

# Approaches to Provide Assurance for Biological Measurements

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January 15, 2020

*Workshop on Ultraviolet Disinfection Technologies & Healthcare  
Associated Infections: Defining Standards and Metrology Needs*

# Lack of Confidence in Biomedical Research



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NATURE | NEWS FEATURE

## 1,500 scientists lift the lid on reproducibility

Survey sheds light on the 'crisis' rocking research.

Monya Baker

Estimated over \$28B spent annually in U.S. on preclinical research that is irreproducible<sup>1</sup>



U.S. Department of Health & Human Services

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## RIGOR AND REPRODUCIBILITY

<https://www.nih.gov/research-training/rigor-reproducibility>

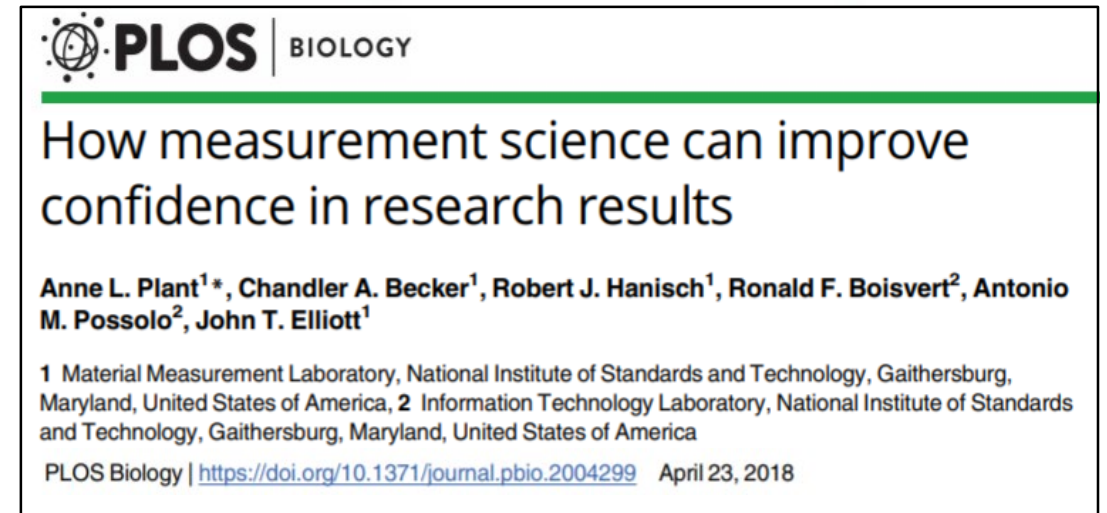
7 January 2019

## The nature of the biological material and the irreproducibility problem in biomedical research

George V Papamokos  

[Author Information](#)

EMBO J (2019) 38: e101011 | <https://doi.org/10.15252/embj.2018101011>



**PLOS** | BIOLOGY

## How measurement science can improve confidence in research results

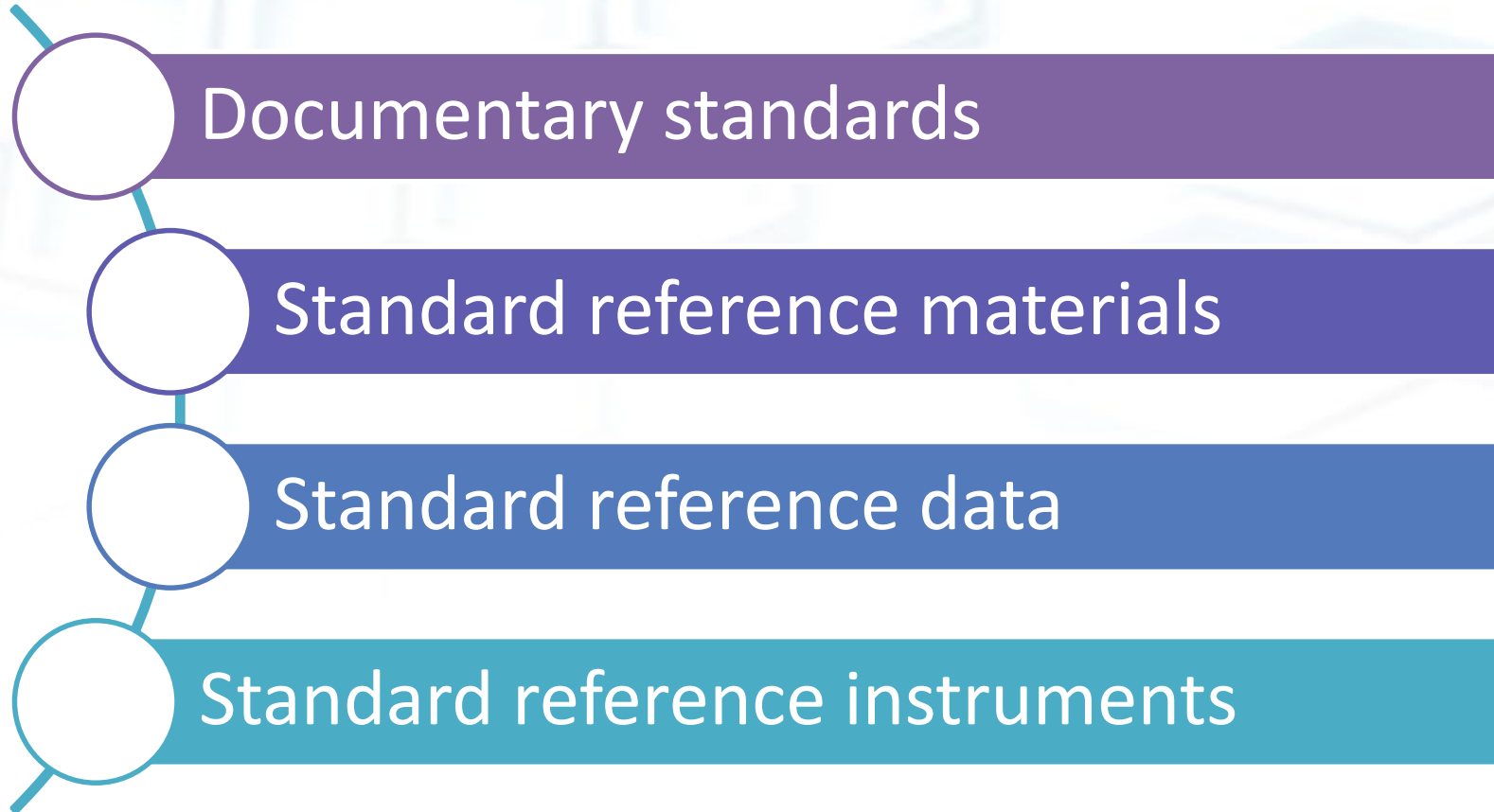
Anne L. Plant<sup>1\*</sup>, Chandler A. Becker<sup>1</sup>, Robert J. Hanisch<sup>1</sup>, Ronald F. Boisvert<sup>2</sup>, Antonio M. Possolo<sup>2</sup>, John T. Elliott<sup>1</sup>

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PLOS Biology | <https://doi.org/10.1371/journal.pbio.2004299> April 23, 2018

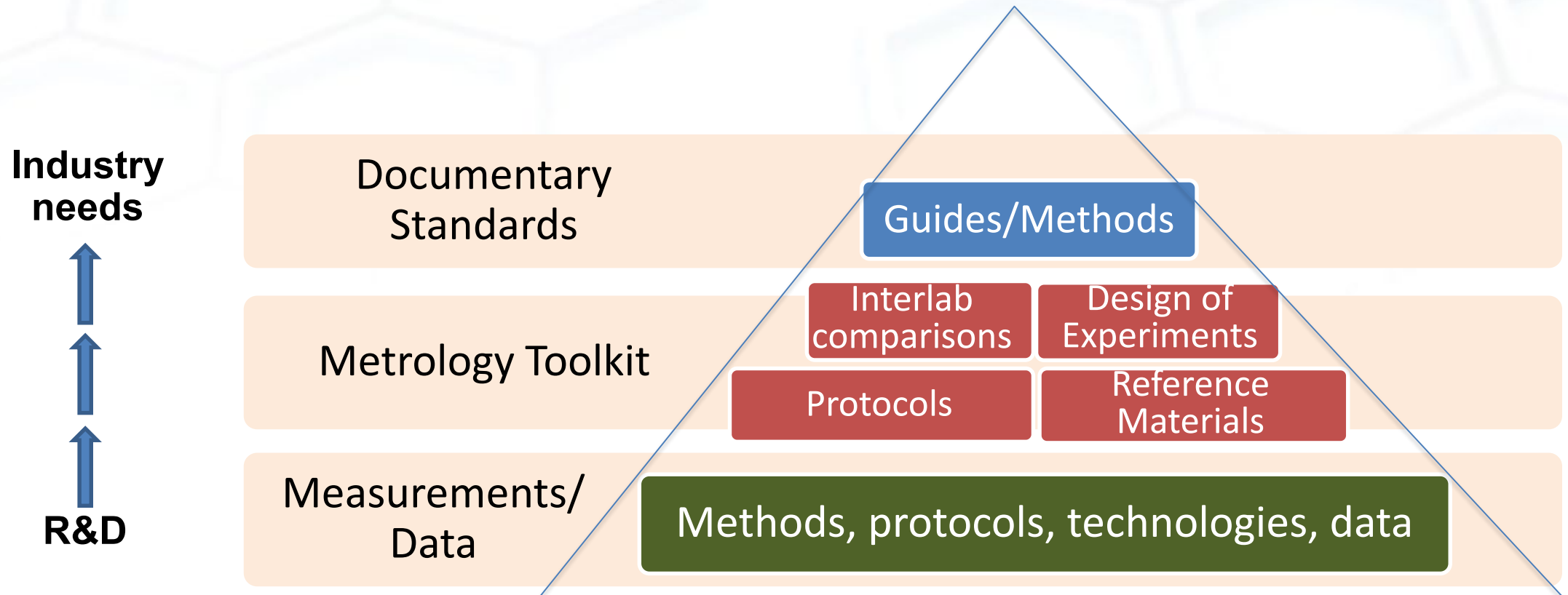
<sup>1</sup> Freedman et al. "The Economics of Reproducibility in Preclinical Research," 2015, PLoS Biol 13(6): e1002165.

# Standards



# Measurement Assurance

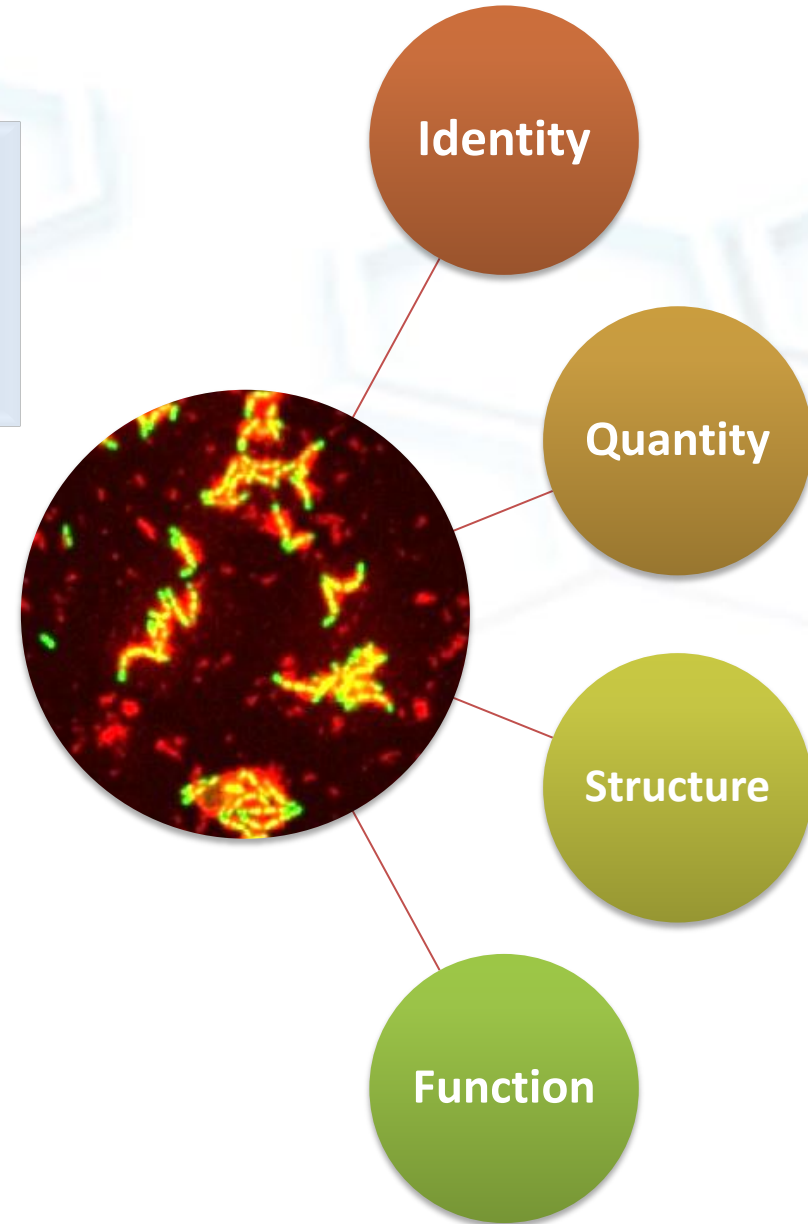
- Provides a known level of confidence to inform decision making
- Is based on supporting data and metadata to provide credibility
- Leads to accelerated technology development and translation



# Microbial Metrology

Developing measurement science, technology, and standards to increase confidence in measurements of microbes and their complex communities and to promote responsible biotechnology innovations

Planktonic cells  
Microbiome Communities  
Biofilms



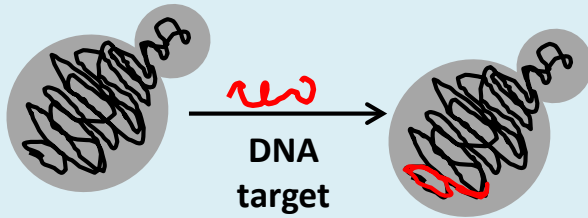
# Candidate RM 8230: Living Cells Characterized for Total Cell Count and CFUs



Sandra Da Silva

*Saccharomyces cerevisiae* NE095

**Homogeneous, Stable, Fit for Purpose**



Measurand	# per vial x 10 <sup>7</sup>
Total cells (Coulter)	<b>3.81 ± 0.51 (13.3 %)</b>
CFUs (Plating)	0.095 ± 0.018 (18.9 %)

“Ground truth” material to

- assess accuracy of total cell count methods
- enable comparison of methods
- evaluate efficiency of antimicrobial approaches
- increase confidence in results



*Antimicrobial testing*  
*Probiotics*  
*Live biotherapeutic products*  
*Food contamination*  
*NGS pathogen detection*  
*Biothreat detection*

## Data processing

coincidence →  
analysis approach →  
subtraction method →  
background →  
count range →  
replicates →

## Operator

user →  
experience →  
pipetting →

## Instrument

aperture clogging →  
model no. →  
calibration →  
temperature →  
← carry over effect  
← electrical noise  
← aperture

## Object Count

flushing delay →  
measurement →  
sample prep interval →  
analytical volume →  
aliquot →  
mixing →  
buffer →  
← debris/bubble  
← particle size  
← particle size dist.  
← concentration  
← coincidence  
← loss to the tube  
← aggregation  
← absolute count

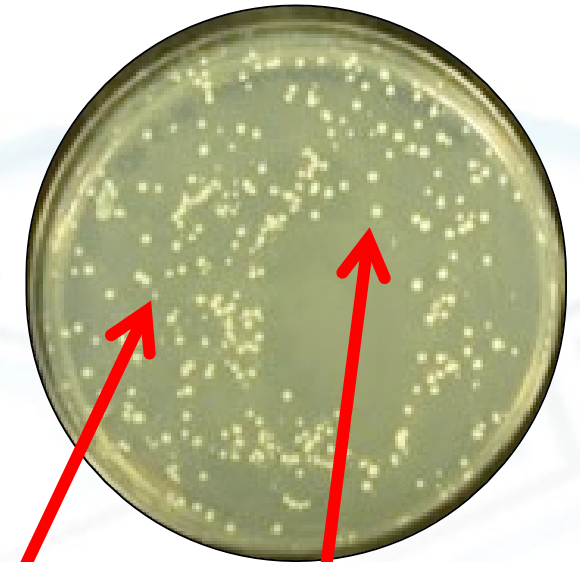
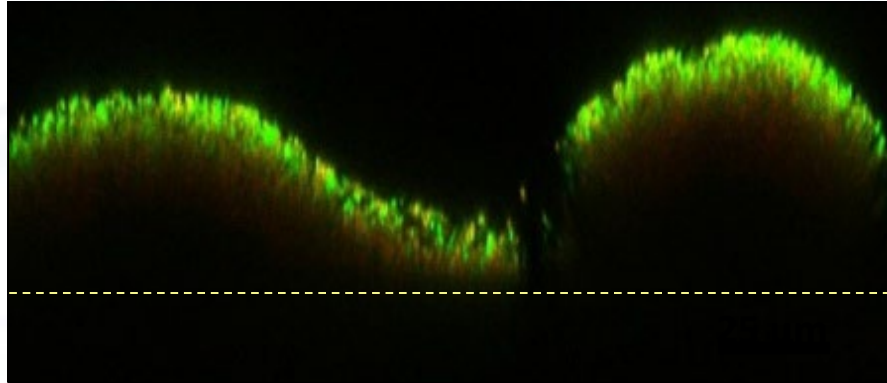
## Protocol

## Sample

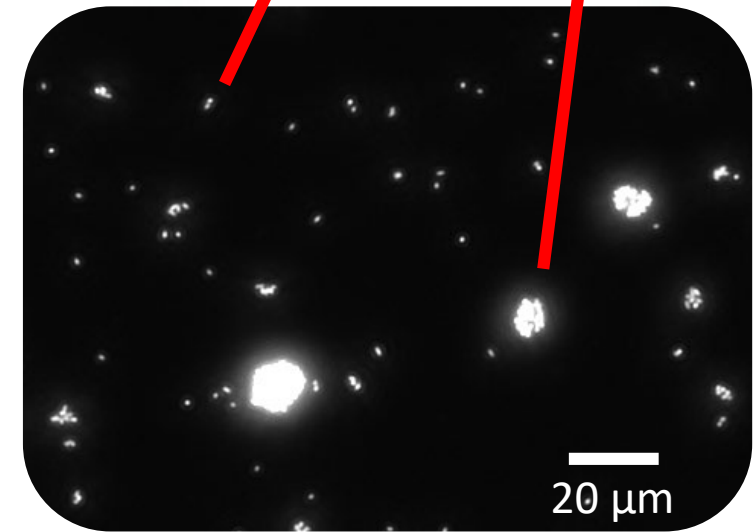
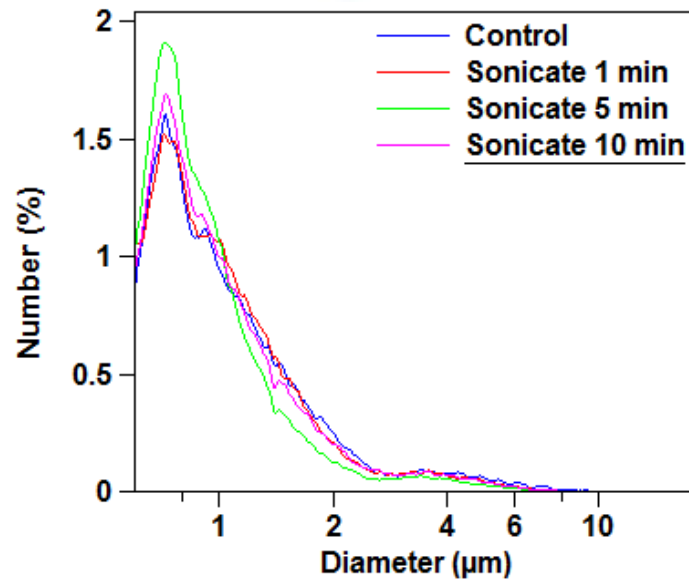
**Fishbone (Ishikawa) Diagram for the Coulter Counter to identify potential sources of uncertainty**

# Check Assumptions When Possible

CFUs for  
Biofilms



Coulter counter  
analysis



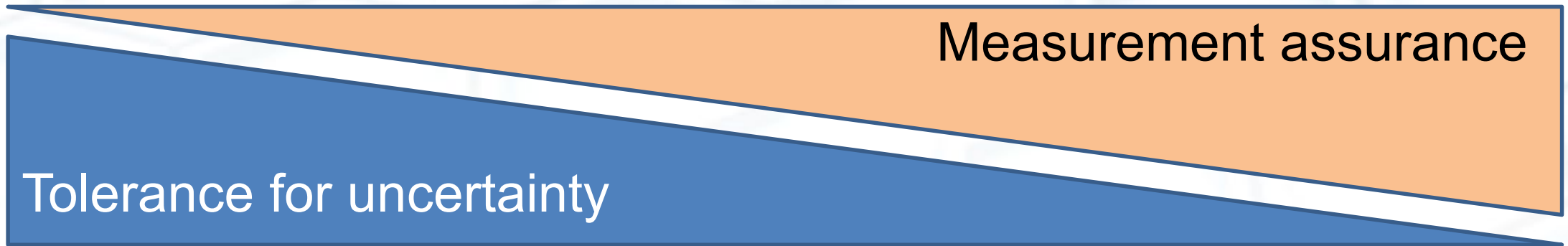


# Concluding Thoughts

Low stakes decisions

High stakes decisions

Trade-off



## Example Efficacy Testing Workflow



Incorporating measurement assurance strategies into each step will increase confidence in results

