EuFMD FMD Vaccine Prequalification Public Summary Report

Endorsed by the Standing Committee for Prequalification of FAST vaccines (SCPQv)

Name of Foot and Mouth Disease Vaccine

[Enter FMD vaccine tradename]

Manufacturer

[Manufacturer/Applicant]

Prequalification number

[PQv unique application number]

Date added to the list of prequalified FMD vaccines (PQv list):

[Date vaccine PQv Listed]

The Public Summary Report (PSR) is a modified version of the full Evaluation Report (ER) considered by the SCPQv with all information of a commercially confidential nature removed.

Background and basis for prequalification listing

This public summary report for [**FMD vaccine tradename]**, manufactured by [**Manufacturer]** has been produced following evaluation of an application for prequalification in line with the 'Administrative Procedure for Applications for Prequalification (PQv) of Foot-and-Mouth Disease Vaccines'. The technical requirements applied are those described in 'Technical Guidance for Application for Prequalification of Foot-and-Mouth Disease Vaccines and Content of the Prequalification Evidence File' with the aim of assuring compliance with at least minimum international standards i.e., the standards defined in the general and specific chapters of the latest version of the Manual of Diagnostic Tests and Vaccines for Terrestrial Animals of the World Organization for Animal Health (the' WOAH Terrestrial Manual').

The Public Summary Report (PSR) is a modified version of the full Evaluation Report (ER) considered by the Standing Committee on Prequalification of Vaccines against FAST diseases (SCPQv) with all information of a commercially confidential nature removed. Further information on the role of the SCPQv in the governance and decision process for the prequalification of FMD vaccines can be found at: https://www.fao.org/eufmd/who-we-are/structure/scpqv.

PQv uses a risk-based approach to focus the data requirements on critical elements of FMD vaccine manufacture and testing supported by evidence that the vaccine holds a full marketing authorization (MA)/product registration issued by a National Regulatory Authority. PQv does not attempt to repeat the evaluation performed by the national regulatory authority(ies) specified in Annex 1 for the purposes of marketing authorization but uses the outcome from the national evaluation procedure(s) as part of the evidence for qualification assurance together with additional information on key properties of the vaccine and its manufacture.

PQv provides an independent and internationally recognized source of information on FAST vaccines that can be used by EuFMD member nations and other parties seeking to control FAST diseases through vaccination. Further details of the PQv scheme can be found at https://www.fao.org/eufmd/global-situation/vaccine-prequalification/key-principles/ or by contacting EuFMD at EuFMD-PQv@fao.org.

Introduction

On **DD/MM/YYYY**, the applicant [**Manufacturer/Applicant]** submitted an application for prequalification for [**FMD vaccine tradename]**.

The Prequalification Evidence File (PEF) was submitted in line with the requirements of the 'Technical Guidance for Application for Prequalification of Foot-and-Mouth Disease Vaccines and Content of the Prequalification Evidence File'.

The Standing Committee for Prequalification of FAST vaccines (SCPQv) endorsed the vaccine for PQv Listing at its meeting on **DD/MM/YYYY**.

The vaccine is indicated for **[Target Species] against FMD serotypes [list serotypes].**

The route of administration is **[intramuscular** and/or **subcutaneous].**

The vaccine is an **[emulsion/double oil emulsion/aqueous vaccine adjuvanted with aluminum hydroxide/saponin].**

The primary vaccination schedule is **[one dose,** or **two doses** separated by an interval of **x weeks]**.

A booster dose is recommended every **[x months/week].**

The vaccine is manufactured by **[Manufacturer]** to the principles of Good Manufacturing Practice (GMP) as certified by the national regulatory authority for GMP **[name of NRA responsible for GMP compliance for manufacture].**

The manufacturing site meets the relevant standards of biosafety and biosecurity preventing release of pathogens from sites of manufacture into the environment as certified by the national regulatory authority for biosafety/biosecurity **[name of NRA responsible for biosafety/biosecurity]**.

Antigen production, QC testing, formulation, filling and packaging takes place at:

Address of manufacturing site(s):

Annex 1. Summary of evidence provided to support PQv Listing for XXXX

Definitions:

Qualification Assurance	Prequalification of vaccines by EuFMD is based on the principle of 'Qualification Assurance'. Qualification of vaccines is performed national competent authorities through granting a national marketing authorization (also termed product license or registration in some areas) based on a comprehensive evaluation of evidence demonstrating the pharmaceutical quality, safety and efficacy of the product in line with respective national legislation. Only vaccines for which a national marketing authorization has been issued by at least one national competent authority are eligible for PQv. PQv does not attempt to repeat the evaluation carried out NRA but relies on a risk-based evaluation of evidence provided by the applicant in the prequalification evidence file (PEF) to demonstrate that the vaccine meets at least the minimum standards in the WOAH Terrestrial Manual with respect to the key properties of the vaccine that are essential for its safe and effective use. The outcome of prequalification is an assessment of the level of assurance that can be placed on the qualification that exists for the vaccine. The level of assurance is rated from 'Full', through 'Partial' to 'Incomplete' to recognize that the level of assurance depends on the amount and quality of data provided. In the case of vaccines rated 'Partial' or 'Incomplete', the outcome of PQv does not call into question the evaluation performed by a national competent authority in qualifying the vaccine but only reflects that data has not been provided to EuFMD to demonstrate compliance with the minimum standards of the WOAH Manual. The PQv Technical Guidelines clarifies the interpretation of the standards defined in the WOAH Manual that will be applied by the Standing Committee on Prequalification of Vaccines Qv in order to provide certainty to applicants in situations where the Manual is open to interpretation.

Full Assurance	Prequalification evidence provided full assurance that the product meets at least the minimum international standards of the WOAH Terrestrial Manual as further elaborated in the PQv Technical Guideline
Partial Assurance	Some prequalification evidence was provided to assure that the product meets at least the minimum international standards of the WOAH Terrestrial manual, but the evidence was not sufficient to provide full assurance as elaborated in the PQv Technical Guideline. An explanation of the basis for the assignment of this category will be included in the summary of evidence.
Incomplete Assurance	Insufficient prequalification evidence was provided to assurance that the product meets at least the minimum international standards of WOAH Terrestrial manual as further elaborated in the PQv Technical Guideline. An explanation of the basis for the assignment of this category will be included in the summary of evidence.
N/A	Not applicable.
Additional information	Additional information is provided in this report where evidence is provided to demonstrate that the standards of manufacture and/or testing meet another internationally recognized standard, for example PIC/S or VICH, or that the evidence provided goes beyond the minimum international standards of WOAH Terrestrial manual.

Country/region where Marketing Authorisation/ Product Registration held	Marketing Authorisation/Product Registration Reference number & Date issued	PQv standard
e.g., France	*e.g., FR/V/123456/2023 01/03/2010*	*Fully assured*
e.g., *Australia*	*e.g., 91351/131935 30/06/2022*	*Fully assured*

PEF Heading/ Section		Prequalification evidence to support PQv listing	PQv standard
1.A	Site Master File (SMF) and evidence of GMP.	*e.g., A valid GMP certificate issued within last three years was provided for the manufacturing site.* *e.g., A Manufacturing Authorization and Site Master File were provided demonstrating compliance with appropriate standards of GMP.* *e.g., A valid GMP certificate issued within last three years was provided for the manufacturing site to the standards of PIC/S (Pharmaceutical Inspections Convention Pharmaceutical Inspection Co-operation Scheme).*	*Fully assured* *Fully assured* *Fully assured with additional information on standard of GMP*
	NRA for GMP	*France* *Agency for Food, Environmental & Occupational Health Safety*	*Fully Assured* *PIC/S*

		Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES) *14 rue Claude Bourgelat* *PA de la Grande Marche - Javené - CS 70611* *FR - 35306 FOUGERES Cedex*	
1.A.1	Biosafety & Biosecurity.	*e.g., Regular inspections are conducted by the national regulatory agency to ensure appropriate standards of biosafety & biosecurity at the site(s) of manufacture.*	*Fully assured*
	NRA for Biosafety & Biosecurity	*HSE UK* *licence is granted by the Health and Safety Executive of Redgrave Court, Merton Road, Bootle, L20 7HS, United Kingdom ("the licensing authority") under Article 4(1) of The Specified Animal Pathogens Order ("SAPO") and authorises the licence holder to have in their possession the specified animal pathogen foot-and-mouth disease virus.*	
1.B	Summary Product Characteristics (SPC).	*e.g., An SPC for the product was provided.* *e.g., Not applicable. An SPC for the NRA is not required.*	*Fully assured* *N/A*
1.C	Labelling and package insert.	*e.g., Copies of the vaccine label and package insert provided.* *e.g., A copy of the vaccine label provided. No package insert required by NRA.*	*Fully assured* *Partially assured*
1.D.	Lot summary protocol.	*e.g., A final batch protocol representative of a batch of vaccine*	*Fully assured*

		released for supply provided. *e.g., A final lot summary provided representative of a batch of vaccine released for supply provided.*	*Fully assured.*
Chapter 2	Manufacture & Control		
2.A	Composition.	*e.g., A Table of the qualitative and quantitative composition of the vaccine with details of the antigen content, adjuvants, excipients and any preservative, expressed as per dose or per ml provided.* *e.g., A Table containing the qualitative details with only the potency expressed for the FMD antigen content of each batch of vaccine*	*Fully assured* *Partially assured*
2.B	Assuredhod of Manufacture		
2.B.1	Description of manufacturing process.	*e.g., Flow chart indicating the steps of manufacture from the Master Seed Virus (MSV) through to the finished product including the in process (IP) and final product (FP) Quality Control (QC) tests provided.* *Test results for three consecutive batches/serials/lots as approved in the MA/product registration or for routine release provided.* *e.g., A brief description of the manufacturing method included.*	*Fully assured* *Partially assured*

		Test results provided from three non-consecutive batches	
2.B.1.a	Validation of the inactivation process.	*e.g., The cultured FMD virus is clarified by an appropriate method and the viral harvest inactivated by the addition of binary ethyleneimine (BEI). After adding the inactivant the batch/lot of virus is transferred to second sterile vessel where inactivation is completed.* *The inactivation kinetics is validated for the time period for chemical treatment and temperature at pilot and industrial scale with the manufacturing equipment used for routine production.* *The inactivation procedure was shown to be satisfactory with a decrease in virus titer, when plotted logarithmically, that was linear, and extrapolation indicated that there is less than 1 infectious virus unit per 10,000 L of liquid preparation at the end of inactivation.* *During the inactivation of each manufactured batch, the virus titer is monitored by a sensitive and reproducible technique using a sensitive cell line to monitor the inactivation kinetics.* *After inactivation any residual BEI in the harvest is neutralized by adding excess sodium thiosulphate to a final concentration of 2% in the antigen batch.*	*Fully assured*

		e.g., The cultured FMD virus is clarified by an appropriate method and the viral harvest inactivated by the addition of binary ethyleneimine (BEI). After adding the inactivant the batch/lot of virus is transferred to second sterile vessel where inactivation is completed. *The inactivation kinetics is validated for the time period for chemical treatment and temperature at industrial scale with the manufacturing equipment used for routine production.* *The inactivation procedure was shown to be satisfactory with a decrease in virus titer, when plotted logarithmically, that was linear, and extrapolation indicated that there is less than 1 infectious virus unit per 10,000 L of liquid preparation at the end of inactivation.* *During the production of each manufactured batch an inactivation test is conducted to confirm the absence of any residual live virus.* *After inactivation any residual BEI in the harvest is not neutralized but the downstream process has been validated to demonstrate removal of the inactivant.*	
2.B.2	Detailed flowcharts.	*Provided in 2.B.1*	

2.C	Production and Control of Starting Materials		
2.C.1	Starting materials of biological origin		
2.C.1.1	Virus Seed.	*e.g., For each virus strain(s) that may be/is included in the vaccine, the source of the isolate has been recorded including details of the country of origin, species, and date of isolation, type of material from which virus was isolated.* *The in vitro passage history of each vaccine strain has been recorded, including details of the ingredients used and any adaptation to growth on a cell line.* *Details of the preparation and passage of the Master Seed Virus (MSV) and Working Seed Virus (WSV) and storage conditions provided (–40°C, –70°C or freeze-dried) were provided as evidence.* *Tests results for the MSV and WSV (Identity, titration, absence of bacteria and fungi (sterility test), absence of mycoplasmas and absence of extraneous agents) were provided as evidence.* *Details on the measures taken to minimize the risk of Transmissible spongiform encephalopathies provided.*	Fully assured

		e.g., additional information that may be included *For each vaccine strain, the genotyping of the VP1 region of the viral capsid has been undertaken.* *The FMD type O India vaccine strain was shown to belong to the FMD type O ME-SA/Ind-2001e sublineage.* *The FMD type O Panasia vaccine strain was shown to belong to the* O/MESA/PanAsia-2^{ANT-10} lineage. *The FMD type A SEA vaccine strain was shown to belong to the ASIA/Sea-97 lineage.* *The FMD Type A Africa vaccine strain was shown to belong to the AFRICA/G-IV lineage.* *The FMD SAT 2 vaccine strain was shown to belong to the SAT 2 topotype II*	Additional information on vaccine strain(s)
2.D	In-Process Controls		
2.D	In-Process controls.	*e.g.,* ***Inactivation kinetics.*** *The decrease in virus titre, plotted logarithmically, is linear and extrapolation indicates that there is less than 1 infectious virus unit per 10,000 L of liquid preparation at the end of inactivation. The Inactivation test method using*	Fully assured

		virus titre is sensitive and reproducible. *e.g., Inactivation control (innocuity test/absence of residual live virus)* *An antigen sample representing at least 200 doses of vaccine shown to be free of infectious virus by inoculation of sensitive cell culture monolayers.* *e.g.,* ***Residues of inactivating agents.*** *neutralisation of BEI by adding excess sodium thiosulphate solution to a final concentration of 2%.* *Validation of the elimination of BEI through the downstream production process so not test required.* *e.g.,* ***FMDV antigen mass (146S) content*** *The 146S antigen content of each batch of bulk inactivated antigen is determined using an in vitro method, for example, by sucrose density gradient centrifugation and ultraviolet spectrophotometry at 259 nm, HPLC-SEC, 146S specific ELISA or other validated method).* *The specification set for release is such that a batch of final vaccine produced according to the authorised manufacturing process contains at least the minimum amount antigen per dose throughout the entire authorised*	Fully assured Fully assured Fully assured Fully assured

		shelf life that that was used to establish the efficacy of the vaccine.	
2.E	Controls on Finished Product		
2.E.1	General characteristics of the finished product.	*e.g., A list of all tests performed, and the release specifications provided*	Fully assured
2.E.2	Identification of active substance(s).	*e.g., A Brief description of the final product identity test performed on each batch of manufactured vaccine was provided.* *Validation reports for the identity of each vaccine strain/serotype provided.* *Presence of the relevant FMD vaccine strains in the bulk or final filled vaccine, and evidence no other serotype could be present in the vaccine demonstrated.*	Fully assured
2.E.3	Batch Potency.	*e.g., Description of the final product batch potency test and validation reports for the potency test that established the specifications for release for each vaccine strain provided.* ***And** Evidence of least one PD_{50} (50 per cent cattle protective doses) challenge test per vaccine strain to establish efficacy in cattle, and demonstrating the vaccine contains at least 3 PD_{50}.* **Or** *Evidence of at least one PGP test (percent protection against*	Fully assured

		generalized foot infection) per vaccine strain to establish efficacy in cattle, and demonstrating the vaccine protects at least 12 out of 16 vaccinated animals that correlates with $3PD_{50}$.	
2.E.6	Safety Tests.	*e.g., Routine batch safety tests not required for PQv. However, the manufacturer is required to conduct target animal batch safety tests in cattle and laboratory animals.*	Additional information
2.F	Batch consistency		
2.F	Batch consistency – Process validation.	*e.g., Batch protocol/Lot summary for three consecutive batches outlining all the production steps, specifications and results for all tests performed during the production process and on the finished product provided and show consistency of manufacture.* *e.g., Batch protocols/lot summaries provided for three non-consecutive batches.*	*Fully assured* *Partially assured*
2.G	Stability		
2.G	Stability.	*e.g., Stability of 3 consecutive batches tested for each container size every 3 months over the claimed shelf life provided and shown to be 24 months.* *e.g., Stability of 3 batches tested regularly over the claimed shelf life provided and shown to be 24 months.*	Fully assured Partially assured

Safety & Efficacy data requirements for the PEF

PEF Heading/ Section		Prequalification evidence to support PQv listing	PQv standards
Chapter 3	Safety & efficacy section – Use in target species		
3.B	Safety Requirements		
3.B.1	Laboratory studies.	*e.g., A summary of the laboratory safety studies in cattle, sheep, goats, pigs & buffalo provided. The safety studies were conducted to the standards of International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) and were in accordance with the principles of Good Laboratory Practice (GLP). VICH safety studies were conducted with a single/double dose and repeat dose.* *The safety studies were performed with vaccines formulated to contain the maximum permitted payload and number of antigens.* *The safety warnings on the SPC/label/package insert reflect the local and systemic reactions observed in the safety studies.* *A warning has been included in the SPC/label/package insert*	Fully assured. Safety studies assured VICH & GLP standards

		that no safety data are available to demonstrate the impact of vaccination on pregnancy/lactation. *No specific studied have been conducted to investigate the interactions with other veterinary medicinal products given at the same time as the vaccine but an appropriate warning has bene included on the SPC/label/package insert.* *e.g., A summary of the laboratory safety studies in cattle and pigs provided. Safety studies were performed with representative vaccine batches administered as a single dose.* *For the other target species on the label, sheep, goats & buffalo field studies demonstrated the safety of the vaccine. There is no warning regarding administration to pregnant/lactating animals but no laboratory safety data in these categories has been provided. However, field usage indicates that the vaccine is safe in these categories.*	Partially assured
3.C	Efficacy requirements (including DIVA claims)		
3.C.1	Laboratory studies.	*e.g., The efficacy of each vaccine strain was demonstrated for cattle using the potency challenge-test. One PD50 (50 per cent cattle protective doses) challenge test was performed using each vaccine strain to establish efficacy in cattle, and demonstrating the vaccine contains at least 3*	Fully assured/Partially assured

		PD50. *The onset of immunity was established using the PD50/PGP potency challenge test at 21 days in cattle of at least 6 months of age that received a single dose of vaccine.* *Additional laboratory studies have been conducted in calves from 4 weeks of age free of FMD antibodies at the time of vaccination. A two-dose primary vaccination schedule provided protection as determined by serology within 10 days of vaccination.* *The duration of immunity was demonstrated by serology. Cattle receiving a primary vaccination. Antibody titers of a representative strain of each of the serotypes were shown to persist for at least 6 months at titers equivalent to those measured at the time of challenge in the PD50/PGP studies.* ***Additional Information*** ***Fitness for purpose study*** *A vaccination-challenge study was performed by using two emergency FMDV vaccines with A22 Iraq 64 (A22 IRQ) and A Malaysia 97 (A MAY 97) strains, against challenge with a variant strain of FMDV A/Asia/G-IX/SEA-97 lineage at 7- and*	Additional information provided on cross-protection against FMDV A/Asia/G-

		21-day post-vaccination (dpv). Vaccines were formulated at >6PD50/per dose. Five calves were protected despite relatively low heterologous neutralizing antibody titers to the challenge virus at the time of challenge.	IX/SEA-97 lineage
3.C.2	Field studies.	*e.g., Field safety and efficacy studies has been performed in cattle, pigs and sheep. Representative commercial batches were use*d	Fully assured
3.D	Assessment reports.		
3.E.2	Post-marketing pharmacovigilance.	*e.g., Periodic safety update reports (PSUR) provided for the past three years 2020-2023. The reports are consistent with the potential adverse reactions on the SPC.*	Full assured

Production & Distribution data requirements for the PEF

Chapter 4	Production and distribution data	Prequalification evidence to support PQV listing	PQv standards
4.1	Provide information on the quantity of finished product distributed domestically and exported in the previous 3 years.	*e.g., Information on batches of FMD vaccine suppled as finished product both domestically and internationally provided for the years 2019-2022.*	Fully assured
4.2	Provide a list of countries where the product is licensed (marketing authorization) and supplied.	*e.g., List of countries where product is authorized/registered provided.*	Fully assured

Update on regulatory actions data requirements for the PEF

Chapter 5	Update on regulatory actions	Prequalification evidence to support PQV listing	PQv standards
5.1	Provide information on post-authorization regulatory actions.	*e.g., The manufacturer confirmed that no regulatory actions had been taken by any NRA where the product is authorized/registered.*	Fully assured
5.2	Provide a list of lots rejected by the NRA, if applicable.	*e.g., The manufacturer confirmed that no final FMD vaccine batch/lots had been rejected by a supervisory authority for release of the product.*	Fully assured
5.3	Describe restrictions on distribution or recalls, including manufacturer-initiated recalls.	*e.g., Information provided on one recall initiated by the manufacturer due to a labelling error.*	Fully assured
5.4	Name clinical trial suspensions, including manufacturer-initiated suspensions	*e.g., The manufacturer confirmed that there have been no clinical trial suspensions, including manufacturer-initiated suspensions.*	Fully assured
5.5	Describe dosage or schedule modifications since the initial marketing authorization/product was granted.	*e.g., Since the first authorization the booster interval in sheep and cattle has been extended from 6 months to 12 months.*	Fully assured
5.6	Provide information on changes in target populations or indications since the initial marketing authorization/product was granted.	*e.g., Since the first authorization, an additional target species, goats has been added to the authorization/registration with the claim for a reduction of clinical signs of FMD.*	Fully assured
5.7	List the GMP and/or	*e.g., The manufacturer provided a list of*	Fully assured

	Biosafety/Biosecurity inspections conducted by NRAs within the previous 3 years, including the scope of each inspection.	*Biosafety/Biosecurity inspections conducted by NRAs within the previous 3 years, including the scope of each inspection.*	
5.8	List inspections conducted by foreign GMP and/or Biosafety/Biosecurity authorities within the previous 3 years, including the scope of each inspection	*e.g., The manufacturer provided a list of inspections conducted by foreign GMP and/or Biosafety/Biosecurity authorities within the previous 3 years, including the scope of each inspection*	Fully assured

Provision of sera from batch release potency tests data requirements for the PEF

6.	Provision of sera from batch release potency tests	Prequalification evidence to support PQV listing	PQv standards
	Manufacturers with PQv listed FMD vaccines should commit to provide sera from batch release potency tests to independent laboratories once the terms for supply and testing have been agreed with stakeholders and published on the PQv website.	*A commitment to provide sera from batch potency tests was provided*	Fully assured