

Measurement science in ICCVAM

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Measurement Science Tools (NIST)

- **Measurements**

- Develop new measurement methods
- Improve accuracy/precision of measurements

- **Reference Materials**

- Well-defined materials for use as a reference when making measurements
- Enables inter-lab comparability
- Physical artifacts for calibrating instruments

- **Standards**

- Documentary standards, ASTM, ISO
- Reference data (chemical spectra)

- **Assay development within ICCVAM**

- No regulatory responsibilities but supports other agencies with improving the quality of assays potentially useful for regulatory purposes
- Interlab comparison with EASA method with NIOSH, FDA, and CPSC/NIST coordinated by NIEHS started in 2017 using cuvette-based method



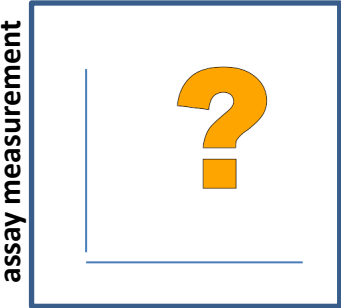
Food-matrix reference materials to facilitate nutritional labeling

NIST Synthetic RNA controls (ERCCs) used in sequencing of Ebola virus genomes to characterize patterns of viral transmission



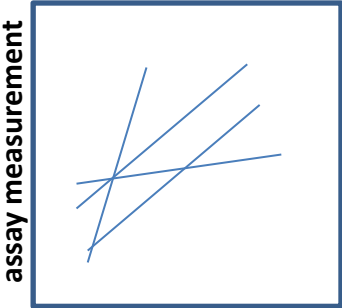
Biological relevance and measurement quality influence predictive power of a new approach method (NAM)

Quality: YES/NO,
Biological
relevance: NO



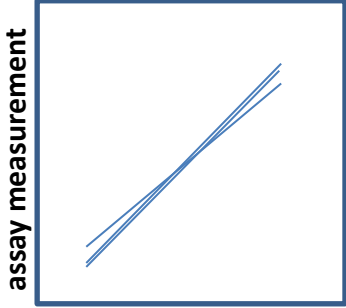
Clinical measurement
Unlikely predictive

Quality: NO,
Biological
relevance: YES



Clinical measurement
Poorly predictive

Quality: YES, Biological
relevance: YES



Clinical measurement
Highly predictive



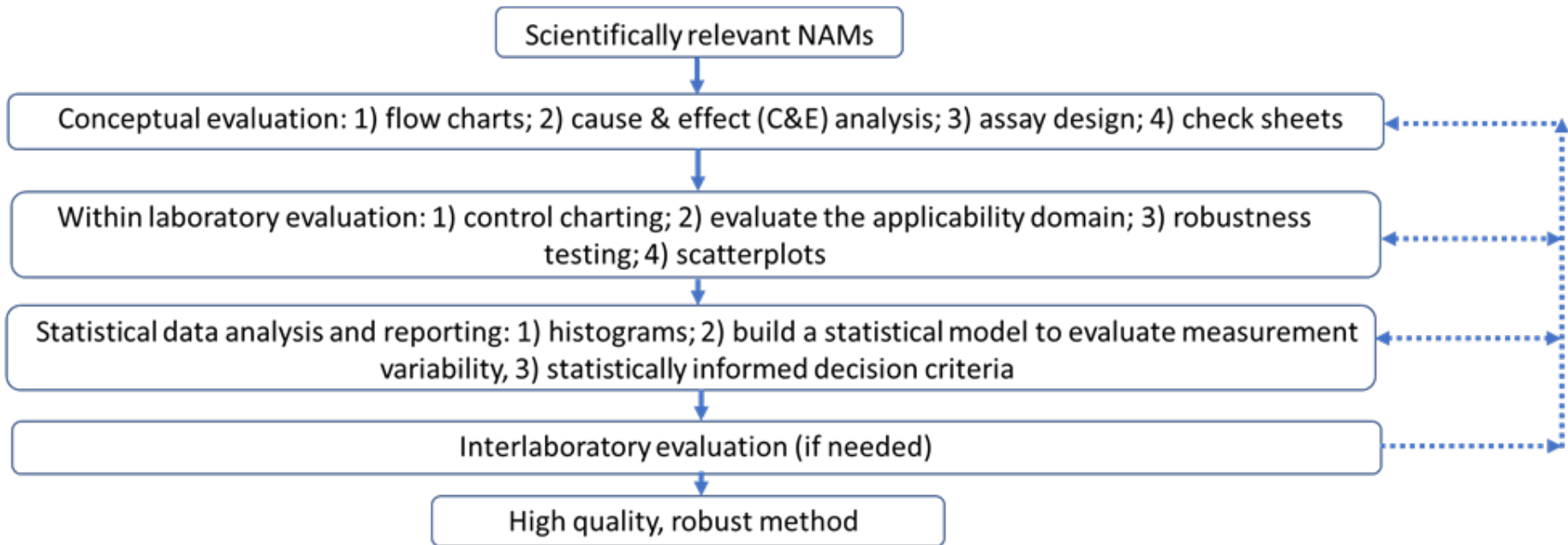
decisions

Technical framework for high quality NAMs

Collaborative partners: CPSC, NICEATM, DOD, EMPA

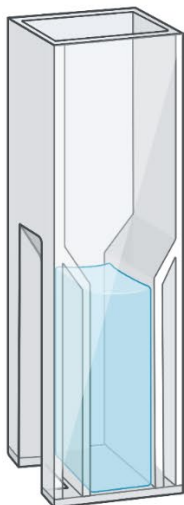
- NAMs need to yield reproducible results across time and among laboratories
- Basic quality tools (cause-and-effect analysis, flow charts, control charts, etc.) can be used to improve confidence in measurement processes
- This technical framework provides general guidance on how to apply these tools to NAMs
- Approaches for adding statistical confidence to decisions based on NAM results is also described
- There may be tradeoffs among different choices during protocol development

Technical framework for high quality NAMs



Electrophilic allergen screening assay adaptation to a 96-well plate

Cuvette-based skin sensitization assay



Measurement quality tools



96-well plate assay with in-process control measurements

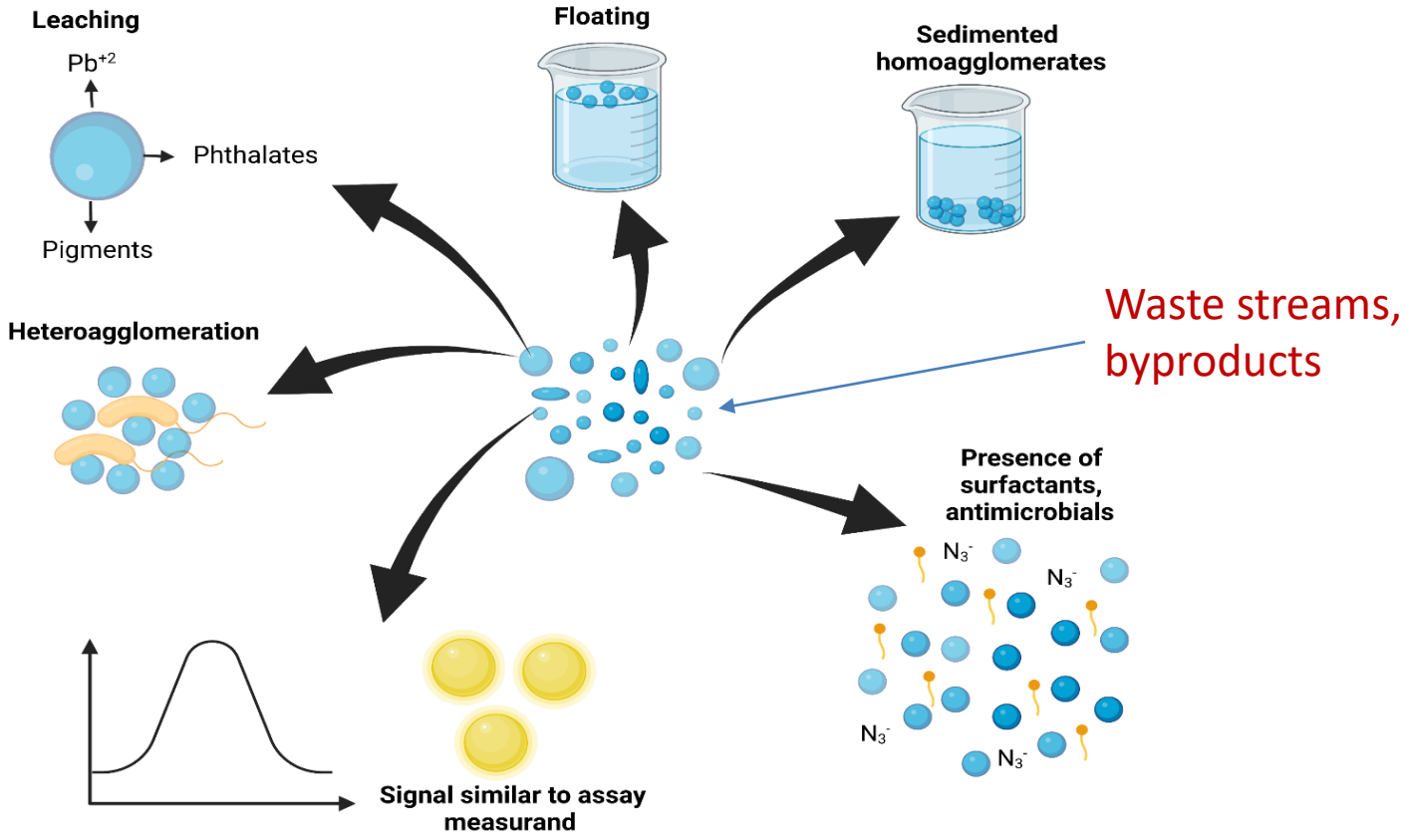
	1	2	3	4	5	6	7	8	9	10	11	12
A	SS	NC	NC	NC	NC	NC	NC	NC	NC	●	●	●
B	SS	NC	PC	PC	PC	TC	TC	TC	TC			
C	SS	NC	PC	PC	PC	TC	TC	TC	TC			
D	SS	NC	PC	PC	PC	TC	TC	TC	TC			
E	SS	NC	PC	PC	PC	TC	TC	TC	TC			
F	SS	NC	PC	PC	PC	TC	TC	TC	TC			
G	SS	NC	PC	PC	PC	TC	TC	TC	TC			
H	SS	NC	PC	PC	PC	TC	TC	TC	TC			

Petersen, E.J.; Uhl, R.; Toman, B.; Elliott, J.T.; Strickand, J.; Truax, J.; Gordon J. Development of a 96-Well Electrophilic Allergen Screening Assay for Skin Sensitization Using a Measurement Science Approach. *Toxics* **2022**, in press.

NIST/NIDCR workshop on NAMs for the biocompatibility of dental devices

- A virtual workshop titled “PREDICTIVE ALTERNATIVE METHODS FOR ASSESSING BIOCOMPATIBILITY OF DENTAL MATERIALS NIST-NIDCR VIRTUAL WORKSHOP” was held on November 10, 2021
- Over 70 people registered
- Invited speakers from different US government agencies (NIEHS, NIDCR, FDA, and NIST) and academic universities gave presentations
- Presentations on the FDA’s medical device development tool (MDDT) were given
- A workshop report is in agency clearance
- Input on future directions for NAM development were received
- Use case- An assay using 3D constructs of the oral tissues to assess irritation is the focus of within laboratory evaluation

Environmental and human health testing: Artifacts and biases during toxicity testing of nanoplastics and microplastics



The above and examples of potential artifacts and biases. A paper has been submitted on this work.