Thinking about target product attributes in basic nanomedicine research can smooth the road to translation

Prof. Lea Ann Dailey
Institute of Pharmacy
Martin Luther University Halle–Wittenberg
European Nanomedicine Meeting 2017
London UK
3–4 April, 2017
Our research interests

Biocompatibility of nanomedicines with an emphasis on new biomaterials/excipients

- Inhaled nanomedicines
- Injectable nanomedicines and diagnostics

Manufacture, characterisation, biocompatibility, optimisation and (performance) testing of protein, lipid and polymeric nanoparticles
Basic science vs. applied science

**Basic science**

- Observation → question → hypothesis → experiment → analysis → new question
- Results are not known in advance
- Applications are not always the driving force of the research question

**Applied science**

- Observation → question → hypothesis → experiment → analysis → new question
- Results are not known in advance
- Applications frame the research questions
Pharmaceutical research vs. development

**Applied Science Research**
- Question/hypothesis driven research (scientific method)
- Creates knowledge and design space for potential products
- Creates new processes or instrumentation

**Development**
- Aims, objectives and specifications
- Experiments are performed to validate expected results
- Works within design space
- Results are used as evidence in quality control studies

The need for optimisation may drive new research questions
Nanomedicine development is high risk

GAINS

- Improved PK
- Reduced toxicity

RISKS

- Added complexity in all development stages
Example study scope in publications

ACCURINS® technology: PEG–PLA polymeric nanoparticles + API
–Bind Therapeutics

Formulation comparison  Physicochemical properties

\textit{in vitro} drug release  \textit{in vivo} efficacy  \textit{in vivo} safety

“...developing nanotherapeutics presents its own set of challenges, as the formulations can be complicated and the manufacturing processes complex.

Developing a thorough understanding of the relationship between biological performance and the chemistry and manufacturing controls which enable the technology is crucial to advance these medicines into the clinic.”

What are pharmaceutical quality parameters?

Example list of quality and operational attributes of a parenterally administered nanomedicine

- Endotoxin content*
- Sterility*
- pH*
- Tonicity*
- Particle dose
- Free drug content
- Drug content and uniformity*
- Particulate matter*
- Drug/excipient purity
- Physicochemical properties
- Drug release profile
- Physchem of reconstituted product
- Reconstitution time
- Viscosity/syringibility
- Residual solvents
- Container closure integrity

- Yield
- Cost
- Filterability
- Process time
- Process efficiency
- Encapsulation efficiency
- Operator safety
- Residual process aid
- Residual surfactant
- Residual solvent (non ICH)

*Pharmacopoeial methods
Where does this list come from?

Quality by Design (QbD)

Define | Develop | Control

“Quality by Design is a systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management” (taken from ICH Q8)
Step 1: Define the product parameters

TARGET PRODUCT PROFILE

New drug molecule (API)
- Indication
- Mechanism of Action
- Efficacy
- Safety
- Length of therapy
- Dosage and Administration
- Value Proposition

Reformulated drug (nanomedicine)
- Altered PK profile
- Improved safety profile
- Length of therapy
- Dosage and Administration
- Value Proposition

What kind of product will be developed? Covers all areas!
Key element: What will be the patient benefit?
Step 1: Define the product parameters

QUALITY TARGET PRODUCT PROFILE

- Route of administration
- Dosage form
- Clinical dosage form
- Tox dosage form (if necessary)
- Dosage strength
- Excipients
- Primary packaging
- Storage
- Shelf life

What properties should the product have? Covers all areas!
Key element: What will be the patient benefit?
Step 1: Define the critical quality attributes

“Potential Critical Quality Attributes are physical, chemical, biological or microbiological properties or characteristics that should be within an appropriate limit, range or distribution to ensure the desired product quality.”

(taken from ICH Q8)
ACURINS® technology: PEG–PLA polymeric nanoparticles + API (Bind Ther)

<table>
<thead>
<tr>
<th>Class</th>
<th>Attribute</th>
<th>Test Method</th>
<th>Typical Acceptance Criteria</th>
<th>Safety</th>
<th>Efficacy</th>
<th>Max</th>
<th>Uncertainty</th>
<th>Criticality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endotoxin</td>
<td>BET</td>
<td>Depends on dose</td>
<td>10</td>
<td>1</td>
<td>10</td>
<td>0</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Sterility</td>
<td>USP</td>
<td>Negative</td>
<td>10</td>
<td>1</td>
<td>10</td>
<td>0</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>CCI</td>
<td>Dye Ingress</td>
<td>Negative</td>
<td>10</td>
<td>1</td>
<td>10</td>
<td>0</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Free drug content</td>
<td>CU-UPLC</td>
<td>Depends on dose</td>
<td>8</td>
<td>6</td>
<td>8</td>
<td>1</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Content uniformity</td>
<td>UPLC</td>
<td>Per USP&lt;905&gt;</td>
<td>8</td>
<td>5</td>
<td>8</td>
<td>0</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Particulate matter</td>
<td>SPOS</td>
<td>&lt; 6,000 (&gt; 10 μm) / container</td>
<td>8</td>
<td>2</td>
<td>8</td>
<td>0</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>ID</td>
<td>UPLC</td>
<td>Conforms to standard</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>0</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Surface properties</td>
<td>Surface PEG by NMR</td>
<td>Report results</td>
<td>4</td>
<td>6</td>
<td>6</td>
<td>2</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Binding/ligand</td>
<td>Depends on formulation</td>
<td>4</td>
<td>6</td>
<td>6</td>
<td>2</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Zeta potential</td>
<td>Report results</td>
<td>4</td>
<td>6</td>
<td>6</td>
<td>2</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Assay</td>
<td>UPLC</td>
<td>Depends on target</td>
<td>7</td>
<td>5</td>
<td>7</td>
<td>0</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Large particles</td>
<td>SPOS</td>
<td>NMT 0.05% 5-50 μm</td>
<td>6</td>
<td>3</td>
<td>6</td>
<td>1</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Drug purity</td>
<td>UPLC</td>
<td>Per ICH</td>
<td>5</td>
<td>4</td>
<td>5</td>
<td>2</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Counter ion content</td>
<td>UPLC</td>
<td>Depends on formulation</td>
<td>4</td>
<td>2</td>
<td>4</td>
<td>3</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Drug release profile</td>
<td>37 C IVR</td>
<td>Depends on formulation</td>
<td>6</td>
<td>4</td>
<td>6</td>
<td>0</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Accel IVR</td>
<td>Depends on formulation</td>
<td>6</td>
<td>4</td>
<td>6</td>
<td>0</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Reconstitution time</td>
<td>Per DFU</td>
<td>&lt; 5 minutes</td>
<td>6</td>
<td>4</td>
<td>6</td>
<td>0</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>pH of reconstitute</td>
<td>Potentiometric</td>
<td>4.0-8.0</td>
<td>6</td>
<td>2</td>
<td>6</td>
<td>0</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Appearance</td>
<td>Visual</td>
<td>Depends on formulation</td>
<td>6</td>
<td>2</td>
<td>6</td>
<td>0</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Particle size by DLS</td>
<td>DLS</td>
<td>70-130 nm, PDI ≤ 0.3</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>2</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Particle dose</td>
<td>SEC</td>
<td>Depends on drug load</td>
<td>4</td>
<td>2</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Residual solvents</td>
<td>GC or UPLC</td>
<td>Per ICH</td>
<td>4</td>
<td>1</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>
Calculating criticality

<table>
<thead>
<tr>
<th>Severity</th>
<th>Score</th>
<th>Description for Safety</th>
<th>Description for Efficacy</th>
<th>Uncertainty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negligible</td>
<td>2</td>
<td>No patient impact</td>
<td>No loss in efficacy</td>
<td>0 Impact established with clinical or in vivo data</td>
</tr>
<tr>
<td>Minor</td>
<td>4</td>
<td>Minor, reversible patient impact not requiring medical intervention</td>
<td>Minor loss in efficacy</td>
<td>2 Impact established in vitro</td>
</tr>
<tr>
<td>Moderate</td>
<td>6</td>
<td>Some impact on patient requiring medical intervention, reversible</td>
<td>Major loss in efficacy</td>
<td>4 Hypothetical impact based on literature</td>
</tr>
<tr>
<td>Major</td>
<td>8</td>
<td>Major, possibly irreversible impact on patient, not life threatening</td>
<td>Complete loss in efficacy</td>
<td></td>
</tr>
<tr>
<td>Catastrophic</td>
<td>10</td>
<td>Life threatening illness or irreversible injury to patient</td>
<td>Negative efficacy (accelerates disease)</td>
<td>6 Unknown</td>
</tr>
</tbody>
</table>

Criticality = Max (safety, efficacy) + Uncertainty

<table>
<thead>
<tr>
<th>Criticality</th>
<th>Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 4</td>
<td>Very low, not a CQA</td>
</tr>
<tr>
<td>4-5</td>
<td>Low, not a CQA unless “max” = 4</td>
</tr>
<tr>
<td>6-7</td>
<td>Moderate, CQA unless “max” ≤ 2</td>
</tr>
<tr>
<td>8-9</td>
<td>High, CQA requiring tight acceptance criteria</td>
</tr>
<tr>
<td>10+</td>
<td>Very high, extremely critical attribute requiring rigid acceptance criteria</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Class</th>
<th>Attribute</th>
<th>Test Method</th>
<th>Typical Acceptance Criteria</th>
<th>Safety</th>
<th>Efficacy</th>
<th>Max</th>
<th>Uncertainty</th>
<th>Criticality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endotoxin</td>
<td>BET</td>
<td></td>
<td>Depends on dose</td>
<td>10</td>
<td>1</td>
<td>10</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Sterility</td>
<td>USP</td>
<td>Negative</td>
<td></td>
<td>10</td>
<td>1</td>
<td>10</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>CCI</td>
<td>Dye Ingress</td>
<td>Negative</td>
<td></td>
<td>10</td>
<td>1</td>
<td>10</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Free drug content</td>
<td>CU-UPLC</td>
<td>Depends on dose</td>
<td></td>
<td>8</td>
<td>6</td>
<td>8</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Content uniformity</td>
<td>UPLC</td>
<td>Per USP&lt;905&gt;</td>
<td></td>
<td>8</td>
<td>5</td>
<td>8</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Particulate matter</td>
<td>SPOS</td>
<td>&lt; 6,000 (&gt; 10 μm) / container</td>
<td></td>
<td>8</td>
<td>2</td>
<td>8</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>ID</td>
<td>UPLC</td>
<td>Conforms to standard</td>
<td></td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Surface properties</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Surface PEG by NMR</td>
<td>Report results</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Binding/ligand</td>
<td>Depends on formulation</td>
<td></td>
<td>4</td>
<td>6</td>
<td>6</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Zeta potential</td>
<td>Report results</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assay</td>
<td>UPLC</td>
<td>Depends on target</td>
<td></td>
<td>7</td>
<td>5</td>
<td>7</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Large particles</td>
<td>SPOS</td>
<td>NMT 0.05% 5-50 μm</td>
<td></td>
<td>6</td>
<td>3</td>
<td>6</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Drug purity</td>
<td>UPLC</td>
<td>Per ICH</td>
<td></td>
<td>5</td>
<td>4</td>
<td>5</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Counter ion content</td>
<td>UPLC</td>
<td>Depends on formulation</td>
<td></td>
<td>4</td>
<td>2</td>
<td>4</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Drug release profile</td>
<td>37 C IVR</td>
<td>Depends on formulation</td>
<td></td>
<td>6</td>
<td>4</td>
<td>6</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Accel IVR</td>
<td>Depends on formulation</td>
<td></td>
<td>6</td>
<td>4</td>
<td>6</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Reconstitution time</td>
<td>Per DFU</td>
<td>&lt; 5 minutes</td>
<td></td>
<td>6</td>
<td>4</td>
<td>6</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>pH of reconstitute</td>
<td>Potentiometric</td>
<td>4.0-8.0</td>
<td></td>
<td>6</td>
<td>2</td>
<td>6</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Appearance</td>
<td>Visual</td>
<td>Depends on formulation</td>
<td></td>
<td>6</td>
<td>2</td>
<td>6</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>Particle size by DLS</td>
<td>DLS</td>
<td>70-130 nm, PDI ≤ 0.3</td>
<td></td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Particle dose</td>
<td>SEC</td>
<td>Depends on drug load</td>
<td></td>
<td>4</td>
<td>2</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Residual solvents</td>
<td>GC or UPLC</td>
<td>Per ICH</td>
<td></td>
<td>4</td>
<td>1</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>
ACCURINS® technology: PEG–PLA polymeric nanoparticles + API (Bind Ther)

<table>
<thead>
<tr>
<th>Non-Critical Quality Attributes</th>
<th>Residual process aid</th>
<th>Various</th>
<th>Report results</th>
<th>2</th>
<th>2</th>
<th>2</th>
<th>1</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Residual surfactant</td>
<td>UPLC</td>
<td>Report results</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Residual solvent (non-ICH)</td>
<td>UPLC</td>
<td>Report results</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Critical Operational Attributes</th>
<th>Yield</th>
<th>NA</th>
<th>NA</th>
<th>1</th>
<th>1</th>
<th>1</th>
<th>0</th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Filterability</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Process time</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Process efficiency</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Encapsulation efficiency</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Operator safety</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Common Pitfalls in Nanotechnology: Lessons Learned from NCI’s Nanotechnology Characterization Laboratory

Nanotechnology Characterization Laboratory, Advanced Technology Program, SAIC-Frederick, Inc., Frederick National Laboratory for Cancer Research, Frederick, MD 21702

Abstract

The Nanotechnology Characterization Laboratory’s (NCL) unique set-up has allowed our lab to handle and test a variety of nanoparticle platforms intended for the delivery of cancer therapeutics and/or imaging contrast agents. Over the last six years, the NCL has characterized more than 250 different nanomaterials from more than 75 different investigators. These submitted nanomaterials stem from a range of backgrounds and experiences, including government, academia and industry. This has given the NCL a unique and valuable opportunity to observe trends in nanoparticle safety and biocompatibility, as well as note some of the common mistakes and oversights of nanofabrication. While not exhaustive, this article aims to share some of the most common pitfalls observed by the NCL as they relate to nanoparticle synthesis, purification, characterization and analysis.

1. Sterility and endotoxin
2. Physicochemical characterization
3. Residual manufacturing components
4. Biocompatibility of components
5. Batch-to-batch consistency
6. In vivo stability
7. Drug release rates
Endotoxin limits in products for humans

Endotoxin limit for parenteral drugs = K/M

K = threshold human pyrogenic dose of endotoxin per kg of body weight,
M = maximum recommended human dose of product per kg of body weight in a single hour period (infusion or multiple injections) or maximum dose per kg (bolus injections)

Intravenous: 5 Endotoxin Units (EU)/kg body weight/hour
Intrathecal: 0.2 EU/kg/hour

Endotoxin limits in preclinical studies

Endotoxin limit for parenteral formulations in preclinical studies

\[ \text{Limit} = \frac{K}{M} \]

\[ K = 5 \text{ EU} / \text{kg} \]

\[ M = \frac{\text{dose (mg or mL (per h))}}{\text{kg}} \]

Example: 100 µL formulation injection into a mouse 1x daily

\[ \frac{5 \text{ EU kg}^{-1}}{(0.1 \text{ mL} / 0.03 \text{ kg})} \]

\[ = 1.5 \text{ EU/mL} \]

# Endotoxin effects *in vitro*

![Graph showing Endotoxin effects *in vitro*](image)

<table>
<thead>
<tr>
<th>Au NPs 4 nm</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Endotoxin (EU/ml) in</td>
<td>Solvent</td>
<td>NPs</td>
</tr>
<tr>
<td>Wet #1</td>
<td>5.9</td>
<td>151.6</td>
</tr>
<tr>
<td>Wet #2</td>
<td>1.1</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>Wet #3</td>
<td>27.8</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td>Wet #4</td>
<td>&lt;1.0</td>
<td>3.4</td>
</tr>
</tbody>
</table>

**Batch to batch variation**

**IL-1β expression in human monocytes**

Li & Borashi (2016) *Nanomed.* Vol. 11, No. 3, 269–287
Importance of testing filterability and product yield (critical safety and operational attributes)

Investigating formulation parameters of photoluminescent π–conjugated nanoparticles for optical imaging and parenteral administration?

Ahmadkhanbeigi (2015) Biomacromol
Abelha (2016) Nanoscale

Improved stability in biofluids and optical properties

F8BT 95% total mass

F8BT 5% total mass

Excipients

Product yield (%) after filtration through a 0.2 µm membrane filter

SDS Solutol C12E6 C18-1E10 C18E20 C12E23 C18E100 PEG-PLGA PEG-PLGA

Nanoprecipitation Microfluidics

Mini-emulsion
Importance of testing residual solvents

Investigating formulation parameters of photoluminescent π–conjugated nanoparticles for optical imaging and parenteral administration?

Impaired mitochondrial activity

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>0:1</th>
<th>20:1</th>
<th>20:1 (680)</th>
<th>20:1 (720)</th>
<th>1:0</th>
</tr>
</thead>
<tbody>
<tr>
<td>% cell population with impaired mitochondrial activity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Addition of ethanol in the formulation

Kemal (2016) RSC Adv
Importance of testing excipient purity and pH over time

All polymers were stored according to manufacturer instructions
Importance of considering particle dose

Reference fluorophore (ICG) in an aq. sol. (100 µg)
100 µg/mL total mass
Clinical dose: 25 mg/kg

vs

100 µg of a novel fluorophore (5%) encapsulated in PEG–PLGA nanoparticles

2000 µg / mL total mass
Projected clinical dose based on same fluorophore content: 500 mg/kg
“Quality by Design is a systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management” (taken from ICH Q8)
Generating “know–how” in research labs

**Knowledge space**
Area for which knowledge exists based on literature, process modelling and experimental data

**Design space**
Range of process conditions that produce a product within the specifications

**Control space**
Range of process conditions used for routine production of the product
Creating the knowledge space adds value

Design of Experiment (multivariate analysis)

Variable 1

H_{V1} L_{V2}  
M_{V1} L_{V2}  
L_{V1} L_{V2}

Variable 2

H_{V1} M_{V2}  
M_{V1} M_{V2}  
L_{V1} M_{V2}

Nelder–Mead Simplex optimisation

Variable 1

Form#3

Variable 2

Form#2

Form#1

Form#4
Creating the knowledge space adds value

Contour plots of data can be used to create the knowledge space and is added value for potential commercialisation of the technology.
Nanomedicine research with translation potential

KEY POINTS

• Understanding the pharmaceutical development process helps us design better research studies

• Using selected experimental design approaches from the industry can add value to the project

• Judicial use of the peer review process can reinforce the importance of quality parameters for research studies
Acknowledgements and Literature

**AbbVie**
Thomas Merdan

**Contributors**
Raha Ahmadkhanbeigi
Thais Abelha
Laura Urbano
Sana Hussain
Rachel Patel
Evren Kemal
Mark Green
Paul Robert Neumann

- ICH Q8 guidelines
- Nanotechnology Characterisation Lab literature in general