

# OTC Products

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# Presentation Outline

- NDAs
- OTC Drug Monographs
- NDA vs. Monographs Comparison
- For More Information
- Q&A

# REGULATORY SYSTEMS

- Two Regulatory Systems
  - New Drug Application (NDA)
  - OTC Drug Monograph
- Rx to OTC Switch Lifecycle



# Marketing under an NDA

# MARKETING UNDER AN NDA

- Requires a pre-approved application
  - May require clinical studies
  - May require a user fee under PDUFA
  - Post-approval NDA maintenance
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- Individual license to market
- May provide marketing exclusivity
- Mandated FDA review timeline

# NDA DEVELOPMENT PROCESS

- An IND (Investigational New Drug) for trials in human subjects
- Typical “milestone” development meetings with FDA
  - Pre-IND
  - End of Phase 2
  - Pre-NDA

# NDA REFERENCES

- For the pre-IND Meeting:  
Guidance entitled “Formal Meetings With Sponsors and Applicants for PDUFA Products”
- For the NDA review process:  
Guidance entitled “Good Review Management Principles for PDUFA Products”
- For IND requirements: 21 CFR 312
- For NDA requirements: 21 CFR 314

# Marketing under an OTC Drug Monograph



# WHY WERE MONOGRAPHS CREATED?

- 1962 Amendments to FD&CA
- Drug Efficacy Study Implementation (DESI)
- 420 drugs of low toxicity deferred
- Developed monographs by therapeutic class (rather than individual product review) for efficiency

# What are OTC Drug Monographs?

- Requires Conditions that are Generally Recognized As Safe and Effective (GRASE)
- Limited routine chemistry, manufacturing and controls (CMC) review
- NDA regulations (Part 314) do not apply

# MONOGRAPH REQUIREMENTS

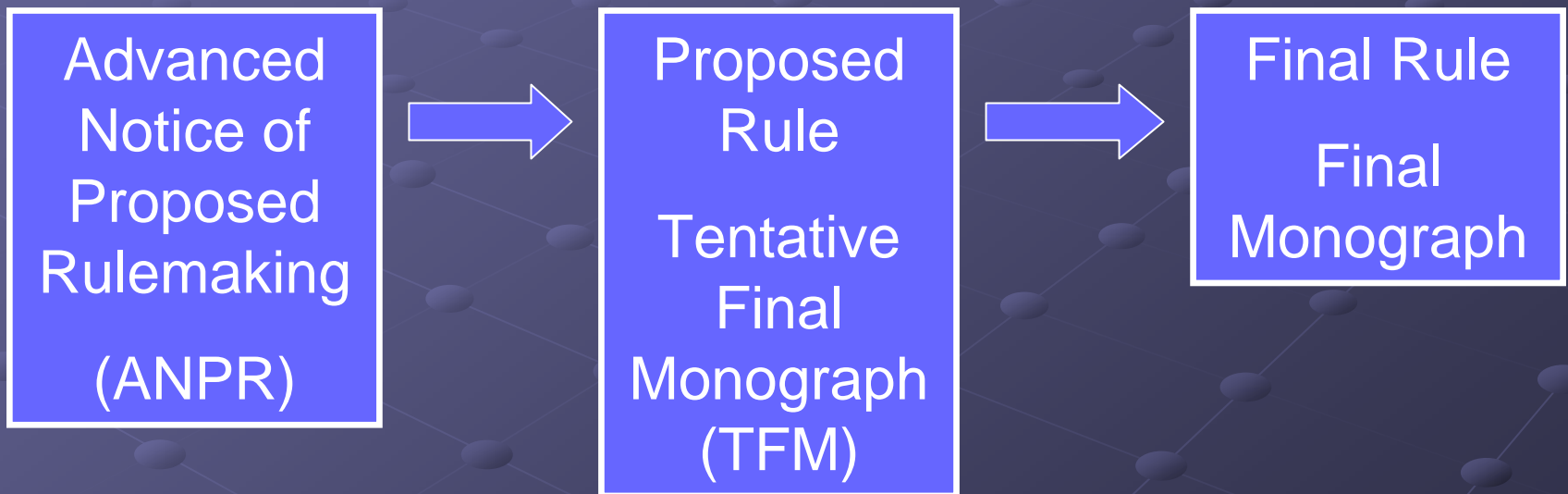
- Active Ingredients
- Dosage Forms
- Dose or Concentration
- Required Labeling
- Packaging and/or Testing Requirements  
(in some cases)

# LABELING REQUIREMENTS

- Uses
- Warnings
- Directions
- Professional Labeling  
(healthcare provider instruction)

# How is a Monograph Established?

- See 21 CFR 330
- Three Step Rulemaking Process



# What is the process to establish a monograph?



## Advisory Review Panel



- Category I: GRASE
- Category II: not GRASE
- Category III: cannot determine if safe and effective; more data needed

# What is the process to establish a monograph?

- Category I: GRASE
- Category II: GRASE
- Category III: GRASE determined





# What is the process to establish a monograph?

## Comments





# What is the process to establish a monograph?

## Comments



## Data



# HOW TO MODIFY ACTIVE INGREDIENTS CONSIDERED UNDER MONOGRAPHS

- Citizen Petition, IF
  - ❖ Product was marketed prior to 1975
- Time and Extent Application (TEA) under 21 CFR 330.14, IF
  - ❖ Product marketed OTC outside of U.S.
  - ❖ Product marketed OTC inside U.S. after 1975
- Both are preliminary to a Proposed Rule

# NDA vs. Monographs

# How are NDAs and Monographs Different?

## NDA

Pre-approval Required

Clinical studies and user fees may be necessary

Review process is proprietary

Approved labeling is unique to your drug

Possible marketing exclusivity

Approved NDA is your license to market

## Monograph

Pre-approval Not Required

Clinical studies may not be necessary and no user fees

Notice and comment process is public

Labeling is the same for all similar drugs

No marketing exclusivity

Final monograph is open to anyone

# How are NDAs and Monographs the Same?

- Standards for safety and efficacy
- Manufacturing and GMP inspections
- Labeling under 21 CFR 201.66
- Advertising regulation

# Ensuring Safety and Efficacy without a Prescription

- Patient safety in an unsupervised setting
  - \* Self-diagnose?
  - \* Self-manage?
  - \* Self-help?
- Label Comprehension Studies
- Actual Use Studies
- U.S. and worldwide adverse event data

# OTC Drug Labeling

## ● “Drug Facts” format

- \* Standard format for labeling of OTC drugs that consumers become accustomed to
- \* “Nutrition Facts” for foods and “Supplement Facts” for dietary supplements

## ● 21 CFR 201.66

## ● Final Rule: 64 FR 13254 (March 17, 1999)



# OTC Drug Advertising

- Federal Trade Commission regulates advertising
- FDA regulates labeling

## FD&CA definition (201.m)

Includes all labels, as well as other written, printed, or graphic matter accompanying the product



# For More Information

## ● Visit the ONP web site

- <http://www.fda.gov/cder/Offices/OTC/default.htm>
- How do the NDA and OTC monograph processes work?
- What NDAs are approved containing the active ingredient of interest?
- What monograph documents pertain to this active ingredient?
- Is this active ingredient a drug or cosmetic?
- What inactive ingredients are allowable?

# For More Information

## ● Call or Email ONP

- Main number 301-796-2060
- For NDAs, contact Leah Christl  
[leah.christl@fda.hhs.gov](mailto:leah.christl@fda.hhs.gov)
- For Monographs, contact Walter Ellenberg  
[walter.ellenberg@fda.hhs.gov](mailto:walter.ellenberg@fda.hhs.gov)
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