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SCIENCE MEDICINES HEALTH

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Committee for Veterinary Medicinal Products (CVMP)

# Concept paper for the development of a guideline on quality aspects of mRNA vaccines for veterinary use

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| Agreed by Immunologicals Working Party | 22 October 2024 |
| Adopted by CVMP for release for consultation | 5 December 2024 |
| Start of public consultation | 8 January 2025 |
| End of consultation (deadline for comments) | 8 April 2025 |

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| Keywords | mRNA, vaccine, development and manufacture, starting materials, active substance, quality, veterinary, finished product |


## 1. Introduction

This concept paper addresses the need to establish a Guideline on the quality aspects of mRNA vaccines. In the area of human medicinal products, the number applications for clinical trials and marketing authorisations for mRNA containing products significantly increased over the last few years and a lot of experience with mRNA vaccines was gained during the COVID-19 pandemic. It is expected that such developments will be seen in the field of vaccines for veterinary use, too. From an analytical and regulatory perspective, mRNA vaccines are different to most of the vaccines which are currently authorised.

mRNA vaccines against infectious diseases must align with the general guidance for veterinary vaccines, however this technology is not fully accounted for in the existing guidance. It is therefore proposed to establish a guideline addressing those specific aspects regarding the manufacturing process, characterisation, specifications and analytical control as well as the definition of active substance and finished product for mRNA vaccines.

The scope of the guideline will be limited to mRNA vaccines against infectious diseases (including self-amplifying mRNA). mRNA-based therapeutics will be out of scope of the document.


**Official address** Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
**Address for visits and deliveries** Refer to www.ema.europa.eu/how-to-find-us
**Send us a question** Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

## 2. Problem statement

Currently there is no guideline which reflects the quality requirements for regulators and industry on mRNA containing vaccines. Considering the scientific developments in recent years including the experience gained during the COVID pandemic in the human medicinal products area and the first expected submissions for mRNA vaccines for veterinary use, such a guideline should be developed to ensure appropriate support in development and manufacturing of mRNA vaccines for veterinary use.

## 3. Discussion (on the problem statement)

mRNA vaccines and their manufacturing process are a novel technology, and the resulting products differ from other types of vaccines. They consist of mRNA (non-replicating or self-amplifying, nucleoside-modified or not) encapsulated in lipid nanoparticles or other kinds of delivery systems and specific quality considerations may apply to these novel products.

This type of vaccine may have some advantages over the direct inoculation of the antigen itself, e.g. it may provide a wider stimulation of the immune system, both cellular and humoral, including the stimulation of a cytotoxic T cell response. It may also have advantages over the use of live attenuated micro-organisms, e.g. the avoidance of the risk of breakthrough of disease arising from possible reversion to virulence. Furthermore, the development and manufacture of mRNA vaccines is likely to be more easily adaptable and scalable and therefore more cost-efficient than for the traditional types of vaccines, as well as providing wider scope to encompass other modes of delivery. Furthermore, mRNA can be considered a vaccine platform technology which can be of advantage for rapidly responding to emerging disease threats. The proposed guideline will provide information and regulatory considerations regarding the following key aspects of the manufacture and quality control:

- Definitions of starting materials, active substance, finished product intermediate, excipients and finished product
- Control of starting materials (linear DNA template for the preparation of mRNA transcript and plasmid DNA where relevant)
- Development of an integrated control strategy for the active substance and finished product manufacturing process to ensure consistent quality of mRNA vaccines, based on relevant critical quality attributes (CQAs)
- Characterisation approaches including investigation of the impurity profile
- Purity control strategy: process-related and product-related impurities as well as other potential contaminants and methods to control them
- Active substance and finished product specifications
- Potency testing: different tests may be required to control various aspects of potency also including functionality (e.g. mRNA expression, protein expression in transduced cells)
- Various aspects with respect to the formulation strategies, including considerations on formation and method of manufacturing of lipid nanoparticles (LNPs) or other delivery systems, and their stability
- Stability studies for active substance and finished product

The proposed guideline will also discuss relevant regulatory considerations and challenges relating to:

- the development and testing of multivalent mRNA vaccines, as well as to changes in mRNA composition
- self-amplifying mRNA (sa-mRNA) packaged in LNPs
- other delivery systems (i.e. non-LNPs)
- the use of platform technology for new targets

The WHO guidance document, Annex 3 "Evaluation of the quality, safety and efficacy of messenger RNA vaccines for the prevention of infectious diseases: regulatory considerations", WHO technical report Series, No.1039, 2022 will be taken into account. Furthermore, reference will be made to current and future Ph. Eur. chapters and/or monographs, where applicable.

# 4. Recommendation

The Committee for Medicinal Products for Veterinary Use (CVMP) recommends the Immunologicals Working Party (IWP) to discuss the drafting of a guideline on quality aspects of mRNA vaccines for veterinary use. The issues identified above will be taken into consideration and options for possible solutions may be included if these are known.

# 5. Proposed timetable

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| December 2024 | Concept paper released for consultation |
| March 2025 | Deadline for comments from stakeholders |
| Q4 2025 | Adoption of the draft guideline by CVMP and release for consultation |
| Q2 2026 | Deadline for comments from stakeholders |
| Q4 2026 | Expected date for adoption by CVMP and publication of the guideline |

# 6. Resource requirements for preparation

The development of the new guideline will involve the IWP (including a drafting group composed of rapporteur, co-rapporteur and 3 IWP members).

The IWP drafting group will meet virtually as required (e.g. 2-3 virtual meetings). Discussion is foreseen in at least 2 IWP plenary meetings.

# 7. Impact assessment (anticipated)

The guideline will clarify requirements for regulators and pharmaceutical industry with respect to the quality aspects of mRNA containing vaccines and consider the concepts of recent developments in the field of mRNA vaccines for human use.

Overall, it is anticipated that the guideline will have a positive impact on the development of veterinary vaccines based on mRNA and is expected to facilitate the submission and authorisation of veterinary vaccines. The guideline can contribute to increased availability of veterinary vaccines and thereby benefit public and animal health.

# 8. Interested parties

Veterinary pharmaceutical industry, veterinary consultants, EU regulatory authorities involved in assessment of marketing authorisation applications.

# 9. References to literature, guidelines, etc.

Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products

Evaluation of the quality, safety and efficacy of messenger RNA vaccines for the prevention of infectious diseases: regulatory considerations, WHO/RNA/DRAFT/22 DECEMBER 2020

Concept Paper on the development of a Guideline on the quality aspects of mRNA vaccines (EMA/CHMP/ BWP/211968/2023)

Relevant Ph. Eur. monographs and chapters