IPEC-Americas Inactive Ingredient Proposals for Consideration during GDUFA Negotiations

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Multiple stakeholders; **one objective.**

International Pharmaceutical Excipients Council

Collaborative solutions for excipient industry stakeholders

The Need for New/Novel Excipients

- **Innovative and novel drug technologies are key to**
  - **improving public health,**
  - **developing high-quality drug products and**
  - **advancing manufacturing science in the pharmaceutical industry**
- To explore innovative systems, develop formulations which can address difficult drug substance property issues (*ie: poor solubility or permeability*) and enhance the use of advanced manufacturing techniques, **the availability of high quality inactive ingredients (excipients) having unique performance capabilities designed for purpose is critical**.

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Independent Safety Review of New/Novel Excipients

- Currently, outside of inclusion in an NDA or ANDA, **there is no regulatory pathway or process** for the Agency to independently review the safety of new or novel excipients.
- The current process has not been effective at getting new or novel excipients used by the industry due to the regulatory risks involved.
- **The lack of an independent FDA excipient safety review process is hindering drug development and innovation in both generic and innovative drugs .**

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Independent Safety Review of New/Novel Excipients

- **Establishment of an independent process for FDA** to review the safety of new/novel excipients **is critical** for both innovative and generic drug development.
- Members of IPEC-Americas plan to propose in our written comments a number of options for FDA to consider which could lead to enhanced innovations in the pharmaceutical industry (both innovative and generic drugs).
- We would like these options to be included in the GDUFA and PDUFA reauthorization negotiations which will take place over the coming months.

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Types of New/Novel Excipients

- New Grade of an existing Family of related Excipients
  - typically little safety assessment needed
- New Co-Processed Excipients (CoPEs)
  - Physical synergistic combination only - No chemical change
  - Analytical data and a safety bridging argument to individual excipients usually enough to establish safety
- New use of an Existing Excipient
  - Higher level of use in a previously used route of administration
  - Use in a new route of administration
- New Chemically Modified Grade of an Existing Excipient
- New Chemical Entity Excipients (NCEs)

The level of safety assessment needed increases as you go down the list

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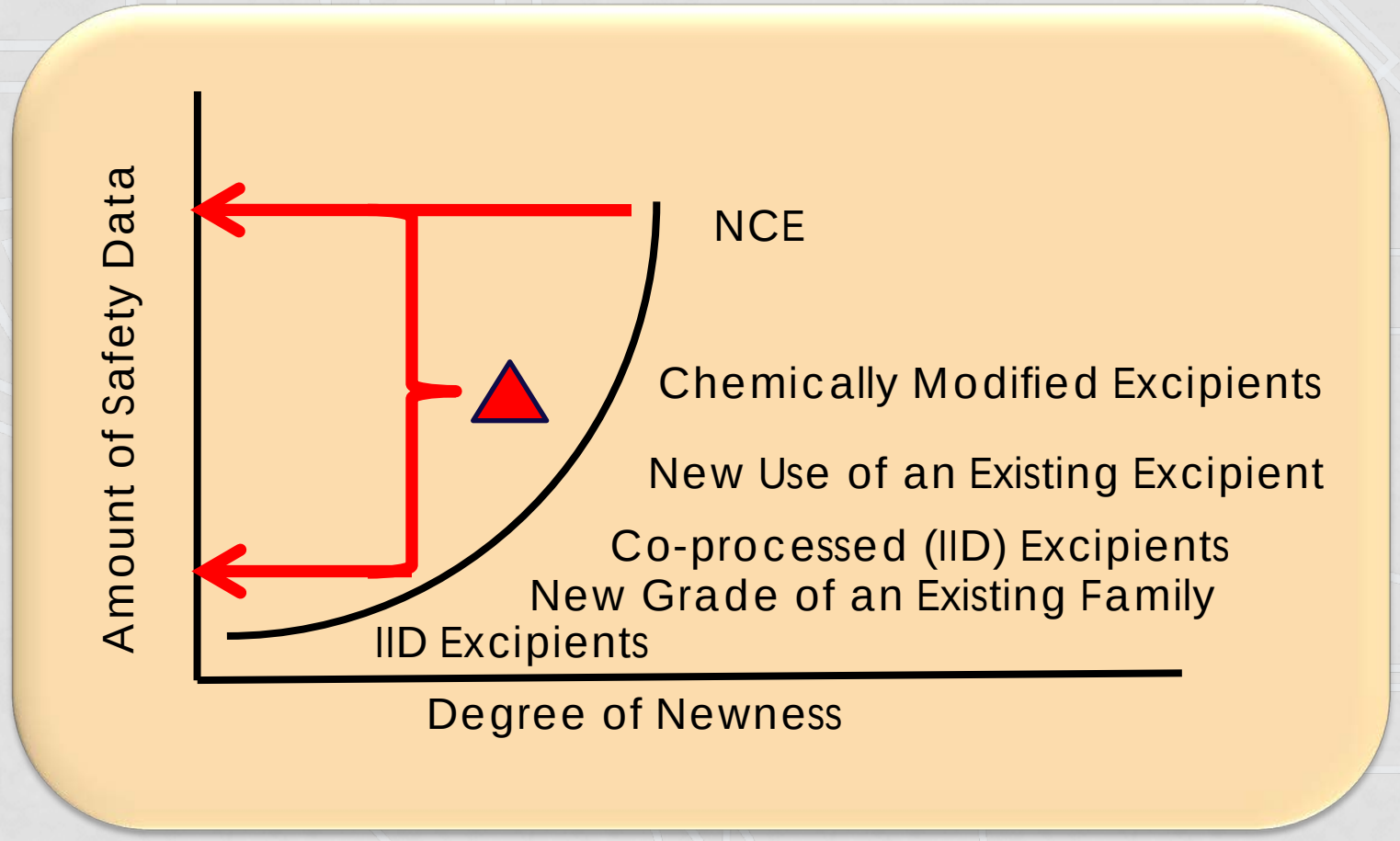
Degree of Newness – Data Requirements



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Independent Safety Review of New/Novel Excipients

- IPEC-Americas will propose concepts for consideration such as:
  - Use of Type IV or V DMFs for submission of inactive ingredient safety information including studies and bridging arguments
  - FDA Independent Safety Assessment of these DMFs outside of a drug application – DMF holder would indicate intended types of use & levels
  - Usefulness of a GDUFA/PDUFA type user fee system which could provide resources to FDA for these independent safety assessments
  - Publication of a list of excipients which have undergone the FDA's independent assessment and are considered to be "endorsed" by FDA for specific intended uses in pharmaceuticals
    - Other similar programs: FDA GRAS Notification, FEMA GRAS, CIR

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Family Approach for Inactive Ingredients Safety Assessment

- **The current Inactive Ingredient Database and the policies regarding it's use are insufficient at the current time to support efficient drug development and approval**

- FDA policies and guidance (ie; RTR, CC) related to the review of inactive ingredients (excipients) in ANDAs **continue to create confusion and results in longer review times for generic drug applications.**

- IPEC-Americas believes that there are several things that can be done **to make the process more efficient** and help the Agency and industry **meet GDUFA commitments.**

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Family Approach for Inactive Ingredients Safety Assessment

- The current FDA practice of requiring toxicology data for **every grade** of an inactive ingredient is **not substantiated by scientific rationale and is not aligned with a risk-based approach.**

- **Utilizing a family approach during a safety review of related grades of excipients** used in a generic drug could lead to **a more efficient review and reduction of FDA resources** without compromising patient safety.

- The safety testing of Excipients within a related family is **normally performed using a bracketing approach** and the same data must be used to evaluate all grades within the family

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Family Approach for Inactive Ingredients Safety Assessment

- Currently, FDA reviewers are "*re-reviewing*" the **same excipient toxicology data over and over for each grade of excipient in a family** – since new data does not exist for each grade - *redundant work*!
- IPEC-Americas has been meeting with FDA's IID Expert Working Group since 2011 **and has supplied significant information to FDA to justify the use of a Family approach** to excipient safety assessment for related excipient grades
- A decision is needed to accept this Family approach, otherwise these issues **will impact the amount of redundant and non-value-added FDA resources** used to evaluate these excipients under GDUFA

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Family Approach for Inactive Ingredients Safety Assessment

- We recognize and applaud the FDA for their recent work at updating and improving information listed in the inactive ingredients database (IID); however,
  - A modern database with improved capabilities is needed to support improved drug development and more efficient FDA reviews – this new database must have the capability to include maximum daily intake (MDI) information
- **IPEC-Americas believes that provisions to build and maintain a new improved IID database should be considered as part of the GDUFA and PDUFA reauthorization and should be funded by GDUFA and PDUFA fees.**

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Questions?

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