Summary Information Format
Category III Veterinary Biologics

I. Introduction

Category III Veterinary Biologics are live recombinant products, either chimeric or containing exogenous genetic material.

A. Provide a brief descriptive summary of the product:

B. Describe the intended use of the product:

1. Target species:
2. Proposed label claim:
3. Route of administration:
4. Geographic area:

II. Description of the Product

For a Category III SIF, the Backbone Biological Agent (BBA) is a live, replicative, commercially available, wild type or commonly available parental organism or cell prior to the genetic manipulation(s) necessary for expression of exogenous product(s). The Donor Biologic Agent (DBA) is the source of recombinant genetic material and may also refer to inserted or synthetic sequences. The Regulated Biological Agent (RBA) is the final product, typically a live replicating, viable agent or cell either synthesized or derived from the BBA via genetic modification.

A. Backbone Biological Agent (BBA)

1. Describe the wild type or modified organism or cell or material used for the BBA, where it was obtained or constructed, and cite the primary literature describing the BBA.

2. Characteristics of the BBA
   a. If the BBA has been modified from its wild-type parent, either via targeted manipulation or through in vitro passage, cite the primary literature, and/or include a flow diagram or explanation of the construction of the BBA.
   b. Describe how the BBA differs from the wild-type, including genetic and phenotypic changes, and the methods and results useful for differentiating the BBA from its wild-type parent and other strains.

B. Donor Biological Agent (DBA) (or inserted sequences)

1. Identify the source of the inserted recombinant sequences, whether obtained from a DBA or synthesized. If obtained from another organism (DBA), provide a thorough history of the origin and characteristics of the DBA organism.

2. Identify each recombinant sequence and the function of the genetic product. Cite literature as appropriate.

C. Regulated Biological Agent (RBA)

1. Identify where the final RBA was initially constructed and where the final product will be made, tested, and manufactured and the biosafety level of the facilities.

2. Provide GenBank accession numbers or nucleic acid sequences in FASTA or FASTQ format (.txt files) for all relevant BBA, DBA, and RBA. Sequence files should contain actual, not theoretical, sequences for any new or altered genetic sequences, including insertion and flanking sequences. Whole genome sequence data should be provided as zipped FASTQ files. Contact CVB for guidance on electronic submission of large sequence files.

3. Provide a flow diagram for the laboratory construction of the RBA. Include the following:
    a. Backbone Biological Agent
    b. Donor Biological Agent or nucleic acid or gene
    c. All plasmids, shuttle vectors or kits and their source
    d. Host cell lines used and source
    e. Describe the selection techniques and methods used to construct the RBA.

4. Describe the characterization of the RBA including the laboratory methods and criteria used to evaluate the RBA. Provide evidence that the genetic modifications occurred as intended.
    a. Describe and show the results of PCR, sequencing, or other genetic test that will discriminate between the BBA and RBA sequences.
    b. Describe the criteria for stability and purity of the RBA Master Seed (X) and highest passage thereof (X+n) desired for use in production.
    c. Provide all detailed protocols and show characterization results of the expressed/target antigen or product, including but not limited to fluorescent antibody and Western blot testing of the BBA, Master Seed and X+n; including positive and negative controls. If appropriate, provide any purification or concentration steps/protocols used for characterization of the expressed/target antigen.
    d. Provide a description of any genetic motifs that may have resulted due to the genetic modifications. Report any known motifs that may promote homologous recombination, insertion, or gene expression of existing or new open reading frames.

D. Safety Considerations

1. Provide the recommended CDC/NIH biosafety level for the BBA, DBA and RBA.

2. Describe, citing literature or internal data as appropriate, both any known virulence associated with and any previous safe use of the BBA, DBA, and RBA in:
    a. Target animal species
    b. Non-target animal species
    c. Humans

3. Clearly identify any antimicrobial resistance genes present or used to create the RBA, and whether these genes will be present in the final product.

4. Describe any expected or possible impact the final product could have on animal/human diagnostic testing, food testing, or disease surveillance programs. Include if a test to differentiate infected from vaccinated animals (DIVA) is available or possible.

III. Biological Properties of the RBA (Provide direct scientific evidence, including any relevant scientific publications, if available. Provide MailLog numbers of studies submitted to CVB where appropriate).

A. Describe the known phenotypic characteristics or effects of the genetic modifications on the RBA.

B. Describe whether the recombinant sequences enhance the virulence or survivability of the RBA in the host.

C. Describe the persistence and tissue tropism of the RBA in target and non-target animals.

D. Describe the potential for horizontal gene transfer or recombination of the RBA. Include any reason to believe that the potential for horizontal gene transfer or recombination is different in target and non-target animals. Include any contributions from the BBA and recombinant sequences in the discussion.

E. Describe the shed/spread capabilities of the RBA. Include target and non-target animal species. Include any contributions to shed/spread capabilities that might be associated with attributes of the BBA and recombinant sequences.

F. Describe the environmental impact and survivability of the RBA. Include whether attributes of the BBA or recombinant sequences enhance the ability to survive in the environment or increase resistance to therapeutic agents.