FORM A COMMENTS ON THE WORK PROGRAMME OR ITEMS DOCUMENTED IN THE REPORT THAT DO NOT INCLUDE ANNEXES	
United States of America	**WOAH Biological Standards Commission February 2026**
	Title of the item in the report or item in the work programme annex: 5.5 Review of *Terrestrial Manual* vaccine chapters (Chapter 1.1.8 "Principles of veterinary vaccine production") **Proposal/Comment:** The United States of America notes that the *February 2026 Report of the Meeting of the WOAH Biological Standards Commission* indicates an interest from the Commission in updating Chapter 1.1.8 "Principles of veterinary vaccine production" of the WOAH *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* (*Terrestrial Manual*). The United States of America agrees with the need to review Chapter 1.1.8 "Principles of veterinary vaccine production" and recommends updating the Chapter to encompass new technologies of vaccines that are available as described in further detail below. **Rationale:** Resolution No. 29 adopted during the 92nd General Session in May 2025 states that the Assembly of Member States recommends: "WOAH develops and updates international standards for the vaccine safety, efficacy, integration of new technologies and, when applicable, safe trade of vaccinated animals and their products, ensuring global recognition and trust". Novel vaccine technologies continue to enter global markets which address our most pressing animal health needs, but which may not be accurately characterized by the existing definitions for vaccines in Chapter 1.1.8 of the *Terrestrial Manual*. In the interest of WOAH international standards remaining current and supportive of safe international trade, the United States of America supports amendments to Chapter 1.1.8. The United States of America recently approved a new class of vaccine that is not currently categorized in Chapter 1.1.8 of the *Terrestrial Manual*: Propagation defective encapsulated RNA vaccines. This class of vaccine meets the definition of an inactivated vaccine; however, the definition of its construct is not included in the current subtypes of inactivated vaccines. Propagation defective encapsulated RNA vaccines differ from the currently-defined constructs for inactivated vaccines in that they use a nucleic acid particle backbone to encode for immune-stimulating proteins. The nucleic acid particles are taken up by cells in the vaccinated animal to self-amplify for a limited period of time and undergo translation to produce antigenic proteins that are transported to the surface of the cell to generate an immune response (Tarpey *et al.* 2025). This mode of action is significantly different from the current constructs listed for inactivated vaccines: microorganisms that have been killed/inactivated; inactivated toxins; subunits extracted from cultures or produced through rDNA procedures.

	Supporting evidence, if relevant:  vaccines-13-01176.pdf

PRINCIPLES OF VETERINARY VACCINE PRODUCTION

VACCINE TYPES OR FORMS

Inactivated (killed) ~~Killed~~ products may contain: 1) Cultures of microorganisms that have been inactivated by chemical or physical means; 2) Inactivated toxins; ~~or~~ 3) Subunits (antigenic parts of microorganisms) that have been extracted from cultures or that have been produced through rDNA procedures; or 4) Propagation defective encapsulated RNA which produce proteins.

United States of America	**Category:** Additions **Proposed amended text:** Inactivated (killed) ~~Killed~~ products may contain: 1) Cultures of microorganisms that have been inactivated by chemical or physical means; 2) Inactivated toxins; ~~or~~ 3) Subunits (antigenic parts of microorganisms) that have been extracted from cultures or that have been produced through rDNA procedures; or 4) Propagation defective encapsulated RNA which produce proteins. **Rationale:** Add “Inactivated” to the beginning of the paragraph to maintain consistent wording with the first paragraph in the section. Propagation defective encapsulated RNA vaccines are a novel class of vaccine which exhibits a mode of action best characterized as “inactivated”. These vaccines present antigenic proteins for immune response via a self-amplifying but propagation defective nucleic acid backbone. They cannot revert to virulence and do not contain any live microorganisms (Mogler and Kamrud, 2014; Tarpey *et al.* 2025). To ensure that Chapter 1.1.8 reflects and accurately categorizes new technologies, this class of vaccine should be added to the subtypes of inactivated vaccine. **Supporting evidence, if relevant:** vaccines-13-01176.pdf Mogler and Kamrud 2014.pdf

PRINCIPLES OF VETERINARY VACCINE PRODUCTION

VACCINE TYPES OR FORMS

Category I consists of non-viable or killed products that pose negligible risk to the environment and present no new or unusual safety concerns. Such products include inactivated microorganisms, either whole or as subunits, created by using rDNA techniques, and propagation defective encapsulated RNA which produce proteins.

United States of America	**Category:** Additions **Proposed amended text:** Category I consists of non-viable or killed products that pose negligible risk to the environment and present no new or unusual safety concerns. Such products include inactivated microorganisms, either whole or as subunits, created by using rDNA techniques, and propagation defective encapsulated RNA which produce proteins. **Rationale:** Propagation defective encapsulated RNA vaccines fall within Category I of veterinary vaccines derived through rDNA technology because they use discreet DNA units to produce the RNA particles which will encode for antigenic proteins (Tarpey *et al.* 2025). As stated above, propagation defective encapsulated RNA vaccines cannot revert to virulence and do not contain live virus. As such, the United States of America recommends that this class of vaccine is listed as a Category I vaccine derived through rDNA technology. **Supporting evidence, if relevant:**  vaccines-13-01176.pdf

FORM A COMMENTS ON THE WORK PROGRAMME OR ITEMS DOCUMENTED IN THE REPORT THAT DO NOT INCLUDE ANNEXES	
United States of America	**WOAH Biological Standards Commission February 2026**
	Title of the item in the report or item in the work programme annex: 5.5 Review of *Terrestrial Manual* vaccine chapters (Chapter 3.1.19 "Rabies [Infection with Rabies Virus and other Lyssaviruses]") **Proposal/Comment:** The United States of America notes that the *February 2026 Report of the Meeting of the WOAH Biological Standards Commission* indicates an interest from the Commission in updating Chapter 1.1.8 "Principles of veterinary vaccine production" of the WOAH *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals* (*Terrestrial Manual*). The United States of America agrees with the need to review Chapter 1.1.8 "Principles of veterinary vaccine production" and additionally encourages the Biological Standards Commission to review, align and update disease-specific chapters as necessary to reflect new vaccine technologies. The following comments contain recommended edits to Chapter 3.1.19 "Rabies (Infection with Rabies Virus and other Lyssaviruses)" intended to align with recommended edits to Chapter 1.1.8 "Principles of veterinary vaccine production" (please see submitted comments on the work programme for the February 2026 Report of the WOAH Biological Standards Commission entitled: "5.5 Review of *Terrestrial Manual* vaccine chapters [Chapter 1.1.8 'Principles of veterinary vaccine production']). **Rationale:** Beside vaccines against canine influenza H3N2 and feline leukemia virus, a propagation defective encapsulated RNA, i.e., via replicon technology, vaccine has been approved by the United States of America for the prevention of rabies in dogs and cats. As such, the United States of America encourages the Biological Standards Commission to amend Chapter 3.1.19 "Rabies (Infection with Rabies Virus and other Lyssaviruses)" of the *Terrestrial Manual* to reflect that this vaccine class exists and has been found acceptable for rabies. The current text in Chapter 3.1.19 Section 2.1 states that "non-replication competent constructs (e.g. virus like particles [VLPs], replicon vaccines, mRNA vaccines, plasmid vaccines or subunit vaccines) or replication restricted rabies vaccine constructs (e.g. single cell cycle rabies vaccines) may be available for injectable use in the future (see Chapter 1.1.8)". This does not reflect the current status of propagation defective encapsulated RNA vaccines and also limits the long-term accuracy of Chapter 3.1.19 by stating that many vaccine technologies may be available in the future. The United States of America recommends revising this chapter to reflect the current profiles of vaccines available for rabies as well as future-proof the WOAH *Terrestrial Manual* as additional technologies rapidly become available moving forward.

	Supporting evidence, if relevant:  vaccines-13-01176.pdf

CHAPTER 3.1.19.

RABIES (INFECTION WITH RABIES VIRUS AND OTHER LYSSAVIRUSES)

SUMMARY

Requirements for vaccines: *For rabies vaccination in animals, inactivated virus (for companion animals and livestock), live attenuated virus (for wildlife and free-roaming dogs), and recombinant vaccines (for wildlife, cats and dogs) are used. Certain vaccines can be categorised in more than one of these groups and may be biotechnology-derived.*

United States of America	**Category:** Addition **Proposed amended text:** *Requirements for vaccines: For rabies vaccination in animals, inactivated virus (for companion animals and livestock), live attenuated virus (for wildlife and free-roaming dogs), and recombinant vaccines (for wildlife, cats and dogs) are used. Certain vaccines can be categorised in more than one of these groups and may be biotechnology-derived.* **Rationale:** Vaccine technologies against rabies in animals continue to evolve. Currently approved vaccines can be categorized into more than one characteristic, including biotechnology-derived. The added text reflects the current and developing state of rabies vaccine technology. **Supporting evidence:** Not relevant.

C. REQUIREMENTS FOR VACCINES

1. General background

Rabies vaccines are defined as a standardised formulation containing defined amounts of immunogens. These immunogens are ~~either~~ inactivated (killed), live-attenuated and/or biotechnology-derived as described in chapter 1.1.8.

United States of America	**Category:** Deletion and addition **Proposed amended text:** Rabies vaccines are defined as a standardised formulation containing defined amounts of immunogens. These immunogens are ~~either~~ inactivated (killed), live-attenuated and/or biotechnology-derived as described in chapter 1.1.8.

	Rationale: Vaccine technologies against rabies in animals continue to evolve. Currently approved vaccines can be categorized into more than one characteristic, including biotechnology-derived. The added text reflects the current and developing state of rabies vaccine technology. For example, propagation defective encapsulated RNA vaccines are both inactivated and derived from biotechnology. **Supporting evidence:** Not relevant.

2. Rabies vaccine for injectable use

2.1. Background

Rabies virus glycoprotein biotechnology-derived vector vaccines are prepared by inserting non-infectious rabies virus nucleic acid coding for rabies virus glycoprotein into a live vector such as avipox for injectable vaccine (WHO, 2018). ~~Alternatively,~~ Additional biotechnology-derived vector vaccines may include: non-replication competent constructs (e.g. virus like particles [VLPs], replicon vaccines, mRNA vaccines, plasmid vaccines or subunit vaccines etc.) or replication restricted rabies vaccine constructs (e.g. single cell cycle rabies vaccines)~~, may be available for injectable use in the future (see Chapter 1.1.8)~~.

United States of America	**Category:** Addition; editorial. **Proposed amended text:** Rabies virus glycoprotein biotechnology-derived vector vaccines are prepared by inserting non-infectious rabies virus nucleic acid coding for rabies virus glycoprotein into a live vector such as avipox for injectable vaccine (WHO, 2018). Additional biotechnology-derived vector vaccines may include: ~~Alternatively,~~ non-replication competent constructs (e.g. virus like particles [VLPs], replicon vaccines, mRNA vaccines, plasmid vaccines or subunit vaccines etc.) or replication restricted rabies vaccine constructs (e.g. single cell cycle rabies vaccines)~~, may be available for injectable use in the future (see Chapter 1.1.8)~~. **Rationale:** This paragraph describes rabies vaccines that are biotechnology-derived. The United States of America recommends editing the paragraph to remove reference to other biotechnology-derived vaccines being available in the future, as this will require updating the text each time a new technology becomes available. We recommend revising the text to state that biotechnology-derived vaccines *may include* the listed constructs for longevity of the Chapter text. **Supporting evidence:** Not relevant.

2.2. Outline of production and minimum requirements for conventional vaccines

2.2.1. Characteristics of the seed

Biotechnology-derived vaccines are prepared in appropriate cell lines using a vector expressing the RABV glycoprotein, or from DNA templates encoding the vector and rabies glycoprotein sequences.

United States of America	**Category:** Addition **Proposed amended text:** Biotechnology-derived vaccines are prepared in appropriate cell lines using a vector expressing the RABV glycoprotein, or from DNA templates encoding the vector and rabies glycoprotein sequences. **Rationale:** The United States of America has approved a rabies vaccine which uses propagation defective encapsulated RNA. This technology uses synthesized DNA sequences to transcribe RNA sequences for rabies glycoprotein and replicon components (Tarpey *et al.* 2025). **Supporting evidence:** vaccines-13-01176.pdf

2.2.2. Method of manufacture

Propagation defective encapsulated RNA vaccines are generally non-viable and therefore do not utilize chemical inactivation during the manufacturing process.

Inactivated rabies vaccines are usually formulated as liquid or freeze dried. The liquid vaccine is usually prepared by adsorbing the antigen onto an adjuvant, for example aluminium hydroxide gel.

United States of America	**Category:** Addition **Proposed amended text:** Propagation defective encapsulated RNA vaccines are generally non-viable and therefore do not utilize chemical inactivation during the manufacturing process. Inactivated rabies vaccines are usually formulated as liquid or freeze dried. The liquid vaccine is usually prepared by adsorbing the antigen onto an adjuvant, for example aluminium hydroxide gel. **Rationale:** Propagation defective encapsulated RNA vaccines use synthesized DNA sequences to transcribe RNA sequences for rabies glycoprotein and replicon components (Tarpey *et al.* 2025). The synthesized DNA sequences and resulting RNA sequences that comprise the vaccines are not viable and do not contain any live virus components. As such, there is not a need to use chemical inactivation during manufacturing. Inactivated rabies vaccines typically require the use of an adjuvant in order to stimulate immune response. Propagation defective encapsulated RNA vaccines may not require the use of an adjuvant due to the vaccine's mode of action. This

	class of vaccine may induce both innate and adaptive immune responses, which in turn negates the need for an adjuvant (Mogler and Kamrud, 2014). The United States of America recommends amending *Section 2.2.2 Method of manufacture* to reflect that inactivated rabies vaccines are *usually* prepared using an adjuvant but may not be required to use one. **Supporting evidence:**  Mogler and Kamrud 2014.pdf