Animal and Plant Health Inspection Service

Veterinary Services

Center for Veterinary Biologics

1920 Dayton Avenue
PO Box 844
Ames, IA 50010

(515) 337-6100

December 9, 2013

CENTER FOR VETERINARY BIOLOGICS NOTICE NO. 13-18

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

FROM: Byron E. Rippke */s/ Byron E. Rippke*
Acting Director
Center for Veterinary Biologics

SUBJECT: Discontinuing the Use of RelPot Software

I. PURPOSE

This Notice pertains to all licensees using relative potency immunoassays for serial release testing of veterinary biologics. It states that RelPot software will no longer be used by the Center for Veterinary Biologics (CVB) and provides guidance for firms to transition to commercial software for estimating relative potency (RP) in approved assays.

II. BACKGROUND

RelPot software for estimating RP in immunoassays has been distributed by the CVB as a convenience to licensees since at least 1991. The most recent version was developed under the Windows 95 operating system. It used an automated segment selection method described in Supplemental Assay Method (SAM) 318. SAM 318, Section 1.4, notes that the method "is based on an algorithm that has no internal validity" and requires external validation. CVB is discontinuing the use of RelPot software and the method of SAM 318 by its laboratories. Firms with approved potency assays that have utilized RelPot are advised to transition to the use of commercial software for serial release.

III. SCOPE

This guidance refers to relative potency immunoassays approved for serial release of veterinary biologics. This guidance addresses the estimation of relative potency in such assays; it does not affect activities which do not require RP estimation, such as reference monitoring.

IV. ACTION

A. The CVB will discontinue the use of RelPot software after December 31, 2013. Licensed firms may continue to use RelPot software for serial release

per approved Outlines of Production and Special Outlines through the end of calendar year 2015. The disposition of all serials will follow the approved Outline of Production.

B. Before January 1, 2016, firms should develop proposals for transitioning each approved assay currently using RelPot software for serial release to other software, and submit such proposals to CVB Policy, Evaluation, and Licensing (PEL) for consultation and approval. Firms may propose an alternate time line for transitioning assays already approved or close to approval as of Jan. 1, 2014.

C. Transition proposals should demonstrate that the proposed procedure and software package will produce appropriate RP estimates suitable for serial release. Provide data to support the proposal. Identify the software in the Outline of Production or Special Outline. Specify the software settings either in the outline or in a separate document such as a standard operating procedure, to be included with the transition proposal. Specify the region of the response curves that will be utilized for RP estimation. For example, full curves may be fit by parallel nonlinear (e.g. logistic) functions, or pseudo-linear regions may be fit with parallel linear regressions. Automated segment selection methods should not be used.

D. Features to consider in software for serial release are the ability to fit a suitable model with the appropriate parameter constraints, estimate RP, provide a graphical depiction of the raw data and model fit, and evaluate validity criteria such as parallelism. While the CVB does not endorse specific software packages, the CVB Statistics Section may be able to provide some technical advice on implementation within some of the available commercial software it is familiar with.

E. In most cases, evaluation of the new software (and the method for using it) for a particular assay may be achieved by demonstrating the suitability of its performance on a representative historical data set. A set of at least 10 serial tests should typically be sufficient. In some cases, fewer tests may be justified, while highly variable assays or nonstandard analysis methods may require more data. Suitability means that the model (e.g. linear regression), data subset (e.g. limited to the pseudo-linear region if applicable), and validity criteria are appropriate for relative potency estimation in light of the procedure being replaced.

F. For confirmation of dating studies initiated prior to the transition, data from before and after the transition may be analyzed using the post-transition software and method.

V. IMPLEMENTATION/APPLICABILITY

This policy will be effective immediately from the date of this Notice. The applicability of this policy is defined in Section III (Scope).