

Servicio Nacional de Sanidad y Calidad Agroalimentaria

SENASA

National Service for Agrifood Health and Quality



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Assuring the Potency, Purity and Quality of Foot and Mouth Disease Vaccines

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FMD VACCINES

- ❑ As tool of control programs in countries that apply vaccination
- ❑ As vaccine bank in countries/ zones recognized as “free without vaccination”: higher potency vaccines for emergency use
- ❑ Safety, potency and purity required
- ❑ Vaccine strains up date: monitoring of field virus - vaccine matching





Requirements for FMD Vaccines

Criteria for FMD vaccines quality control in South America includes the Official Veterinary Services approval of:

- Facilities
- Licensing of the product
- Batch to batch quality control



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Requirements for FMD Vaccines

FMD vaccine manufacturers shall comply:

- GMP certification
- OIE Guidelines on Vaccine Production
- OIE requirements for Biosafety: containment group 4



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Requirements for FMD Vaccines

Raw materials controls

- Absence of adventitious agents in master seed virus and master cell stock
- Sera, and other raw materials of animal origin used in the process, should be free of adventitious agents and originated in countries with negligible risk of TSEs



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FMD VACCINE QUALITY CONTROL

- Innocuity (residual live virus)**
- Potency/Efficacy**
- Purity (induction of NSP antibodies)**
- Safety (tolerance)**



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FMD VACCINES: INNOCUITY CONTROL

- Inactivant BEI (ethyleneimine)
- Manufacturers should perform the kinetics of each inactivation process
- Validation of cell cultures sensitivity
- Official control is performed in the final product



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FMD VACCINE POTENCY

- ❑ Direct methods: Protective Dose (PD50) and PGP test (Percentage of Protection against Generalised foot infection)
- ❑ Indirect methods: level of antibodies post vaccination.

Statistical validated correlation with direct methods PD50 or PGP

Liquid-Phase ELISA used in South America



FMD Vaccine Potency Test Argentina

For registration	PGP: Challenge at 90 dpv Protection $\geq 75\%$ LP-ELISA at 60 dpv EPP $\geq 75\%$
For batch control	LP-ELISA at 60 dpv EPP: $\geq 75\%$



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CORRELATION PGP and LP-ELISA

- Data of challenged bovines at 90 days post vaccination**
- Correlation with data of LP ELISA at 60 days post vaccination**
- Expected Percentage of Protection (EPP) derived from correlation data**

O1 Campos

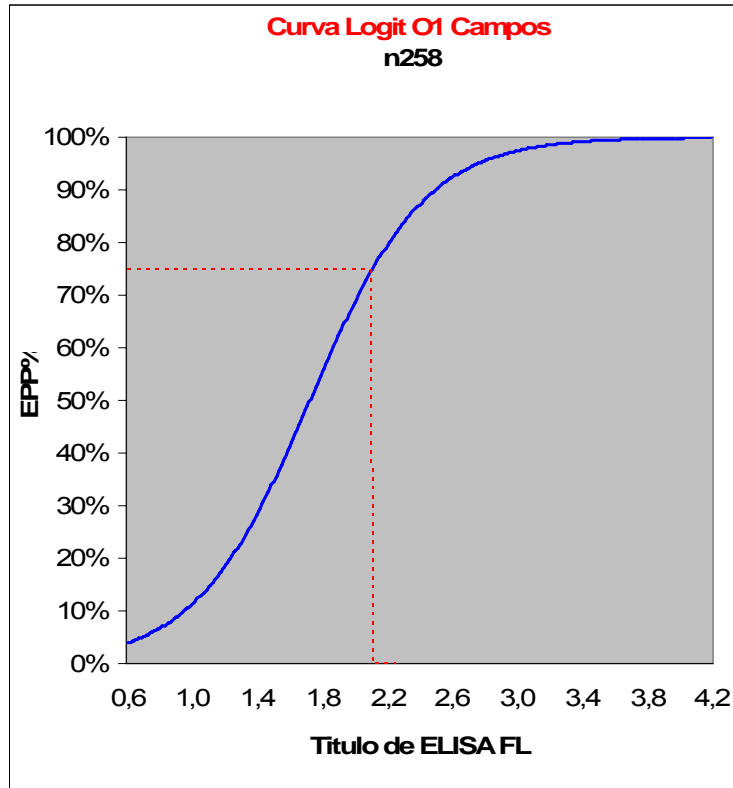


TABLA O1 CAMPOS

Titulos ELISA FL	EPP	Titulos ELISA FL	EPP	Titulos ELISA FL	EPP	Titulos ELISA FL	EPP	Titulos ELISA FL	EPP	Titulos ELISA FL	EPP
0.60	3.9%	1.20	18.3%	1.80	55.3%	2.40	87.2%	3.00	97.4%	3.60	99.5%
0.61	4.0%	1.21	18.8%	1.81	56.0%	2.41	87.6%	3.01	97.5%	3.61	99.5%
0.62	4.1%	1.22	19.2%	1.82	56.7%	2.42	87.9%	3.02	97.6%	3.62	99.5%
0.63	4.2%	1.23	19.6%	1.83	57.4%	2.43	88.2%	3.03	97.6%	3.63	99.6%
0.64	4.4%	1.24	20.1%	1.84	58.1%	2.44	88.5%	3.04	97.7%	3.64	99.6%
0.65	4.5%	1.25	20.6%	1.85	58.8%	2.45	88.7%	3.05	97.8%	3.65	99.6%
0.66	4.6%	1.26	21.0%	1.86	59.5%	2.46	89.0%	3.06	97.8%	3.66	99.6%
0.67	4.7%	1.27	21.5%	1.87	60.2%	2.47	89.3%	3.07	97.9%	3.67	99.6%
0.68	4.9%	1.28	22.0%	1.88	60.9%	2.48	89.6%	3.08	97.9%	3.68	99.6%
0.69	5.0%	1.29	22.5%	1.89	61.5%	2.49	89.8%	3.09	98.0%	3.69	99.6%
0.70	5.1%	1.30	23.0%	1.90	62.2%	2.50	90.1%	3.10	98.0%	3.70	99.6%
0.71	5.3%	1.31	23.5%	1.91	62.9%	2.51	90.3%	3.11	98.1%	3.71	99.7%
0.72	5.4%	1.32	24.0%	1.92	63.5%	2.52	90.6%	3.12	98.2%	3.72	99.7%
0.73	5.6%	1.33	24.5%	1.93	64.2%	2.53	90.8%	3.13	98.2%	3.73	99.7%
0.74	5.7%	1.34	25.1%	1.94	64.9%	2.54	91.1%	3.14	98.3%	3.74	99.7%
0.75	5.9%	1.35	25.6%	1.95	65.5%	2.55	91.3%	3.15	98.3%	3.75	99.7%
0.76	6.0%	1.36	26.1%	1.96	66.1%	2.56	91.5%	3.16	98.3%	3.76	99.7%
0.77	6.2%	1.37	26.7%	1.97	66.8%	2.57	91.7%	3.17	98.4%	3.77	99.7%
0.78	6.4%	1.38	27.3%	1.98	67.4%	2.58	91.9%	3.18	98.4%	3.78	99.7%
0.79	6.5%	1.39	27.8%	1.99	68.0%	2.59	92.2%	3.19	98.5%	3.79	99.7%
0.80	6.7%	1.40	28.4%	2.00	68.6%	2.60	92.4%	3.20	98.5%	3.80	99.7%
0.81	6.9%	1.41	29.0%	2.01	69.3%	2.61	92.6%	3.21	98.6%	3.81	99.7%
0.82	7.1%	1.42	29.6%	2.02	69.9%	2.62	92.8%	3.22	98.6%	3.82	99.7%
0.83	7.3%	1.43	30.2%	2.03	70.5%	2.63	92.9%	3.23	98.6%	3.83	99.8%
0.84	7.5%	1.44	30.8%	2.04	71.0%	2.64	93.1%	3.24	98.7%	3.84	99.8%
0.85	7.7%	1.45	31.4%	2.05	71.6%	2.65	93.3%	3.25	98.7%	3.85	99.8%
0.86	7.9%	1.46	32.0%	2.06	72.2%	2.66	93.5%	3.26	98.8%	3.86	99.8%
0.87	8.1%	1.47	32.6%	2.07	72.8%	2.67	93.7%	3.27	98.8%	3.87	99.8%
0.88	8.3%	1.48	33.2%	2.08	73.3%	2.68	93.8%	3.28	98.8%	3.88	99.8%
0.89	8.5%	1.49	33.9%	2.09	73.9%	2.69	94.0%	3.29	98.9%	3.89	99.8%
0.90	8.7%	1.50	34.5%	2.10	74.4%	2.70	94.1%	3.30	98.9%	3.90	99.8%
0.91	8.9%	1.51	35.2%	2.11	75.0%	2.71	94.3%	3.31	98.9%	3.91	99.8%
0.92	9.2%	1.52	35.8%	2.12	75.5%	2.72	94.4%	3.32	98.9%	3.92	99.8%
0.93	9.4%	1.53	36.5%	2.13	76.0%	2.73	94.6%	3.33	99.0%	3.93	99.8%
0.94	9.7%	1.54	37.1%	2.14	76.5%	2.74	94.7%	3.34	99.0%	3.94	99.8%
0.95	9.9%	1.55	37.8%	2.15	77.0%	2.75	94.9%	3.35	99.0%	3.95	99.8%
0.96	10.2%	1.56	38.5%	2.16	77.5%	2.76	95.0%	3.36	99.1%	3.96	99.8%
0.97	10.4%	1.57	39.2%	2.17	78.0%	2.77	95.1%	3.37	99.1%	3.97	99.8%
0.98	10.7%	1.58	39.8%	2.18	78.5%	2.78	95.3%	3.38	99.1%	3.98	99.8%
0.99	11.0%	1.59	40.5%	2.19	79.0%	2.79	95.4%	3.39	99.1%	3.99	99.8%
1.00	11.3%	1.60	41.2%	2.20	79.5%	2.80	95.5%	3.40	99.2%	4.00	99.8%
1.01	11.6%	1.61	41.9%	2.21	79.9%	2.81	95.6%	3.41	99.2%	4.01	99.9%
1.02	11.8%	1.62	42.6%	2.22	80.4%	2.82	95.8%	3.42	99.2%	4.02	99.9%
1.03	12.2%	1.63	43.3%	2.23	80.8%	2.83	95.9%	3.43	99.2%	4.03	99.9%
1.04	12.5%	1.64	44.0%	2.24	81.3%	2.84	96.0%	3.44	99.2%	4.04	99.9%
1.05	12.8%	1.65	44.7%	2.25	81.7%	2.85	96.1%	3.45	99.3%	4.05	99.9%
1.06	13.1%	1.66	45.4%	2.26	82.1%	2.86	96.2%	3.46	99.3%	4.06	99.9%
1.07	13.4%	1.67	46.1%	2.27	82.5%	2.87	96.3%	3.47	99.3%	4.07	99.9%
1.08	13.8%	1.68	46.8%	2.28	82.9%	2.88	96.4%	3.48	99.3%	4.08	99.9%
1.09	14.1%	1.69	47.5%	2.29	83.3%	2.89	96.5%	3.49	99.3%	4.09	99.9%
1.10	14.4%	1.70	48.2%	2.30	83.7%	2.90	96.6%	3.50	99.4%	4.10	99.9%
1.11	14.8%	1.71	48.9%	2.31	84.1%	2.91	96.7%	3.51	99.4%	4.11	99.9%
1.12	15.2%	1.72	49.7%	2.32	84.5%	2.92	96.8%	3.52	99.4%	4.12	99.9%
1.13	15.5%	1.73	50.4%	2.33	84.9%	2.93	96.9%	3.53	99.4%	4.13	99.9%
1.14	15.9%	1.74	51.1%	2.34	85.2%	2.94	97.0%	3.54	99.4%	4.14	99.9%
1.15	16.3%	1.75	51.8%	2.35	85.6%	2.95	97.0%	3.55	99.4%	4.15	99.9%
1.16	16.7%	1.76	52.5%	2.36	85.9%	2.96	97.1%	3.56	99.5%	4.16	99.9%
1.17	17.1%	1.77	53.2%	2.37	86.3%	2.97	97.2%	3.57	99.5%	4.17	99.9%
1.18	17.5%	1.78	53.9%	2.38	86.6%	2.98	97.3%	3.58	99.5%	4.18	99.9%
1.19	17.9%	1.79	54.6%	2.39	86.9%	2.99	97.3%	3.59	99.5%	4.19	99.9%
										4.20	99.91%



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Duration of Immunity and Stability studies

- ❑ Vaccine manufacturers has to demonstrate the duration of immunity for the specific formulation, in target species
- ❑ The stability of vaccines should be demonstrated as part of the shelf - life determination study for registration of the product



FMD VACCINE PURITY CONTROL

The term vaccine purity is related to the lack of immunogenicity against non structural proteins induced by FMD vaccines.

Requirements for Vaccine Licensing

0 days	60 days post vac	90 days post vac
Vaccination 16 cattle	Revaccination 16 cattle NSP Ab evaluation	NSP Ab evaluation

For batch control: evaluation of NSP antibodies is done in vaccinated animals used in the potency test



FMD VACCINES APPLIED IN SOUTH AMERICA

❑ Vaccine Strains:

Argentina

O1 Campos
A24 Cruzeiro
A Arg 2001
C3 Indaial

Bol- Brazil-Par

O1 Campos
A24 Cruzeiro
C 3 Indaial

Ecu-Col-Per-Uru-Ven

O1 Campos
A24 Cruzeiro

❑ Inactivation: BEI

❑ Oil vaccine

❑ Single emulsion

❑ Dose: 2, 3, 5 ml.

❑ Route of administration: I.M./ S.C.





FMD VACCINES APPLIED IN SOUTH AMERICA

FMD Vaccine Producers in South America

- Argentina (4)
- Brazil (4)
- Colombia (3)
- Paraguay (2)
- Venezuela (2)

Production in private laboratories

All batches controlled by Official laboratories

Doses produced/ year: 550 – 600 millions



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Harmonization of FMD Vaccines Official Quality Control in South America

Regulations/ Tests / Exigencies

- OIE FMD Reference Laboratories in S.A.
PANAFTOSA and SENASA - Argentina
- Twinning Projects
- PAMA Project – CVP
- Multilateral harmonization meetings



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