

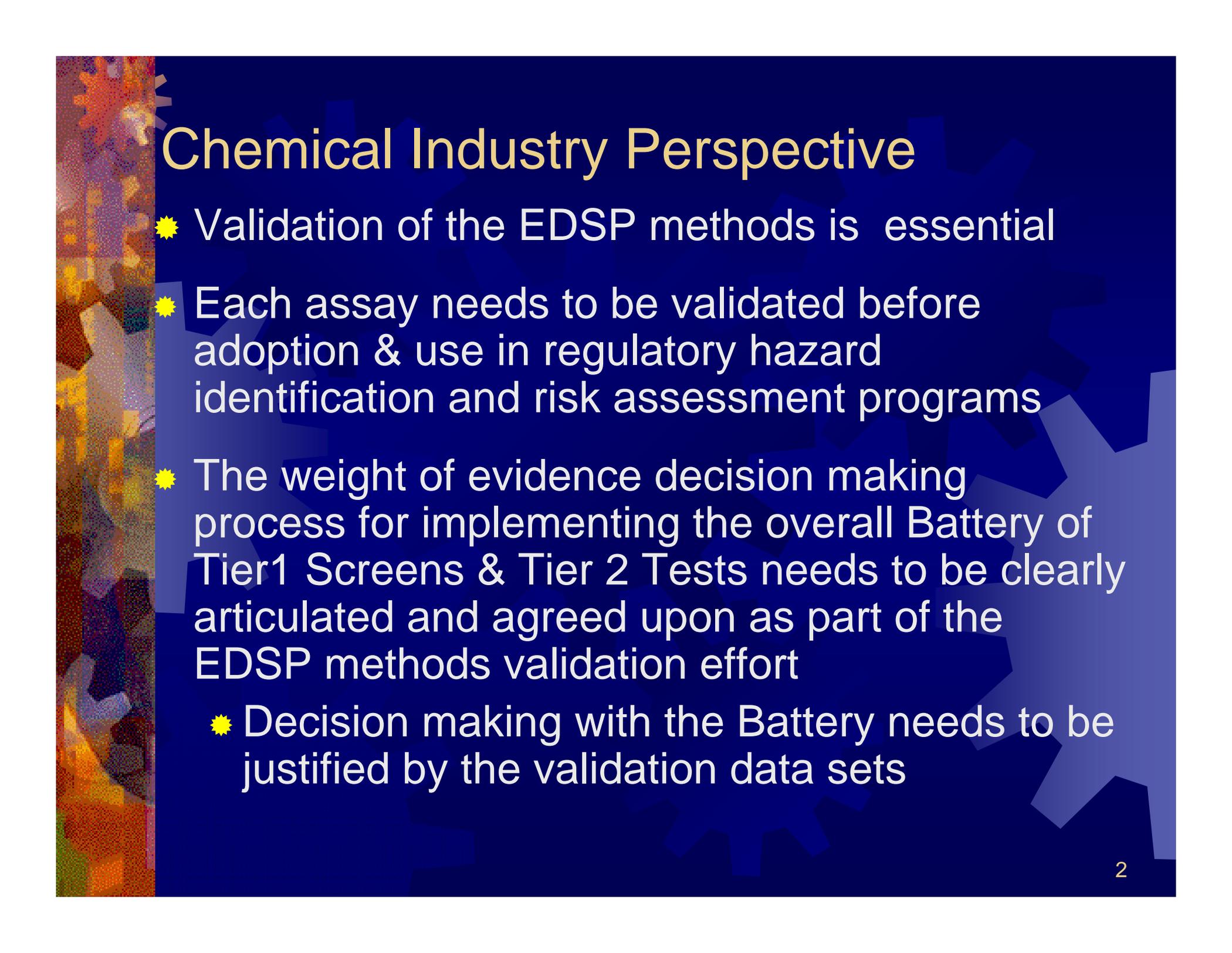


# **Validation of EDSP ASSAYS**

## **Perspective of the American Chemistry Council**

**Richard A. Becker, Ph.D., DABT  
American Chemistry Council**

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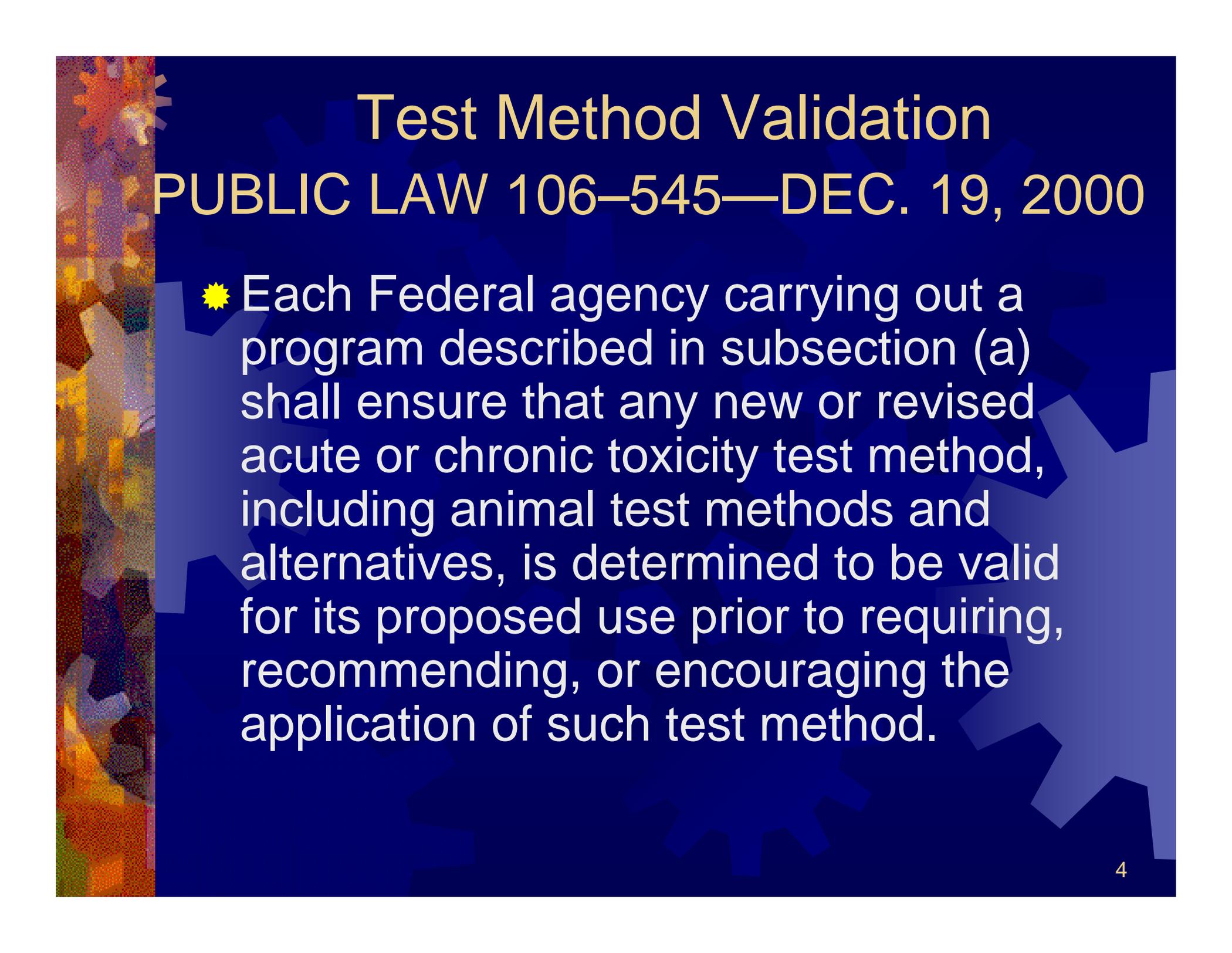


# Chemical Industry Perspective

- ✦ Validation of the EDSP methods is essential
- ✦ Each assay needs to be validated before adoption & use in regulatory hazard identification and risk assessment programs
- ✦ The weight of evidence decision making process for implementing the overall Battery of Tier1 Screens & Tier 2 Tests needs to be clearly articulated and agreed upon as part of the EDSP methods validation effort
  - ✦ Decision making with the Battery needs to be justified by the validation data sets

# Validation

- ★ Validation is essential & required by FQPA & ICCVAM authorization Act of 2000
- ★ Validation must be completed prior to incorporating assays into routine testing programs
- ★ Validation establishes relevance & reliability
- ★ Validation is necessary for interpreting results & understanding significance
- ★ One size does not fit all, a replacement, a modification, a screen are all different
- ★ Resources – need to be realistic and practical
- ★ Guidance - but avoid extremes of absolute perfection vs. a sham
- ★ Judgments are necessary - but need solid rationale, dialog, documentation and transparency



# Test Method Validation

PUBLIC LAW 106–545—DEC. 19, 2000

- ★ Each Federal agency carrying out a program described in subsection (a) shall ensure that any new or revised acute or chronic toxicity test method, including animal test methods and alternatives, is determined to be valid for its proposed use prior to requiring, recommending, or encouraging the application of such test method.

# Screening vs. Testing

Screening assays provide qualitatively different information than definitive tests

- ✦ Results from these dissimilar assays should be used in a manner that is consistent with the scientific basis and purpose of each
- ✦ Screening assays should provide mechanistic understanding of potential to interact with one or more components of endocrine system
- ✦ Definitive tests yield information on apical endpoints for use in risk assessment

**Reliability**  
reproducibility & transferability  
(in a given lab, across labs,  
across time)

**Method (this is a  
Decision Tool (for  
a specified purpose)**

=

**Test System**

+

**Prediction Model**  
(for a specified purpose)

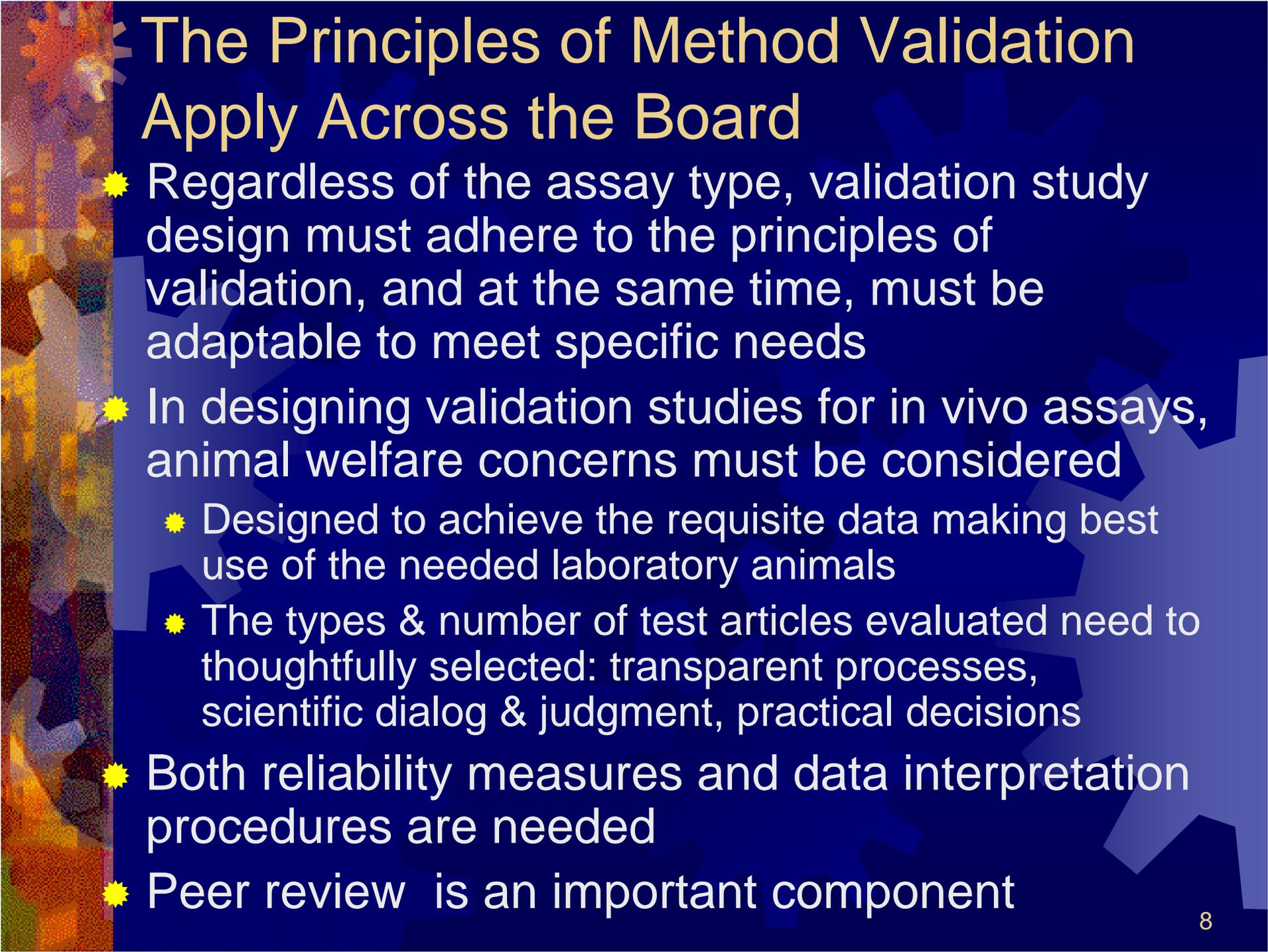
**Relevance:  
Scientific  
basis**

**Predictive  
capacity**



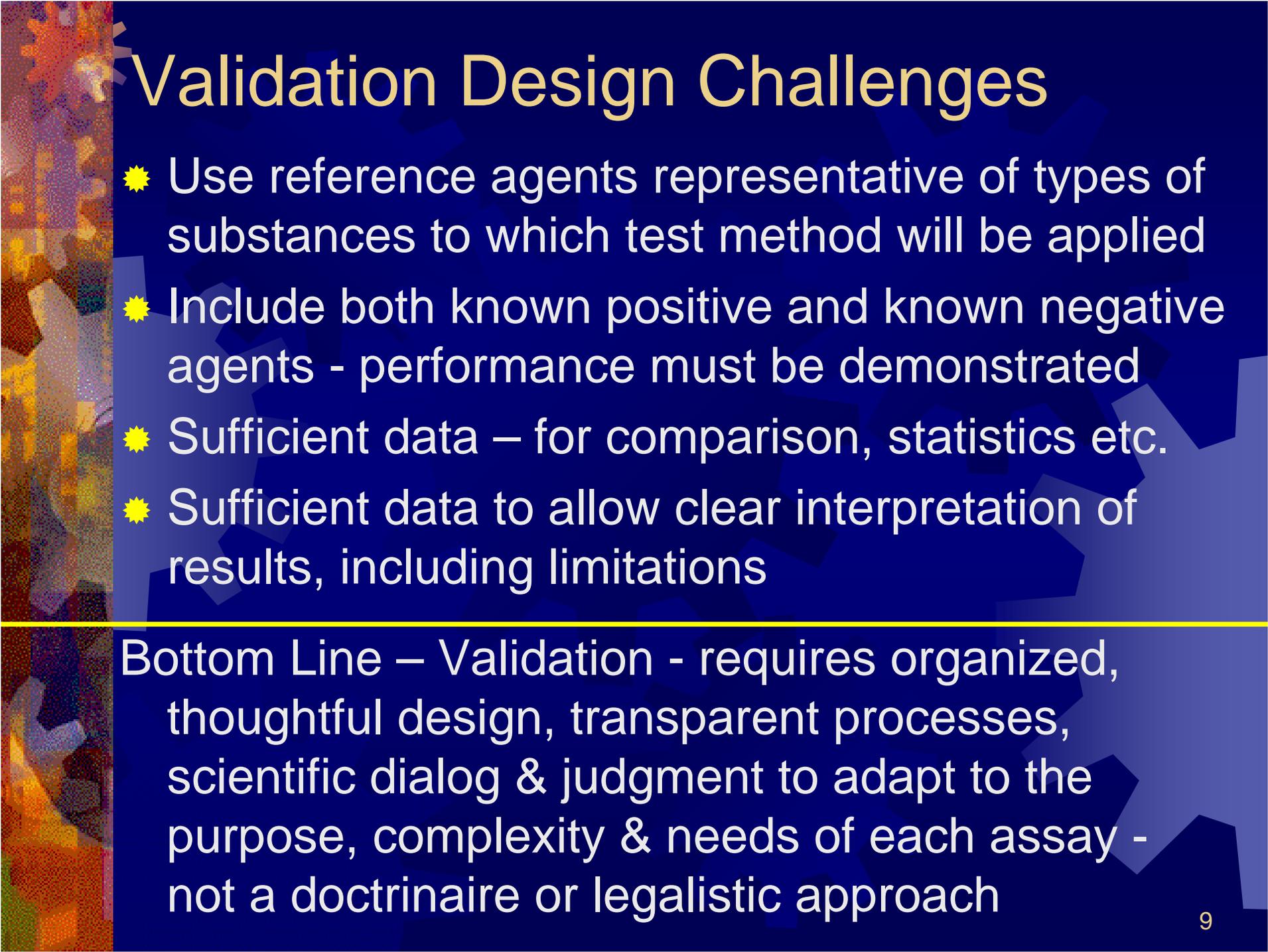
# Validation Should Address

- ★ Relevance of the method to the endpoint
- ★ Test method specificity, sensitivity, reliability and reproducibility
- ★ Criteria for appropriate use
- ★ Strengths, limitations, and uncertainties in data interpretation
- ★ (if a replacement ) - sufficient data should be provided to permit a comparison of the proposed substitute test with that of the test it is designed to replace



# The Principles of Method Validation Apply Across the Board

- ★ Regardless of the assay type, validation study design must adhere to the principles of validation, and at the same time, must be adaptable to meet specific needs
- ★ In designing validation studies for in vivo assays, animal welfare concerns must be considered
  - ★ Designed to achieve the requisite data making best use of the needed laboratory animals
  - ★ The types & number of test articles evaluated need to be thoughtfully selected: transparent processes, scientific dialog & judgment, practical decisions
- ★ Both reliability measures and data interpretation procedures are needed
- ★ Peer review is an important component



# Validation Design Challenges

- ☀ Use reference agents representative of types of substances to which test method will be applied
- ☀ Include both known positive and known negative agents - performance must be demonstrated
- ☀ Sufficient data – for comparison, statistics etc.
- ☀ Sufficient data to allow clear interpretation of results, including limitations

Bottom Line – Validation - requires organized, thoughtful design, transparent processes, scientific dialog & judgment to adapt to the purpose, complexity & needs of each assay - not a doctrinaire or legalistic approach