presentation Takeaways

- The goal of the Administrative Order process under the CARES Act is to streamline the OTC drug marketing process, but . . .
  - It still involves a multistep process; and
  - It will probably only be as fast as FDA believes it has capacity to move
- There are many unknowns – Until FDA issues guidances, questions will remain unanswered
  - However, based on FDA's statements in its Goals letter, it seems that FDA expects to release guidances in the next couple of years
  - How much of Goals letter will FDA keep?
- Scope of Minor Dosage Form change unclear until FDA guidance issues
  - OMOR availability is an open question
  - Default: NDA

Biography

Rebecca Dandeker

Washington, DC
Phone
+1.202.739.5614
Fax
+1.202.739.3001

Rebecca Dandeker represents clients in matters involving products regulated by the US Food and Drug Administration (FDA), including prescription and nonprescription pharmaceuticals, dietary supplements, cosmetics, and alternative therapies. Rebecca advises on diverse regulatory, policy, and compliance issues pertaining to pharmaceuticals, including preapproval pathways for innovators and generics, clinical studies, Hatch-Waxman issues, Drug Efficacy Study Implementation (DESI) drugs, over-the-counter (OTC) monograph drugs, homeopathics, Rx-to-OTC switches, and postapproval compliance. Her clients range from manufacturers, distributors, and pharmacies to healthcare providers, clinical investigators, and entrepreneurs.

Biography

Ann Begley
Washington, D.C.
Phone
+1.202.739.5613
Fax
+1.202.739.3001

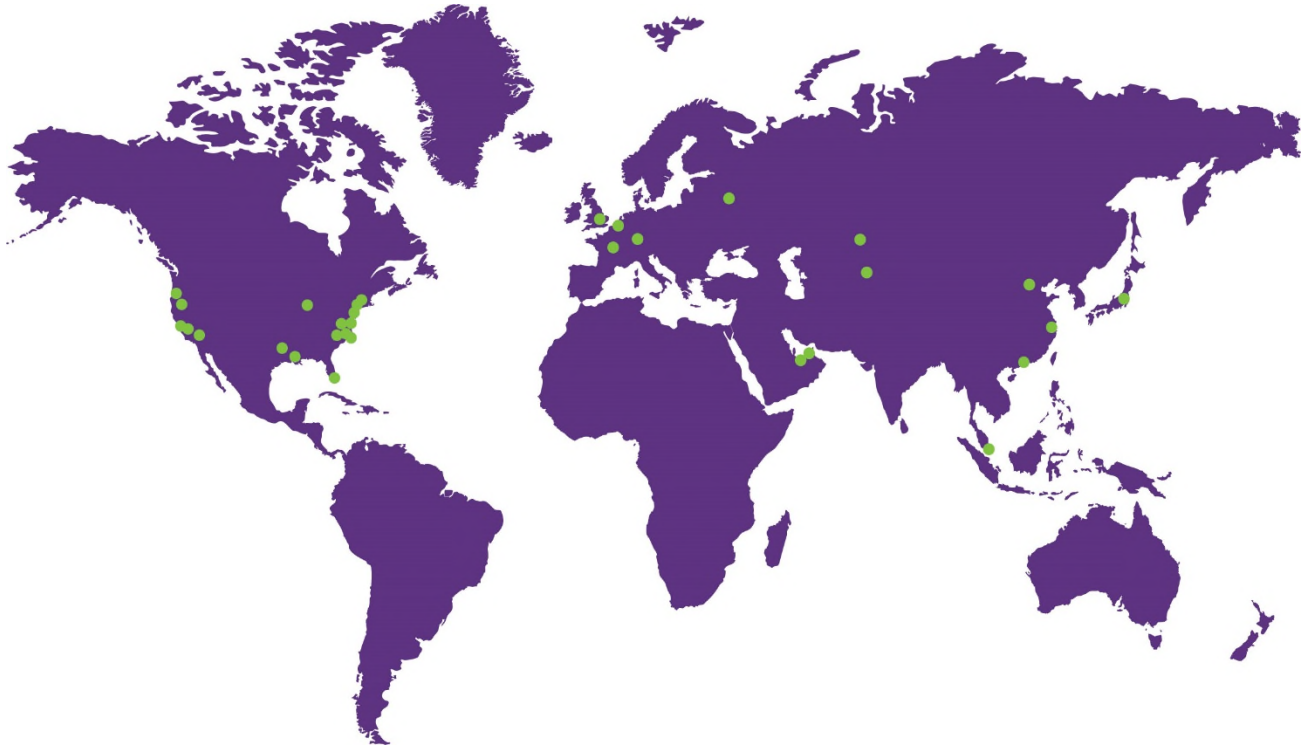
Ann M. Begley advises clients on a range of US Food and Drug Administration (FDA) legal and regulatory issues relating to drug, cosmetic, dietary supplement, food, and medical device products, with an emphasis on matters involving clinical practice and over-the-counter (OTC) drugs. Ann counsels institutional review boards, clinical investigators, and sponsors on compliance and strategic issues. She also provides extensive guidance on product approval pathways, formulation, labeling, and product advertising.

Our Global Reach

Africa
Asia Pacific
Europe
Latin America
Middle East
North America

Our Locations

Abu Dhabi
Almaty
Beijing*
Boston
Brussels
Century City
Chicago
Dallas
Dubai
Frankfurt
Hartford
Hong Kong*
Houston
London
Los Angeles
Miami
Moscow
New York
Nur-Sultan
Orange County
Paris
Philadelphia
Pittsburgh
Princeton
San Francisco
Shanghai*
Silicon Valley
Singapore*
Tokyo
Washington, DC
Wilmington



Morgan Lewis

*Our Beijing and Shanghai offices operate as representative offices of Morgan, Lewis & Bockius LLP. In Hong Kong, Morgan Lewis operates through Morgan, Lewis & Bockius, which is a separate Hong Kong general partnership registered with The Law Society of Hong Kong as a registered foreign law firm operating in Association with Luk & Partners. Morgan Lewis Stamford LLC is a Singapore law corporation affiliated with Morgan, Lewis & Bockius LLP.

THANK YOU