UNIVERSITY of MARYLAND
SCHOOL OF PHARMACY

NIPTE The National Institute for Pharmaceutical Technology and Education

Improving quality and lowering costs of pharmaceuticals™

Critical Issues In The Use and Evaluation of Excipients In Dosage Forms Such As Pediatric, Geriatric and Abuse Deterrent Dosage Forms

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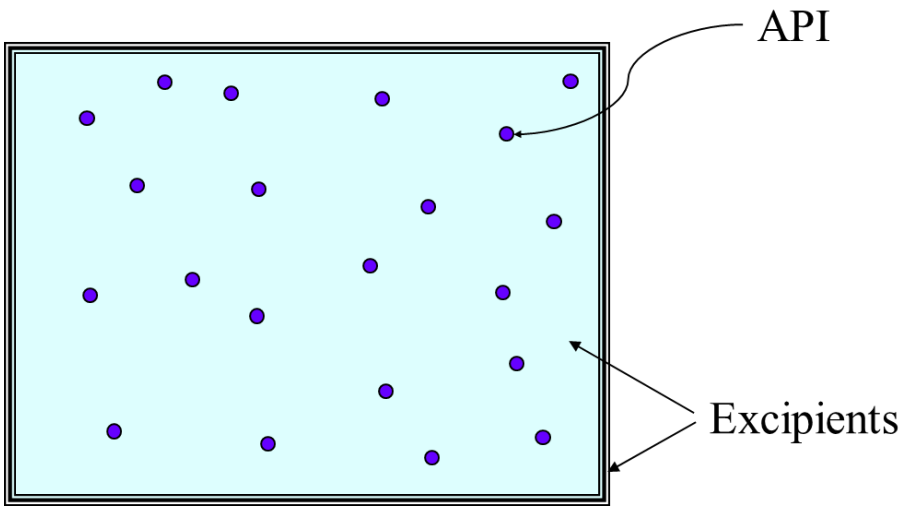
Outline

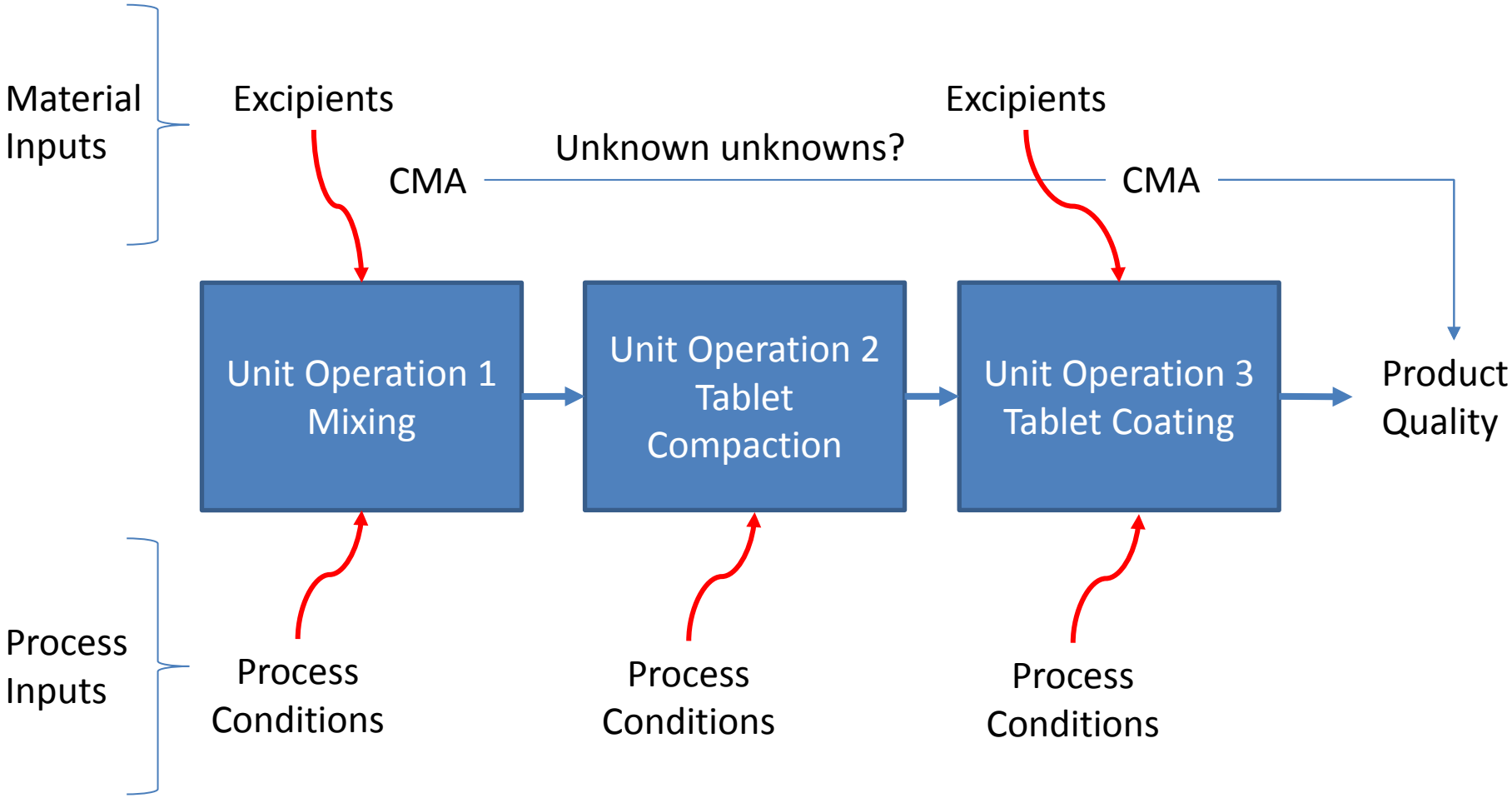
- Introduction to research needs for excipients
- Fundamental research needs
- Specialty excipient needs
- Continuous manufacturing
- Stream line approval for new excipients

Excipients are Key to Quality

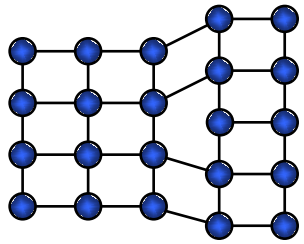
- Excipients are added to provide:
  - Manufacturability
  - Stability
  - Patient acceptance
  - Drug delivery attributes
  - And many other properties
  - Excipients aren't inactive ingredients

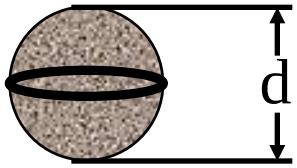


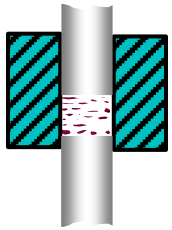
Excipient Control is Key to Quality

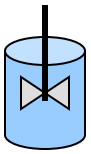


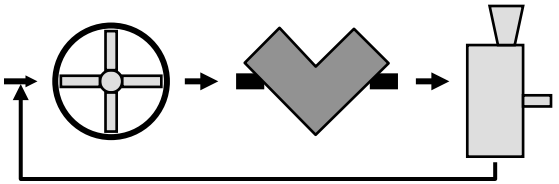
Scale	Analysis
Molecular	Physicochemical e.g. - Tm, Tg,
Particulate	Particulate e.g. – size, distribution
Volume Element	Solid - Moduli Powder - Flow Liquid - Viscosity
Unit Operation	Mixing Patterns Resident Times
Manufacturing	Process optimization









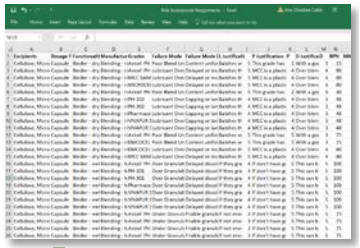


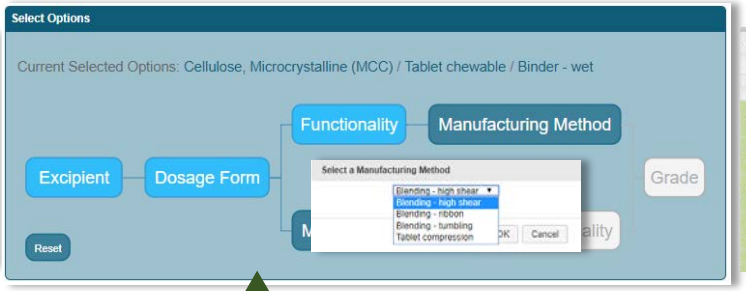
Poor understanding

Lack of methods & Standardization

Adapted from: Perry's Chemical Engineers' Handbook 7th Ed, RH Perry DW Green, Ch20

User Interface





Data Load | **Decision-making** | **Risk Discovery**

Data Platform

DATA IMPORT
- Spreadsheet Upload
- Risk Data Processing

DECISION SUPPORT
- Data Acquisition
- Hierarchical Data Selection
- Rules Validation
- Visualization

DATA VIEW
- Data Definition Language
- Interactive Data Exploration

SOFTWARE COMPONENTS

KNOWLEDGE BASE
- DECISION VARIABLES
- MASTER LISTS
- RULES
- VALID PATHS
- FMEA STRUCTURE
- RPN RISK ASSIGNMENTS
- SUPPORT DATA

hubzero web ecosystem

Specialty Applications

- Years of experience provides at least some empirical rules for tradition IR manufacturing
  - E.g., particle size and flow
  - Best practices for Mg Stearate blending
  - Etc.
- But some formulation types don't have well established best practices and a lot of research is needed to establish best practices
  - Pediatric dosage forms – taste masking
    - Especially neonates and infants
  - Low solubility
  - Abuse deterrent Formulations (ADF)
  - Biotech products

Continuous Manufacturing

- It appears continuous manufacturing will only grow in importance
- Because knowledge of excipient performance is empirical and not fundamental in nature
  - It is unknown how the empirical experience and rules in a batch process will translate to a continuous process
    - Some will and some won't
    - E.g., are there scale or shear differences for Mg Stearate mixing
- Need to better understand how excipients perform in continuous process and identify CMA for continues processes
- Research is needed to determine CMA and best practices for excipient use in continuous processes

Approval of New Excipients

- Currently not many new excipients are entering the market
  - Most introductions are co-processed blends of old excipients
  - Previously mentioned specialty areas would greatly benefit from new excipients with enhanced materials properties would help bring drugs to market faster and with less expense
  - Markets are small enough there is not sufficient financial incentive to develop new excipients
  - Currently new excipients are approved by piggy backing on big pharma product that needs the a certain excipient and once this product is approved the excipient is put in the inactive ingredient database (IID)
    - This approach limits and delays the introduction of new excipients into the market and underserves excipients for niche markets
- Research is needed to streamline the process for approving new excipients especially for niche markets