

Preclinical Breakout Projects

The background of the slide is a solid blue color. In the bottom right quadrant, there are several overlapping, wavy, light blue lines that create a sense of motion or depth, resembling a stylized landscape or a decorative graphic element.

Project 1: Towards standards

Project 2: Imaging Techniques for nanotechnology-based materials

Project3: Compartmental transfer

Project 1: Towards Standards

[for the standardization, characterization &
control of Nanomaterial properties]

Presented by: Roland Fleck

Issue to be Solved

- Nanopharmaceuticals require:
 - Accurately defined product by
 - Type, purpose, endpoint
 - Defined SOP, QA/QC and manufacturing parameters
 - Credible, reliable, reproducible data
 - Accepted methodologies and protocols defined by purpose and type of NM

Issue to be Solved (continued)

- Standard characterization/reporting and classification
- Selection and adoption of appropriate/pertinent existing or new international standards relating to the endpoint of the study
 - reference materials
 - animal models
 - bioassays
 - functional cell based bioassays
- Permitting inter laboratory comparison of data

Project Description

- Identify/verify/promote that there are credible characterization tools of nanopharmaceuticals/materials
- Identify/verify/promote that there are credible imaging methodologies for experimental pre-clinical studies and product characterization
 - Appropriateness of methods for each NM class
 - Carrier
 - Payload
 - Carrier + Payload

Project Description (continued)

- Promote nano-biomarker library:
 - Proteome
 - Genome
 - Cytokine
 - Binding of carrier to proteins and other biomolecules; extracellular and intracellular
- Define bioassay
- Biological impact and genomic-driven variation in binding, transport, etc.

Way Forward

- Coordination with NanoHealth Enterprise, NIH, ICON, NCI/NCL, etc. regarding standards work that has or is being conducted regarding nomenclature, ontology, chemical description, physical characteristics, etc.
 - Identify and leverage existing efforts
 - Provide influence and input into those efforts
- Engage national and international measurement authorities to establish and provide necessary reference standards/metrology

Expected Results (applicability)

- **How the outputs will address the issue:**
 - Will facilitate product development,
 - Will generate credible, reliable, reproducible data

Cost effectiveness

- How widely useful are the outputs?
 - Broadly applicable across nano-product development
- What is the benefit value of the project?
 - Supports Critical Path Initiative
 - Informs pre-clinical studies
 - Facilitates appropriate regulatory action at all phases,
 - including post-market

Critical Study Design Elements and Data Output Elements

- **Design**

- Interface with
 - NIH NanoHealth Enterprise
 - NIST
 - NCL
 - Other international metrology organizations

- **Output**

- Promote program to develop international standards and protocols leading to credible, reliable, reproducible data.

Timeline/ Level of Effort

- **Timeline**
 - Early implementation is important
- **Level of effort**
 - Creating momentum – **high** (getting appropriate international regulatory and standards agencies engaged)
 - Implementation – **low** (but could take time)

Project 2:

Imaging Techniques for
nanotechnology-based materials

Presented by Sandy McEwan

Issue to be Solved

- Understanding the use of imaging modalities to characterize *in vitro* behavior of nanopharmaceuticals
- Understanding the use of imaging modalities to characterize *in vivo* behavior of nanopharmaceuticals
 - Sub-cellular
 - Cellular
 - Ex-vivo
 - In-vivo

Issues to be Solved

- Standardized chemistry
 - Carrier specific
 - Payload
 - Ligand/surface modification

Issues to be Solved

- In vitro image modalities –
 - quantitative/qualitative
 - AFM, SEM, TEM, CryoTEM,
 - NMR
 - FACS
 - Fluorescence/bioluminescence
 - DLS

Issues to be Solved

- In vivo image modalities –
 - quantitative/qualitative
 - NMR
 - Live cell imaging
 - Fluorescence/bioluminescence
 - Animal imaging
 - MR probes – images/spectra
 - Radiolabeled probes – PET and single photon
 - Optical imaging

Why?

- Applications of techniques
 - ADME
 - Cellular trafficking and distribution
 - Transition states
- Recognition of techniques developed for other biomedical applications
- Imaging
 - Carrier/surface modification/stability
 - Payload
 - Construct

Expected Results (applicability)

- **Output**
- Review article or position paper regarding gap (define platform and gap)
- Chemistry/morphology taxonomy
- Standardized imaging protocols (quantitative where possible)
 - Appropriate granularity for scale
- Reference to standard drug ADME
- **How the outputs will address the issue**
 - Standardized methodologies/repeatability/reproducibility
 - Cross platform comparisons and validation

Cost effectiveness

- **Standardization**
- **Referencibility**
- **Off the shelf testing**
 - (Relatively) low cost method of defining boundaries and knowledge
- **Stability within review system**
- **Reduced time to approval**

Timeline/ Level of Effort

- **Timeline**
 - Modality/technique specific
- **Gap analysis**
 - Imaging – shorter timeline
 - Taxonomy- relatively quick for first attempt
 - Chemistry – longer timeline - ? Evolutionary
- **Methodologies**
 - Within short time frames for standardization of imaging protocols
- **Level of effort**
 - Some is low hanging fruit

Practical Example

Compartmental Transfer

Presented by Abby Jacobs

Example Issues

- Projects 1 & 2 are required to assess, for example:
 - Batch to batch variation
 - Product stability
 - What are the parameters that define transport/transfer,
 - Placenta
 - BBB
 - Size, shape and charge
 - Carrier + payload