An update on the CODATA Uniform Description System for Nanomaterials

and its use in supporting NanoEHS work

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Today’s Presentation

- What is the UDS today?
- What is next for the UDS?
- The UDS in support of Read Across and QSAR
- Conclusions and recommendations

CODATA Uniform Description System for Nanomaterials Today

- Version 2.0 released on www.codata.org/nanomaterials on 25 May 2016; freely available for use
- Review workshops have been held in U.S. , Europe, and Asia
  - Feedback on improvements for definitions, ambiguity (reduction thereof), clarity, etc.
- Insights from the nanoparticle ontology (NPO), ISA-TAB Nano, eNanoMapper, caNanoLab

- Final review is gathering new comments

Modeling Nanomaterials

Issues

- Complexity of information
- Lack of important knowledge in key areas
- No comprehensive collection of data
- Multi-disciplinary with multiple user communities
- Premature standardization

Consequences

- Difficulty in modeling
- Modeling unknown data
- No vigorous test of model
- Difficult to get everyone together
- Standardizing concepts and definitions prematurely

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CODATA Approach

- Data modeling
  - Natural language
  - “Elementary” level
  - Understandable by researchers and users of nanomaterials
  - Emphasis on clarity of definitions
- Information categories and detailed descriptors
- Ease of use by implementers
- Broad multi-disciplinary, multi-user WG

Nanomaterials in the UDS

Types

*Nano-objects *

*Collections of nano-objects

*Described in the UDS

- Nano-objects in bulk materials (solid and liquid)
- Bulk materials with nano-scale features

Information Categories

* Characterization

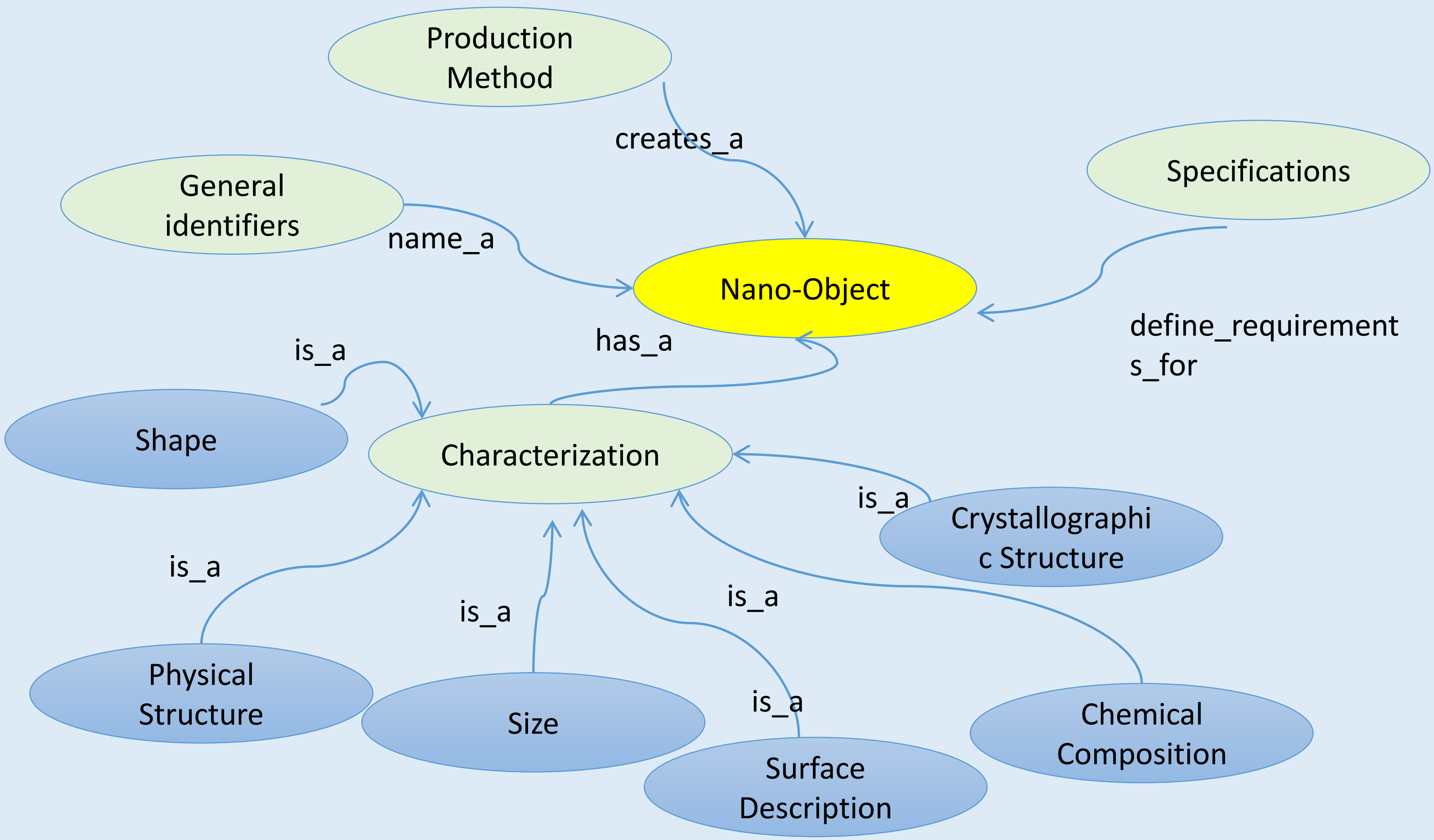
* Production

* Specification

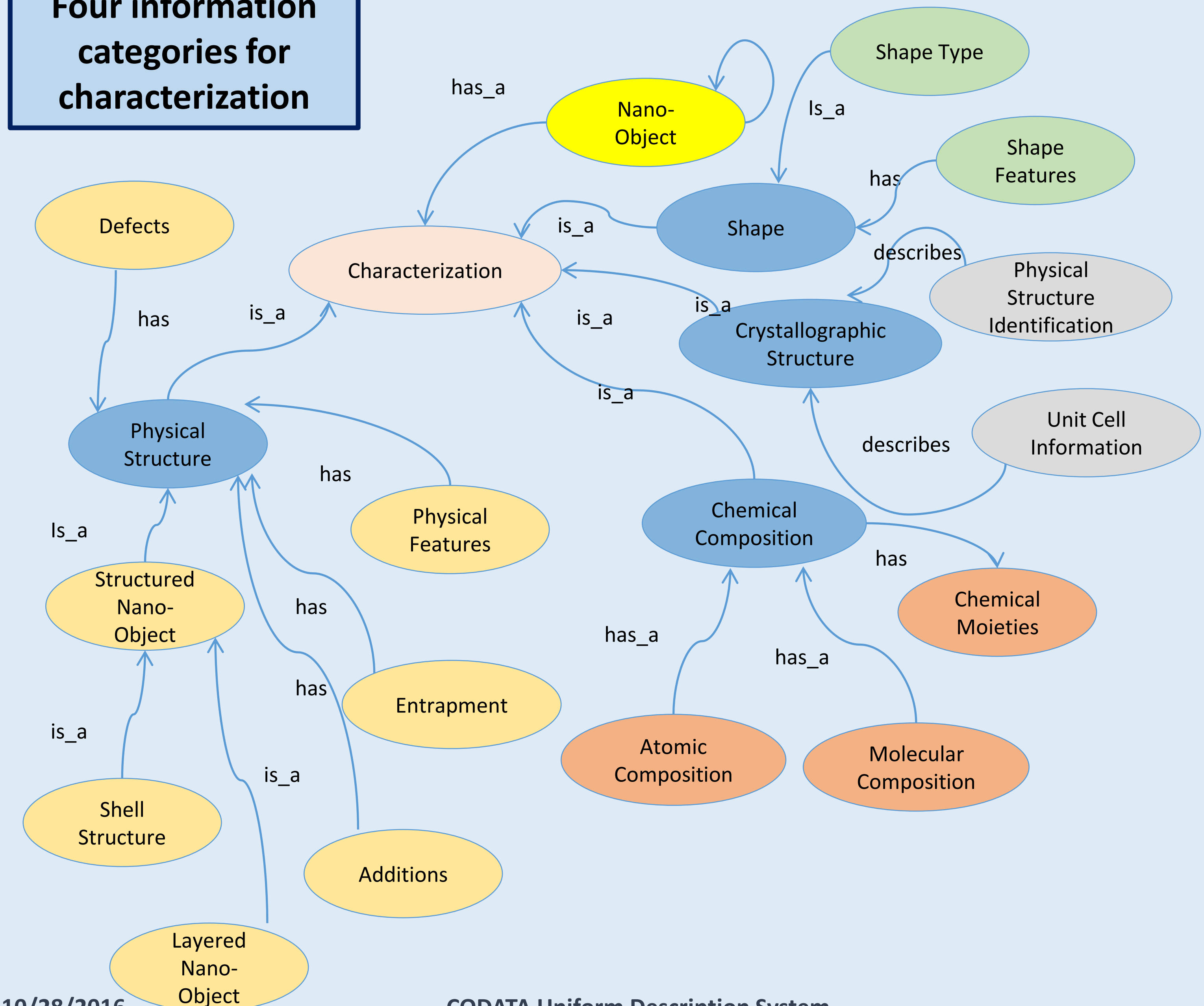
* General Identifiers

*Described in the UDS

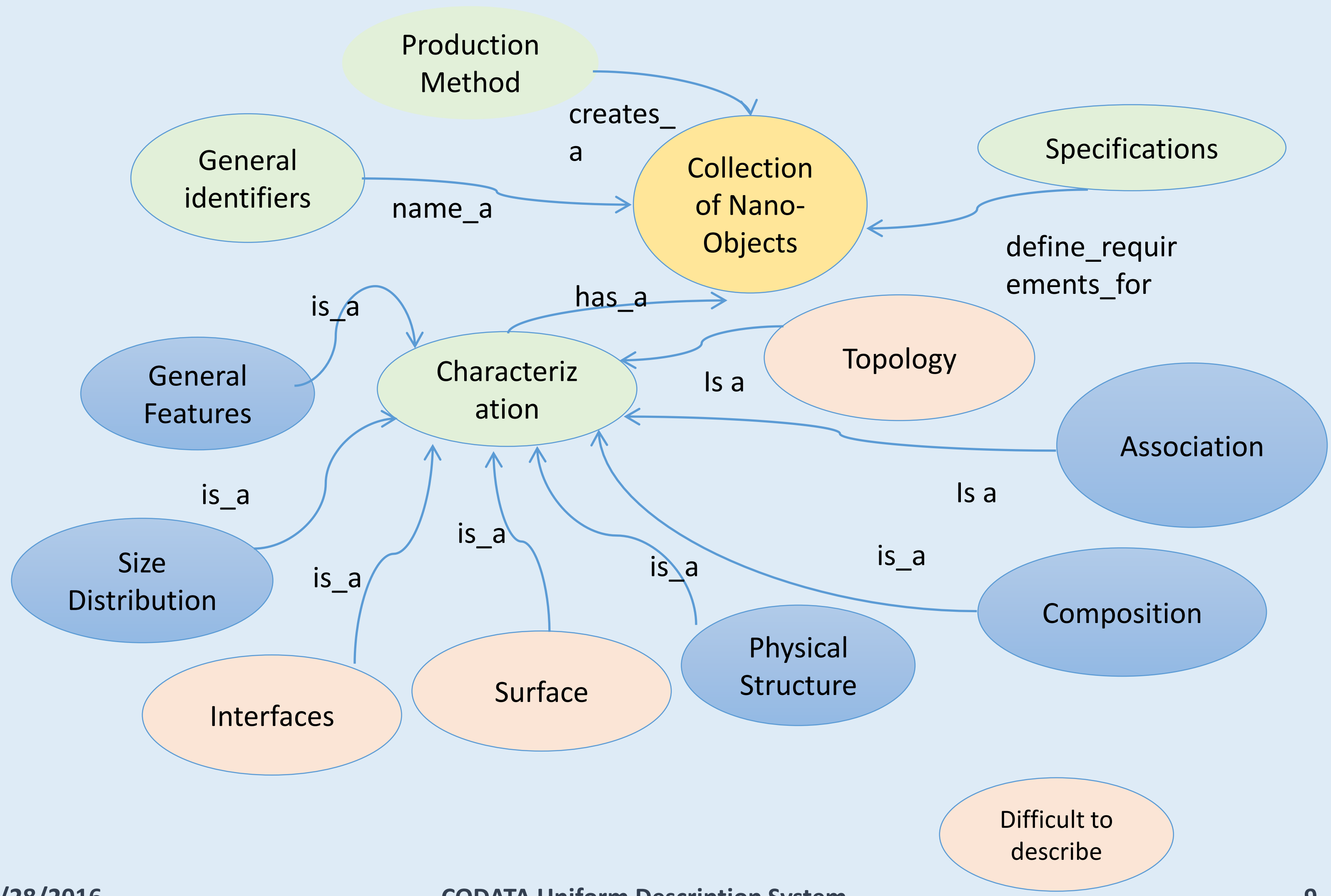
Description of Nano-objects



Four information categories for characterization



Description of Collection of Nano-objects



What is a Nanomaterial?

- ISO TC 229 definition

  "A Nanomaterial is a material with any external dimension in the nanoscale [approximately 1 nm to 100 nm] and/or having internal structure or surface structure in the nanoscale."

- Emphasizes aspects of <u>an individual nanomaterial</u>
- Almost equivalent to a nano-object (ISO definition of nano-object)

  "A material with one, two, or three external dimensions in the nanoscale" (as defined in ISO/TS 80004-3:2010(en), 2.2)

What is a Nanomaterial?

EU definition

"A natural, incidental or manufactured material containing particles, in an unbound state or as an aggregate or as an agglomerate and where, for 50 % or more of the particles in the number size distribution, one or more external dimensions is in the size range 1 nm - 100 nm.

"In specific cases and where warranted by concerns for the environment, health, safety or competitiveness the number size distribution threshold of 50 % may be replaced by a threshold between 1 and 50 %."

- Emphasizes fact that <u>real situations involve collections of nano-objects</u>
- Does not specify any characteristic except "external dimensions"

What is next for the UDS?

- Working with ASTM E56 on Nanotechnology to develop guide for nano-objects (just starting)
- CODATA WG on Nanomaterials is being extended
  - New chairs: CEINT Christine Hendren U.S.) and CEREGE (France)
  - Extending ISA-TAB-nano and integrating the UDS into it
- Using the UDS with categorisation efforts (with Univ College Dublin and Future Nano Needs project)
- Applying UDS to update existing ontologies and supporting creation of data repositories

The UDS and Read-Across and QSAR

- Useful to go back to what we are really trying to do by these efforts in RA and QSAR

  - *To predict a property and functionality (behavior) of a substance, without making the necessary measurement, based on the similarity of that substance to other substances for which we have measurements.*

  - *Further to do this on the basis of scientific evidence, which includes reproducibility, accurate uncertainties, and sound physical principles.*

Property = Function (Nanomaterials, Measurement Conditions)

To achieve our goal of prediction, we must answer the following questions:

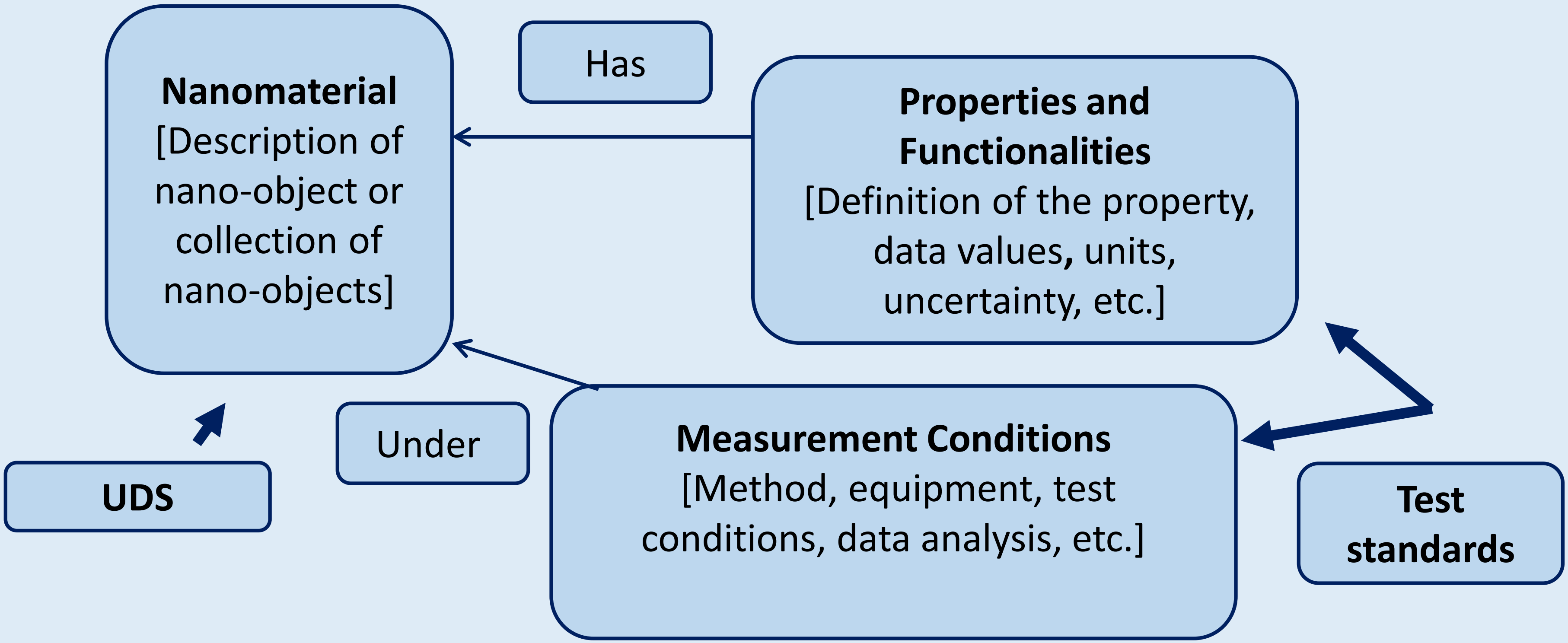
1. Which nanomaterials features affect a property?
2. Which measurement conditions affect a property?
3. What is the function that links nanomaterials features and measurement conditions to the property, that is, how do they affect the property?

UDS and NanoEHS

This is not a moot conversation

- Regulations are being developed about nanomaterials based on their real and supposed impact on people, animals, and the environment
- Read across (RA) and QSAR methods rely on accurate definitions of independent variables and parameters that govern functionality
- If we don’t know which nanomaterial feature causes an effect, we are in big trouble

Model of Nanomaterial Property Data

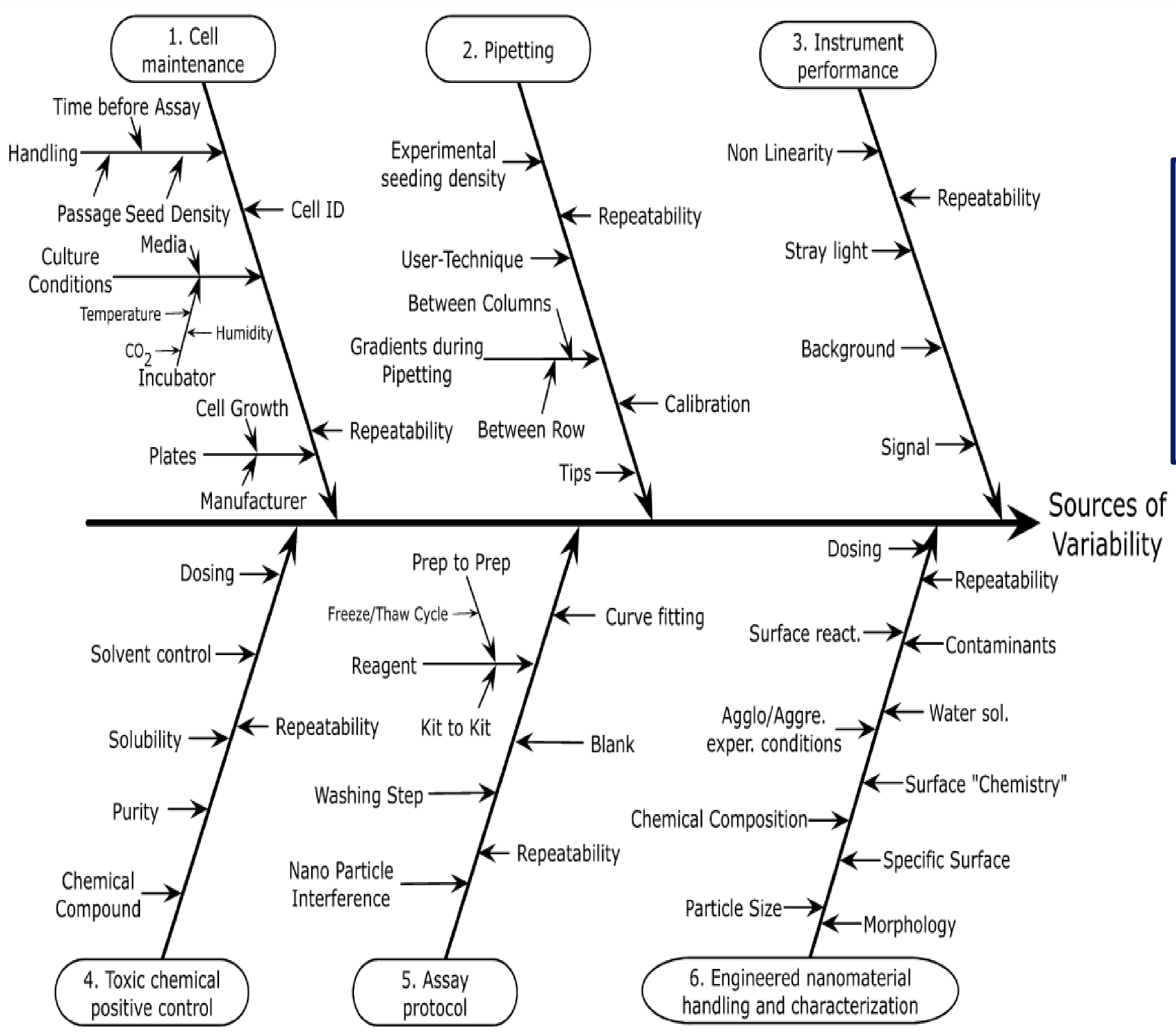


Number of possible independent nanomaterial features and measurement conditions is large

Features of Nano-objects	Features of a Collection of Nano-objects	Classes of Measurement Conditions
Shape	General features	Specimen preparation
Size	Size distribution	Measurement type
Chemical composition	Interfaces	Measurement procedure
Crystallographic structure	Surface characteristics	Instrument descriptions
Surface characteristics	Physical Structure	Test environment
Physical structure	Composition	Initial test results
Production method	Topology	Data analysis
Specifications	Association	
	Production method	
	Specifications	

Some Complexities

- Nanomaterials ae complex: the “same” nanomaterials may differ in significant details – e.g. stars may have varying size points
- Actual mechanisms of actions can be difficult to discern, and relying on gross effects, while proving possible hazardous effects, may not determine what actually caused that effect
- Even reproducibility does not clarify cause and effect.
- As Krog has shown, most measurements showing gross effects have not control important gross level conditions so that proposed nano-object mechanisms are suspect.



From Harald Krug talk; Quality Nano Meeting, Crete July 2015

UDS and NanoEHS

We can describe

- the “starting” nanomaterial and the step-wise changes,

  or

- the tested nanomaterial and the processes used to make it from a starting nanomaterial,

  or

- the nanomaterial at each step

Regardless,

- need better definition of the relationship between the test results and the original nanomaterial
- present ontologies and data models do this in an encompassing manner that makes it difficult to trace cause and effect,
- i.e., which features (independent variables) really govern the results obtained?

Consider this sequence of events a nanomaterial experiences during "testing"

Manufactured, Natural, or Prepared Nanomaterial

This is the "substance" for which users, regulators, and the public want results: Almost always a collection of nano-objects

As received

In spite of precautions, changes occur during shipping and storage: agglomeration, aggregation, reactions, degradation: The collection has changed in some way

As prepared for testing

Usually some processing takes place, including purification, reactions, reversal of shipping and storage effects: Perhaps restoring the nanomaterial to its "original" state

Which nanomaterial needs to be described and how?

As sampled

A subset of the nanomaterial is taken for testing, using standard, specified, or ad hoc procedures: Hopefully fully representative of the original material

In test environment

Once in the test environment, the nanomaterial may experience reactions, additions, alterations, including coronas, surface modification, pH changes, etc.: What is the relationship to the original material

Data and NanoEHS

- Unlike organic and biochemistry, large comprehensive data sets of nanomaterials properties and test results are not yet available
- Available data sets are sparse and do not contain the richness of data that years of testing of organic and bio-chemicals have produced

- The research culture in nanomaterials is still in the exploratory stage with emphasis of finding new phenomena and gross effects

Data and NanoEHS

- Even present projects to systematically explore cause and effect have challenges
- Present standards are not detailed enough to enable valid data analysis to determine cause and effect in most instances
    - reporting test results
    - description of nanomaterials
    - standard test procedures
    - deviations from standard procedures
    - bio-assays
- See recent review by Lowry *et al* on zeta potentials

Questions

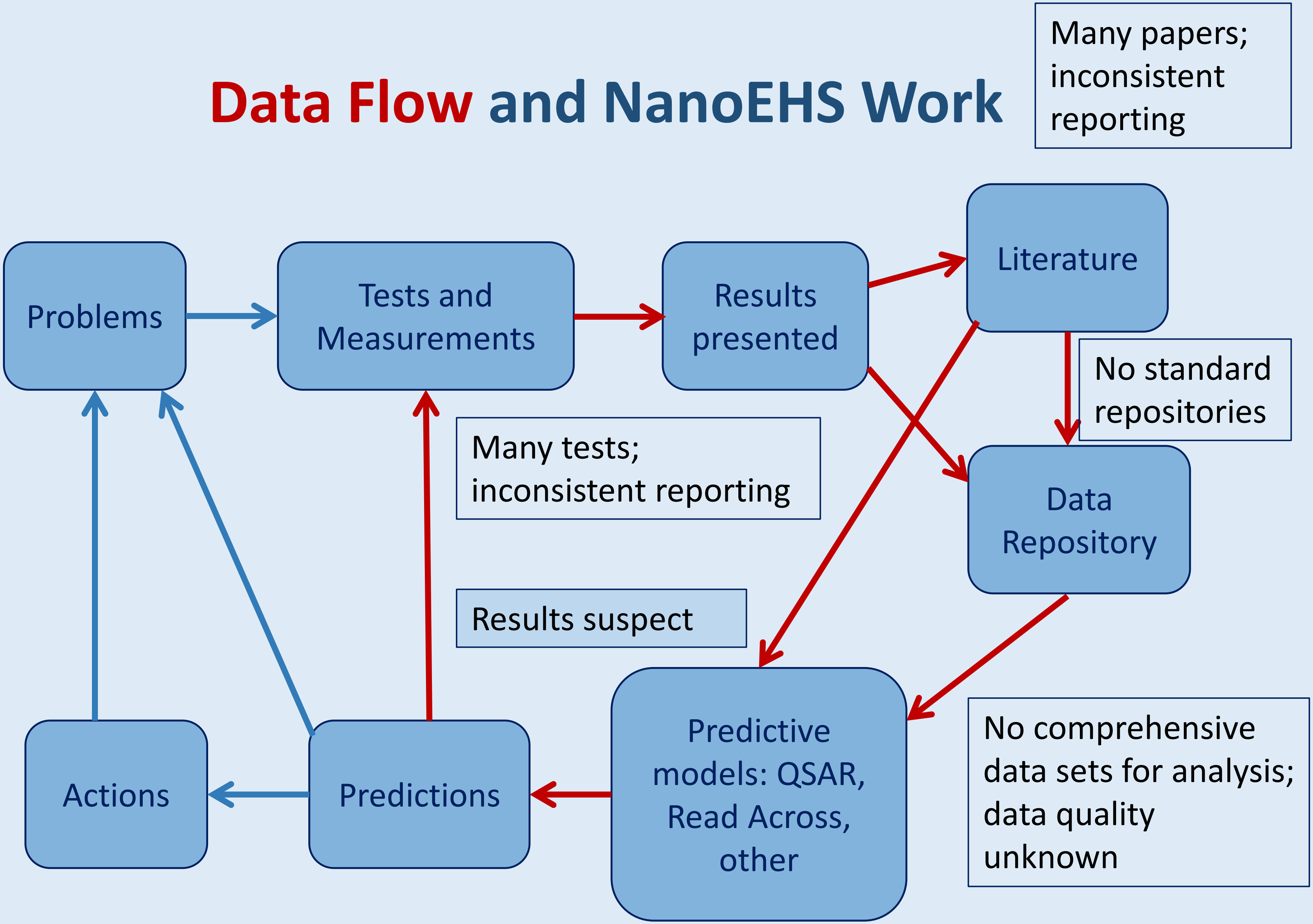
- Is the present body of data on the measurement of nanomaterials properties sufficiently complete and of high enough quality to support RA and QSAR in the broad sense?
- If not, is the body of data sufficiently complete with enough quality to support RA and QSAR in specific areas, e.g. specific nanomaterials or biological outcomes?
- If the data are not complete enough or of inadequate quality, or both, what can be done to improve the quantity and quality of needed nanomaterial property data?
- How can one assess the quality of existing nanomaterial data, even if the data sets are not complete with respect to number of nanomaterials, properties measured, and metadata reported?

Questions

- Are data recording formats for biological and environmental assays for nanomaterials, such as OECD templates, ISA-NANO-tab, eNanoMapper, etc., good enough to capture all relevant metadata (nanomaterials features and measurement conditions)? If not, how can they be improved?
  - E.g. recent reporting requirements for zeta potentials

- If the body of data is not sufficient to support fully RA and QSAR, can scientifically useful approaches be developed to compensate for the lack of completeness or quality?

Data Flow and NanoEHS Work



Conclusions and Recommendations

Some conclusions

- RA and QSAR results highly dependent on quantity and quality of available data
- Data reporting requirements are partially available but lacking sufficient detail to support high quality RA and QSAR
- Few viable repositories
- Data quality is poor or unknown

Some recommendations

- Strong need for comprehensive repositories with mandatory deposition(15 minute tool!)
- Develop next generation ontologies and test results reporting

Other Comments

- QSAR and Read-Across can work only with adequate high quality data
- Data cannot retroactively be archived; must plan for and enforce data capture at very beginning of project
- Research (and measurement) community must be involved from beginning in setting ontologies, repositories, and data management (capture) plans
- CODATA WG on Nanomaterials will continue to partner with NanoEHS projects internationally