

**The Need for Science and Risk-based Excipient Safety Assessment during generic drug review – Impact on formulation quality and performance**

**David Schoneker**  
**Vice Chair for Science and Regulatory Policy – IPEC-Americas**

**[dschoneker@colorcon.com](mailto:dschoneker@colorcon.com)**

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



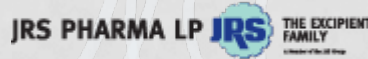
Jost Chemical

Avantor

Shell Chemical



AbbVie



ADM

Croda



Genentech

Evonik

Roquette

Teva

CP Kelco

Celanese

Lyondell Basell



Johnson & Johnson



Sanofi

Merck & Co.

Mingtai

Capsugel

Biogen



Ligand



Dow Corning

SPI Pharma

Nisso

Abitec

Purdue Pharma

Cytec Solvay



Baxter Healthcare



Mallinckrodt Pharmaceuticals

Monument Chemical

Henkel Trelyst

Vanderbilt Minerals

# IPEC-America's Key Concerns

- ▶ Current FDA OGD policies and guidance for generic drugs related to excipient safety review are **NOT** science and risk based.....nor aligned with other areas within FDA
- ▶ The current policies and guidance (such as RTR, CC) related to the use of the IID are creating barriers to innovation and significant confusion throughout industry
- ▶ IPEC-Americas/GPhA have been working with FDA since **2011** to improve the IID and process for excipient safety reviews; however, key decisions have **still NOT** been made or implemented by FDA in **2016**
  - There is a need for better coordination of these concepts between OPS and OGD



# FDA Key Input Areas – IPEC Comments

1. Opportunities for scientific or technical advancements that would help to overcome specific barriers for industry that currently limit the availability of generic drug products.
  - OGD's current Excipient Safety Review and IID related policies are stifling innovation, wasting FDA resources and are resulting in the development of non-optimized generic drug product formulations
5. Identification of specific issues related to generic drug products where scientific recommendations and/or clarifications are needed in developing and/or revising FDA's guidance for industry.
  - A Read-Across approach to excipient toxicology review is needed for evaluation of excipient families (the Family Approach) in order to facilitate streamlined assessments based on good science. This practice is already performed in other parts of the FDA
6. Strategies for enhancing quality and equivalence risk management during generic drug product development, during regulatory review, and/or throughout the drug product's lifecycle.
  - Acceptance of the Family Approach and an Independent Novel Excipient Qualification Process can speed up generic drug development, improve drug quality and performance and enhance the use of advanced manufacturing techniques such as continuous manufacturing

# ANDA Process - Impact of the IID

- ▶ FDA needs to improve the efficiency of the ANDA process for excipient safety review to:
  - Help the Agency and industry meet GDUFA goals
  - Apply science-based risk assessment principles
  - Minimize reviews of **redundant** excipient toxicology information
  - Reduce confusion regarding the IID
- ▶ The current IID and associated policies is insufficient to support efficient drug development and approval

**We MUST streamline this process and use good science to assess the REAL risk!**

# Use of Excipients in Generic Drug Development

- ▶ **New uses of existing excipients and novel excipients (that are not new chemical entities) will:**
  - Enhance high quality generic drug development and equivalent performance to innovator drugs
  - Improve manufacturing productivity and help control the cost of generic drugs
- ▶ **Many generics are being designed with **less than optimum formulations** due to barriers in the excipient safety review process for ANDAs**
- ▶ **The process should be consistent with:**
  - Risk management concepts
  - Good science and global toxicology practices
  - Quality by Design principles

# How to Facilitate the Review of Excipients in ANDA Submissions?

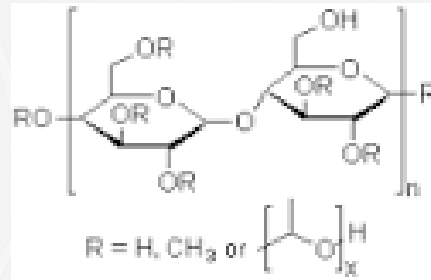
Standardize the approach for supplying inactive ingredient information to streamline the submission and review process

Use the excipient **family approach** to facilitate common pharm-tox evaluations for related excipients

Prioritize a one time review of excipient families

Revise FDA guidance documents by correcting contradictory and inconsistent information





## What is the Family Approach?

Many Excipients (such as polymers) are chemically similar but may have various grades in the family that all are the same from a toxicological standpoint



# Benefits of the Family Approach

- ▶ Transparency to drug formulators on maximum excipient use levels by route as supported by toxicity data.
- ▶ Minimizes need for multiple FDA reviews of the same excipient toxicology data once a maximum use level has been accepted.
- ▶ Expedites FDA review of ANDA's.
- ▶ Minimizes errors and resources to maintain IID
- ▶ Reduces the complexity of the IID

# IPEC-Americas Requests

- ▶ **Formalized acceptance** by FDA OGD for use of the **Family Approach** for excipient safety review
  - If needed, work can be done under the GDUFA Regulatory Science Initiative to develop improved guidance or answer any unanswered questions so a decision can be made to move forward with the use of this technique by OGD
- ▶ **Revision** of the RTR and CC Guidance **to facilitate innovation** related to the use of novel excipients that are not based on a new chemical entity
- ▶ Work with Industry to investigate the development of an **independent novel excipient qualification process**
- ▶ Set up an **Industry Working Group** to **collaborate** with FDA on the development of the GDUFA Regulatory Sciences Initiatives and monitor progress of projects



# Questions?