NANoREG-Proposed ISA-TAB-Nano Template Expansion:

How Do we Add Commentary into Templates?

&

How Will We Incorporate Nanoparticle Instances?

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NanoWG Presentation

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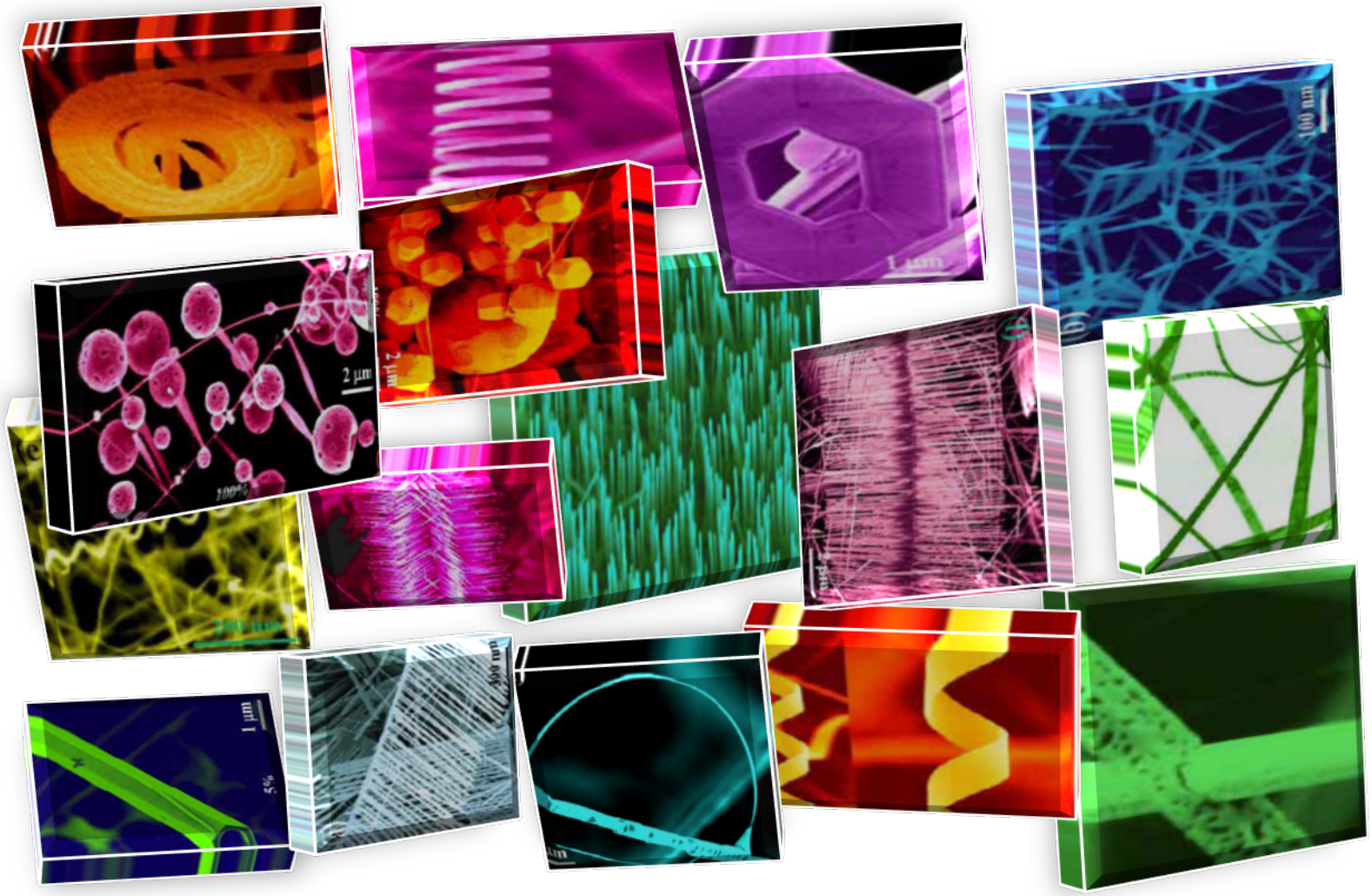
CEINT

Duke University · Carnegie Mellon · Virginia Tech · Howard University · Stanford University · UK University of Kentucky · Baylor University · NSF · United States Environmental Protection Agency

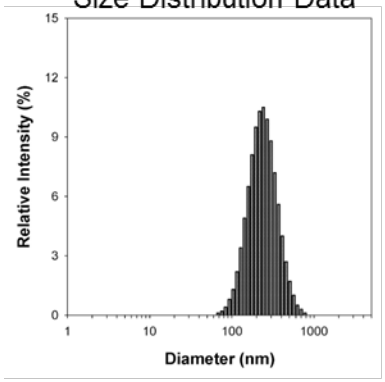
Nanomaterials are Complex



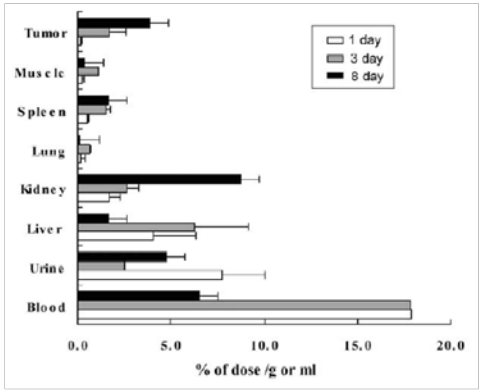
https://wiki.nci.nih.gov/display/ICR/ISA-TAB-Nano

Assay and Data Diversity

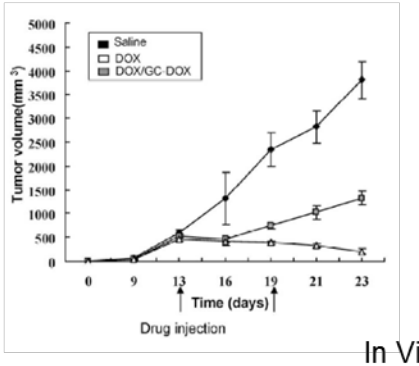
Size Distribution Data

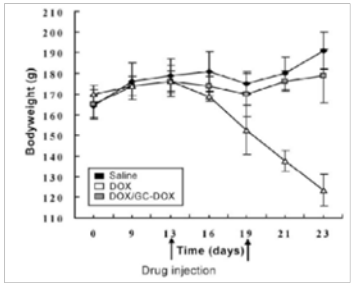


Tissue Biodistribution



Anti-tumor Activity





Zeta Potential

Table 1
Zeta potential values of control and tamoxifen loaded nanoparticles[a]

Nanoparticle formulations	Zeta potential (mV)
Control nanoparticles	6.7±1.2[b]
Tamoxifen-loaded nanoparticles	25.4±1.4

[a] Zeta potentials of the nanoparticle suspension in deionized distilled water were measured using the Brookhaven's Zeta PALS instrument.
[b] Mean ±S.D ($n = 8$).

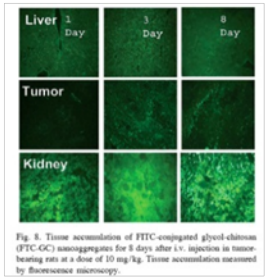
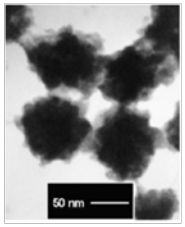
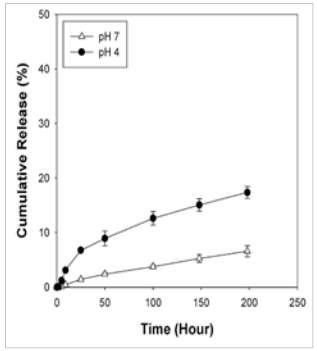


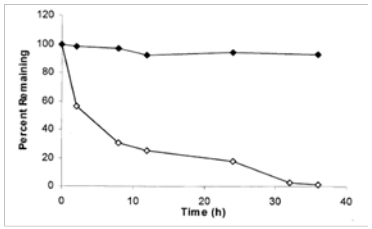
Fig. 8. Tissue accumulation of FITC-conjugated glycol-chitosan (FTC-GC) nanoaggregates for 8 days after i.v. injection in tumor-bearing rats at a dose of 10 mg/kg. Tissue accumulation measured by fluorescence microscopy.

Surface Morphology Data

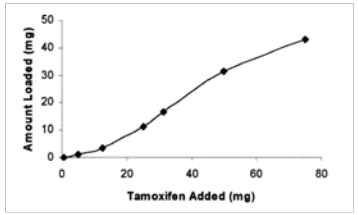


In Vitro Drug Release



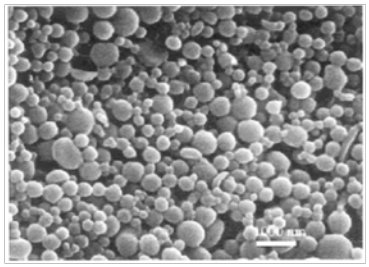


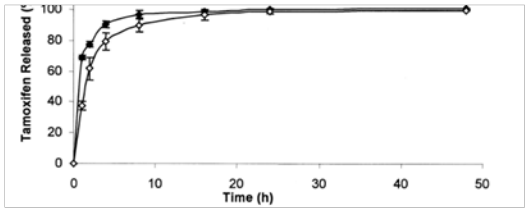
Drug Loading Data



Preparation

Chemical Composition of Nanoparticle Formulation





Source: Chawla JS et al, *Int J Pharm*, **249**, 127-38 (2002), Son YJ et al, *J Control Release*, **91**, 135-145 (2003)

https://wiki.nci.nih.gov/display/ICR/ISA-TAB-Nano

Issue: Nanomaterial & Study Diversity

Nanophase structure/behavior are far more complex/diverse than analysis of Chemical Composition may suggest

Diversity of test systems

- Ecosystem vs. organism vs. cell vs. test tube
- Species, cell line
- Age, gender, weight

Diversity of measurements and assays

- Physical-chemical: size, potential, surface chemistry, shape (*morphology & structure*), aggregation vs. agglomeration, …
- Biological: toxicity, recognition & association, uptake, delivery, …
- Exposure: dose & concentration, timing, duration, …
- Thermodynamic stability (nanophase formation/transformation), energetics of the surface (surface enthalpy, adsorption/desorption enthalpies) >> future work

Diversity of data resources with lack of common standard for data exchange

Slide modified from https://wiki.nci.nih.gov/display/ICR/ISA-TAB-Nano

ISA-TAB-Nano Evolution

Expands the Investigation/Study/Assay (ISA-TAB) format

- **ISA is the standard tab-delimited file format**
- **Developed by the European Bioinformatics Institute (EBI) for representing a variety of assays and technology types**
- ***ISA-TAB-Nano* adds *Materials* to the standard ISA format**

Incorporates into the ISA standard tab-delimited format for describing data all of the following:

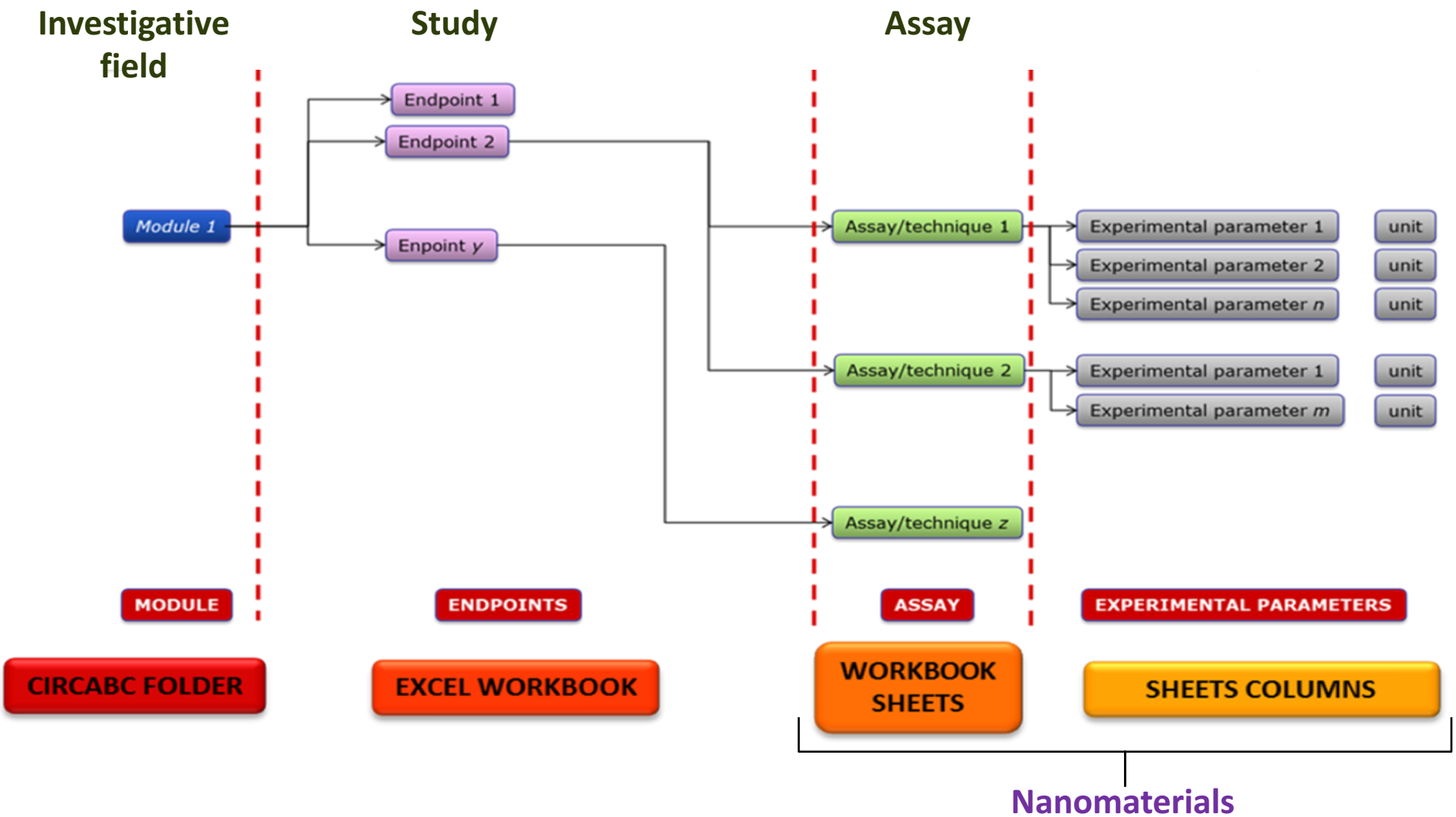
- **Investigative fields, e.g. Modules**
- **Studies, e.g. Endpoints (Excel workbooks)**
- **Assays (Excel worksheets)**
- **Materials; nanomaterials (added into the Assay worksheets)**
- **Nanomaterials terminology and concepts from the NanoParticle Ontology (NPO) as well as other ontologies**

CEINT NIKC is expanding NANoREG-based templates to capture:

- **functional assays (reaction systems), media characterization data, and nanomaterial transformations over time (instances)**

Slide modified from https://wiki.nci.nih.gov/display/ICR/ISA-TAB-Nano

Investigation Study Assay (ISA)-TAB-Nano



From flowchart in ISA-TAB-Nano template workbook

Progress on NANoREG-Proposed ISA-TAB-Nano Templates

- Templates have been prepared for comments
- Physical-Chemical templates have my comments
  - Minimal commentary on the biological templates, so far
- Templates uploaded into Google Docs (March 15th)
  - Commenters were invited to make comments (Christine's talk 3/16/17)
- *Commentary from others is needed*
  - Templates are available: ceint.duke.edu > NIKC > ISA-TAB-Nano
  - Review/incorporate changes & report again to NanoWG
  - Another round of comments/revisions, before finalizing (date?)
- Questions about incorporating nanomaterial instances

NANoREG-Proposed ISA-TAB-Nano Templates: How to Make Comments

CEINT Center for the Environmental Implications of NanoTechnology

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ISA TAB Nano

WHAT IS ISA-TAB-NANO?

The ISA-TAB-nano file sharing format, developed under the National Cancer Informatics Program Nanotechnology Working Group (NCIP NanoWG), is an accepted ASTM standard (ASTM International E2909-13).

In 2016, the European project NANoREG adopted and adapted the ISA-TAB-nano format to consistently organize the results of their broadly distributed network of researchers. To create the templates they have followed the logic of the original ISA-TAB-nano formatting, but have also drawn upon relevant existing ontologies and extended it to incorporate additional endpoints and methods not addressed in the original standards. The resulting templates can be downloaded here.

Offer your comments!

Also in 2016, CEINT has taken on the leadership of updating and extending the ISA-TAB-nano templates, in collaboration with researchers at Oregon State University and with the continued efforts of the NCIP NanoWG. As part of this effort we are collating input from all interested stakeholders who wish to offer commentary on the NANoREG-proposed ISA-TAB-nano templates.

Physical-Chemical Characterizations Comment Forms

https://drive.google.com/open?id=0BzDfkK3j1-1ULTdLVG93N0dtc3c

https://drive.google.com/open?id=0BzDfkK3j1-1UelpGTzVmbWRJYTg

From the CEINT website, *click* on one of the Google Drive hyperlinks. Google Drive contains a list of folders (the Modules) in which the template workbooks (the Endpoints) are located.

Open one of these Endpoint workbooks and therein you'll find excel tabs for various experimental techniques (the Assays).

Within an Assay tab, you'll input information into boxes for Experimental Parameters, or worksheet columns:

- **Commenter column - name, date, and institution**
- **Along the row containing commenter information, input suggested revisions, or comments.**

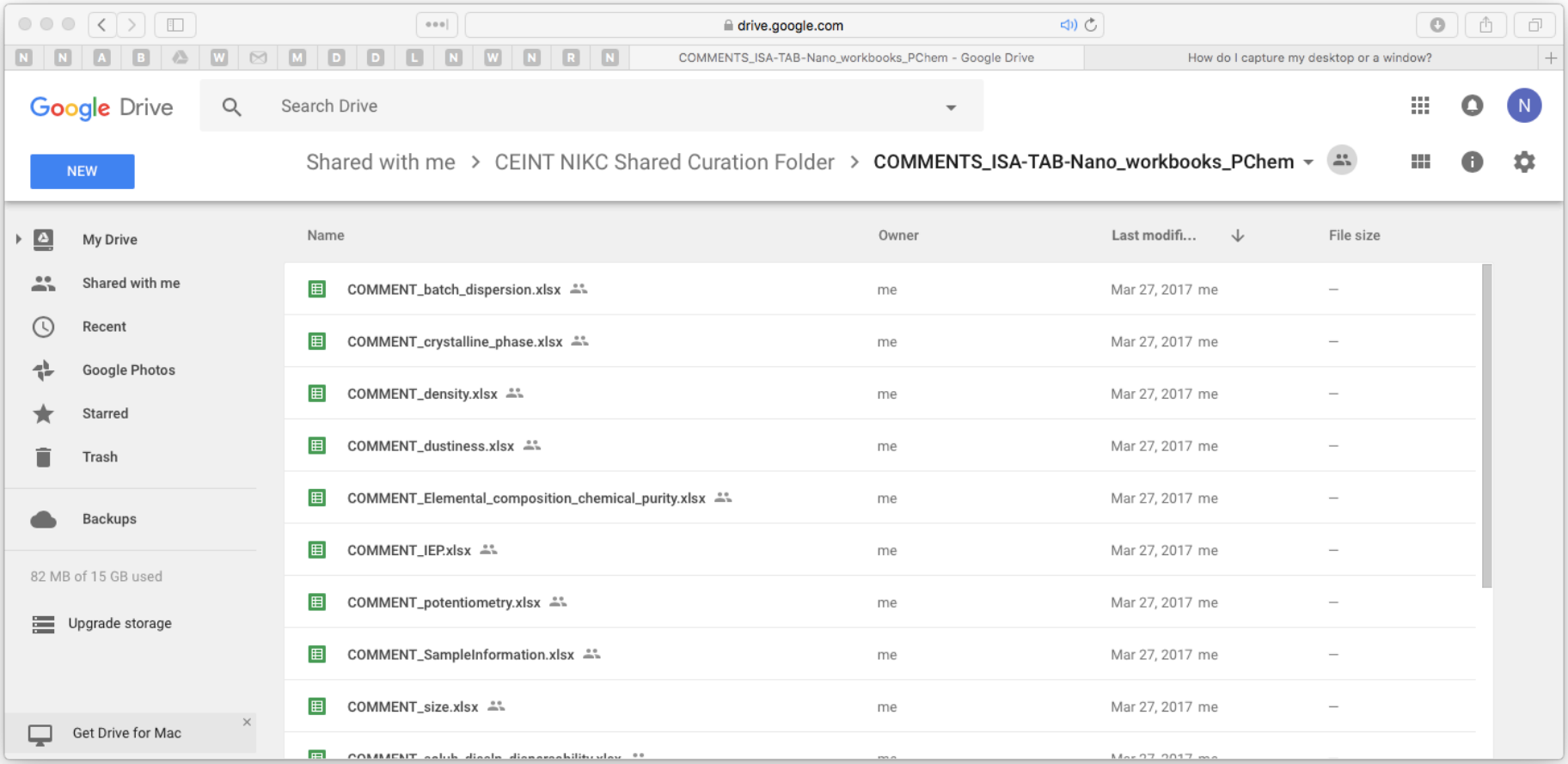
Let's look at an example together…Physical-Chemical Module

https://ceint.duke.edu/research/nikc/isa-tab-nano

After Clicking on a Google Drive hyperlink from the CEINT website...

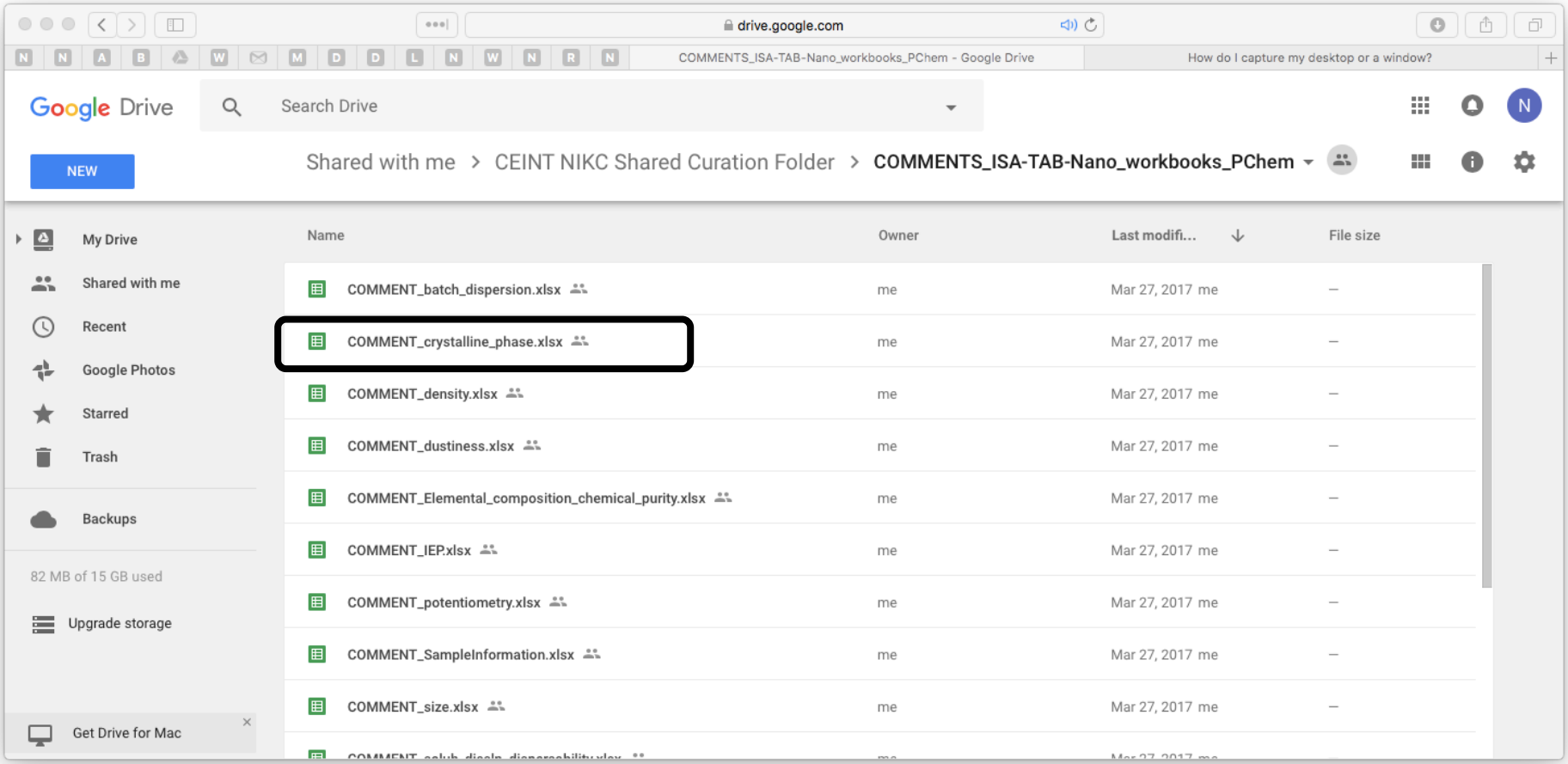
Physical-Chemical Characterizations Comment Forms

e.g. This hyperlink is for the Physical-Chemical Module folder labeled: COMMENTS_ISA-TAB-Nano_workbooks_PChem

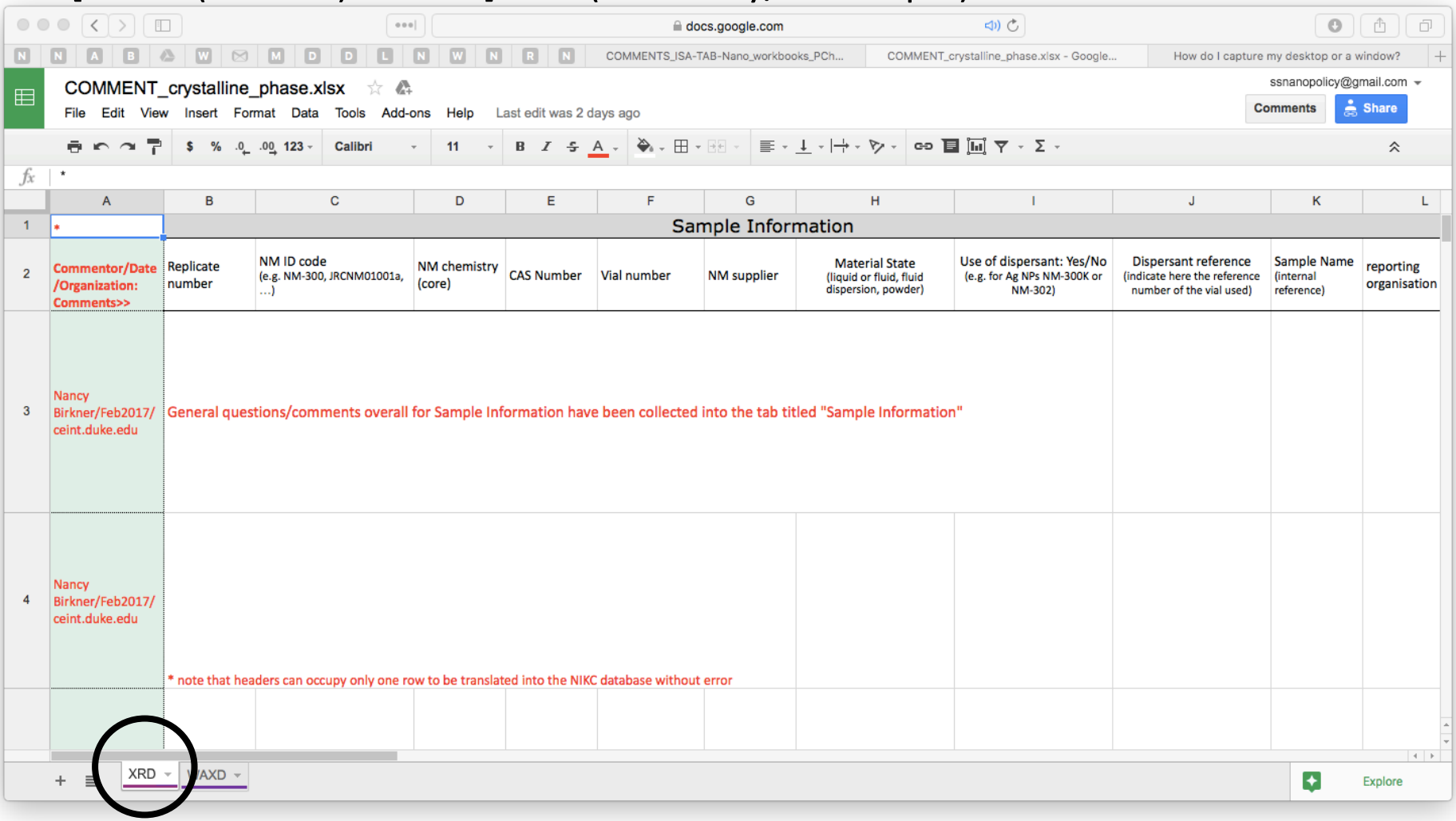


Within the Physical-Chemical Module folder labeled: COMMENTS_ISA-TAB-Nano_workbooks_PChem

[***select*** (click on) a workbook] COMMENT_crystalline_phase.xlsx (Endpoint)



Within the workbook (Endpoint), COMMENT_crystalline_phase.xlsx, [***select*** (click on) the tab] XRD (the Assay/Technique)



Left: highlighted in mint-green is the column for input of commenter's information.
Right: comment fields/columns (Experimental Parameters). Click & type in the box.

Still within the workbook (Endpoint), COMMENT_crystalline_phase.xlsx, [XRD tab] (the Assay/Technique)

COMMENT_crystalline_phase.xlsx

	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD
1	Sample preparation		Method and instrument information									
2	Heading is needed, see below	Heading is needed, see below	Capillary diameter	Source	Geometry	Detector	Monochromator	Wavelength (nm)	2θ range	2θ step	2θ scan speed	Scanning Mode
3	Sample preparation header is needed: e.g. Sample mount	Sample preparation header is needed: e.g. Sample preparation technique or referenced peer-reviewed article or SOP	I don't understand what Capillary diameter refers to here.	is this standard XRD or high energy source XRD at a synchrotron? If it's standard XRD then the choices are Cu or Mo.								
4	which zero background silicon (Si) plate was used?	what, if any, fixation agent was used (e.g. ethanol, or dry nano powder)	*For nanomaterial powder X-ray diffraction samples are not mounted using a capillary tube, instead a zero background silicon (Si) plate is used*	maybe a dropdown list for the source of the X-Rays								
	General comment about XRD sample preparation: For nanomaterial powder X-ray											

Example of comments made in each column of interest, suggesting or commenting or questioning. Should we add dropdown lists? Why is Capillary diameter used?

Still within the workbook (Endpoint), COMMENT_crystalline_phase.xlsx, [XRD tab] (the Assay/Technique)

COMMENT_crystalline_phase.xlsx

File Edit View Insert Format Data Tools Add-ons Help All changes saved in Drive

Results

	AG	AH	AI	AJ	AK	AL	AM	AN	AO	AP	AQ
1	Results										
2	Headers are needed for crytal system details, see corresponding cells, below, for specific heading suggestions. I suggest, use a dropdown for the unit cell geometry (there are seven of them) for each mineral phase. Side lenths (units of Angstron										
3	I suggest, a drop-down list that indicates either single phase or mixed phase nanomaterial	I suggest, a drop-down list for the unit cell geometry (e.g. cubic, orthorhombic, monoclinic, hexagonal, triclinic, rhombohedral, tetragonal) for the sample whether it is a single phase or the major phase (e.g. the major phase)	I suggest, a drop-down list for the unit cell geometry of the minor phase (second phase of a mixed phase sample), and perhaps include the selection, not applicable (NA), if the sample is a single phase (pure mineral phase sample)	sidelength A	sidelength B	sidelength C	angle alpha	angle beta	angle gamma	Space group	Point group
4		Excellent reference: The International Tables for Crystallography, a database of crystallographic tables, for reference source or further details (Edited by Mois I. Aroyo)									

XRD WAXD

Example of comments suggesting that we include XRD crystal system information

Your commentaries are needed

CEINT ISA-TAB-Nano Extension:
https://ceint.duke.edu/research/nikc/isa-tab-nano

or

Physical-Chemical Characterizations Comment Forms:
https://drive.google.com/drive/folders/0BzDfkK3j1-1UWFZUY3cxQjBmSWc

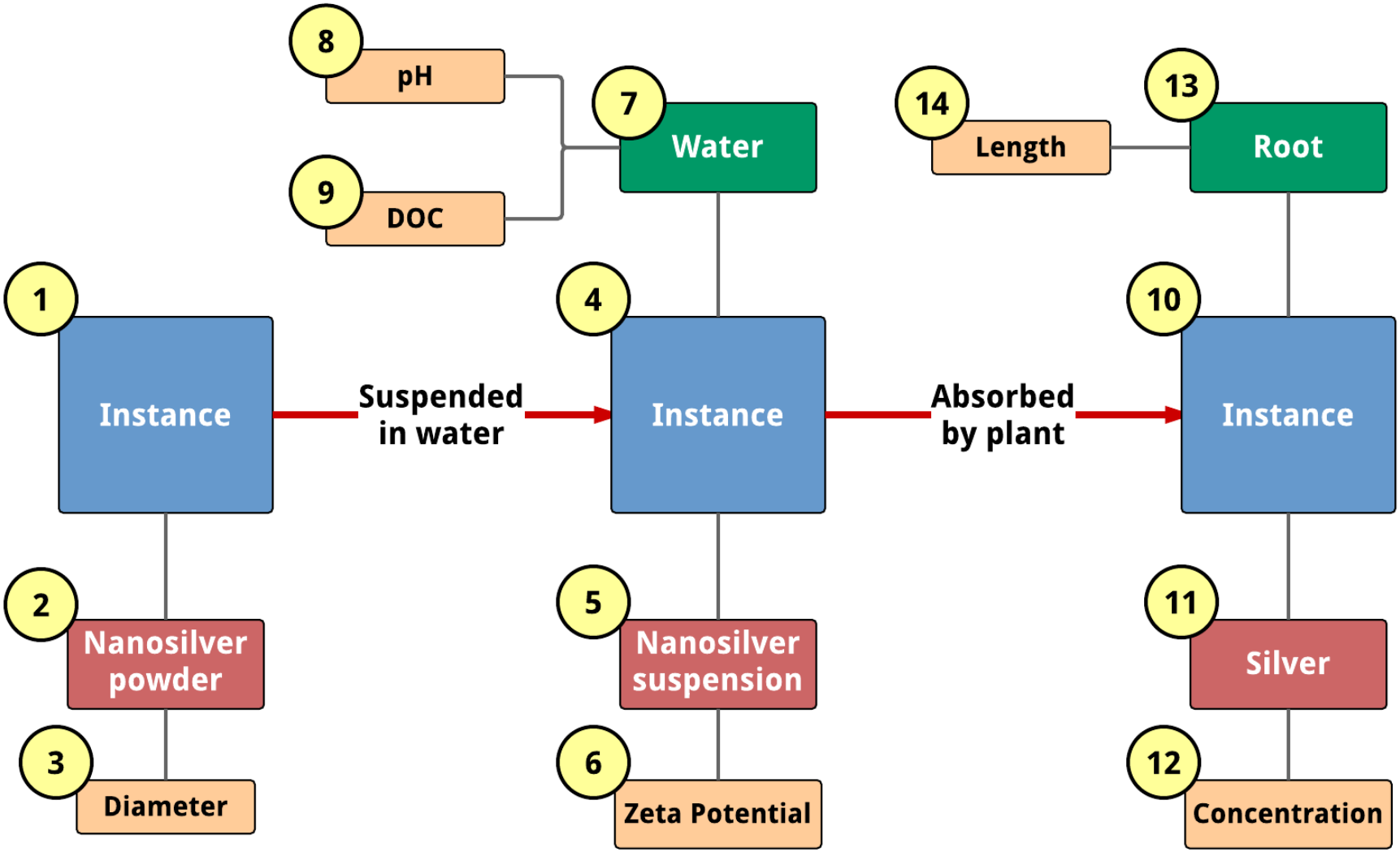
Mammalian Toxicity (*in vivo*) Comment Forms:
https://drive.google.com/open?id=0BzDfkK3j1-1ULTdLVG93N0dtc3c

Mammalian Toxicity (*in vitro*) Comment Forms:
https://drive.google.com/open?id=0BzDfkK3j1-1UelpGTzVmbWRJYTg

How to Represent Nanoparticle (NP) Instances?

- NP Instance 1: Nascent NP
  - Synthesized NP is then characterized (XRD, TEM, …)
- NP Instance 2: Functionalized NP
  - Nascent NP surface functionalization followed by characterization (e.g. XRD, TEM, ICP-OES…)
- NP Instance 3: Functionalized NP put into Media
  - NP is then characterized again (size, phase ID, purity, …)
- NP Instance 4… : NP exposed to full experiment
  - NP characterization after/during final experiment - exposure to the substrate or system in question

Visualizing the NIKC Concept of "Instance": Tracking the Life-cycle of a Nanomaterial



In Summary:
Where Are We Now & What's Next

- **Suggest a deadline for completion of comment collection and the next steps.**
  - **End of July for the final collection of comments?**
  - **Followed by integration of comments and then finalize the templates.**
  - **Upload onto share site by middle of August (say, 08/18/17)?**
- **Decide/agree on how to represent nanoparticle instances**
- **Development of additional physical-chemical templates. Currently preparing surface association affinity template.**
  - **Please contact me if you've an interest in working together to produce a specialized template**
- **Produce audio-visual presentations (e.g. YouTube) that demonstrate nanomaterial template development method, to guide others who want to create their own templates.**

Your commentaries are needed

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or

Physical-Chemical Characterizations Comment Forms:
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The combined effort of over 130 researchers

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Image: http://pratt.duke.edu/about/news/setting-ground-rules-nanotechnology-research

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