IPEC-Americas' Comments for Over-the-Counter Monograph User Fees

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Multiple stakeholders; **one objective.**

International Pharmaceutical Excipients Council

Collaborative solutions for excipient industry stakeholders

IPEC-Americas is a non-profit trade association representing many excipient makers and users

Eli Lilly

Apotex

Catalent

Sensient

Jost Chemical

Shell Chemical

Avantor

ADM

AbbVie

Roquette

Croda

Genentech

Teva

CP Kelco

Evonik

Celanese

Lyondell Basell

Johnson & Johnson

Sanofi

Merck & Co.

Mingtai

Capsugel

Biogen

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Dow Corning

SPI Pharma

Cytec Solvay

Purdue Pharma

Baxter Healthcare

Trelyst

Henkel

Mallinckrodt Pharmaceuticals

Monument Chemical

Vanderbilt Minerals

IPEC-Americas Supports OTC Monograph User Fee Concept

- IPEC-Americas supports improvements in the OTC monograph system to provide sufficient FDA resources to facilitate a more expeditious review process
- A user fee system may enable FDA to gather better quality data on OTC manufacturers because the facilities would need to be identified or registered
- A user fee system would be a viable means to fund the necessary resources but careful consideration should be given to the types of fees and which parties would be responsible for paying them

IPEC-Americas' Key Concerns

- Who would be responsible for paying the user fees?
  - Finished OTC drug product supplier and/or manufacturing facility?
  - Ingredient supplier and/or manufacturing facility?
    - Under GDUFA, API manufacturers are subject to fees. What would be the impact of setting fees for excipients, APIs or ingredients used as "Atypical Actives" in OTC drug products?
- Fees applied to ingredient manufacturers/suppliers could be prohibitive
  - Could lead to shortages or withdrawal of ingredients from this market by suppliers who cannot justify this cost
- IPEC-Americas would support user fees for resources to review OTC monographs and resources to evaluate OTC finished drug manufacturing facilities (i.e. GMPs), including foreign facilities (e.g. similar to GDUFA)
- Since many OTC drug products contain atypical actives, a different user fee approach regarding active ingredients than is used with GDUFA is needed

What is an “Atypical Active”?

- An excipient, food additive or cosmetic ingredient that is being used as an “active ingredient” in a formulation
  - Unlike traditional APIs, “Atypical Actives” usually have a physical effect rather than a purely pharmacological effect
  - Common in OTC products
  - Most OTC drug formulations existed long before ICH Q7 was developed as the GMP guideline for APIs
    - Atypical actives have a long history of safe use
  - In some cases it is the only ingredient in the drug product

Some Examples of OTCs Containing "Atypical Actives"

- **Glycerin Suppositories**
  - Glycerin
- **Anti-gas Tablets/Capsules**
  - Dimethicone/Simethicone
- **Kaopectate**
  - Kaolin
- **Rubbing Alcohol**
  - Isopropyl Alcohol
- **Opthalmic Solutions**
  - Cellulose Derivatives (HPMC, CMC, HPC)
- **Hand Sanitizers**
  - Ethanol

Product Category	Examples
Topical Antitussives	Camphor, menthol, eucalyptus oil
Stimulants	Caffeine
Acid Reducers	Bismuth-based antacids, magnesium-based antacids, calcium (carbonate or phosphate)
Antiflatulents	Simethicone
Laxatives	Polycarbophil, polyethylene glycol 3350, cellulose, magnesium hydroxide
Lubricants	Mineral oil
Poison Treatment	Ipecac syrup, activated charcoal
Skin Protectants	Dimethicone, zinc oxide, petrolatum
Acne Products	Resorcinol, salicylic acid, benzoyl peroxide
Astringents	Witch hazel, calamine

Potential Consequences of User Fees for OTC Ingredients

- If fees were imposed on API manufacturers/suppliers and they were required to register and comply with ICH Q7 GMPs, many ingredients may no longer be available
- If fees were imposed on the ingredients, withdrawal of OTC drug product from market could result in:
  - Potential adverse impact to patient/consumers
  - Leading to possible **drug shortages** for common OTC Drugs
- Due to the nature of the manufacturing processes and distribution channels, it would be very difficult (or impossible) to apply API (ICH Q7) GMPs when manufacturing "Atypical Actives".
  - The costs to apply ICH Q7 would rarely be justified from a business perspective due to limited profit margins and market size relative to other applications.

IPEC-Americas' Recommendations Regarding OTC Monograph User Fees

- User fees, including facility registration, should not be imposed on ingredients used in OTC drug products, but rather, on the finished OTC drug products
  - User fees for OTC active ingredients or facilities could have a adverse impact on availability of many OTC medicines
  - Many suppliers of ingredients used in OTC drug products are not always aware of how their products are being used and would not be willing to pay fees based on their use in OTC drug products
- Any user fee system should have a FDA commitment for completing pending OTC monographs

Questions?