United States Department of Agriculture

Animal and Plant Health Inspection Service

Veterinary Services

Center for Veterinary Biologics

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CENTER FOR VETERINARY BIOLOGICS NOTICE 23-06

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

FROM: Dr. Dave White
Acting Director
DAVID WHITE Digitally signed by DAVID WHITE
Date: 2023.03.24 12:40:26 -05'00'

SUBJECT: Antimicrobial Resistance (AMR) Genes in Veterinary Biological Products

I. PURPOSE

The purpose of this notice is to outline current policy regarding the presence of antimicrobial resistant (AMR) genes in veterinary biologics administered to animals. This policy is applicable to products licensed under Title 9, *Code of Federal Regulations*, Part 102.5 (9 CFR) and products produced under 9 CFR 107.1. This policy does not apply to diagnostics except for those administered to animals.

II. BACKGROUND

Vaccines are often used as an example of a tool to address AMR. However, animal vaccines have not historically been tested for the presence of AMR genes. The spread of AMR has become a major public health concern, and responsible actions are required to mitigate any potential contributors to the issue.

The Center for Veterinary Biologics (CVB) is currently investigating the presence of AMR genes in biologics, particularly those capable of vertical and lateral transfer and regardless of the occurrence of an AMR phenotype.

III. ACTION

All veterinary vaccines which could contain AMR genes capable of environmental spread will be analyzed by CVB to determine what, if any, AMR genes are present. This includes products licensed under 9 CFR 102.5, as well as vaccines manufactured under 9 CFR 107.1. As per 9 CFR 107.1, any persons exempt from licensure that are shipping products containing live organisms must provide any information CVB may require prior to shipment, or at any other time deemed necessary, in order to assess the products' safety and effect on the environment. CVB may request additional information from parties exempt from licensure.

Concerns surrounding AMR will be incorporated into the risk/safety assessment for all veterinary biologics, except diagnostics unless administered to animals. For newly licensed products, biologics should not contain any AMR genes. Exceptions are possible based on CVB's review of a complete risk assessment. CVB strongly recommends licensees/permittees take action to remove AMR genes from any currently licensed products that may contain AMR genes. In the future, CVB may consider labeling requirements or even market removal of products that contain AMR genes, based on a risk assessment. Products produced under 9 CFR 107.1 will be subject to the same requirements.

CVB uses tools and databases from the National Center for Biotechnology Information (NCBI) to evaluate next generation sequencing and other genetic data generated from master seeds for the presence AMR genes. Specifically, master seed sequence data is analyzed using the NCBI AMRFinder tool. CVB recognizes that tools and databases evolve with time and that decision makers use the best data available at the time of testing. There may be multiple routes to replicate sequence-based testing, whether internally or via an external laboratory. Note: Testing identical to that conducted by CVB is available on a fee-for-service basis via the USDA National Veterinary Services Laboratories by submitting a VS 10-4 form and specifying AMR testing through whole genome sequencing. Please submit any questions regarding sequence-based testing to your reviewer.

IV: IMPLEMENTATION/APPLICABILITY

Updated policy in this Notice is effective immediately.