USDA
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IMPLEMENTATION OF THE AMENDMENTS TO APHIS'NEPA REGULATIONS

(CATEGORICAL EXCLUSIONS)

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Regulatory Authorities

- 1913 Virus-Serum-Toxin Act (VSTA)
- 1969 National Environmental Policy Act (NEPA)
- 1985 Food Security Act: intrastate, export commerce
- 1995 APHIS' NEPA Procedures (7CFR Part 372)
  - Replication competent biotech products undergo an environmental assessment per NEPA
- 2018 revision to APHIS' Implementing Procedures for NEPA
  - Categorical exclusions may apply to live biotech products

Risk Assessment for Live Biotech Vaccines To Identify Hazards - Unchanged by NEPA Revision

- Examine genotypic + phenotypic stability *in vitro* + in target animals (backpassage/reversion to virulence – VSM 800.201)
- Evaluate zoonotic potential, any changes in tissue tropism or host range
- Assess shed/spread capabilities + effect of overdosing
- Consider recombination potential + consequences
- Assess survivability in environment, target + nontarget animals

Risk Analysis: Assessment, Characterization, Communication, Management

- Risk review by CVB of proposed field trials
  - Environmental assessment (EA) for any live vaccine's effects on animal safety, public health, or the physical environment
  - The firm submits a Risk Analysis (RA) to CVB + a CBI-redacted version
- NEPA compliance for field safety trial
  - Environmental impact statement (EIS) needed?
  - Decision: significant impact on animals, humans, the environment? input from SMEs - EA or EIS? So far: > 50 EAs, no EIS – all FONSI.
  - Alternative actions are evaluated; any mitigation is identified
  - Action is taken to mitigate possible risk, e.g. restriction to only government use for wildlife vaccines
  - The public is notified of possible risk by Federal Register Notice

Federal Register (FR) Process for Live Biotechnology-Derived Vaccines (Not Done if Categorical Exclusion Applies)

- CVB provides the FR Notice, EA, + FONSI (public documents) to the firm for review, then sends the FR Notice, CBI- RA, + EA to Riverdale for agency + departmental review
  - PPD/RAD, OGC, CVB, OA, MRPBS/OSEC, DA (signs docket)
  - Announcement in FR of pending field trials and tentative Finding of No Significant Impact (FONSI)
  - Placement of the CVB-prepared Environmental Assessment and firm's CBI-redacted Risk Analysis in the FR docket
  - Public comment period, minimum 30 days required
  - If no significant issues arise: signed FONSI, approval of field trials

Review of the Final Rule

- Published in the Federal Register on 5/24/2018

"Categorical exclusions" (372.5(c)): where testing +/or monitori has shown no significant adverse impact on the human environment

  - Less time + resources for redundant studies
  - Benefit to industry, APHIS, + the consumer

Applicable to viable, recombinant, biotech-derived vaccines; but not applicable to diagnostic, inactivated, allergenic, or antibody products

Following publication of the final rule, CVB posted a draft VS Memo with guidelines; comments incorporated, now waiting on DA's signature

Revision to APHIS' Implementing Procedures for NEPA

- Categorical exclusion to the FR process for safe, well-characterized vectors or recombinants if no adverse impacts to the environment
- Some potential candidates: fowlpox/other pox virus, canarypox, HVT, adenovirus vectors (although bacterial vectors may also be considered)
- New types or scientifically controversial biotech vaccines will go through the FR process at least once; even a potential CatX'd vector may have a unique circumstance that makes it unacceptable for CatX
- Provisions made for rapid response to emergencies

NEPA Provisions

- **An EA or EIS will be prepared for the FR process if there is a higher degree of novelty or uncertainty regarding vaccine safety or potentially hazardous use**
  - An EA is prepared for actions with limited scope + potential effect
- **CatX actions could include:**
  - New GE'd vaccines or existing vaccines given to new species if given in a controlled + limited manner, where impacts can be predicted;
  - Vaccination trials designed to limit interaction with similar animals, where controls are used that mitigate potential risk;
  - Authorization to field test unlicensed GE'd vaccines
- **Exceptions for CatX:** when the biologic is shown to be unsafe, is used in a substantially different way, or involves new species or novel modifications that raise new issues

Implementation of Categorical Exclusions

- **What data needed to show a product can be CatX'd?**
  - Case-by-case basis: e.g., change of insert without significant effect on performance of the vaccine + insert is nontoxic, non-allergenic
- **If one firm has multiple products licensed, would it count for other products from that firm?**
  - If same or very similar vector and manufacturing process
  - If change in primers, promoters, insertion size, etc. not significant
  - If same product type? –e.g. all influenza products? Not required
- **Other firms using same or similar vector?**
  - Need their own well-characterized products, or a technology transfer

Questions?