



Animal and Plant  
Health Inspection  
Service

Veterinary Services

Center for Veterinary  
Biologics

1920 Dayton Avenue  
PO Box 844  
Ames, IA 50010

(515) 337-6100

## CENTER FOR VETERINARY BIOLOGICS NOTICE NO. 17-14

**TO:** Veterinary Services Leadership Team  
Directors, Center for Veterinary Biologics  
Biologics Licensees, Permittees, and Applicants

**FROM:** Byron E. Rippke  
Director

**SUBJECT:** Relative Potency Terminology for References and Related Preparations

### I. PURPOSE

The purpose of this Notice is to provide definitions related to certain types of potency assays for the release of biological products.

### II. BACKGROUND

Center for Veterinary Biologics (CVB) Notice No. 16-13 announced the cancellation of Veterinary Services (VS) Memorandum 800.90, which had become obsolete with the publication of more recent guidance documents, including VS Memorandum 800.112, Guidelines for Validation of In Vitro Potency Assays, and VS Memorandum 800.211, Guidelines for Master Reference Qualification and Requalification. Those documents do not fully clarify certain terms used in relative potency assays that are defined in title 9, *Code of Federal Regulations*, part 101.5. Clarification of those terms and policies related to them are provided here.

### III. TERMINOLOGY

- A. *Master Reference*. A preparation of the vaccine, bacterin, antigen, immunomodulator, antiserum, antibody, or toxoid derived from the Master Seed, Sequence, or Master Cell and prepared according to the approved Outline of Production within the specified range of passage levels and formulated as final product or maintained as a nonadjuvanted harvested culture of microorganisms or as a purified preparation of the protective antigen that has been characterized by methods acceptable to APHIS. It is used as the analytical reference for evaluating the potency of serials and for establishing the potency of Working References and Qualifying Serials. The Master Reference is qualified for use in a procedure approved by APHIS that demonstrates a correlation between the amount of the protective antigen or component and efficacy, protection, or therapeutic effect in the target species or an approved surrogate animal. The Master Reference may be prepared from a concentrate and stored under conditions to enhance stability.

## CENTER FOR VETERINARY BIOLOGICS NOTICE NO. 17-14

Page 2

- B. *Working Reference.* The reference preparation used in the in vitro potency method for the release of serials. The Working Reference may be:
- The qualified Master Reference or dilution of the Master Reference concentrate.
  - A serial of the product prepared and established for use as a Working Reference in a manner acceptable to APHIS.
  - A purified preparation derived from harvested material prepared according to the approved Outline of Production and established for use in a manner acceptable to APHIS.
  - A nonadjuvanted harvested culture of microorganisms prepared according to the Outline of Production and established for use in a manner acceptable to APHIS.
- C. *Qualifying Serial.* A serial of biological product used to qualify the Master Reference when the Master Reference cannot be used because it is not formulated as the finished product; e.g., a purified antigen or nonadjuvanted harvest material. Qualifying Serials must be produced in accordance with the filed Outline of Production. A qualifying serial that is used to requalify or extend the dating period of a Master Reference must be tested for efficacy, be unexpired, and prepared according to the currently approved Outline of Production.

### IV. REFERENCE POTENCY

- A. *Master Reference.* The potency of the qualified Master Reference or dilution of the Master Reference concentrate is either defined as the actual amount of the protective antigen or component present in the biological product at the time of qualifying study, or 1.0 in relative units
- B. *Working Reference.* Working References used in relative potency assay methods must have a relative potency  $\geq 1.0$  when compared to the Master Reference while those used in assay that quantify the actual amount of protective antigen or component must have an antigen or protective component concentration similar to the Master Reference. The geometric mean potency of the Working Reference when compared to the Master Reference must be established in the approved potency assay by five or more independent assays.
- C. *Qualifying Serial.* The geometric mean potency of the Qualifying Serial, when compared to the Master Reference, must be equal to or less than the potency of that reference in the approved potency assay as established by five or more independent assays.

### V. IMPLEMENTATION/APPLICABILITY

Terminology provided in this Notice shall remain in force until further notice.