U.S. FOOD & DRUG ADMINISTRATION

# Over-the-Counter Drug Monograph

# United States Food and Drug Administration Approach

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# OUTLINE

- Organizational Structure
- U.S. Regulatory Frameworks for Over-the-Counter (OTC) Drugs
  - New Drug Application
  - OTC Drug Monograph
- Origins of the OTC Drug Monograph
- OTC Monograph Review Process
- Future of the OTC Monograph

# FDA ORGANIZATION RELEVANT TO OTC DRUGS

- **Office of Medical Products and Tobacco**
  - **Center for Drug Evaluation and Research**
    - **Office of New Drugs**
      - **Office of Drug Evaluation IV**
        - **Division of Nonprescription Drug Products**

# OTC DRUG PRODUCTS

OTC drug products generally have these characteristics:

- Can be adequately labeled such that
  - The consumer can self-diagnose, self-treat, and self-manage the condition being treated
  - No health practitioner is needed for the safe and effective use of the product
- Drug has low potential for misuse and abuse
- Safety margin is such that the benefits of OTC availability outweigh the risks

# TWO REGULATORY PATHWAYS

| New Drug Application | OTC Monograph |
|---|---|
| Product specific (including formulation and labeling) | Therapeutic category-specific regulations (product can contain permissible active ingredients in a monograph compliant formulation) |
| Certain subsequent labeling and formulation changes require prior approval through supplemental application | Changes do not require approval when in compliance with monograph |
| Confidentiality during the approval process | Public process for monograph changes |
| Safety and effectiveness testing required for each individual product | Safety and effectiveness testing of each individual product not required if compliant with monograph |
| Application submitted for premarket approval | No FDA product-specific premarket application or preapproval |
| Application fees (i.e., user fees) | No user fees |
| Adverse event and other reporting requirements | Limited reporting requirements (serious adverse events only) |
| Comply with good manufacturing practices | Comply with good manufacturing practices |
| A period of market exclusivity (if certain conditions are met) | No market exclusivity |

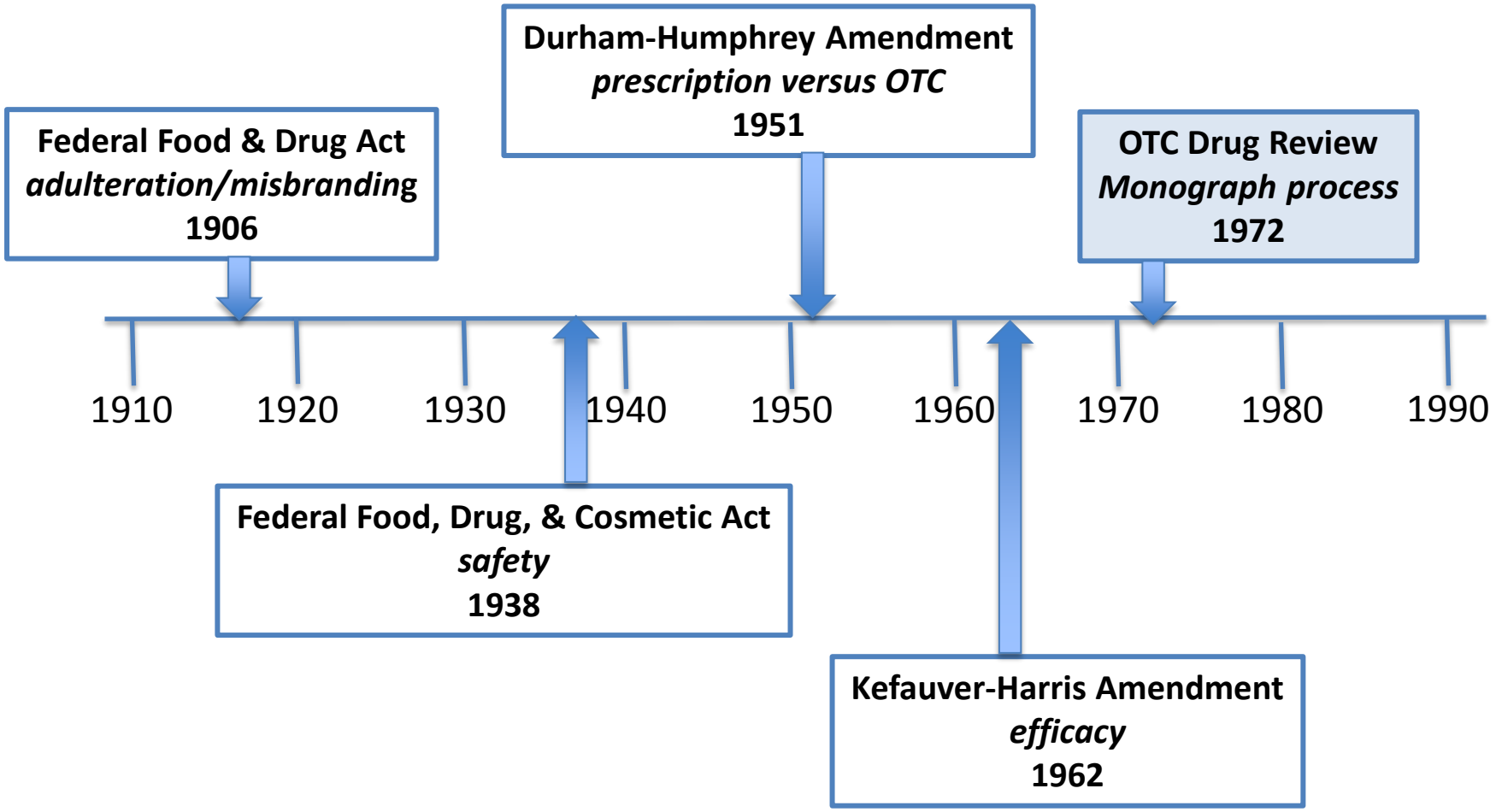
# New Drug Application OR MONOGRAPH?

# EXAMPLES OF OTC MONOGRAPH DRUG CATEGORIES

- Antacids
- Laxatives
- Antidiarrheal products
- Antiemetics
- Antiperspirants
- Sunscreens
- Cough and cold products
- Wart removers
- Sedatives/Sleep aids
- Stimulants
- Ophthalmic products
- Hemorrhoidal products
- Dandruff products
- Anticaries products
- Otic products
- Analgesics
- Allergies

# ORIGINS OF THE OTC MONOGRAPH

# HISTORICAL DEVELOPMENT OF FDA DRUG REGULATION



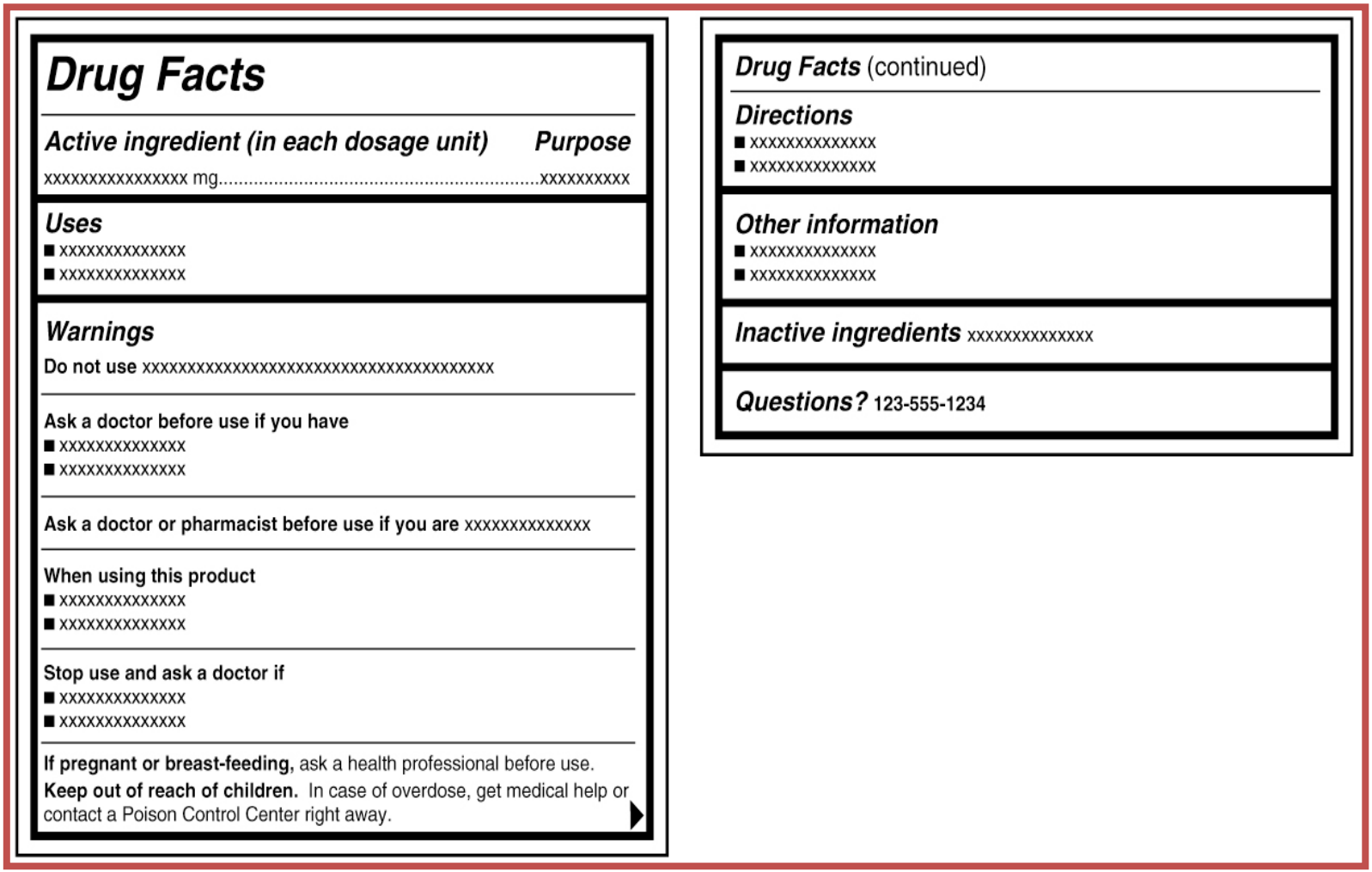
# CURRENT OTC MONOGRAPH PROCESS

- OTC drug review established in 1972
  - Implemented 1962 Congressional directive to review the safety and effectiveness of drugs
- Rather than review hundreds of thousands of individual OTC products, FDA began issuing monographs establishing conditions under which OTC drugs are generally recognized as safe and effective (GRASE)
  - Monographs are “rulebooks” establishing indications, strengths, dosing information, warnings, etc., for OTC products containing the covered ingredients to be GRASE
  - Each monograph generally provides for the marketing of hundreds or thousands of products
  - Products meeting the specifications of a monograph are not required to be reviewed by FDA before marketing
- The monographs cover some 800 active ingredients for over 1,400 different uses and over 100,000 products
- Each monograph is established by regulation
  - There are >150 final rules related to OTC drugs
  - Approximately 88 ongoing rulemakings in 26 broad therapeutic categories

# WHAT GOES IN A MONOGRAPH?

- Conditions include:
  - Active ingredients (must comply with a USP drug monograph)
  - Dosage strength and form and route of administration
  - Patient population (age, gender) and indications for use
  - Required labeling: • Uses • Warnings • Directions
  - Final formulation testing, if required for the specific product (not all monographs)

# OTC DRUG FACTS LABEL OUTLINE



## Drug Facts

**Active ingredient (in each dosage unit)** **Purpose**

xxxxxxxxxxxxxxxx mg.....xxxxxxxxxx

**Uses**
- xxxxxxxxxxxxxx
- xxxxxxxxxxxxxx

**Warnings**

**Do not use** xxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx

**Ask a doctor before use if you have**
- xxxxxxxxxxxxxx
- xxxxxxxxxxxxxx

**Ask a doctor or pharmacist before use if you are** xxxxxxxxxxxxxx

**When using this product**
- xxxxxxxxxxxxxx
- xxxxxxxxxxxxxx

**Stop use and ask a doctor if**
- xxxxxxxxxxxxxx
- xxxxxxxxxxxxxx

**If pregnant or breast-feeding,** ask a health professional before use.
**Keep out of reach of children.** In case of overdose, get medical help or contact a Poison Control Center right away.

## Drug Facts (continued)

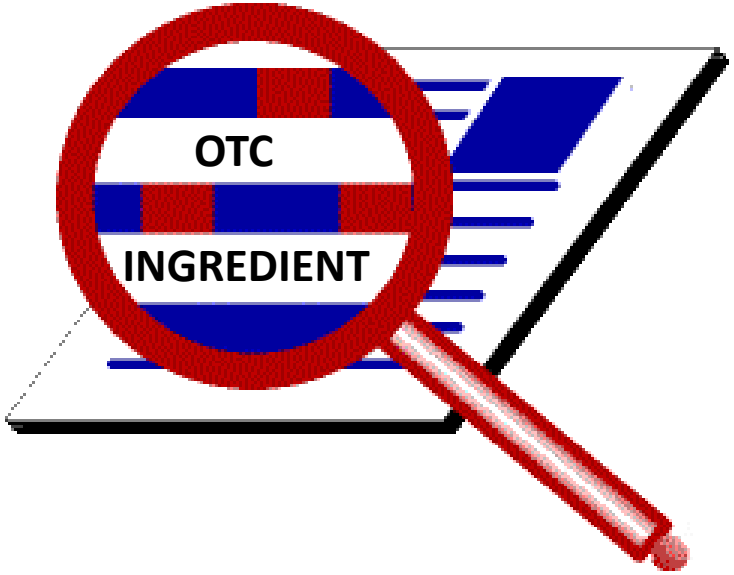
**Directions**
- xxxxxxxxxxxxxx
- xxxxxxxxxxxxxx

**Other information**
- xxxxxxxxxxxxxx
- xxxxxxxxxxxxxx

**Inactive ingredients** xxxxxxxxxxxxxx

**Questions?** 123-555-1234

# THE OTC MONOGRAPH REVIEW PROCESS



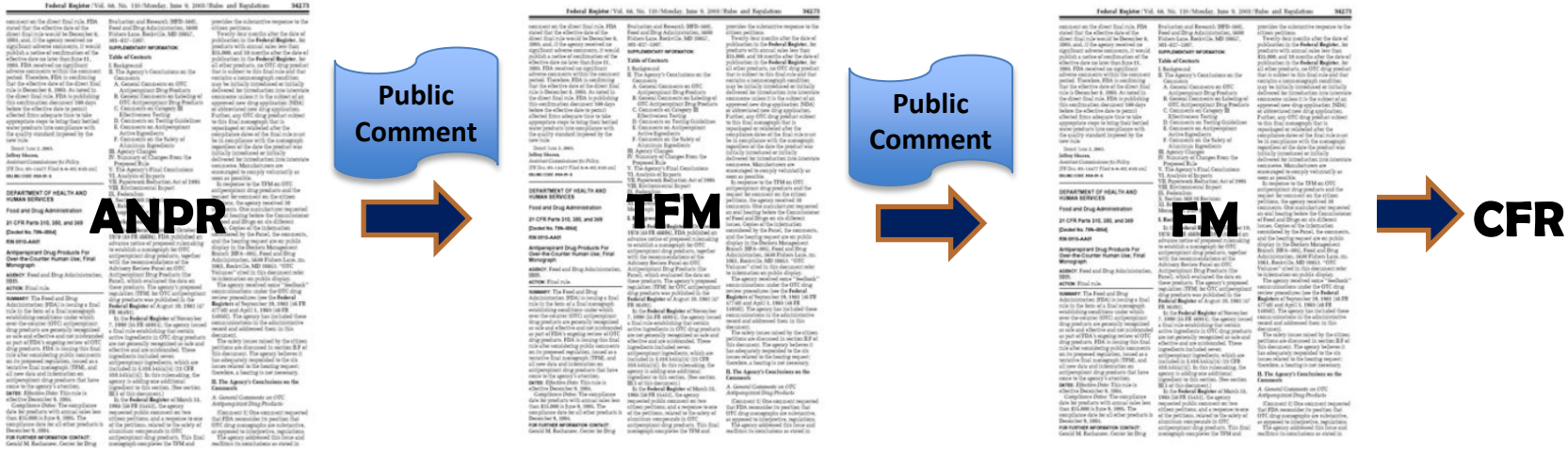
# GRASE CATEGORIES

- In 1970s, Advisory Review Panels reviewed therapeutic classes of OTC drugs and put products into three categories:
  - Category I: GRASE (Generally Recognized as Safe and Effective)
  - Category II: not GRASE
  - Category III: insufficient data available to determine if generally recognized as safe and effective
- Monograph products using original ingredients may stay on the market until FDA makes a final determination of ingredient status

# CURRENT OTC MONOGRAPH RULEMAKING PROCESS

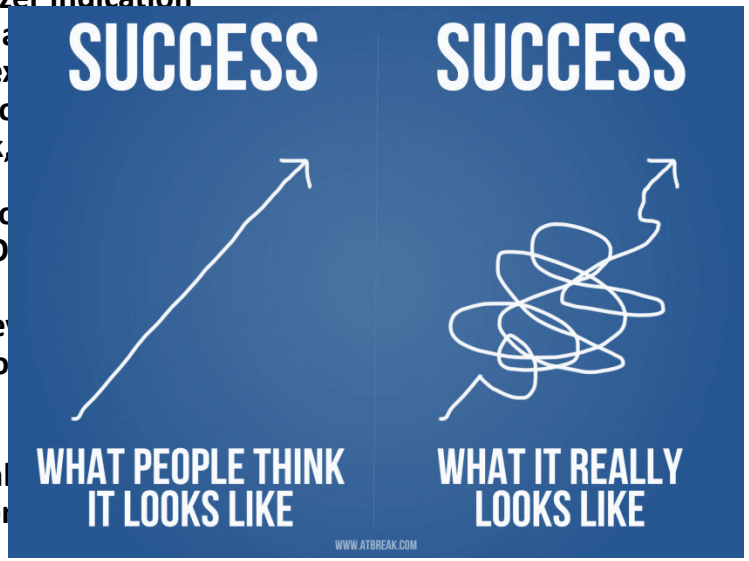
Requires a three-step public notice and comment rulemaking process

- Advance Notice of Proposed Rulemaking
- Tentative Final Monograph
- Final Monograph→ Code of Federal Regulations



# REALITY OF THE MONOGRAPH PROCESS

| Published | Fed Reg citation | Topic |
|---|---|---|
| 12-4-79 | 44FR69768 | **ANPR for External Analgesic Drug Products** |
| 2-5-80 | 45FR7820 | Correction |
| 9-26-80 | 45FR63878 | Reopening of administrative record |
| 9-7-82 | 47FR39412 | Reopening of administrative record |
| 12-7-82 | 47FR54981 | Correction |
| 12-28-82 | 47FR57738 | Extension of comment and reply periods |
| 2-8-83 | 48FR5852 | TFM (Tentative Final Monograph = Proposed Rule) |
| 3-11-83 | 48FR10373 | Correction |
| 10-2-85 | 50FR40260 | Amend TFM to add male genital desensitizer indication |
| 7-30-86 | 51FR27360 | Amend TFM to add seborrheic dermatitis a |
| 8-25-88 | 53FR32592 | Amend TFM warnings and directions for ex |
| 4-3-89 | 54FR13490 | Amend TFM to remove astringent drug pro |
| 10-3-89 | 54FR40818 | Amend TFM to add poison ivy, poison oak, bite indications |
| 1-31-90 | 55FR3370 | Amend TFM to address fever blister and co |
| 2-27-90 | 55FR6932 | Amend TFM to make hydrocortisone 1% O |
| 3-27-90 | 55FR11291 | Correction |
| 6-20-90 | 55FR25234 | Amend TFM to address treatment and prev |
| 8-30-91 | 56FR43025 | Hydrocortisone; Notice of Enforcement Po |
| 6-19-92 | 57FR27654 | FR (Final Rule) Male genital desensitizer |
| 12-18-92 | 57FR60426 | FR (Final Rule) Diaper rash labeling |
| 8-29-97 | 62FR45767 | Amend TFM to add warning about diphenl |
| 11-19-97 | 62FR61710 | Reopening of administrative records to co |



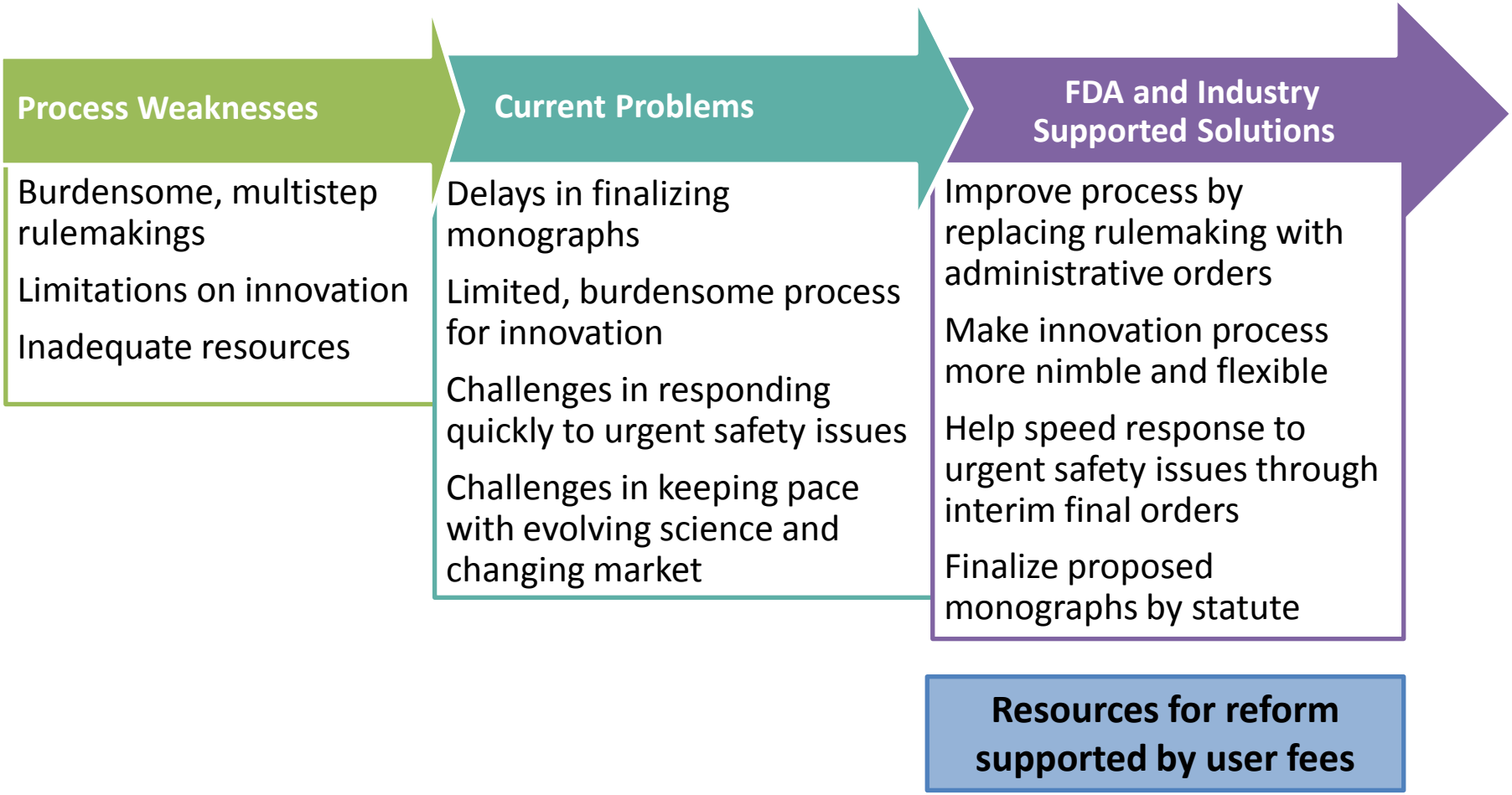
# FUTURE OF THE MONOGRAPH

# BENEFITS AND CHALLENGES OF THE MONOGRAPH SYSTEM

- Well-functioning OTC drug market should promote self-care, patient choice, and industry innovation
- But the current process is not working well
  - Burdensome, multi-step rulemakings take years to complete
    - Even urgent safety issues are subject to lengthy rulemakings, frustrating FDA, industry and patient groups
    - The difficulty in staying up-to-date impairs consumer confidence
  - Process is backward-looking
    - Intended to cover products on the market in 1972
    - Innovation has stalled
  - Program not supported by user fees
    - Significantly under-resourced
  - Status quo does not serve public health or industry well

# OTC DRUG REFORM PROPOSAL

## (Under Consideration by Congress)

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