Utilizing the OTC Regulatory Process for Marketing OTC Drugs

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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
- General OTC 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

- 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

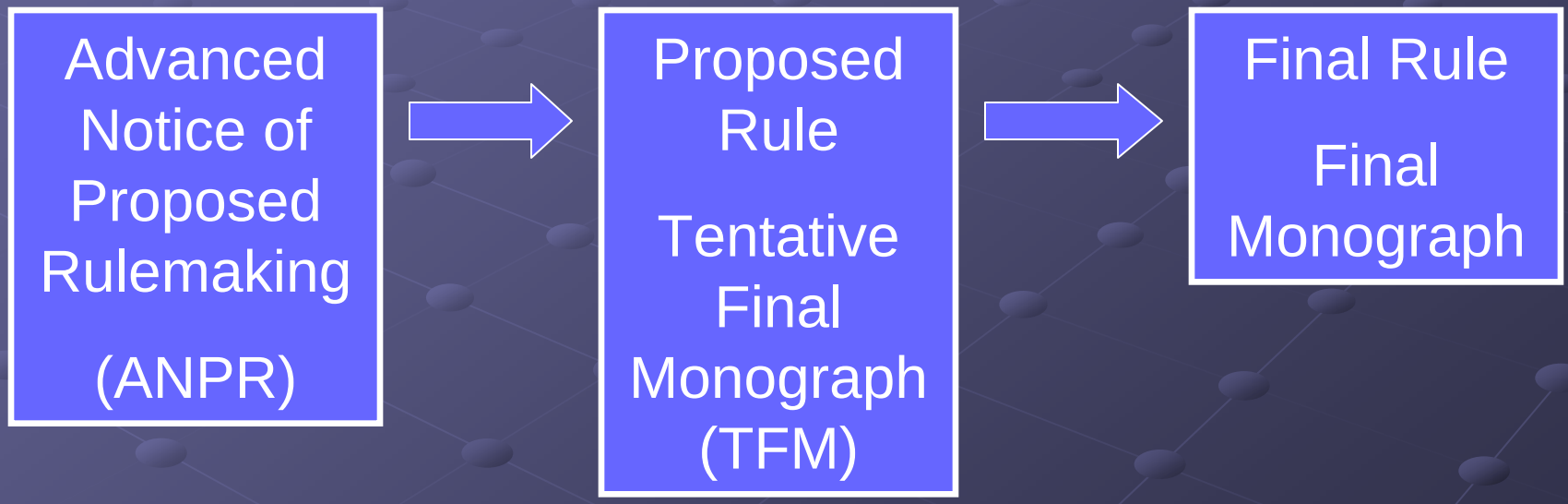
- Active Ingredients
- Dosage Forms
- Dose or Concentration
- Required Labeling
- Packaging and/or Testing Requirements (in some cases)

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
- Categ RASE
- Categ termined

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	Monograph
Pre-approval Required	Pre-approval Not Required
Clinical studies and user fees may be necessary	Clinical studies may not be necessary and no user fees
Review process is proprietary	Notice and comment process is public
Approved labeling is unique to your drug	Labeling is the same for all similar drugs
Possible marketing exclusivity	No marketing exclusivity
Approved NDA is your license to market	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

- Same standards for effectiveness as prescription products
- Patient safety in an unsupervised setting
  - Self-diagnose?
  - Self-Treat?
  - Self-Manage?
- Label Comprehension Studies
- Actual Use Studies
- U.S. and worldwide adverse event data

OTC Drug Product Labeling

General Concepts

- All labeling directed to the consumer
- Labeling needs to ensure that consumers can:
  - Diagnose the underlying condition
  - Determine whether a drug is appropriate for them
  - Self-administer safely and effectively
  - Avoid potential serious consequences
  - Recognize when to see a physician or seek emergency assistance

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

<u>FD&CA definition (201.m)</u>

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

- Categorical listing of all OTC monographs
  http://www.fda.gov/cder/otcmonographs/rulemaking_index.htm
- Over-the-Counter (OTC) Related Federal Register Notices, Ingredient References,
  and other Regulatory Information
  http://www.fda.gov/cder/offices/otc/industry.htm
- Questions for Drug Listing contact:
  - Phone: 301-210-2840 or 301-796-3110
  - Email: druginfo@fda.hhs.gov
- Questions for Drug Registration
  - Email: dfrm@fda.hhs.gov

For More Information

- Call or Email ONP
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  - For NDAs, contact Leah Christl
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