Title: Plan for Approach to the Understanding and Predicting Excipient Properties and Functionality

NIPTE - National Institute of Pharmaceutical Technology and Education

Excipient Database Development Project

March 31, 2011 update

Purdue University

Outline

- Introductions
- Database overview
  - Steve Hoag and Ting Wang
- PharmHub overview
  - Ann Christine Catlin and Sumudinie Fernando
- Test methods overview
  - Carl Wassgren and Kristine Alston
- Database demonstration
- Feedback summary
  - Wish list for features
  - Future steps
  - Database sustainability

NIPTE

NIPTE The National Institute for Pharmaceutical Technology and Education

Improving quality and lowering costs of pharmaceuticals

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- **More info can be found on:**
  - www.nipte.org

Goal to promote Pharmaceutical Technology research in US universities and Education

FDA Sponsored Research

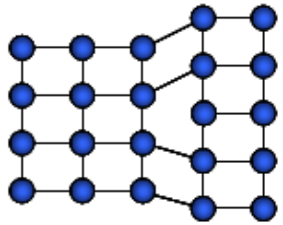
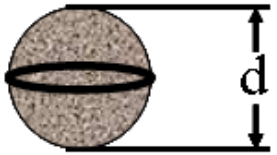
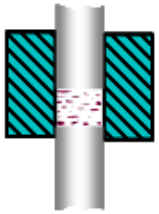
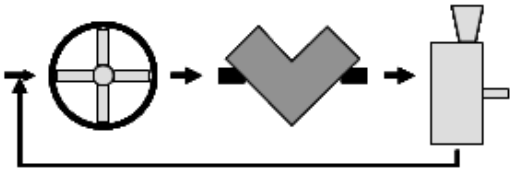
NIPTE Personnel	Affiliation	Role
Stephen W. Hoag Ting Wang	University of Maryland, Baltimore School of Pharmacy	PI Data collection Data modeling
Carl Wassgren Kristine Alston	Purdue University Dept. of Mechanical Engineering	Data collection Data modeling
Ann Christine Catlin Sumudinie Fernando Sudheera R. Fernando	Purdue University Rosen Center for Advanced Computing	Database technology and development Hub Cyber Infrastructure
Linas Mockus	NIPTE/Purdue	Database data entry development
Prabir Basu	NIPTE	Director of NIPTE Administrative

Raw Material Inputs → CQA

Excipient Properties
- Crystal form
- Particle size
- Bulk density
- Etc.

Relationships Not well understood

Critical Quality Attributes
- Hardness
- Disintegration time
- Dissolution
- CU/mixing

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

Development Strategy

- **Won't solve problem of excipient functionality with one project**
  - **Thus, focus on first step which is material properties of excipients**

- **Goal to develop database infrastructure with limited resources**
- **Start with DC and will expand to other categories as database grows**
  - **Current properties**
    - **Chemical Description**
    - **Flow**
    - **Compactability**

Comparison of different grades from different manufacturers--MCC

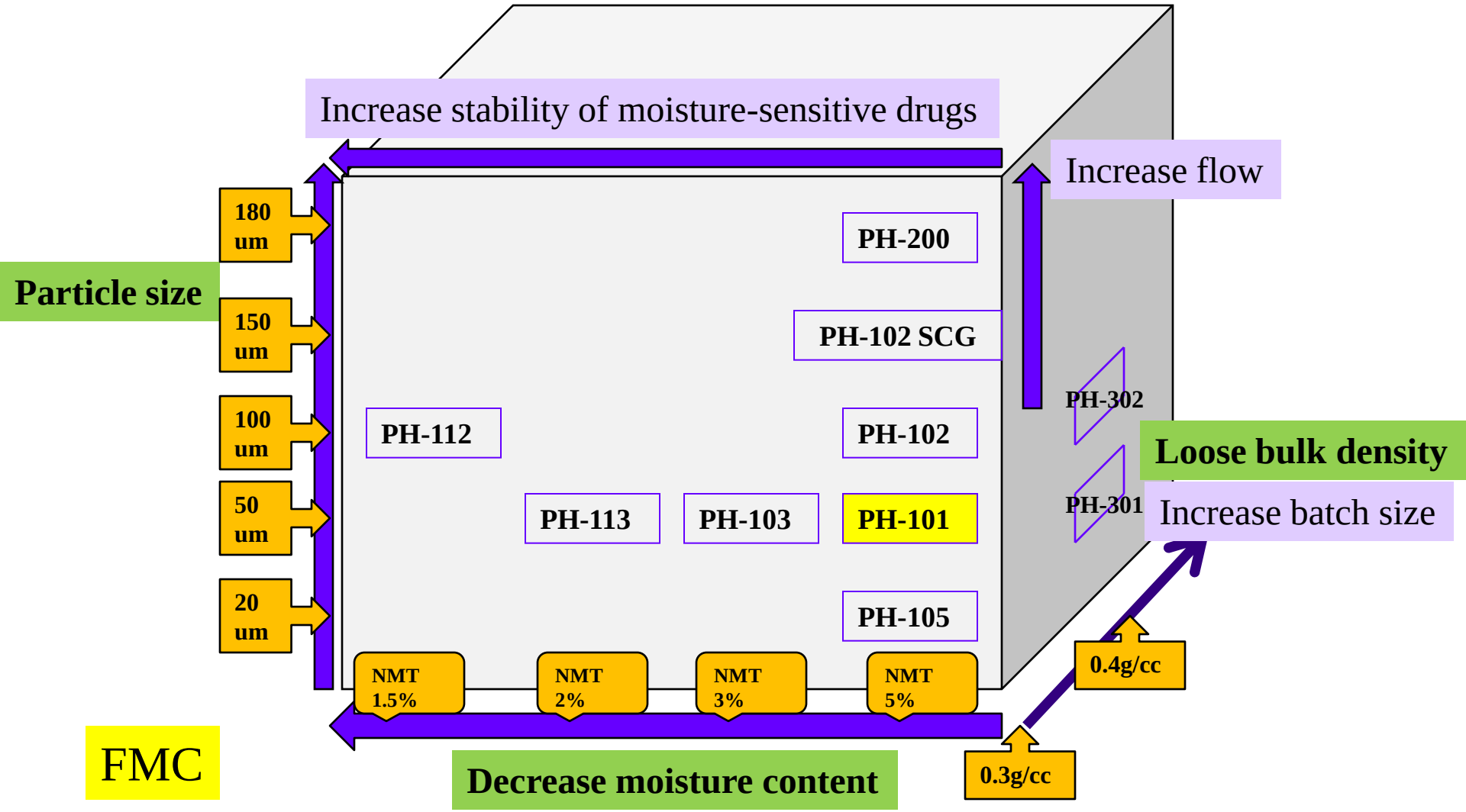
FMC = FMC BIOPOLYMERS

JRS = J Rettenmaier & Söhne GmbH and Co.KG

AKC = Asahi Kasei Corporation

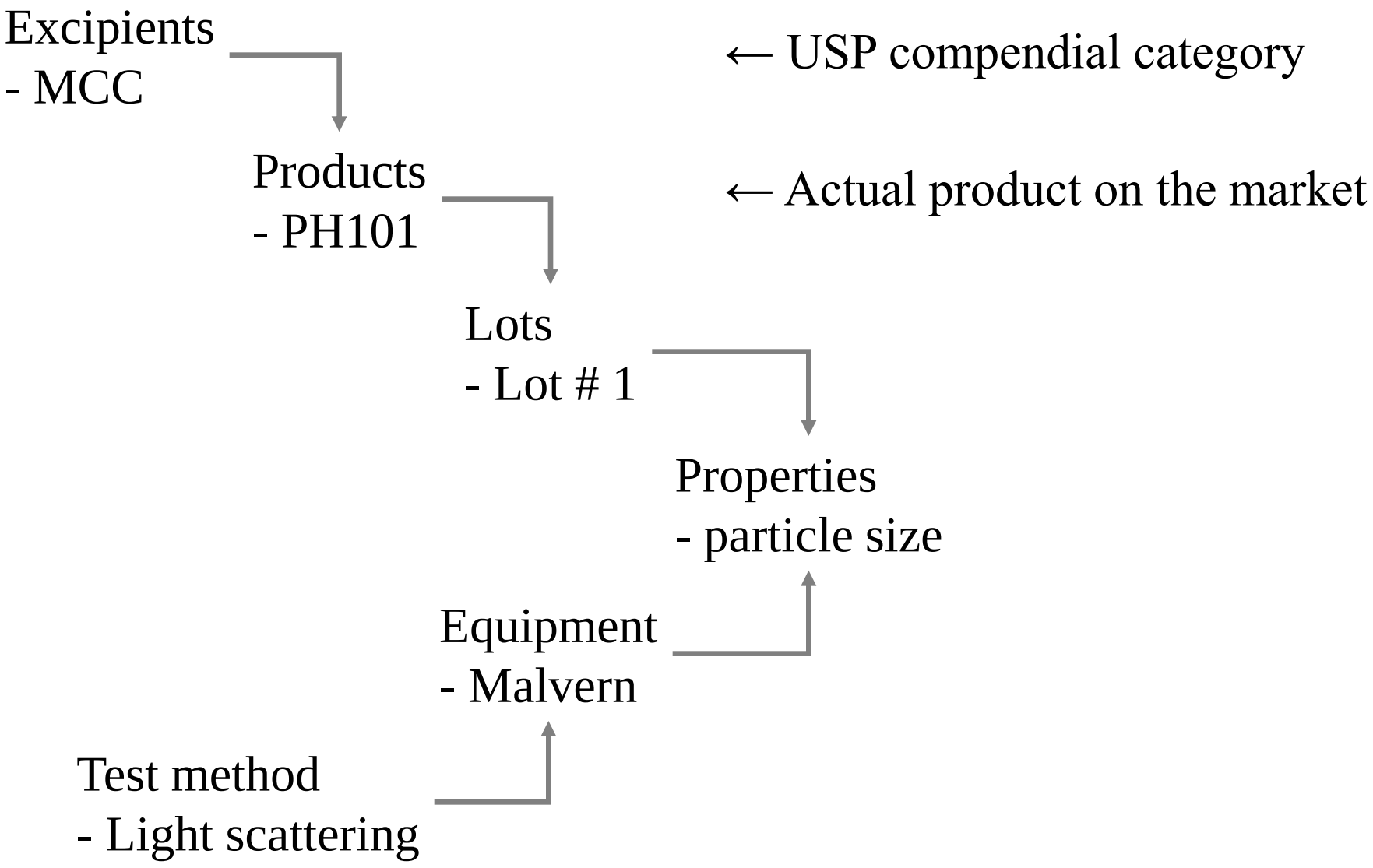
Manufactures	Grades	Particle Size, μm	Moisture, %	Loose Bulk Density, g/cc
FMC	Avicel PH101	50	3.0-5.0	0.26-0.31
JRS	Vivapur 101	65	--	0.26-0.31
	Emcocel 50M			0.25-0.37
AKC	PH-101	50	2.0-6.0	0.22
	UF-711			0.21
	KG-802			0.12
	KG-1000			0.29
FMC	Avicel PH-102	100	3.0-5.0	0.28-0.33
JRS	Vivapur 102	100	--	0.28-0.33
	Emcocel 90M			0.25-0.37
AKC	PH-102	90	2.0-6.0	0.30

Comparison of different grades of MCC



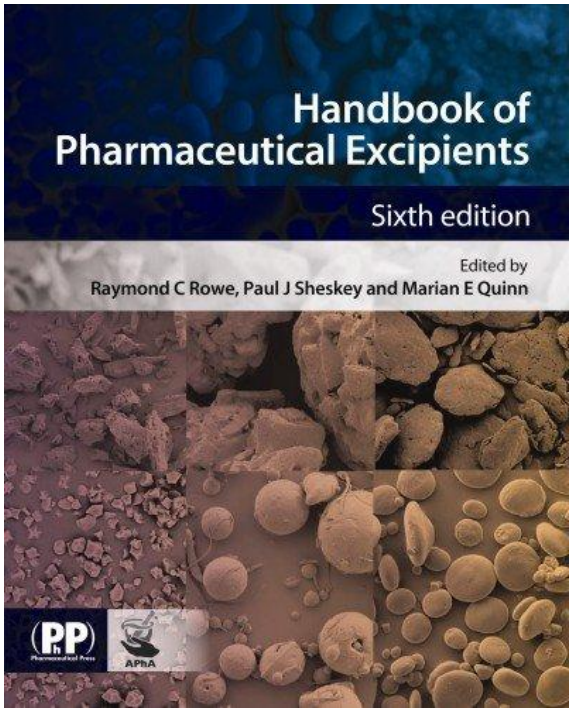
NMT= not more than

Database Structure

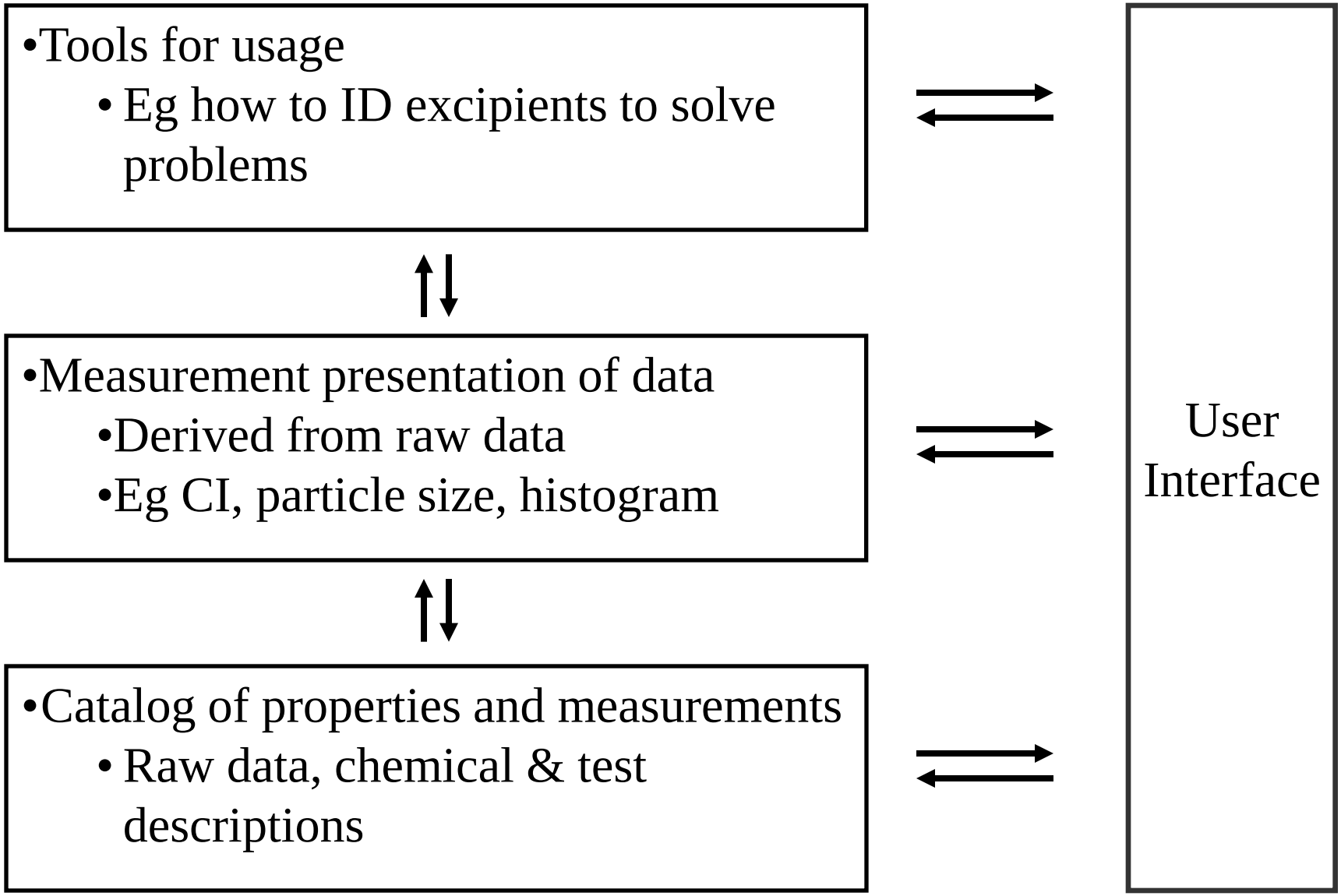


Handbook of Excipients

- **Handbook of excipients**
  - **1. Nonproprietary Names**
  - **2. Synonyms**
  - **3. Chemical Name and CAS Registry Number**
  - **4. Empirical Formula and Molecular Weight**
  - **5. Structural Formula**
  - **6. Functional Category**
  - **7. Applications in Pharmaceutical Formulation or Technology**
  - **8. Description**
  - **9. Pharmacopeial Specifications**
  - **10. Typical Properties**
    - **Angle of repose**
    - **Density (bulk, tapped and true)**
    - **Flowability**
    - **Melting point**
    - **Moisture content**
    - **NIR spectra**
    - **Particle size distribution**
    - **Solubility**
  - **11. Stability and Storage Conditions**
  - **12. Incompatibilities**
  - **13. Method of Manufacture**
  - **14. Safety**
  - **15. Handling Precautions**
  - **16. Regulatory Status**
  - **17. Related Substances**
  - **18. Comments**
  - **19. Specific References**



Database Structure



Presentation Style

- **We would like this to be interactive discussion not a lecture**
  - **Please feel free to interrupt at any time!!!**
- **Can you…**
- **What would happen if….**
- **Can you show me….**

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