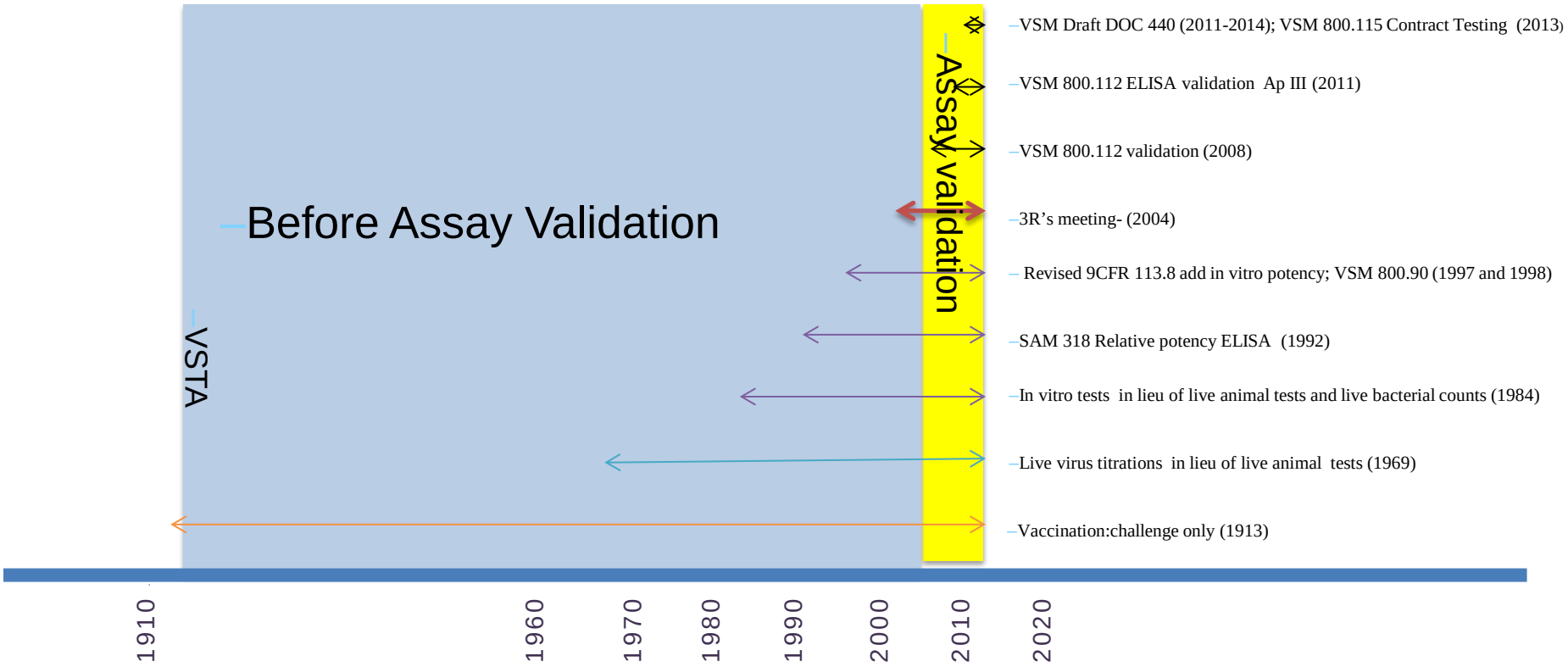
Introductory Session-Historical Perspective on Regulation of Potency (testing) of USDA Regulated Vaccines

David M. Dusek
Staff Reviewer
Center for Veterinary Biologics
USDA
Ames, Iowa

History? Various Opinions

- History is indeed the witness of the times, the light of truth. (Cicero)
- Those who cannot remember the past are condemned to repeat it. (Santayana)
- History is more or less bunk. (Henry Ford)

Overview of Relevant Events



Summary

1913 VSTA -For the first 60 years exclusively animal potency tests with some changes.

- Shift from host animal to laboratory animal
- Shift from vaccination/challenge to vaccination/serology

1969

- Virus titrations in lieu of animal testing

1984

- In vitro tests in lieu of animal tests for immunogenicity
- Counts for live bacterial vaccines

Summary

1992

- SAM 318 Relative potency method for enzyme immunoassays (revised 7/9/2001)

1997 Publication of revised 9CFR 113.8

- Regulation describing criteria for a relative potency immunoassay

1998

- VSM 800.90: Guidelines for Veterinary Biological Relative Potency Assays and Reference Preparations Based on ELISA Antigen Quantification

Summary

2003-2004 Review of potency testing policy

- Animal welfare concerns –reduce, refine, replace (3R's) *in vivo* potency testing
- Guidelines for developing test methods
- Consistency across products
- Adopt new technology

2004 Meeting Ames, Iowa "Technology and Approaches to Reduce, Refine, and Replace Animal Testing"

- Proposed changes for potency testing.
- Presentation on various types of bio-analytical methods

Proposed Policy Changes

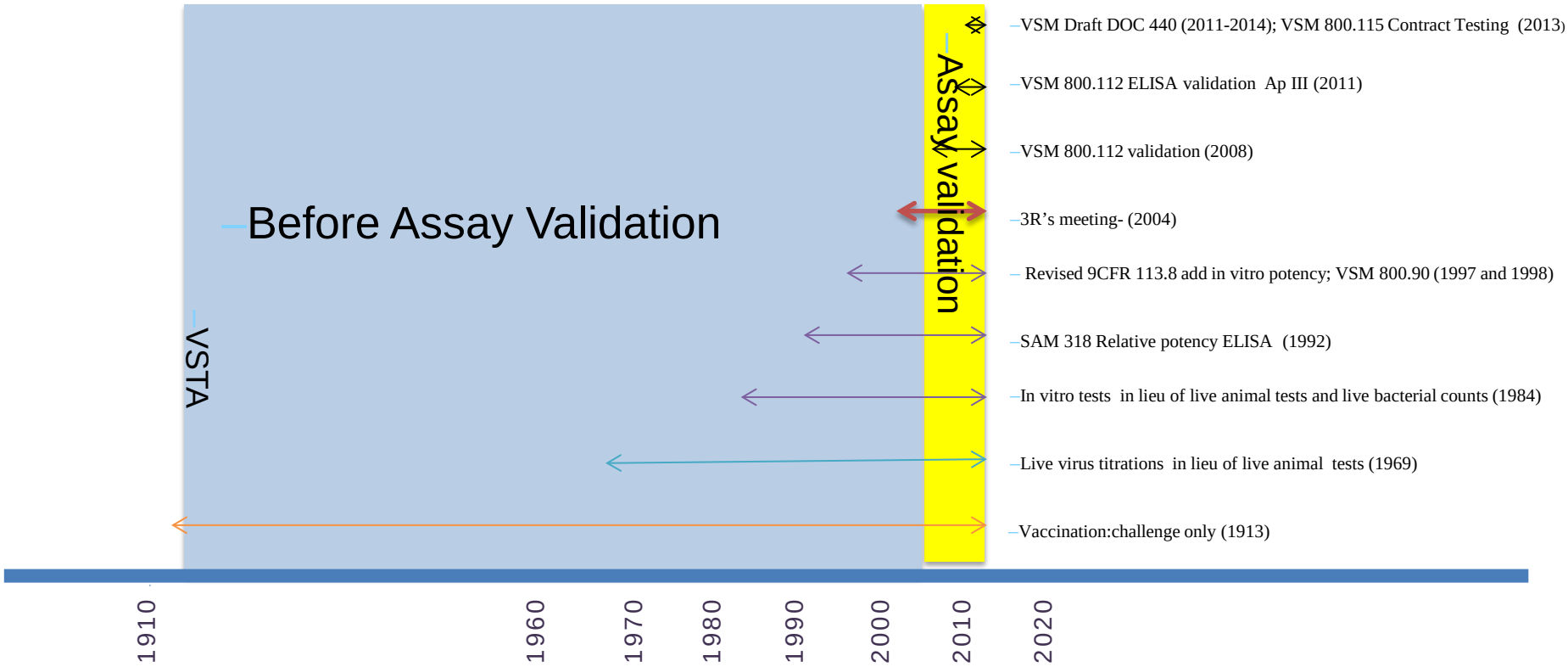
Common policy for ALL potency tests, that included clearly defined requirements for

- Validated assay methods
- Quality assurance programs for assays and references
- Develop criteria for evaluation of product and reference stability and expiration dating
- Reemphasize direct antigen quantification *(µg/mL versus relative potency)*

Proposed Policy Changes

- Real-time stability studies –stability indicating assays
- Contract testing
- Non-protective surrogate antigen correlated to efficacy in lieu of measuring protective antigen

Overview of Relevant Events



Summary

2008-VS Memorandum 800.112 Guidelines for Validation of In Vitro Potency Assays

- Detailed guidance for validating potency testing methods developed in collaboration with industry

2011-VS Memorandum 800.211 Guidelines for Master Reference Qualification and Requalification

- Extended useful dating period of Master References
- Response to industry concerns about resources committed to Master Reference qualification studies

2011-VS Memorandum 800.112 Guidelines for Validation of In Vitro Potency Assays Appendix III (ELISA validation)

- Requested by and developed in collaboration with industry.

Summary

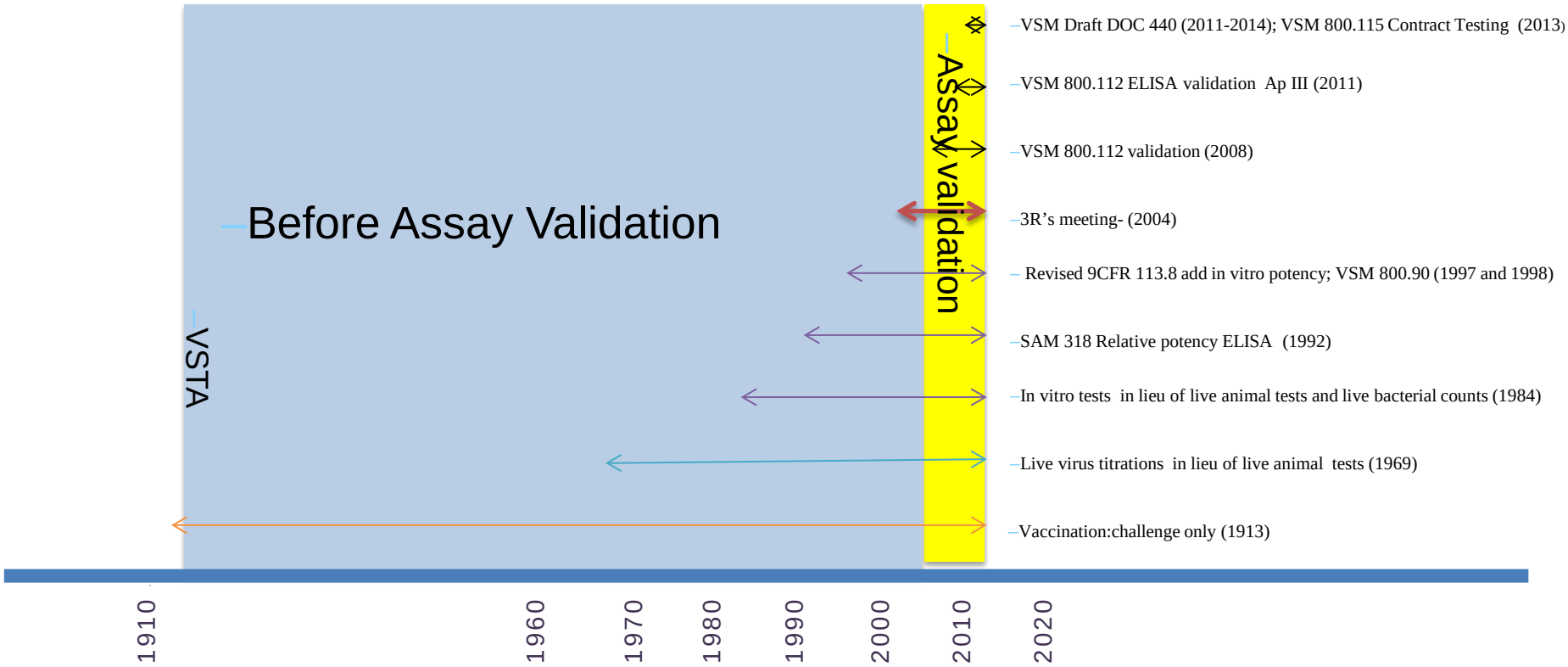
2011-2014 VSM Draft Doc #440 Guidelines for Determining Release and Throughout-Dating Potency Specifications ,

- Several drafts for public comment.

2013 VS Memorandum 800.115 Potency Testing by Unlicensed Facilities (June 21, 2013)

- Potency testing by contract labs

Overview of Relevant Events



A Dichotomy: Before Validation vs After Validation

Why is this important?

- The majority of potency tests have not been validated
  - Not stability indicating assays
  - Not good measures of product potency or stability
- New assays will be stability indicating assays and will be valuable for evaluating stability and product dating.
- Guidance is in place to improve or replace older assays resulting in relevant measures of product potency and stability
- Proposed guidance indicates how we can apply this to have consistent measures of product dating and release values that are science based and data driven

Why is this important?

- Industry needs consistency and predictability
- Regulators need to be consistent and have sound basis for policy and decisions
- Both need to be adaptable to changing technology and the scientific knowledge base
- CVB continues to be on its journey for upgrading potency and other assays to support serial release and stability of product and references

What version of History do you subscribe to?

- History is indeed the witness of the times, the light of truth. (Cicero)
- History is more or less bunk. (Henry Ford)
- Those who cannot remember the past are condemned to repeat it. (Santayana)
- Don’t know much about history…..what a wonderful world this would be. (Sam Cooke, 1959)

Questions?