Policy: **IBC/IACUC RCT01-17**	Version: **2017**
Name: **Veterinary Clinical Trials Involving Recombinant Nucleic Acids and/or Recombinant Microbes**	Approved: **February 15, 2017**
Areas Affected: **All veterinary clinical trials, experimental treatments, or adoptions involving animals exposed to recombinant nucleic acids and/or recombinant microbes**	Next Review: **February, 2018**

I. PURPOSE, APPLICABILITY & SCOPE

Veterinary clinical research often involves patient enrollment for the purpose of conducting clinical trials, experimental treatments, etc. for the development of new medications, procedures or therapies. The results of these trials may be instrumental in Food and Drug Administration and/or Unites States Department of Agriculture approval of new drugs or treatments. While some clinical trials may fully fall to the discretion of the coordinating clinician(s), some require additional institutional and/or regulatory approvals. One example of the latter, and the focus of this policy, is the use of novel, unlicensed recombinant DNA molecules and/or recombinant microbes (vaccine agents, nucleic acid delivery vectors, or challenge agents used in infectious disease models). Such studies are subject to approvals by the Institutional Animal Care and Use Committee as well as the Institutional Biosafety Committee (studies in containment) and/or regulatory agencies (studies involving environmental release, release to owners, or adoption of research animals).

This joint IBC/IACUC policy applies to veterinary research, clinical trials, experimental treatments or adoptions involving animals exposed to recombinant nucleic acids and/or recombinant microbes (including vaccine agents).

II. ABBREVIATIONS, ACRONYMS & DEFINITIONS

A. *Abbreviations & Acronyms*

1. APHIS – Animal & Plant Health Inspection Service
2. CFR – Code of Federal Regulations
3. CVB – Center for Veterinary Biologics
4. DNA – Deoxyribonucleic Acid
5. FDA – Food & Drug Administration
6. FFDCA – Federal Food, Drug & Cosmetic Act
7. IACUC – Institutional Animal Care and Use Committee
8. IBC – Institutional Biosafety Committee

9. NIH – National Institutes of Health
10. USDA – United States Department of Agriculture
11. VSTA – Virus, Serum, Toxin Act

B. ***Definitions***

1. **Biological Products** – all viruses, serums, toxins (excluding substances that are selectively toxic to microorganisms, e.g. antibiotics), or analogous products at any stage of production, 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 used in clinical trials fall under the VSTA. This includes, but is not limited to, vaccines, bacterins, allergens, antibodies, antitoxins, toxoids, immunostimulants and diagnostic components of natural or synthetic origin, or that are derived from synthesizing or altering various substances or components of substances such as microorganism, genes or genetic sequences, proteins, antigens, allergens or antibodies. "Biological product" does not apply to antimicrobials, corticosteroids, steroidal and non-steroidal anti-inflammatories, hormones, and products intended to treat disease with a primary mechanism of action that is not immunological.
2. **Containment** – the use of (i) a set of standard practices that are generally used in microbiological laboratories; (ii) special procedures, equipment, and laboratory installations that provide physical barriers that are applied in varying degrees according to the estimated biohazard; and (iii) highly specific biological or natural barriers that limit either the infectivity of a vector or vehicle (plasmid or virus) for specific hosts, or its dissemination and survival in the environment. Special practices and physical containment requirements for recombinant/synthetic nucleic acids or organisms in animals are outlined in Appendix G and Appendix Q (large animals) of the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules*. Considerations for biological containment can be found in Appendix I.
3. **Drugs –** articles intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease in man or other animals and articles intended to affect the structure or any function of the body of man or animals. "Drugs" also includes agents intended to improve animal performance, such as increased production, weight gain and enhanced feed efficiency.
4. **Environmental Release** – the intentional or accidental release of recombinant/synthetic nucleic acids or organisms outside of containment as defined in the *NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules* (see 'Containment' above).
5. **Recombinant DNA and Synthetic Nucleic Acid Molecules** – in the context of the *NIH Guidelines*, recombinant and synthetic DNA molecules are defined as:
    i. molecules that (a) are constructed by joining nucleic acid molecules and (b) can replicate in a living cell, i.e., recombinant nucleic acids;

ii. nucleic acid molecules that are chemically or by other means synthesized or amplified, including those chemically or otherwise modified but can base pair with naturally occurring nucleic acid molecules, i.e., synthetic nucleic acids; or

iii. molecules that result from the replication of those described above.

III. REVIEW AND APPROVAL AUTHORITY & PROCEDURES

A. *Submission and Review*

During the process for IACUC approval to conduct a veterinary clinical trial at the university, the protocol will be evaluated by the Biosafety Office to assess whether recombinant nucleic acids/agents will be used and to determine whether IBC and/or other regulatory approvals are necessary. Initial IACUC submissions, amendments, and updates will be evaluated in a like manner. The Biosafety Officer will work with the coordinating clinician(s) to obtain the appropriate approval if IBC approval is needed. In cases where an outside regulatory body approval is needed, efforts to guide the clinician to the appropriate regulatory body will be taken.

B. *Institutional Biosafety Committee Approvals*

The IBC establishes, recommends, and approves policies ensuring the prudent management of biological hazards, including recombinant and synthetic nucleic acids. IBC review and approval will generally be required for clinical trials involving recombinant/synthetic nucleic acid molecules and/or modified agents, particularly if the recombinant reagents have not been licensed or otherwise deregulated by a federal regulatory authority such as USDA or FDA (see below). During the approval process, the IBC will verify that the proposed physical containment and safety procedures adequately address the risks posed by the proposed recombinant materials. The IBC only has the capacity to approve clinical trials involving recombinant nucleic acids/agents *in containment*. *NIH Guidelines*-defined practices and physical containment requirements must be stringently followed. Resultantly, release of affected animals into the environment, return to owners, or adoption cannot be approved by the IBC and will require additional approvals from a regulatory authority.

C. *Regulatory Oversight of Veterinary Clinical Trials*

While the IBC can provide institutional approvals for clinical trials involving recombinant/synthetic nucleic acids or organisms in containment, they do not have the regulatory authority to approve such trials outside of containment (e.g. environmental release of animals, including return to owners or adoption). While IBC approval may still be required for safety assessments, a regulatory authority will also need to issue approval for release per their respective risk assessment and in accordance with the following:

1. Biological products are subject to approval by the USDA APHIS CVB per the conditions of the Virus-Serum-Toxin Act (VSTA), 21 CFR Part 151; 9 CFR Part 101.

2. Drugs are subject to approval by the FDA per the conditions of the FFDCA, 21 CFR Parts 321 & 510 (*inter alia*)

All approval conditions issued by the respective regulatory agency must be communicated to the Biosafety Office/IBC. The Biosafety Office will work with the coordinating clinician to ensure that all conditions and stipulations are met.

IV. GUIDELINES, STANDARDS & REGULATORY REFERENCES

The following regulations, standards, guidelines and policies apply to this policy. In case of conflict between requirements of the regulatory agencies, the more protective regulations shall prevail, as appropriate.

A. The *NIH Guidelines for Research Involving Recombinant or Synthetic DNA Molecules* (April, 2016):
http://osp.od.nih.gov/sites/default/files/resources/NIH_Guidelines.pdf
http://osp.od.nih.gov/sites/default/files/NIH_Guidelines.html

B. The Virus, Serum & Toxin Act (VSTA): 21 CFR Part 151; 9 CFR Part 109

C. The Federal Food, Drug, and Cosmetic Act (FFDCA): 21 CFR Parts 321 & 510 (*inter alia*)

D. Memorandum of Understanding between the Animal and Plant Health Inspection Service, United States Department of Agriculture and the Food and Drug Administration, Department of Health and Human Services:
https://www.aphis.usda.gov/animal_health/vet_biologics/publications/APHIS_FDA_biologics_MOU.pdf