Animal and Plant Health Inspection Service

Regulatory Pathway for Replicating Recombinant Veterinary Biologics

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USDA’s Center for Veterinary Biologics in Ames, Iowa Regulates Veterinary Biologics vaccines, immunotherapeutics, antisera, diagnostic test kits, etc.
The definition of a biologic (9 CFR 101.2)

Biological products. The term biological products, also referred to in this subchapter as biologics, biologicals, or products, shall mean all viruses, serums, toxins (excluding substances that are selectively toxic to microorganisms, e.g., antibiotics), or analogous products at any stage of production, shipment, distribution, or sale, which are intended for use in the treatment of animals and which act primarily through the direct stimulation, supplementation, enhancement, or modulation of the immune system or immune response. The term “biological products” includes but is not limited to vaccines, bacterins, allergens, antibodies, antitoxins, toxoids, immunostimulants, certain cytokines, antigenic or immunizing components of live organisms, and diagnostic components, that are of natural or synthetic origin, or that are derived from synthesizing or altering various substances or components of substances such as microorganisms, genes or genetic sequences, carbohydrates, proteins, antigens, allergens, or antibodies.

The term treatment shall mean the prevention, diagnosis, management, or cure of diseases of animals.
JURISDICTION IS THE FIRST QUESTION

The applicable FDA regulation: 21 CFR PART 510 -- NEW ANIMAL DRUGS
Subpart A--General Provisions Sec. 510.4 Biologics; products subject to license control.

Memorandum of Understanding between CVB and CVM:

Jurisdictional Institutional Review Committee (JIRC) Standing Monthly Meetings
<table>
<thead>
<tr>
<th>Category I</th>
<th>Category II</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>I-A-1</strong> Non-replicating recombinant antigen(s)-vaccine</td>
<td>40  II Live Gene Deleted</td>
</tr>
<tr>
<td><strong>I-A-2</strong> Non-replicating recombinant antigen(s)-kits</td>
<td>29  <strong>Category III</strong></td>
</tr>
<tr>
<td><strong>I-B-1</strong> Monoclonal antibody-therapeutic/prophylactic use</td>
<td>4   III-A Live Vectored</td>
</tr>
<tr>
<td><strong>I-B-2</strong> Monoclonal antibody-used in diagnostic tests</td>
<td>82  III-B-1 Transgenic plant-based vaccine</td>
</tr>
<tr>
<td><strong>I-C-1</strong> Synthetic peptide-therapeutic/prophylactic use</td>
<td>3   III-B-2 Transgenic plant-based diagnostic kit</td>
</tr>
<tr>
<td><strong>I-C-2</strong> Synthetic peptide/oligonucleotide-in diagnostic</td>
<td>23  <strong>Category IV</strong></td>
</tr>
<tr>
<td><strong>I-D-1</strong> Nucleic Acid-Mediated (not Synthetic)-vaccine</td>
<td>6   IV Non-replicating Platform Derived Count</td>
</tr>
<tr>
<td><strong>I-D-2</strong> Nucleic Acid-Mediated (not Synthetic)-diagnostic</td>
<td>1</td>
</tr>
</tbody>
</table>
Biotech Products by Category and Year

Number

Category 1
Category 2
Category 3
Category 4
• CVB has an iterative licensing process

• Products must be demonstrated to be safe and effective

• Early communication with the agency will save time and expense

• Live products must be evaluated for safety and environmental impact prior to environmental release

• Live recombinants must go through defined National Environmental Policy Act (NEPA) implementing procedure which is not simple
APHIS Implementing NEPA Procedures

DEPARTMENT OF AGRICULTURE
Animal and Plant Health Inspection Service

7 CFR Part 372 [Docket No. 93-165-3] RIN 0579-AA33

National Environmental Policy Act Implementing Procedures

AGENCY: Animal and Plant Health Inspection Service, USDA.

AGENCY: Final rule.

SUMMARY: These final procedures set forth the principles and practices the Animal and Plant Health Inspection Service will follow to comply with the National Environmental Policy Act of 1969, the Council on Environmental Quality regulations, and the U.S. Department of Agriculture regulations implementing the National Environmental Policy Act. These procedures replace APHIS Guidelines Concerning Implementation of NEPA Procedures.


FOR FURTHER INFORMATION CONTACT: Mr. Robert E. Pizel, Branch Chief, Biotechnology, Diagnostics, and Environmental Protection, APHIS, USDA, P.O. Drawer 810, Riverdale MD 20738. The telephone number for the agency contact will change when agency offices in Hyattsville, MD, move to Riverdale, MD, during January 1996. Telephone: (301) 436-8565 (Hyattsville); (301) 734-8565 (Riverdale).

SUPPLEMENTARY INFORMATION:

Background

The regulations of the President's Council on Environmental Quality (CEQ) implementing section 102(2) of the National Environmental Policy Act (hereinafter referred to as NEPA) are applicable to and binding on all agencies of the Federal Government. Pursuant to the CEQ implementing regulations, the Animal and Plant Health Inspection Service (APHIS) is implementing procedures to ensure that its planning and decisionmaking are in accordance with the policies and purposes of NEPA. The CEQ implementing regulations direct that agencies shall include, at a minimum, procedures required by 40 CFR 1501.2(d), 1502.1(c)(3), 1505.1, 1506.6(e), 1507.3 (b)(2), and 1508.4 (1992). APHIS' procedures supplant the APHIS Guidelines Concerning Implementation of NEPA Procedures originally published in the Federal Register on August 29, 1979 (44 FR 50381-50384) and corrections as published in the Federal Register on August 31, 1979 (44 FR 51272-51274). On June 3, 1994, we published in the Federal Register (59 FR 29444-29447; Docket No. 93-165-3) another proposed rule implementing
Regulatory Gray Area

Live recombinants being tested in client-owned animals as model for an ultimate human-only product:

- NIH is requiring government regulatory approval prior to environmental release
- FDA does not “approve” studies at this stage of development
- CVB does not have regulatory jurisdiction over a product that is being developed for use in humans just because it is being tested in an animal model
- If a license is being pursued for both animals and humans, the CVB NEPA process would need to be followed prior to environmental release