OTC Products

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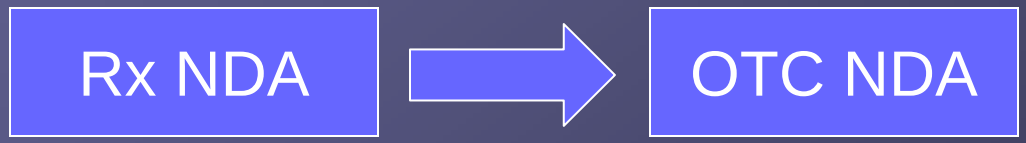
…FDA…HHS…USA…

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

- 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)

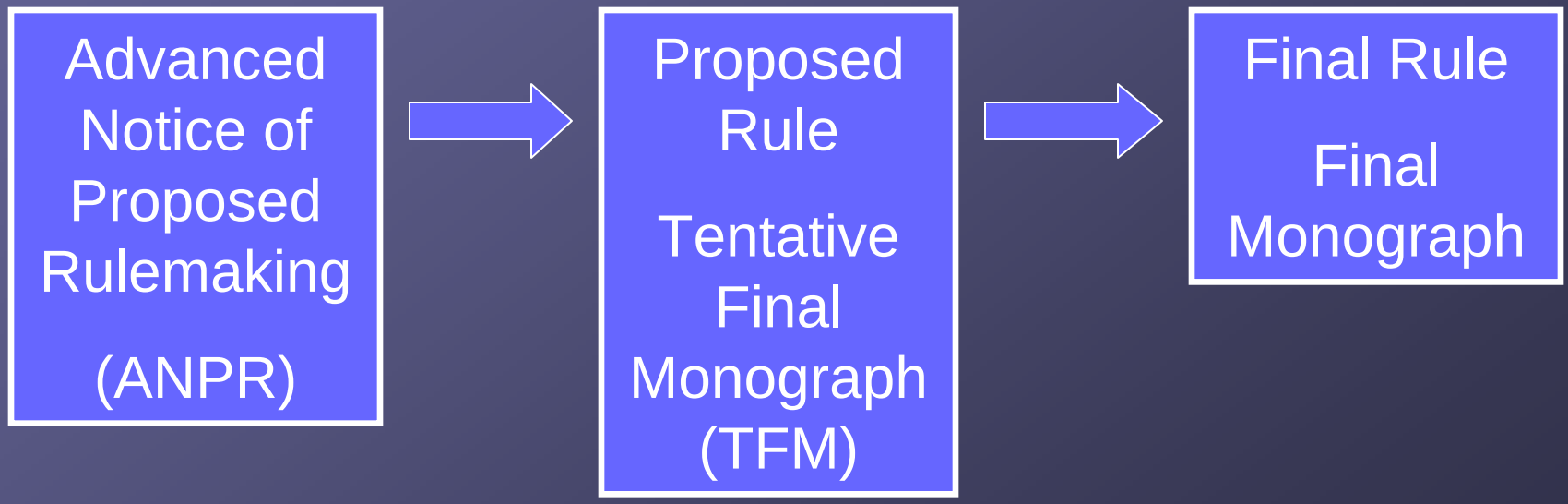
LABELING REQUIREMENTS

- 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

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comment on the direct final rule. FDA stated that the effective date of the direct final rule would be December 8, 2003, and, if the agency received no significant adverse comments, it would publish a notice of confirmation of the effective date no later than June 8, 2004. FDA received no significant adverse comments on the proposed rule. Therefore, FDA is not issuing that the effective date of the direct final rule is December 8, 2003. As stated in the direct final rule, FDA is publishing this confirmation document 180 days before the effective date to permit affected firms adequate time to take appropriate steps to bring (bat) bottled water products into compliance with the quality standard imposed by the new rule.

Dated: June 2, 2003.

Jeffrey Shuren,

Assistant Commissioner for Policy.

[FR Doc. 03-14477 Filed 6-6-03; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 310, 350, and 369

[Docket No. 78N-0004]

RIN 0910-AA01

Antiperspirant Drug Products For Over-the-Counter Human Use; Final Monograph

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is issuing a final rule in the form of a final monograph establishing conditions under which over-the-counter (OTC) antiperspirant drug products are generally recognized as safe and effective and not misbranded as part of FDA's ongoing review of OTC drug products. FDA is issuing this final rule after considering public comments on its proposed regulation, issued as a tentative final monograph (TFM), and after reviewing the administrative record of antiperspirant drug products that have come to the agency's attention.

DATES: *Effective Date:* This rule is effective December 8, 2004.

Compliance Dates: The compliance date for products with annual sales less than $25,000 is June 8, 2005. The compliance date for all other products is December 8, 2004.

FOR FURTHER INFORMATION CONTACT: Gerald M. Rachanow, Center for Drug Evaluation and Research (HFD-560), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-2307.

SUPPLEMENTARY INFORMATION:

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I. Background

In the Federal Register of October 10, 1978 (43 FR 46682), FDA published its proposed procedures for establishing a monograph for OTC antiperspirant drug products, together with the recommendations of the Advisory Review Panel on OTC Miscellaneous External Drug Products (the Panel). The Panel evaluated the data on these products. The agency's proposed regulation (TFM) for OTC antiperspirant drug products was published in the Federal Register of August 30, 1982 (47 FR 36492).

In the Federal Register of November 7, 1990 (55 FR 46901), the agency issued a final rule establishing that certain active ingredients in OTC drug products are not generally recognized as safe and effective and are misbranded. These ingredients included seven antiperspirant ingredients, which are included in § 310.545(a)(4) (21 CFR 310.545(a)(4)). In this rulemaking, the agency is adding one additional ingredient to this section. See section II.E of this document.

In the Federal Register of March 10, 1993 (58 FR 13435), the agency requested public comment on two citizen petitions, and a response to one of the petitions, related to the safety of aluminum compounds in OTC antiperspirant drug products. This final monograph completes the TFM and provides the substantive response to the citizen petitions.

Twenty four months after the date of publication in the Federal Register, for products with annual sales less than $25,000, and 24 months after the date of publication in the Federal Register, for all other products, no OTC drug product that is subject to this final rule and that contains a nonmonograph condition, i.e., an ingredient, dosage form, or delivered for introduction into interstate commerce unless it is the subject of an approved new drug application (NDA) or abbreviated new drug application. Further, any OTC drug product subject to this final monograph that is repackaged or relabeled after the compliance dates of the final rule must be in compliance with the monograph regardless of the date the product was initially introduced or initially delivered for introduction into interstate commerce. Manufacturers are encouraged to comply voluntarily as soon as possible.

In response to the TFM an OTC antiperspirant drug products and the Panel for comment on the citizen petitions, the agency received 11 comments. One manufacturer requested an oral hearing before the Commissioner of Food and Drugs on six different issues. Copies of the information considered by the Panel, the comments, and the hearing request are on public display in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. "OTC Volumes" cited in this document refer to information on public display.

The agency received seven "feedback" communications under the OTC drug review procedures (see the Federal Register of September 29, 1981 (46 FR 47740) and April 1, 1985 (50 FR 13320)). The agency has included these communications in the administrative record and addressed them in this document.

The safety issues raised by the citizen petitions are addressed in section II.F of this document. The agency believes it has adequately responded to the six issues related to the hearing request; therefore, a hearing is not necessary.

II. The Agency's Conclusions on the Comments

A. General Comments on OTC Antiperspirant Drug Products

(Comment 1) One comment requested that FDA reevaluate its position that OTC drug monographs are substantive, as opposed to interpretive, regulations.

The agency addressed this issue and reaffirms its conclusions as stated in

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

- 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
    christll@fda.hhs.gov
  - For Monographs, contact Walter Ellenberg
    ellenbergw@fda.hhs.gov
  - If I can help,
    johnsonsu@fda.hhs.gov