



Animal and Plant
Health Inspection
Service

Veterinary Services

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VETERINARY SERVICES MEMORANDUM 800.215

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

FROM: for Jack A. Shere
Deputy Administrator

SUBJECT: Guidelines Regarding the Revision to Animal and Plant Health
Inspection Service (APHIS) Implementing Procedures for the National
Environmental Policy Act (NEPA)

I. PURPOSE

This memorandum provides guidance to licensees, permittees, and applicants regarding the revision to APHIS' implementing procedures for the NEPA of 1969, as it relates to the licensure of veterinary biologicals, specifically viable, replicating, recombinant, biotechnology-derived vaccines. The memorandum is not applicable to diagnostic, inactivated, allergenic, or antibody products.

II. BACKGROUND

NEPA requires federal agencies specify which actions entail preparation of an environmental impact statement (EIS), preparation of an environmental assessment (EA), or are categorically excluded (title 40, *Code of Federal Regulations* (CFR), [part 1507.3\(b\)](#)). In 1995, APHIS set out its implementing procedures for NEPA ([7 CFR 372](#)). Since then, the Center for Veterinary Biologics (CVB) sought NEPA compliance for all field safety trials of experimental vaccines that met testing requirements and are approaching licensure. In so doing, the CVB evaluated numerous live recombinant vaccines for potential significant impact on animals, humans, or the physical environment. Many of these vaccines used similar or even identical vectors that differ only in the insertion of genetic sequence coding for another pathogen's immunogen.

To establish the safety of these vaccines, the CVB often sought input from subject matter experts to determine whether to consider alternative actions or any mitigations, and whether an EA or EIS would be required. In all cases thus far, it was determined that EAs were sufficient to evaluate risk, and the CVB issued a finding of no significant impact (FONSI). To maintain compliance with NEPA, APHIS announced pending field safety trials through publication in the Federal Register to notify the public and provide an opportunity to comment on the proposed action. Following publication in the Federal Register, APHIS did not reverse any of the FONSI as a result of public comments or concerns not previously addressed and resolved by the CVB.

On May 24, 2018, APHIS amended the 1995 regulations that set out implementing procedures for NEPA, with publication of a Final Rule in the Federal Register. The amendments include revision of the categories of actions for which an EIS or an EA might be completed, and expansion of the list of potential actions APHIS might grant a categorical exclusion from additional environmental evaluation and documentation. These changes reflect the new activities, advances, and data accumulated since 1995. By establishing more appropriate use of categorical exclusions, APHIS can remove the need to prepare time-consuming, costly, redundant, and unnecessary NEPA documents, and move vaccines to market in a more timely manner.

III. POLICY [or GUIDELINES]

A. NEPA considerations

1. Risk assessment for viable, replicating biotechnology-derived vaccines at the CVB will continue to include examination of genotypic and phenotypic stability in cell culture and target animals, zoonotic potential, changes in tissue tropism, shed/spread capabilities, effect of overdosage, recombination potential and consequences, and survivability in the environment and in target and non-target animals.
2. The biologics firm will submit the appropriate information in its Risk Analysis (RA), consisting of Summary Information Format and Risk Assessment documents. The CVB will conduct a risk review of proposed field trials and assess potential effects of the live vaccine on animal safety, public health, and the physical environment, consulting with subject matter experts as needed, to determine if an EA or EIS is required. The CVB will summarize its conclusions regarding whether to categorically exclude a proposed action in a record of environmental consideration. If the CVB cannot categorically exclude a proposed field safety trial from public notification in the Federal Register, the firm will submit an RA with confidential business information redacted. The CVB will send the redacted document along with the EA or EIS prepared by the CVB and a Notice announcing pending field trials for Federal Register publication.
3. Alternately, if the CVB applies a categorical exclusion based on review of the RA, the CVB will not submit documents for further agency and departmental review, and will not publish a Notice in the Federal Register. In these cases, sufficiently similar vaccines have previously been through the Federal Register process, comment period, and FONSI determination with satisfactory results. Categorical exclusions will be applicable to well-characterized, safe vectors or recombinant vaccines that, through prior experience and monitoring, have no significant impact on animals, humans, or the physical environment. Curtailing the preparation, submission, and review of further documents will provide

benefit to APHIS, the public, and biologics manufacturers by saving time and resources to bring qualified vaccines to market.

4. When an exception for a categorically excluded action occurs, i.e., a condition that suggests a normally excluded action has the potential for a significant adverse effect on the environment ([7 CFR 372.5](#)), the CVB will determine if that circumstance requires further analysis in an EA or EIS. The CVB expects new types of live biotechnology-derived vaccines will go through the Federal Register process. Even a vector that might otherwise qualify for a categorical exclusion may have an exceptional circumstance requiring further assessment. If a risk assessment indicates uncertainty regarding vaccine safety or potentially hazardous use, an EA or EIS will be prepared for publication. Scientifically controversial vaccines may go through the Federal Register process more than once if concerns remain.

B. Circumstances under which categorical exclusions may apply

1. Previous data for the same or sufficiently similar vector(s), as determined by the CVB, has led to licensure of more than one product, following Federal Register publication, comment period, and satisfactory field safety trial; and
2. The same biologics firm that previously licensed vaccines using the same or sufficiently similar vector(s) is submitting a new recombinant produced by using the same or a sufficiently similar manufacturing process, as determined by the CVB.
 - a. The new vectored vaccine does not have to be of the same product type, e.g. only an influenza vaccine; but changes in species, route of administration, or other conditions may be considered an exception that requires the Federal Register process be completed. Vaccines using the same vector given across multiple species, with demonstrated safety data in the target species, would be eligible for consideration for categorical exclusion by the CVB.
 - b. Different firms using a similar vector may not receive a categorical exclusion solely on the basis of exclusions granted to another manufacturer. However, following satisfactory technology transfer from the manufacturer that has categorical excluded vaccines, as determined by the CVB, another firm using the same or similar vector(s) may apply for a categorical exclusion.

IV. IMPLEMENTATION/APPLICABILITY

This policy applies to all viable, recombinant, biotechnology-derived vaccines and is effective 30 days from the date of this memorandum.