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Risk of withdrawal of foot-and-mouth disease vaccine in Mato Grosso do Sul and consequent loss of herd immunity for reintroduction of foot-and-mouth disease virus in the State

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***Abstract*—** *The state of Mato Grosso do Sul - MS, has one of the largest cattle herds in the country, and the state is known nationally for the quality of bovine genetics, because the productive system is highly technical, where it seeks the precocity and high quality of pastures provided to animals. Because it is an organized productive sector, it has the longing to have its bovine herd free of foot-and-mouth disease without vaccination, which is already occurring in several states of the federation. However, a long way is already being traveled in order for this dream to come true for the entire beef chain of the state. In view of this situation, the objective of this study is to conduct a study on the sanitary measures adopted, with the objective of removing the vaccine against aphthous from the cattle herd of the state of Mato Grosso do Sul and possible impacts. For this, the State Agency for Animal and Plant Sanitary Defense - IAGRO has not measured efforts with its entire technical team to achieve this goal. With this, it has enhanced its actions in traffic control, in the technical training of its employees, in health education activities, successes in the coverage of all its vaccination campaigns against foot-and-mouth disease and in the results of serological surveys, restructuring of the defense service, as well as*

animal health legislation and active surveillance for the early detection of foot-and-mouth disease virus infection. In addition, it is worth mentioning that IAGRO has been available to comply with all the determinations established by the Ministry of Livestock Agriculture and Supply - MAPA, so that the status of an area free of foot-and-mouth disease without vaccination can be implemented in the state of Mato Grosso do Sul, which validates the work of this agency before MAPA and meet the demand of the productive sector of the state that yearlike this election.

I. INTRODUCTION

Restrictions on trade in animal products and by-products used by some countries is based on the health status of the exporting country, status of foot-and-mouth disease free with vaccination is vetoed by countries that pay better for meat, and by important countries both by high consumption power, as well as by purchasing power, such as countries in Europe, Japan, Canada and the USA , countries that have long eradicated foot-and-mouth disease.

Based on the opening of new markets, the private sector makes a great strength with the agencies responsible for the Brazilian States to advance in the conquest of a new health status, so that they can drain their production to new countries and with greater added value.

By the end of the 2011-2020 Action Plan, the territory of South America with official recognition of foot-and-mouth disease-free status had increased from 67.6% in 2010 to 94.7% at the end of 2019. The herds free of foot-and-mouth disease, which at the beginning of the current action plan represented 63.7%, increased to 97.4%, and the population of free cattle and buffaloes went from 84.4% to 95.4%. Approximately 5% of the territory, herds and bovine population of South America, remains without health recognition at the end of 2020, and comprises the entire territory of Venezuela, which constitutes a significant achievement of national programs and the PHEFA Action Plan 2011-2020 [1].

The improvement in the defense service, traffic control and systematic vaccination, and control programs, led these countries to demonstrate the absence of viral circulation and infection in their territories, which in the 1980s was endemic and in the last decade in isolated cases, today the picture is of absence of both the disease and the presence of the virus.

In 2018, Moraes (2018), points out that in cases of countries or zones free of foot-and-mouth disease where vaccination is applied, the recognition of disease-free status has always been a major challenge for the official veterinary service, when compared to areas where vaccination is not performed. This is partly due to the difficulties of demonstrating the absence of the viral agent in herds submitted to massive and systematic vaccination[2].

"In addition to the general conditions, a Member State applying for recognition of the status of a foot-and-mouth disease-free country or zone with vaccination shall provide evidence of the existence of an effective clinical disease surveillance programme and demonstrate that foot-and-mouth disease has not been present in the country or area for at least the last 2 years. In addition, surveillance of foot-and-mouth disease virus infection should show that the virus has not circulated in the vaccinated population in the last 12 months. For this purpose, serological surveillance will be necessary that includes evidence capable of detecting the presence of antibodies against PNEs, as described in these guidelines. It is recommended to provide evidence of the effectiveness of the vaccination program" [2][3].

According to the Panaftosareport, in 2017, the maintenance of immunization programs as a risk mitigation measure is only justified when there is somewhat significant evidence or probability of transmission or introduction of foot-and-mouth disease virus [4].

Therefore, this study aims to conduct a study on sanitary measures with the objective of withdrawal of the vaccine against aphthous from the cattle herd of the state of Mato Grosso do Sul and possible impacts.

a) Survey at Latin American level of vaccine withdrawal and risk of reintroduction of foot-and-mouth disease virus

Only three Latin American countries are considered totally free of foot-and-mouth disease without the need for vaccination, Chile, Guyana and Peru. In addition to these, there are disease-free zones without vaccination in portions of Argentina, Bolivia, Ecuador and Colombia (fig. 1).

In Brazil, the states of Santa Catarina, Paraná, Rio Grande do Sul, Acre, Rondônia and part of Amazonas and

Mato Grosso are recognized as free without vaccination by the OIE.

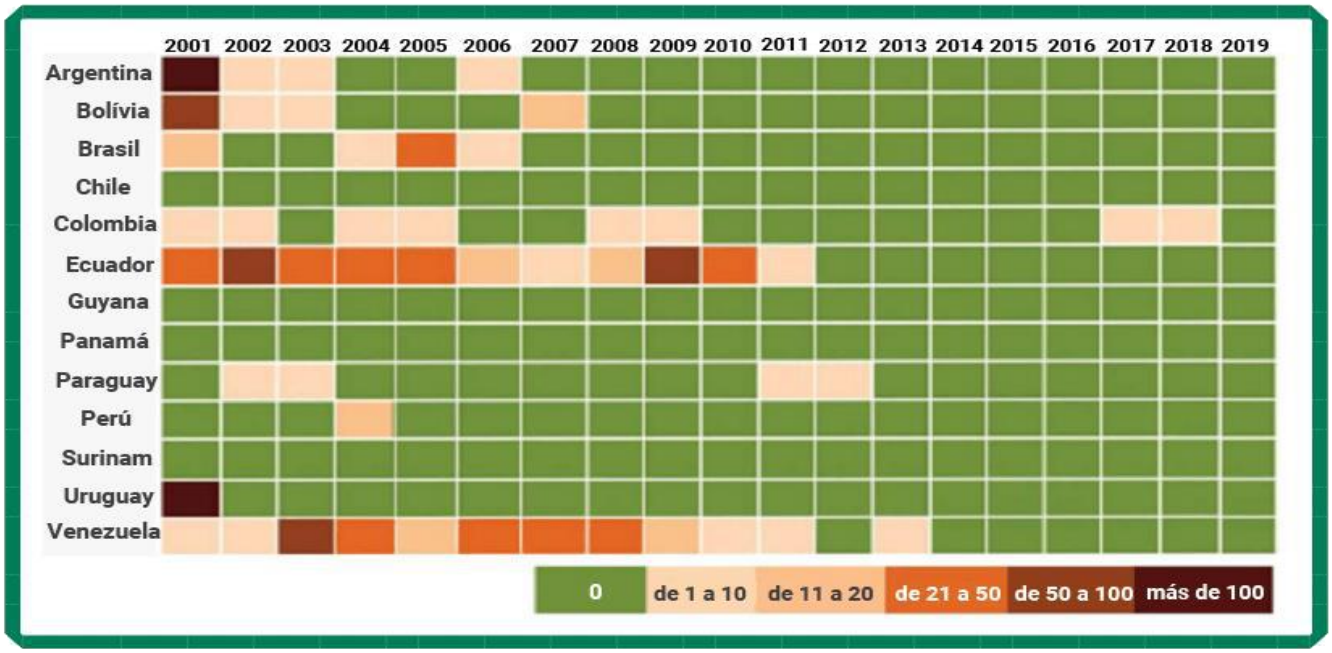

Fig. 1: Geographical distribution of historical risk of foot-and-mouth disease incidence in South America

Source: Cosalfa, 2020

The main risks for the reintroduction of foot-and-mouth disease in these countries are control of income from regions of different status, control of the risk of introduction associated with formal and formal livestock practices in communities and livestock farms that share an administrative border [4].

Dutra et. al. (2006), carried out a study seeking information to assist health actions involving the prevention of the entry of the Foot-and-Mouth Disease virus into the gaucho herd. Rural properties with high movement of bovídeos, located in border regions, close to dairy products or slaughterhouses of animals are classified as high-risk properties for the introduction of foot-and-mouth disease virus. In the second half of 2006, under the coordination of veterinarians of the Department of Animal Production of the Department of Agriculture and Supply of Rio Grande do Sul, a study was conducted on rural properties in the state, finding that 0.88% are classified as high risk to the introduction of foot-and-mouth disease virus. With integrated work among rural producers, plus active surveillance by DPA/SAA employees, in high-risk properties to the introduction of the virus, the probability of introducing this virus into RS is quite low, allowing the state to maintain its health status free of foot-and-mouth disease with vaccination [5].

The most recent work found was by Gavião (2017), who reports on "RISK PERCEPTION OF THE DIFFERENT ACTORS INVOLVED IN THE CONTROL OF FOOT-AND-MOUTH FEVER ON THE WESTERN BORDER OF RIO GRANDE DO SUL". In this work, the placement of Gavião (2017) was clear, where he concludes that it is extremely important for the SVO to mitigate the risk of foot-and-mouth disease, not only in the supervision of vaccination and other control activities performed, but also through health education actions that lead to the breaking of the paradigm that surveillance should be exercised exclusively by government inspection agencies. As well as, intensify the surveillance of the transit of animals and products of animal origin and surveillance activities on the properties identifying animals introduced illegally [6].

b) History of foot-and-mouth disease vaccination in Brazil and the state of Mato Grosso do Sul

In Brazil, a milestone in the institutionalized struggle against the disease was the promulgation of Decree 52,344 of August 9, 1963, with the institutionalization of the Campaign Against Foot-and-Mouth Disease (CCFA). At that time, the activities were basically summing up in the action in foci and vaccination against foot-and-mouth disease. At the same time, during the 1960s, laboratory

infrastructure, personnel training and producer awareness occurred, initiating systematic control of the disease with vaccine production, notification of outbreaks and diagnosis of the disease [1].

Animal health systems and state veterinary services were established one by one, improving surveillance, inspection and coordination, and the private sector participated in actions against the disease, especially vaccination. Strategies to combat foot-and-mouth disease were limited to vaccination campaigns; registration of holdings with susceptible animals; identification and prohibition of transit from holdings with sick animals (where the ban lasted up to two incubation periods from the cure of the last sick animal); and the control of the movements of susceptible animals [1].

Another important milestone in the 1970s was the implementation of vaccine quality control and the identification of problem areas through the study of animal transit and its comparison with the occurrence of the disease.

A sharp drop in the number of outbreaks was observed from 1980, when vaccination campaigns were expanded and control activities carried out by the Official Veterinary Service (SVO) were strengthened [1].

In Brazilian cattle, vaccination against foot-and-mouth disease (AF) virus is fundamental for the initial phase of eradication of the disease. Even with the quality of the vaccine having strict control made by the official agencies, technical variables still not monitored such as manipulation, transportation and conservation by the consumer, dose, place and form of application that interfere in the immune response [7].

The use of mandatory preventive vaccination only in cattle and buffaloes in the areas free of foot-and-mouth disease with vaccination. At the discretion of the Ministry of Agriculture, Livestock and Supply, emergency vaccination can be used as part of strategies to contain outbreaks of foot-and-mouth disease in the country, as provided for in manuals and plans made available by the Department of Animal Health (Article 19 of IN 48/2020). [8].

In Brazil, only cattle and buffaloes are vaccinated, because these species are considered important in the manifestation of foot-and-mouth disease virus in nature, because they develop persistent infections. Therefore, if the spread of the virus is controlled in these species, sheep, goats and pigs and also wild animals will not have anywhere to contract the disease [9].

c) History of serology in Mato Grosso do Sul

Seroepidemiological studies aim to support the certification of no transmission of foot-and-mouth disease virus and are carried out in addition to other components of the surveillance system implanted in the areas under evaluation. In this context, seroepidemiological studies, especially in herds submitted to massive and systematic vaccination, involve the detection of animals in the serological lyological population compatible with foot-and-mouth disease virus infection and require the use of laboratory tests to identify the presence of antibodies against non-structural proteins – PNEs [2]

In the period of 1995 and 1996, in order to evaluate whether the actions to combat foot-and-mouth disease, especially the annual vaccination strategy with oily vaccine, were sufficient to cut the cycle of endemic transmission of the viral agent, Moraes et al. (1996-1997) conducted a serological study in the Pantanal region of Mato Grosso.. The study involved 311 rural properties, randomly selected in a universe of 2,183 herds, and the collection of 3,885 blood serum samples in cattle aged 6 to 24 months. The samples were evaluated by PANAFTOSA, using viaa-idga test as screening test and as confirmatory test the EITB (enzyme-linked immunoelectrotransfer blot). In general, 0.30% (6/1,972) of seropositive cattle aged 6 to 12 months and 0.31% (6/1,913) were identified at 13 to 24 months of age. The results were incompatible with viral agent transmission and motivated local health authorities to follow the objective of eradication of the disease in the State, maintaining the annual vaccination strategy in the cattle herd and buffalo located in the Pantanal of Mato Grosso [2].

From the adoption by the OIE of the concept of zonification, epidemiological studies to support the certification of absence of foot-and-mouth disease virus transmission have been incorporated into the surveillance system for the disease in South American countries. In Brazil, several studies were conducted from 1996 to 2017, with the objective of implantation or recovery of the zoosanitary condition of foot-and-mouth disease free. Complementary work was also carried out to maintain free zones or to meet the demands of importing markets, highlighting: in 2008, serological surveillance at international borders with the states of Mato Grosso do Sul, Mato Grosso, Rondônia and Acre; in 2009, serological study in the Amazon River, Amazonas State, and in the State of Acre (repeated studies in 2010 and 2011); in 2010, serological and clinical surveillance in the State of Santa Catarina (foot-and-mouth disease-free zone without vaccination) and in the foot-and-mouth disease-free zone with vaccination, and a longitudinal study in the high surveillance zone established in the State of Mato

Grosso do Sul; in 2012, a new longitudinal study in the high surveillance zone established in the State of Mato Grosso do Sul; in 2014, serological and clinical surveillance in the foot-and-mouth disease-free zone with vaccination; and in 2016 and 2017, the implementation of longitudinal studies in the State of Santa Catarina [2].

In 2018, surveillance activities were conducted in 5 Brazilian states (Rio Grande do Sul, Paraná, Mato Grosso do Sul, Mato Grosso and Roraima) in the region bordering Uruguay, Argentina, Paraguay, Bolivia and Venezuela. (MAP, 2018) In August 2019 and March 2020, serological surveillance was carried out in the zones free of foot-and-mouth disease with vaccination, where the border regions with Argentina, Bolivia, Paraguay, Uruguay, Peru and Venezuela were carried out, involving the states of Rio grande do Sul, Paraná, Mato Grosso do Sul, Mato Grosso, Rondônia, Acre and Roraima, and each of these regions involved has their particularities [10].

The current epidemiological scenario of the Continent is favorable to the maintenance of free zones with vaccination and the expansion of free zones without vaccination, despite the critical situation of Venezuela and the occurrences in Colombia in 2017 and 2018. In this context, countries should mainly strengthen the surveillance system for early detection of the viral agent and to prevent reintroduction of the disease. However, there is also a need to maintain mechanisms for certification of the absence of viral transmission in the region, mainly to meet OIE standards, to confirm the annual health status and to present the requirements of commercial partners. (MAPA, 2018a)

Serology has a limiting factor, because the program for eradication and prevention of foot-and-mouth disease in Brazil uses the vaccination of box. The EITB test is able to differentiate vaccine antibodies from those produced in natural infection, however, in some cases, non-structural proteins, present in vaccines and that have not been eliminated during filtration, can provoke false-positive reactions Thus, vaccinated animals with suspected foot-and-mouth disease, which react positively to The EITB, should be tested in the "probang" test and, therefore, to be considered negative, the virus cannot be isolated in 3 consecutive tests with an interval of 30 days [9].

Sheep, goats, pigs and wild animals can be used in seroepidemiological surveillance programs to detect viral activity [9].

d) Health defense activities developed by the Agency for Animal and Plant Sanitary Defense - IAGRO

Registration of rural properties; Promotion and supervision of vaccination of cattle and buffaloes; Supervision of vaccination in hazardous areas or properties; Serology; Control of the transit of animals and their products and by-products (intra and interstate); monitoring the distribution and trade of vaccines against foot-and-mouth disease; Attendance to outbreaks of the disease, as well as notifications of suspected vesicular disease and eradication of foci; Health education, organization and encouragement to community participation; Development of the animal health information and surveillance system at the state level; Supervision of livestock events (fairs, exhibitions, auctions and other agglomerations); Inspection of animals and their products and by-products and human resources training [11].

e) Health defense measures adopted by countries bordering Brazil

In 2012, the member countries of the World Organization for Animal Health (OIE) approved a global strategy for the control of foot-and-mouth disease, led by this body together with the Food and Agriculture Organization of the United Nations (FAO), which recognized the Hemispheric Program for the Eradication of Foot-and-Mouth Disease (PHEFA) as a guideline for the control and eradication of the disease on the American continent. Which is conducted by the Hemispheric Committee for the Eradication of Foot-and-Mouth Disease (COHEFA) and the South American Commission to Combat Foot-and-Mouth Disease (COSALFA), and coordinated by the Pan American Foot-and-Mouth Disease Center of the Pan American Health Organization [12].

The last PHEFA Action Plan that was in force during the period 2011 to 2020 allowed 94.7% of the territory of South America to achieve the recognition of official status of foot-and-mouth disease free in 2019, with approximately 97% of its cattle and buffalo herds free of foot-and-mouth disease with or without vaccination. However, Venezuela was the only country that remained without health recognition until the end of 2020, according to Fig. 2, generating a risk to the north of the Andean region and being responsible for the focus that occurred in Colombia during the years 2017 and 2018 [12].

Fig. 2: Official status of Foot-and-mouth Disease in South America.

Source: https://bit.ly/3xsDN2Q

Members and recognised areas free of foot-and-mouth disease without vaccination.

Members and recognised areas free of foot-and-mouth disease with vaccination.

Country and zone without official OIE recognition for foot-and-mouth disease

The PHEFA's 2011-2020 Action Plan has enabled an advance in out-of-date health programs since 2010 and the preservation of status in the free countries of the Southern Cone, i.e., Argentina, Bolivia, Brazil, Chile, Paraguay and Uruguay, where there were sporadic outbreaks in vaccinated populations. However, most free countries with vaccination did not advance to free status without vaccination, as had been proposed [12]

Therefore, the current Action Plan 2021-2025, approved in 2020 by the Hemispheric Committee for the Eradication of Foot-and-Mouth Disease (COHEFA), is responsible for this eradication throughout the American continent by 2025, which also provides for the strengthening of official surveillance services. Its guidelines include: the eradication of the virus active in Venezuela, in order to mitigate the risk to the Northern Andean region; change the official status of free countries with vaccination to without vaccination; and preserve the health status of foot-and-mouth disease-free territories without vaccination [4][12].

In this article, we will emphasize the countries bordering the state of Mato Grosso do Sul, that is, we will discuss the sanitary measures adopted by Bolivia and Paraguay.

Historically, in Bolivia, the Cochabamba region has been affected by outbreaks of the disease with high morbidity, mainly involving type O and A viruses, including having affected vaccinated herds, during the years 1968 to 1969. In the following year, another outbreak with type A virus (provisionally called A/Bolivia/70) affected this region and santacruz, as well as numerous outbreaks caused by the Type O1 virus also in Cochabamba. In 1971, type A and C viruses were typified and the disease manifested itself in seven of the nine departments of the country [13].

Law No. 2061 of 16/03/2000 established the National Service of Health and Agri-Food Quality - SENASAG, as an operational structure of the Ministry of Agriculture, Livestock and Rural Development of the country, responsible for agricultural health and food safety in Bolivia, and in 2001 the National Program for the Eradication of Foot-and-Mouth Disease - PRONEFA was implemented [14].

According to Fig. 3, the country currently has international OIE recognition of three zones free of foot-and-mouth disease with and without vaccination: Chiquitania (with 10 municipalities in 2003), Altiplano (with 58 municipalities in 2012) and Chaco and Valles (with 50 municipalities in 2013). The last record of the disease in this country occurred in the region of Santa Cruz between January and February 2007 [14].

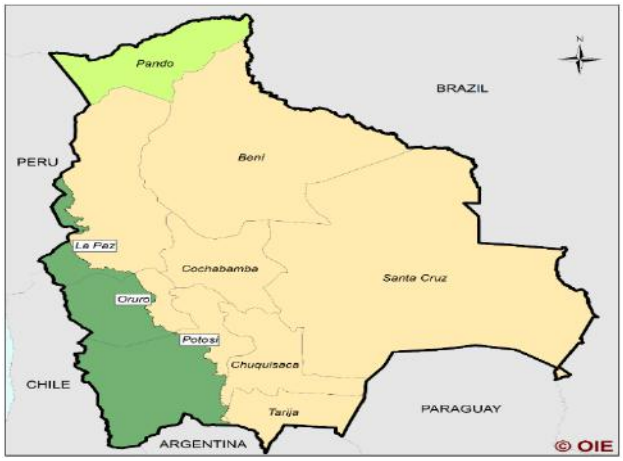

Fig. 3: Official status

Source: World Animal Health Organization - OIE

Foot-and-mouth disease-free zone without vaccination (part of the Altiplano region).

Foot-and-mouth disease-free zone without vaccination (Department of Pando).

Zone free of foot-and-mouth disease with vaccination (chaco, valles and part of Amazonas and Altiplano).

Through senasag's 2014-2018 Institutional Strategic Plan, it was possible: the strategic vaccination of the herd, carried out every six months, with minimum vaccination coverage of 90%, preserving the High Surveillance Zone as an area free of foot-and-mouth disease; the analysis of corrective actions for the non-conformities pointed out by the Process for the Performance of Veterinary Services - PVS/OIE; the technical and structural improvement of the official laboratories and operational capacity of SENASAG through economic support to PRONEFA by the Foot-and-Mouth Disease Free Action Plan – PAMA/MERCOSUR; the computerization and registration of agricultural data through the implementation of the Gran Paititi Software in order to facilitate sanitary management by SENASAG; the implementation of the National Registration and Identification System of the Cattle Herd - SIRINGA; the accreditation of competent professionals responsible for animal health; the registration update of rural properties; updating the list of diseases of mandatory notification with the manual of the National Epidemiological Surveillance System - SINAVE; seroepidemiological studies of the viral circulation of foot-and-mouth disease in the country; the implementation of the National Council of Pork (CONAPOR) to approach swine health and approval of the National Swine Health Regulation; the installation of incinerators at international airports; strengthening the National Herbivorous Rabies Control Program together with Peru, Guatemala and Honduras, as well as the Surveillance Plan against Bovine Spongiform Encephalopathy – BSE; the registration and control of refrigerators and industries in the food industry; the intensification of supervision and the health registry of companies in the food sector; the regulation of inspection and certification for the import and export of food; the control of organic production; technical training of personnel; the implementation of the Bolivian Cattle Traceability System; and technical training in relation to Good Agricultural Practices through the Safety Assurance Program – PAI [14].

In Paraguay, SENACSA is the national body responsible for the preparation, regulation, coordination, implementation and supervision of national policy and management of quality and animal health. In this context, it uses the National Program for the Eradication of Foot-and-Mouth Disease, which has the legal support of Law 808/96, and has as its main objective to keep the national territory free of foot-and-mouth disease virus (FMD) [15].

The strategy consists of carrying out actions to maintain a high level of immunity in the bovine population, through systematic and massive vaccination campaigns, procedures for the care of suspected diseases (interdictions, movement control, strategic vaccinations, etc.), detection of compatible clinical cases and in case of possible outbreak of foot-and-mouth disease, eliminate the sources of infection, through the eradication of sick animals and contacts, disinfection and other tasks [15].

The objective of the National Program for the Eradication of Foot-and-Mouth Disease is to control, eradicate and prevent the re-entry of the disease, in a sustainable way, throughout the territory and in the population of species susceptible to it [15].

The central strategic axes of combating the disease are based on:

- *The drastic decrease in the susceptibility of the bovine population (a single species that gives conditions to sustain endemicity), through systematic and mandatory vaccination campaigns to interrupt the process of transmission of the infection,*
- *A very strict control of disease outbreaks supported by a well-structured surveillance system, timelydetection and rapid emergency response. With the support of a very efficient cattle handling control system, based on a very well structured information system (SIGOR and SISA).*
- *A very robust diagnostic system that includes a maximum safety laboratory, and diagnostic regimens capable of detecting infection through serology in vaccination environments, and determine with high efficiency the level of immune coverage and the quality of vaccines used in the program.*
- *A robust public-private alliance to carry out the program's actions in a delegated manner.*

Systematic vaccination campaigns, surveillance of vaccinated cattle and capture of herd registration data [15].

This study aims to conduct a study on sanitary measures to remove the anti-foot-and-mouth vaccine from the cattle herd of the state of Mato Grosso do Sul and possible impacts.

II. METHODOLOGY

a) Research design

This work regarding its nature is applied research, because once it is intended to conduct a survey of sanitary measures that have been carried out over the last 3 years by the Agency for animal and plant health defense IAGRO do Mato Grosso do Sul, among them an analysis of the latest seroepidemiological studies carried out, with the objective of the withdrawal of the vaccine against aphthous in the cattle herd.

The research is characterized as exploratory and explanatory, since a bibliographic survey will be conducted on information on the subject, providing greater familiarity with the problem and identifying the factors that determine or contribute to the occurrence of phenomena [16].

The scientific basis, makes it necessary since in Brazil other states of the federation that have already gone through the process of withdrawal of the vaccine from their cattle herd, and this process, has not yet occurred with the state of Mato Grosso do Sul, causing a program of measures that are being implemented to achieve this objective.

b) Animal and Vegetable Sanitary Defense Agency of Mato Grosso do Sul IAGRO

The State Agency for Animal and Plant Sanitary Defense of the State of Mato Grosso do Sul - IAGRO, was created by Decree-Law No. 9, of January 1, 1979. Linked to the State Secretariat for The Production of Agrarian Development, Industry, Trade and Tourism [17].

IAGRO, through the delegation of the Ministry of Agriculture Livestock and Supply, implements the**actions of the Animal and Plant Health Programs** that aims to: implement public policies of education, health, inspection and inspection in order to promote, maintain and recover animal and plant health, the quality of its products and by-products through health defense, control, inspection and inspection of products and by-products of agricultural origin, inspection of agricultural inums and biosafety activities to ensure human health. Comply with and enforce the operational obligations delegated by the Executive Branch, which deals with legislation on the protection of animal and plant health and the control and inspection of agricultural products, goods and services, processes and technologies achieved by the agricultural health care system [18].

c) Collection standards for serology

In 2018, the seroepidemiological study was directed to the border region with the following countries: Uruguay, Argentina, Paraguay, Bolivia, and Venezuela, and had the involvement of 5 Brazilian states (RS, PR, MS, MT, RR). According to MAPA, 2018 for the selection of properties that participated in the studies were considered the following indicators: presence of cows (properties with more than 30 cows); Steer/Cow ratio (Males from 25 to 36 months/Total females older than 36 months greater than 0.7); Total cattle (properties with more than 100 cattle). Within the cattle herd the target population were animals from 6 to 24 months of age, this choice was due to the history of lower doses of vaccines applied in these animals as well as the higher frequency of movement between rural properties. For the study, 100 properties were selected among the states mentioned, as described in Table 1 [19].

Another seroepidemiological study to verify viral transmission was conducted between August 2019 and March 2020, was also a study directed to the border zone and had the participation of 7 Brazilian states (RS, PR, MS, MT, RO, AC and RR). According to MAPA, 2020, a 15 km border strip that is usually used to define the area of protection and surveillance delimited the target population in the study, as illustrated in Fig. 4. Because they presented lower immunity results and because they are more susceptible in the transmission of the virus, the bovine population selected for the study were young animals, preferably up to 12 months of age [20].

Fig. 4: Map of the study area, highlighting the region involved and the distribution of the sampled properties.

Source: Ministry of Agriculture, Livestock and Supply - MAPA

III. ANALYSIS AND INTERPRETATION OF DATA

In the serological study conducted in 2018 by MAPA, the properties were distributed according to the border range and the Zones of High Surveillance of the selected States, according to Table 1 [21].

Table 1: Information on total properties in border municipalities and those selected for monitoring in border regions [21].

State	Establishments in bordermunicipalities		Properties chosen for monitoring
	Properties	Cattle	Total
PR	12.108	275.319	15
MS	18.286	7.100.358	20
MT	4.553	1.479.816	15
RR (Pacaraima)	73	20.556	20
RS	33.875	2.830.983	30
Total	**68.895**	**11.707.032**	**100**

Already in the Fig. 5, allows you to visualize the spatial distribution of properties in Mato Grosso do Sul state.

Table 2 shows the information on the number of animals collected in each zone, as well as the laboratory results found in the study conducted in 2018 [21].

Table 2: Number of animals collected and laboratory results, per zone, in theseroepidemiological study for foot-and-mouth disease in the border region [21].

Zone	Participating States	Number of cattle selected for monitoring	Number of reagent cattle in the first serology	Number of cattle selected for the second serology	Number of reagent cattle in the first serology	Cattle that had LEF samples collected in a paired fashion with a "Not Detected" result for FA
2	RS	1.619	43	980	28	27
3	MT,RR,PR e parte do MS	2.739	91	2.019	64	61
4	Parte do MS	578	27	351	8	8
Total	**RS, MT, RR, PR e MS**	**4.936**	**161**	**3.350**	**100**	**96**

Table 3 shows the final data of the first serology of the study conducted in the years 2019 and 2020 of the animals of the study, with the indication of the number of properties, number of animals collected and laboratory results per zone [21] .

Table 3: Number of properties, collected animals and laboratory results, per zone, in the first serology of the seroepidemiological study for foot-and-mouth disease in the border region conducted in 2019, where R= Reactive and I= Undetermined [21].

General data			ELISA 3ABC/EITB (1º sorology)						
UF	**Zone**	**Nº of properties**	**Samples**	**Negative Sample (N)**	**Relative Frequency**	**Reactive Sample(R)**	**Reactive frequency(R)**	**Samples inderterminates(I)**	**Relative Frequency (I)**
RS	2	97	4.714	4.666	98.98%	28	0.59%	20	0.42%
RR	3	12	230	224	97,39%	4	1,74%	2	0,87%
RO	3	34	1.798	1.787	99,39%	7	0,39%	4	0,22%
PR	3	17	269	261	97.03%	1	0.37%	7	2.60%
MS	3 e 4	62	3.360	3.314	98.63%	14	0.42%	32	0.95%
MT	3	54	3.359	3.302	98.30%	22	0.65%	35	1.04%
AC	3	66	3.180	3.160	99.37%	8	0.25%	12	0.38%
Total		**342**	**16.910**	**16.714**	**98.84%**	**84**	**0.50%**	**112**	**0.66%**

Already in the Fig. 6, it'sshows a spatial distribution of the properties studied in Mato Grosso do Sul, in the years 2019 and 2020[10].

Table 4: Number of animals collected and laboratory results, per zone, in the second serology of the seroepidemiological study for foot-and-mouth disease in the border region conducted in 2019, where R= Reactive and I= Undetermined [20].

General Data					ELISA 3ABC/EITB (1º sorology)					
UF	**Zone**	**Predicted sample**	**Animals sampled**	**% of recuperation**	**Reactive Sample(R)**	**Relative frequency(R)**	**Samples indertermin ates (I)**	**Relative Frequency (I)**	**Properties sampled**	**Properties with sampled R or I**
RS	2	1956	1884	96.32 %	4	0.21%	14	0.74%	37	13
RR	3	150	141	94.00 %	1	0.71%	1	0.71%	4	1
RO	3	404	394	97.52 %	0	0.00%	7	1.78%	8	5
PR	3	105	85	80.95 %	0	0.00%	0	0.00%	6	0
MS	3 e 4	1870	1824	97.54 %	3	0.16%	23	1.26%	30	15
MT	3	2094	2045	97.66 %	6	0.29%	22	1.08%	34	16
AC	3	941	927	98.51 %	2	0.22%	9	0.97%	18	8
Total		**7520**	**7300**	**97.07 %**	16	0.22%	76	1.04%	137	58

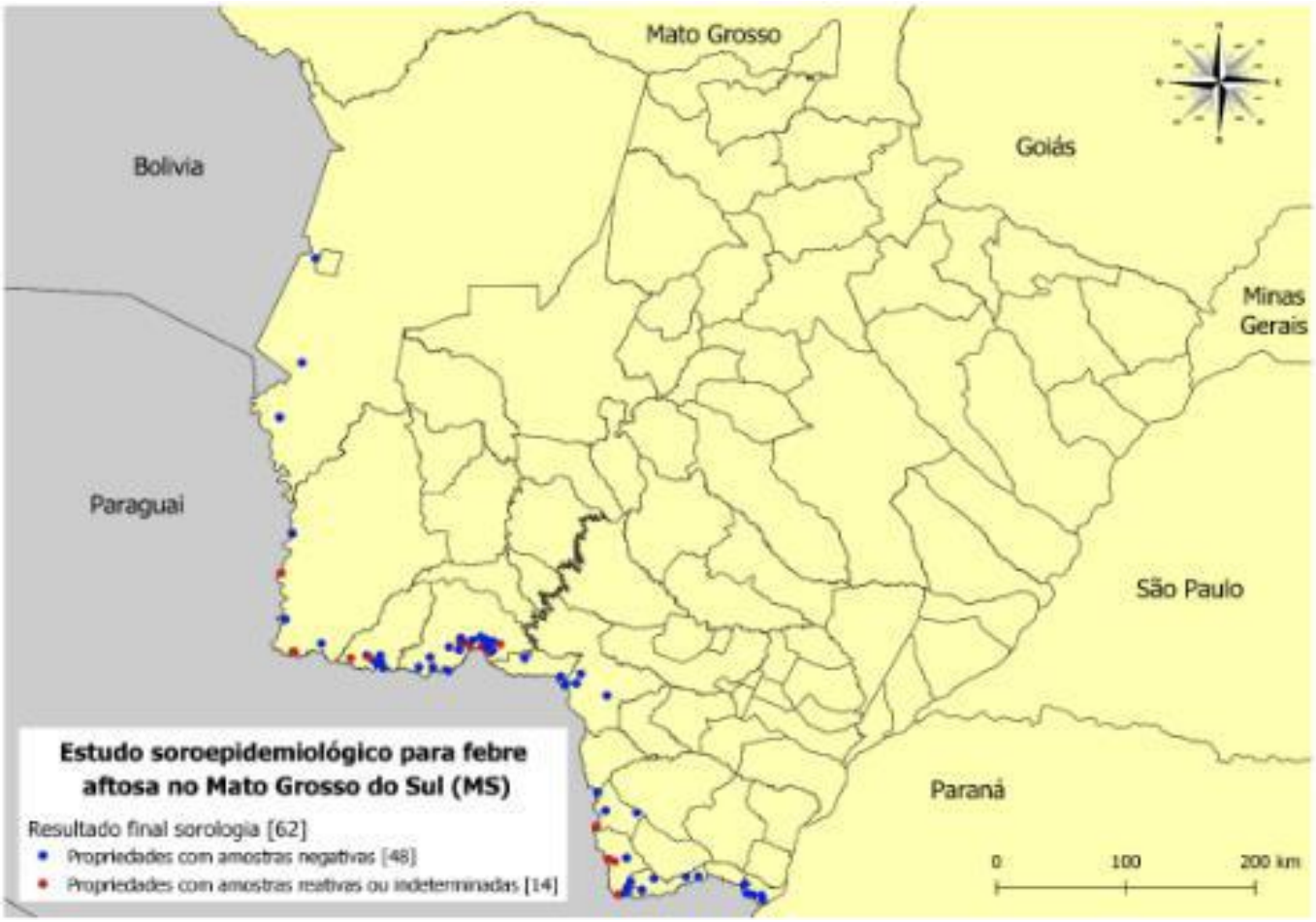

Fig. 6 - Distribution of properties and final results in serology - Mato Grosso do Sul

As foreseen in the study design, a second serology of all animals sampled on properties that had at least one reactive or indeterminate animal in the first serology was performed. With results described in Table 4 and Table 5[20].

Fig. 5: Border region of Mato Grosso do Sul [21].

It was observed that there was no significant increase in the total number of positive animals, already allowing the discarding of viral transmission. However, to obtain greater safety, samples of esophageal-pharyngeal fluid (LEF) were collected from all animals with a positive result of the second serology, where the presence of foot-and-mouth disease virus was not detected, ending studies in these years [10]

IV. RESULTS AND DISCUSSION

a) Measures implemented by IAGRO to obtain the withdrawal of the vaccine

According to the Technical Guide to the Last Stage of the Hemispherical Foot-and-Mouth Disease Eradication Program 2017, Risk Management should consider three levels of action in a free zone without vaccination to mitigate the impact of a possible outbreak of foot-and-mouth disease.

First level of Action: Prevention against the introduction of foot-and-mouth disease virus, objective is an effective separation of the population with the free status without vaccination of other animal populations with a different health status, as well as an effective control of the entry of animals and livestock goods for control by the health authority.

At the second level of action would be risk management measures aimed at reducing the exposure of an animal population to foot-and-mouth disease virus would be associated with a particular route, whereby a commodity contaminated by foot-and-mouth disease virus can enter free territory and reach a susceptible animal, such as feeding pigs with remains of animal origin.

At the third level of action are management measures leading to rapid detection and rapid response in the event of an incursion of foot-and-mouth disease virus into an animal population. These measures aim to limit the spread of a focus and reduce its impact.

Considering the State of MS, where we have borders with 2 countries (Bolivia and Paraguay) where they are free with vaccination, and with the States of MT, GO, MG and SP that also has free status with vaccination, it is essential to effectively control traffic in these borders in case of suspending the vaccine in the south-matogrossense territory, and the withdrawal of the vaccine in block would be a valuable strategy for these states.

In the process of transition to free status without vaccination, the state veterinary service should strengthen prevention, detection and early response measures. Among the measures implemented by IAGRO we can mention: traffic control, restructuring of the defense service, as well as animal health legislation, health education, serology and active surveillance for the early detection of AF virus infection.

Vaccination against foot-and-mouth disease of cattle and buffaloes is the responsibility of producers, and IAGRO is responsible for regulating, disseminating, health education and supervising the activity. In recent years, the State of Mato Grosso do Sul (MS) has achieved excellent vaccination rates of animals against foot-and-mouth disease above 99% (data referring to the stages of May of each year), which demonstrates the commitment of the

entire producing class in the execution of activities, as shown in Fig. 7.

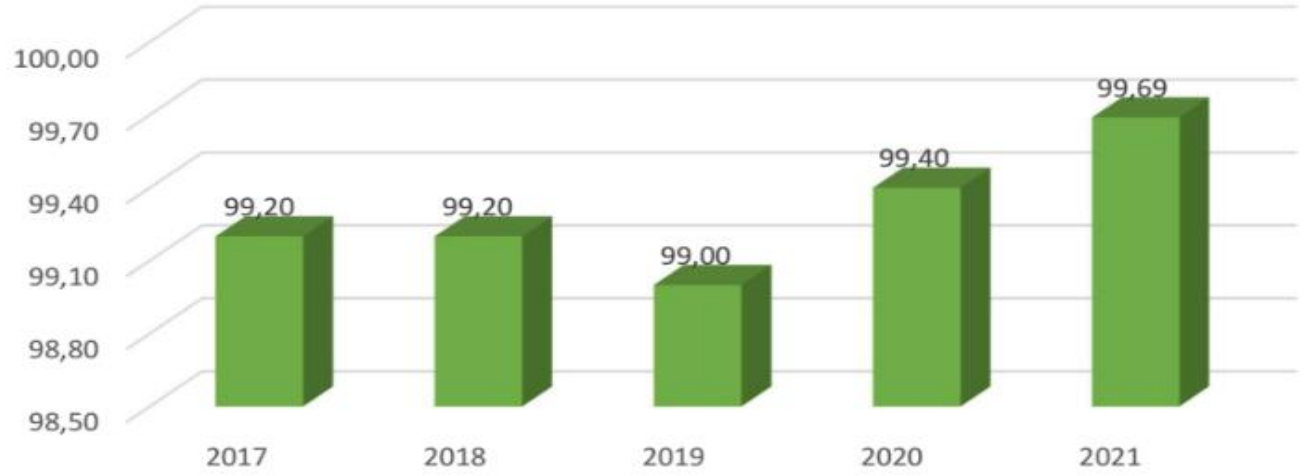

Fig. 7: Animal vaccination rates (%) against foot-and-mouth disease in the State of Mato Grosso do Sul in the years 2017 to 2021 (data referring to the stages of May of each year).

Since 2005, the State Veterinary Services (SVEs), coordinated by the Department of Animal Health of the Ministry of Agriculture, Livestock and Supply (MAPA), conduct seroepidemiological studies, with the objective of estimating the percentage of immune coverage of the bovine population achieved by vaccination campaigns against foot-and-mouth disease. In 2020, a study was conducted to the Federation Units (UFs) qualified for the export of fresh beef to the European Union (EU), covering part of the foot-and-mouth disease-free zone with vaccination (Minas Gerais, Espírito Santo, São Paulo, Mato Grosso do Sul, Mato Grosso and Goiás), in order to meet the certification commitment signed with that economic bloc (Fig. 8).

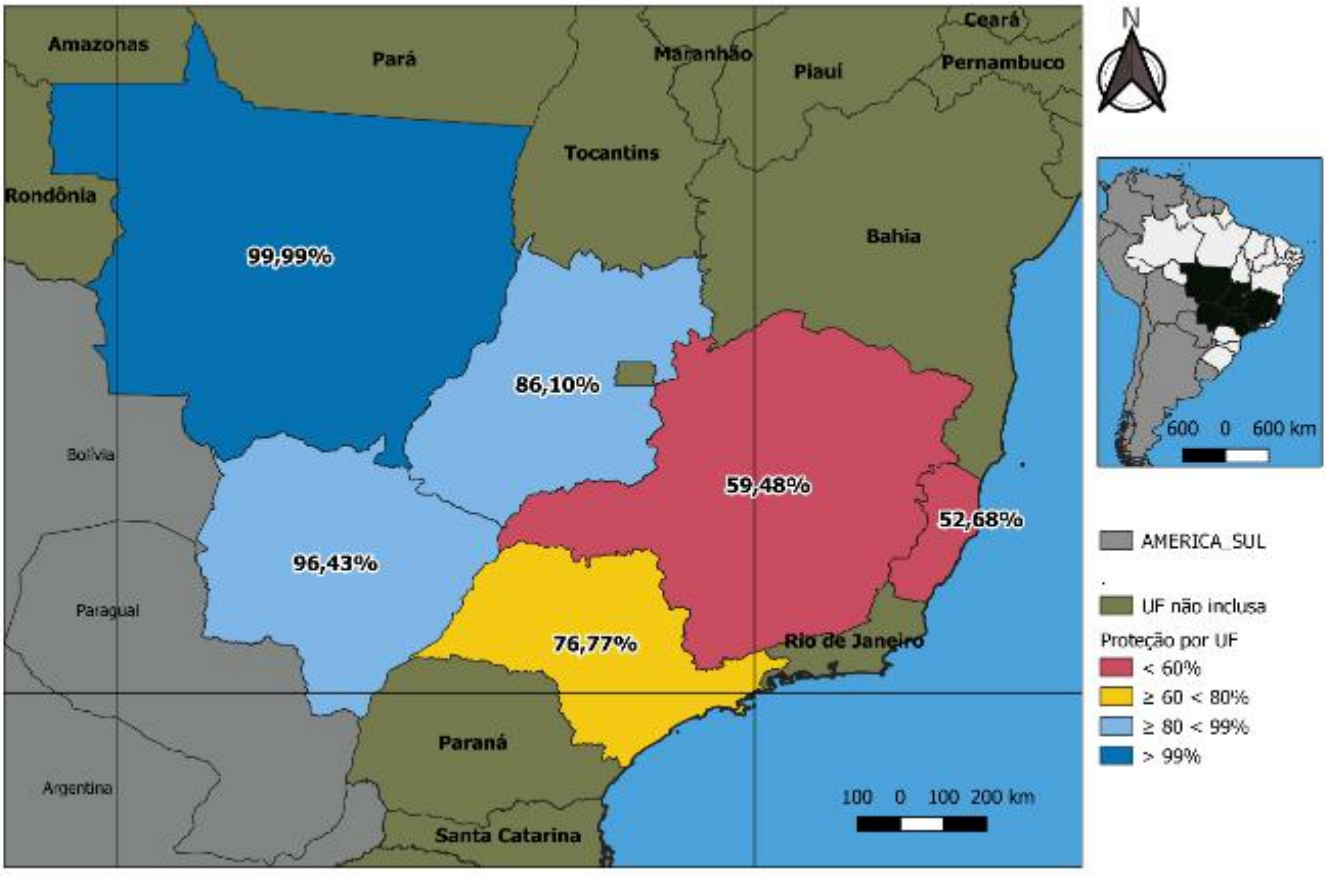

Fig. 8. Distribution of corrected prevalence of cattle immunized by federative unit

b) Serology

In order to meet the OIE standards, for the annual confirmation of health status and to present the requirements of commercial partners, there is a need to maintain mechanisms for certification of absence of viral circulation in the State, therefore, the epidemiological study was structured to detect, through sampling, the presence of AF virus transmission [8], therefore serology and the evaluation of the quality of the official veterinary service (QUALISV), are the main control tools for the conquest and maintenance of health status.

Table 5: List of the main epidemiological studies conducted with the objective of supporting the claims to recognize the condition of foot-and-mouth disease-free zone with the OIE, 1997 to 2017, Brazil.

ID	Goal	Year		Location involved	Subpopulations considered in the design	UPA[1]	Prop[2]	Esp[3]	age group (months)	Samples[4]			Laboratory tests used[5]
		Study conduct	Recognition or restitution							Total	Positives		
1	Recognition	1996/1997	1998	RS e SC	7	780		Cattle	>6	8.326	9	0.11 %	VIAA-IDGA/EITB
								PR	>3	1.993	2	0.10 %	VIAA-IDGA
2	Recognition	1999	2000	PR, SP, GO, MT, DF andparto of MG	3	1.053	2.312	Cattle	6 a 24	35.410	420	1.19 %	ELISA/EITB
3	Recognition	2000	2001	MS, TO, BA, SE, ES, RJ and part of GO, MG,MTand SP	6	1.280		Cattle	6 a 24	35.410	420	1.19 %	ELISA/EITB
4	Restitution	2001	2002	Região norte RS andfrontier SC/Argentina	2	167		Cattle	6 a 24	1.899	0	0.00 %	ELISA/EITB
5	Restitution	2002	2002	RS E SC	3	381	716	Cattle	6 a 24	4.353	20	0.46 %	ELISA/EITB
								PR	> 3	1.343	0	0.00 %	VIAA-IDGA
6	Recognition	2002	2003	RO	1	344	709	Cattle	6 a 24	8.918	142	1.59 %	ELISA/EITB
7	Recognition	2003/2004	2005	AC and part of AM	1	335	448	Cattle	6 a 24	15.598	71	0.46 %	ELISA/EITB
8	Recognition	2003/2004	2007	South-central region of PA	2	649	941	Cattle	6 a 24	32.078	88	0.27 %	ELISA/EITB
9	Recognition	2005	2007	South-central region of PA	2	650	1.101	Cattle	6 a 24	30.137	678	2.25 %	ELISA/EITB
10	Recognition	2006/2007	2007	SC (free without vaccination)	3	468	1.347	Cattle	6 a 36	11.059	48	0.43 %	ELISA/EITB
11	Restitution	2006	2008	forbidden area MS	1	382		Cattl	6 a 24	7.458	214	2.87 %	ELISA/EITB

								e						
12	Restitution	2006	2008	forbidden area PR	1	576		Cattle	6 a 24	9.826	34	0.35 %	ELISA/EITB
13	Restitution	2006	2008	Area not forbidden MS	1	483		Cattle	6 a 12	11.568	26	0.22 %	ELISA/EITB
14	Restitution	2006	2008	Area not forbidden PR	1	932		Cattle	6 a 12	7.797	24	0.31 %	ELISA/EITB
15	Restitution	2006	2008	SP	1	455		Cattle	6 a 12	9.100	3	0.03 %	ELISA/EITB
16	Restitution	2006/2007	2008	Áreainterditada MS	1	444		Cattle	6 a 12	7.986	219	2.74 %	ELISA/EITB
17	Restitution	2007	2008	Áreainterditada MS	1	245	611	Cattle	6 a 12	5.681	168	2.96 %	ELISA/EITB
18	Restitution	2007	2008	Pantanal	1	300	482	Cattle	6 a 12	11.537	133	1.15 %	ELISA/EITB
19	Restitution	2007	2008	Planalto	1	307	452	Cattle	6 a 12	8.846	251	2.84 %	ELISA/EITB
20	Restitution	2007*	2011	Fronteira MS e Paraguai (zona de alta vigilância)	1	298	501	Cattle	6 a 12	8.635	283	3.28 %	ELISA/EITB
21	Recognition	2010	2011	Zona proteção BA	1	294		Cattle	6 a 12	3.804	6	0.16 %	ELISA/EITB
								PR	> 3	1.433	0	0.00 %	VIAA-IDGA
22	Recognition	2010	2011	Zona proteção TO	1	289		Cattle	6 a 12	3.322	1	0.03 %	ELISA/EITB
23	Recognition	2010	2011	Zona proteção RO	1	58		Cattle	6 a 12	1.257	1	0.08 %	ELISA/EITB
24	Recognition	2012/2013	2014	AL, CE, MA, PB, PE, PI, RN e parte do PA	5	1.756	1.942	Cattle	6 a 24	48.840	27	0.06 %	ELISA/EITB
								PR	>3	9.888	103	1.04 %	ELISA
25	Recognition	2014/2015	2018	RR, AP, AM e partes do PA	3	910	1.103	Cattle	6 a 24	19.225	67	0.35 %	ELISA/EITB
26		2017			5	162	162	Cattle	6 a 24	3.982	9	0.23 %	ELISA/EITB

Source: Moraes, 2018

*Na fronteira do MS com o Paraguai, além do estudo realizado em 2007, foram realizados estudos longitudinais na zona de alta vigilância em 2008 e 2009

1. UPA = unidade primária de amostragem; 2. Prop. = propriedade rural; 3. Esp. = espécie(Bov=bovinos/bubalinos, PR=Pequenos ruminantes) 4.Amostras referentes à primeira coleta (não estão incluidas amostras referente às investigações complementares desencadeadas nas UPAs com pelo menos um animal soropositivo)

5. Testes sorológicos para detecção de anticorpos contra PNEs. Dependendo de cada estudo, foram utilziados

outros testes laboratoriais complementares, como teste de reação em cadeia da polimerase de transcrição inversa, em tempo real – RT-PCR, para amostras de líquido esofágico-faríngeo, ou teste de ELISA CFL (competição em fase líquida) para detecção de anticorpos estruturais em animais não vacinados.

c) Measures implemented by IAGRO to obtain the withdrawal of the vaccine

The strengthening of the traffic control of animals within an area free of aphthous without vaccination, is a very important factor for the claim of the new health status. IAGRO - State Agency of animal and plant health defense of MS, created a new management, specific to the issue of Traffic control, made investments in structure and mainly uses artificial intelligence for analysis of intrastate and interstate traffic, created a situation room that monitors all animal traffic in the State (fig. 9 and 11), has in real time, the location of Iagro's teams, and attendance of anomalies within the E-Saniagro system, has in the implementation phase the control through application of the transport of animals, registering the carrier and linking the trip to the GTA's (fig. 10), thus allowing the visualization of the point of embarkation and landing of the animals, the flyunits are guided through these analyses in which area they will act, and in which fixed posts will be activated, always with teams formed by employee of the agency, as employee of public security agencies.

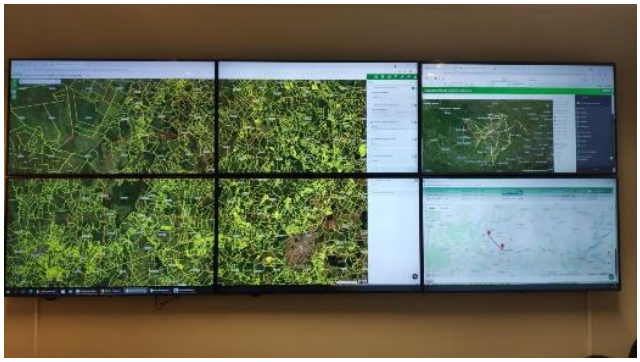

Fig. 9: Geographical Viewing Panel through Business Intelligence

An unprecedented cooperation agreement has been signed in the country, an agreement for the exchange of information and joint actions with the Paraguayan defense service SENACSA, an example is the sharing of the bank of brands of the institutions, thus enabling the identification of the origin of the animals.

Fig. 10: Bovine Movement Network from the state of Mato Grosso do Sul to other states.

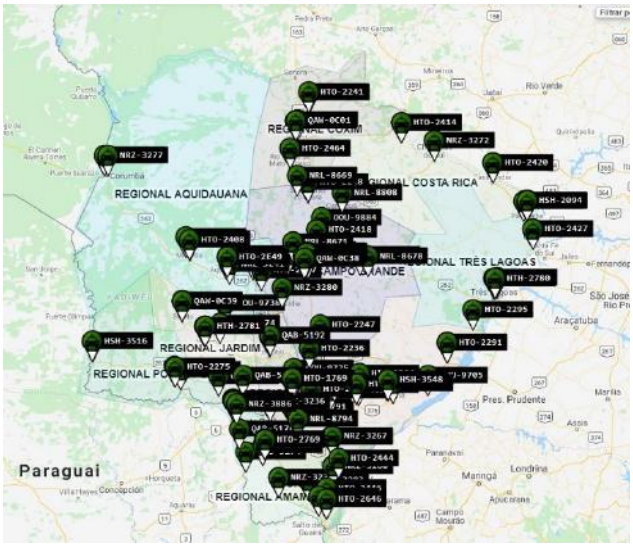

Fig. 11: Inspection points in the state of Mato Grosso do Sul.

d) Restructuring of the defence service

Another limiting factor for the achievement of the new status is the issue of investments in the health defense structure, investments in both structure and human resources become essential to have an efficient sanitary control that can ensure the withdrawal of the vaccine and permanence within the new context.

It is expected to open a public tender in early 2022, with the aim of supplying the vacancy cases of recent years, and the continuous training of employee.

After a few years with few investments in the agency, the Government of the State of MS landed between 2020 and 2021 almost ten million in the acquisition of vehicles, furniture and air conditioners. The forecast for 2022 is for investments of more than 18 million with reforms in local and regional units and in the Central.

The State also created a public fund, Financial Reserve for Animal Health Defense Actions (REFASA), where 65% of its appeal is for indemnification and 35% for investments or costing in the defense agency. The private sector created in 2021, the Private Fund, FUNDEFESA also to give greater assurance and agility in the use of resources for indemnification and defense actions both in costing and investments.

Another important tool is the terms of cooperation with other organs of the State, federal agency and even WITH SENACSA (Paraguayan defense agency) allows an exchange of information and indispensable resource, an example is the availability of aircraft for the use of health defense in partnership with the Secretariat of Public Security of MS, where IAGRO has its availability an airplane and a helicopter seized from drug trafficking, for your use

e) Restructuring of legislation

Although the Official Veterinary Service has standards, plans and infrastructure that allow them to face epidemics and health emergencies, in the transition to free status without vaccination the strategy to mitigate the risk of introduction and the appearance of new outbreaks should be reviewed, so the restructuring of the legal framework is underway is of fundamental importance for the plan to maintain the free zone without vaccine.

f) Health education

Health education is of paramount importance for the conquest and maintenance of the claim, it provides the approximation of the rural producer to the defense agency, shows society the importance of sanitary control and the fundamental role that the producer, and liberal professionals have in ensuring the new status, through notifications of suspected diseases, the sooner they are notified, the faster the defence service can act, providing a quick containment response and elimination of any health problems.

IAGRO uses digital communication tools that guide the producer on diseases, procedures, information and contacts in case of emergencies.

Another important tool used is the participation of local inspectors in the COMUSAS (Municipal Animal Health Committees) where there is an approximation of municipal leaders, and the effective participation in local decisions.

Health education also coordinates the training activities of the employees, keeping its technical staff updated and prepared to perform their functions, important partnerships are established, such as IFMS, MAPA, UFMS, UEMS, GOV School and other institutions.

V. CONCLUSION

The status of foot-and-mouth disease-free zone without vaccination is the main objective of the work that has been carried out by the Agency for Animal and Vegetable Sanitary Defense of Mato Grosso do Sul - IAGRO. However, in order to achieve this goal, the direction of IAGRO and its entire technical staff have not measured efforts in all its animal health defense activities throughout the state.

With the support of the state government and the entire productive sector that yearing for this achievement, there has been success in several actions, such as vaccination coverage throughout the state, satisfactory results in serological studies, actions in animal traffic control in

fixed and mobile posts throughout the state, health surveillance actions throughout the border region, the restructuring of the agency, the implementation and updating of legislation and health education actions, among other activities has given subsidy for the request for the election.

Moreover, the responsibility for the quality of the service already performed, as well as the commitment to meet all the demands of the Ministry of Agriculture Livestock and supply with regard to having the state as an area free of foot-and-mouth disease without vaccination, are commitments that will be assumed before mapa and society south matogrossense in the face of this great victory for the state.

Despite all the weather, such as the pandemic, the difficulty of investments and the global crisis, the State of Mato Grosso do Sul, through the Agency for Animal Sanitary Defense and - Vegetal de MS- IAGRO, has been galloping in strides to obtain the status of free zone without vaccination. There have been several achievements, such as the creation of funds and applied technological innovation, which enables the analysis of information in real time through applications used in the field and transport, very important for quick decision making and for an immediate response to any notifications.

The challenges are enormous, mainly due to the geographical location of the State of MS in the face of the extension of international currencies, making traffic control a critical point. However, this challenge must have numerous partners, such as MAPA, public security agencies and, mainly, rural producers. Another limiting factor of this journey, as in other States, is still the structuring of personnel, which should be saneada with tender scheduled for the beginning of 2022.

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