

Zika vaccine: development, assemblages, and sociotechnical controversies

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Abstract: The theoretical essay discusses the controversies about the zika vaccine development, highlighting negotiations which involve technical-scientific choices and the effects of defining the Vaccine Target Product Profile (TPP) for use only in the emergency scenario. Three perspectives of analysis are presented aligned with the Social Studies of Science: the flows of normative establishment provided by the World Health Organization (WHO), the narratives published in specialized journals and the discuss of a group of interviewees. We conclude that the definition terms of TPP supported the establishment of the WHO ontological policy, implying in exposure, accountability and culpability of women for the prevention of Congenital Zika Syndrome; definition of certain vaccination strategies; making other possible scenarios invisible; greater acceptance of certain platforms; widening global inequalities. Such an ontological policy engendered a potent emergency rationality that distinguished the vaccine from the social need for vaccination, pushing the second one towards invisibility.

► **Keywords:** Zika Virus. Zika Virus Infection. Vaccines. Vaccination. Global Health Strategies.

Received on: 7/2/2022

Revised on: 5/12/2023

Approved on: 7/31/2023

Corrected on 05/24/2024

DOI: <http://dx.doi.org/10.1590/S0103-7331202434SP105en>

Editor: Jane Russo

Reviewers: Gustavo Matta and Sergio Rego

Introduction

In July 2016, a new threat to public health was characterized as congenital Zika virus syndrome (SCVZ), brought to the global stage by the microcephaly epidemic in Brazil and the public health emergency of international concern (ESPII). The possibility of its transnational outbreak and the lack of treatment required the search for prevention and surveillance measures. The development of accurate serological diagnostic methods, innovative mosquito vector control devices and safe and efficient vaccines was prioritized, boosting interests and financial resources for biotechnological research and development.

The World Health Organization (WHO) mobilized itself in ordering technical-scientific considerations regarding regulation (WHO, 2016a) and the “vaccine target product profile” (TPP) against the Zika virus (ZIKV) (WHO, 2016b). It organized forums with recognized researchers in the field and encouraged the identification of markets for the products developed. Even recognizing at least two vaccination contexts (emergency and routine/endemic), the institution focused on the TPP for exclusive use in that emergency and subsequent ones (WHO, 2016b).

More than five years after the end of ESPII, serological diagnostic methods still leave room for doubt (Zhang *et al.*, 2021), the mosquito continues to be the villain in the epidemiological spectacles of arboviruses and there is no viable medication horizon, or a vaccine available for any scenarios highlighted (Castanha; Marques, 2020). This situation of uncertainty has effects: it makes it difficult to understand the engagements related to the control of the SCVZ; does not expose the diversity of possible actions; and makes controversies that go beyond technical-scientific boundaries invisible.

This article arose from concerns identified in meeting areas between formal and non-formal forums for the production of knowledge, in networks of people affected by SCVZ made up of: scientists, mothers, family members, professionals and managers. Why was the Covid-19 vaccine produced and the Zika vaccine not? Did the end of ESPII imply a reduction in investments for research? What stage of development are the studies at? What are the prospects for a new epidemic?

Based on these questions and the tensions they produce, we discuss the controversies surrounding the development of the Zika vaccine, highlighting the negotiations that involve technical-scientific choices. We question the effects of

defining the TPP for emergency use only, limiting the analysis to the Zika event. We assume that the vaccination scenario sanctioned by the WHO implies ways of ordering institutional, professional and social relationships. This is because the development of vaccines and vaccination are part of societal projects and are implemented in public health – a field of practices, knowledge and policies. Thus we recognize the importance of carrying out the debate in the academic domain, as well as in the public arena.

Engaging controversies

We assume that the controversies linked to the development of the vaccine make it possible to examine power games and efforts undertaken to erase constraints, oppositions and possibilities for constructing different logics (Callon; Lascoumes; Barthe, 2001; Law, 2004). An arena constituted by practices and interests, defined in the movement of actions, resistance and the production of knowledge. Interests that understand the ways in which science leaves the laboratory and produces agencies to make viable paths. Dynamics that require thinking about the consequences of applying scientific results.

We pay attention to institutions and practices, considering the contexts that shape them, without producing definitive answers. We propose three scenarios for engendering strategies, actors, interests and statutes: the flows of establishing regulation and the TPP; narratives published in specialized magazines; and the narratives of a group of interviewees.

The document organization of the first two scenarios (institutional regulations and scientific articles) began with a bibliographic search and checking the list of regulations available on the WHO virtual page. The search was mediated by descriptors such as “Zika virus”, “Congenital Zika Syndrome”, “Vaccines”, “Vaccination”. The movement took place on the Virtual Health Library (VHL) and PubMed platforms, favoring review studies performed by experts on the subject, between 2016 and 2021, without the intention of reaching the total number of publications.

Interviews were carried out as part of a project linked to research into the present history of Zika. Between September and October 2021, we interviewed, for an average of 50 minutes, mothers and family members, scientists, health and education professionals, focusing on prevention, care and scientific production. The debates helped to carry out the questions of this study.

We analyzed the narratives of articles, documents and interviews in dialogue with the theories and practices of Social Studies of Science. We present evidence that supports the discussions, although they are not the focus of supporting the argument. We characterize the study as a theoretical essay about the games of forces that involve the relations of technical-scientific production, their agencies and social implications (Castiel, 2021). We operate in a way that provokes reflection, raising tensions, possibilities and barriers to vaccine development. We emphasize what is noticeable in the speeches; that which is absent but still manifest; and what is absent and is not or cannot be uttered (Law, 2004).

The project and research followed Resolutions CNS/MS nº 510, of April 7, 2016, and CNS/MS nº 466, of December 12, 2012. The research was approved by the Research Ethics Committee (CEP) of the School National Public Health Sergio Arouca.

Regulations and agencies

WHO's consultation with experts to prepare the TPP and regulate the development of the vaccine, in 2016, took place at a time of possible territorial expansion of Zika, during ESPII. Certain aspects about the link between SCVZ and the virus had already been highlighted; however, the lack of knowledge about its nature and causes generated controversies, contributing to a diversity of acceptable interpretations of the facts. The processes involved institutional actors, through the performances of their experts. Most of the organizations that participated in the initial movements came from the United States. Other countries were represented: Brazil, United Kingdom, Germany, France, Japan, South Africa, Austria, Mexico and India (WHO, 2016a; 2016b).

Uncertainties put pressure on the recently started biotechnological "race" which, from February to June 2016, had 30 vaccines registered in the pre-clinical phase (WHO, 2016a). As this was a health emergency, it was possible to activate the "Emergency Use Assessment and Listing Procedure" for candidate vaccines (EUAL). The device recommended safety, quality and efficacy guidelines, helping to determine the "acceptability of the use of a specific vaccine under investigation in the context of a" ESPII (WHO, 2015, p. 1). It was aimed at vaccine manufacturers, outlining recommendations for national regulatory authorities and United Nations

purchasing agencies (*Ibid.*). An important factor, as the lists of professionals invited to participate in the construction of regulation and the TPP (WHO, 2016a; 2016b) showed the direct involvement of countries and companies recognized for their biotechnological production capacity – actors who also had a particular interest in mitigating that and other crises.

The WHO consultation report on the regulation of candidate products was published in 2016 and explained that the content did not “necessarily represent the decisions or declared policy of the World Health Organization” (WHO, 2016a, p. 7). However, the list of participants showed that the WHO itself and the United Nations Children’s Fund were the second largest representation at that meeting (*Ibid.*). The TPP was created at the same time and contained product development considerations, associated with ideal and minimum vaccine characteristics (WHO, 2016b). The gap between ideal and minimum attributes creates a space for acceptance of candidates in national regulatory processes.

After defining the emergency scenario, the TPP’s first agency was the target population standard: women of childbearing age, including adolescent and pre-adolescent girls nine years of age or older, as well as men in the same age range. However, the pragmatism demanded by a health emergency, associated with the cost-benefit logic, restricted it to women between 15 and 49 years old. The construction of the standard assumed that mass female vaccination could promote the mitigation of sexual transmission of Zika from infected men (WHO, 2016b).

Restricting the public had predictable implications. Safety/reactogenicity regulations prioritized non-replicating viral platforms, such as inactivated vaccines, those based on subunits or those that use alum adjuvant. From a risk-benefit perspective, plausible safety information constituted criteria for minimum emergency approval of live viral vaccine platforms, single-cycle replication vectors or using adjuvants other than alum, increasing the space for acceptance of certain products. In this sense, technologies that had already been developed for other vaccines were declared favored (*Ibid.*).

The TPP determined that there were no contraindications for pregnant or lactating women and that data on the absence of teratogenicity needed to be produced before authorization for use in outbreaks. However, exceptional use among this public was accepted, according to the emergency scenario – the benefit of vaccination would outweigh the potential risks of the product (*Ibid.*).

The regulatory narrative highlighted the need for ethical considerations about the risk *versus* benefit of vaccinating these women, in circumstances of accelerating target population analyses, in territories with scarce resources. However, it linked the emergency acceptance process to special post-licensing studies, stating that there were issues that could only be assessed after authorization to use the product (WHO, 2016a).

The acceptance space for many products decreased with other ideal arrangements. The estimated outcome was to prevent ZIKV-linked clinical disease of any severity (WHO, 2016b). The standards of excellence for efficacy provided for virological confirmation of disease prevention in at least 80% of the tested population (WHO, 2016b). It is worth remembering that effectiveness is the ability to promote expected experimental results, under controlled conditions and with predefined criteria (Marinho; Façanha, 2001). The minimum acceptance of additional efficacy measures, such as serological markers of protection, depended on studies in animal models or prospective studies. However, there was still no possibility of standardizing these other measures, as they remained undefined: the link between viremia levels and fetal pathology; the mechanisms by which asymptomatic Zika leads to SCVZ; the most suitable animal models for research; the accuracy of diagnostic methods (WHO, 2016b). Uncertainties persisted regarding the assessment of clinical disease prevention as a marker of outcome. However, the logic of the emergency established in the EUAL reaffirmed its prioritization as a goal of vaccination programs, in times of outbreaks (WHO, 2015).

The agency that increased the acceptance space for certain products in relation to expiration dates restricted the definition of an ideal vaccine platform. The TPP determined a minimum shelf life of 6 months, in storage at -20°C , and evidence of stability for at least 6 hours, at temperatures of $2-8^{\circ}\text{C}$. At that time, DNA and RNA platforms were stored at -20°C and vaccines using alum adjuvant cannot withstand this temperature (WHO, 2016b). The document also recommended that the developed vaccine could be administered in a preparation that included other already licensed immunizers, an important measure in routine vaccination strategies, especially in endemic scenarios. However, there was leniency with the use of a monovalent product during an emergency (WHO, 2016b).

The consonances, dissonances and interests of the negotiations that constituted the regulatory processes and the TPP created spaces for the acceptance of products

suitable for use in emergencies. A space that tends to increase with the expansion of the frontiers for admitting new characteristics, and to decrease, as it is reduced to the ideal. It may also vary, inversely, with the rigor of regulation in each country of submission. A greater acceptance space makes the development of certain vaccines more feasible. The shorter interval, in addition to reducing this universe of possibilities, may even make its approval unfeasible (Lacey, 2014). It remains to be seen what the implications of these designs are for the development of vaccine products.

Expert reviews

Clinical research for the development of bioproducts is organized into stages, concerned with safety and efficacy. In the pre-clinical stage, testing on animals takes place. In phase I, products are tested on a few humans and, if the results are not extremely harmful, the study can continue. Phase II trials are controlled and randomized, including about a hundred people. In them, the product is applied to one group and another group receives a placebo. Although concern about harmful effects continues, attention is focused on the benefits. Phase III includes thousands of people and only happens when the results obtained are promising. It can be carried out in many countries and last several years. In general, for regulatory agencies to approve a candidate for clinical use, there must be several phase III trials showing good efficacy. Phase IV studies take place after formal approval from regulatory agencies (Stegenga, 2018).

In traditional vaccine development, a study takes approximately three years to complete phase I, five to complete phase II and approximately 10 years until approval by regulatory agencies (*Ibid.*). During the Covid-19 health emergency, to speed up the process, the phases were performed simultaneously. Around two years into the pandemic, some studies went from phase III to phase IV (PAHO, 2020).

More than five years have passed since the start of the Zika biotechnological “race”, and no study has reached phase III (Castanha; Marques, 2020), which raises doubts about the future of research. For Callon, Lascoumes and Barthe (2001), the processes that involve technical-scientific production do not necessarily engender certainties; on the contrary, they convey meanings of not knowing. From this perspective, the presentation of the articles’ narratives seeks to highlight problems and challenges interspersed along this path.

Poland *et al.* (2018) revealed the uncertainty of the occurrence of another SCVZ outbreak. They stated that the diverse set of animal hosts, in which antibodies against ZIKV were found, could contribute to the emergence of recombinant strains and facilitate viral spread. The drop in the number of cases of the syndrome, which began in 2017, provided a counterpoint to the authors' concerns and caused efforts to develop vaccines to decline (Castanha; Marques, 2020). Chestnut and Marques; and Pielnaaa *et al.* (2020) returned to the issue: new cases of the syndrome continued to occur; ZIKV had become endemic in some countries and could re-emerge in places with previous transmission; and a major Zika epidemic was expected in the next 10 to 15 years.

The doubt about new SCVZ epidemics coexists with the challenge highlighted by Castanha and Marques (2020): (a) develop vaccine products that are ready to activate phase III trials and, simultaneously, (b) promote the acceleration of industrial production of these vaccines, during an epidemic. The first part touches on estimating the effectiveness of the vaccine. Britto *et al.* (2018) explained that measuring effectiveness would be difficult in the Latin American scenario, due to the decline in the incidence of clinical disease, given the population's wide exposure to ZIKV. In that context, the impact of the vaccine would also be difficult to determine (*Ibid.*). The lack of specificity in the clinical manifestations of the disease and the scarcity of diagnostic modalities suitable for ZIKV would make the process doubtful. The calculation would require measuring the incidence rate of primary and secondary outcomes: clinically apparent or laboratory-confirmed ZIKV infection; and herd immunity or disease complications, respectively. Furthermore, although the prevention of SCVZ is relevant to public health and was the ideal outcome regulated by the TPP, Wilder-Smith *et al.* (2018) considered the parameter unfeasible, due to: restriction to the female target audience, diversity of clinical manifestations of the syndrome, demand for large sample sizes and ethical issues.

The second part of the challenge, accelerating the production of candidate vaccines in an epidemic context, is also related to serological tests. Zhang *et al.* (2021) showed that the specificity and sensitivity of these devices is essential to meet the demands in endemic areas, warning of the difficulty posed by low viral loads and the cross-reactivity of Zika, mainly with the dengue virus (DENV). This is because serological tests are not specific enough to guarantee the differentiation of

diseases. These factors weaken the detection of ZIKV and reveal uncertainty about the safety of vaccines under development (*Ibid.*).

For some authors (Castanha; Marques, 2020; Britto *et al.*, 2018; Pielnaaa *et al.*, 2020; Poland *et al.*, 2018), there was no conviction whether the Zika vaccine would lead to the so-called “antibody-dependent intensification” (ADI), resulting from cross-reactivity between ZIKV and DENV, in endemic areas. ADI is an immunological event characterized by an increase in the harmful effects of dengue in individuals who have not fully developed protection against the virus. The chance of this happening would occur in the case of a new infection or vaccination (Castanha; Marques, 2020). Such uncertainty raises the challenge of knowing how the immunity induced by candidate vaccines can affect other flavivirus epidemics and *vice versa* (*Ibid.*) – remembering that the Zika, dengue and yellow fever viruses belong to the flavivirus genus. New issues for vaccine development that require time and investment to resolve.

At this point, Poland, Ovsyannikova and Kennedy (2019) reinforced the need for clarification about the pathological mechanisms that cause neurological changes, such as Guillain-Barré syndrome and SCVZ. As it is a direct result of a viral infection, it would have major implications for studies, as it would reduce the possibilities of choosing certain platforms (Wilder-Smith *et al.*, 2018). Mainly because the development of animal models required additional validation to verify: infection, disease, maternal-fetal transmission and fetal ZIKV infection (*Ibid.*).

According to Castanha and Marques (2020), in pre-clinical and clinical studies, numerous platforms were developed and tested, most of them without published results. Chart 1 shows the candidates in clinical trials, published by the authors. In May 2022, the information was updated, with data available on the American virtual platform of the National Library of Medicine (NIH). Most of these studies were carried out in non-endemic areas of the United States and Europe.

Chart 1. Zika vaccine candidates in clinical trials

Platform	Sponsors	Research	Phase	State
Inactivated virus	National Institute of Allergy and Infectious Diseases (NIAID); Walter Reed Army Institute of Research (WRAIR)	NCT02937233	I	Complete
	NIAID	NCT02952833	I	Complete
	NIAID	NCT02963909	I	Complete
	NIAID	NCT03008122	I	Complete
	Takeda	NCT03343626	I	Complete
	Valneva Austria GmbH; Emergent BioSolutions	NCT03425149	I	Complete
	Bharat Biotech International Limited	NCT04478656	I	Complete
Genetic (DNA)	NIAID; National Institutes of Health Clinical Center (CC)	NCT02996461	I	Complete
		NCT02840487	I	Complete
	NIAID	NCT03110770	II	Complete
	GeneOne Life Science, Inc.; Inovio Pharmaceuticals	NCT02809443	I	Complete
		NCT02887482	I	Complete
Genetic (RNA)	ModernaTX, Inc., Biomedical Advanced Research and Development Authority	NCT04064905	I	Complete
	ModernaTX, Inc.; Biomedical Advanced Research and Development Authority	NCT03014089	I	Complete
	ModernaTX, Inc.,	NCT04917861	II	Recruiting
Live attenuated virus	NIAID	NCT03611946	I	Active/not recruiting

continue...

Platform	Sponsors	Research	Phase	State
Viral vector	Themis Bioscience GmbH	NCT04033068	I	Complete
		NCT02996890	I	Complete
	University of Oxford	NCT04015648	I	Active/not recruiting
		NCT04440774	I	Complete
	Janssen Vaccines and Prevention B.V.	NCT03356561	I	Complete

Source: Castanha & Marques (2020); NIH (2022).

For Castanha and Marques (*Ibid.*), the vaccine platforms studied have advantages and disadvantages (Chart 2). Poland, Ovsyannikova and Kennedy (2019) listed the predicates of an ideal vaccine: requiring a single dose; can be administered to anyone; result in durable immunity; prevent clinically significant outcomes of infection; be safe and highly effective; and does not require a cold chain or complex logistics to store and manage. The different modes of Zika transmission, and the different existing vaccination scenarios, may impose different vaccine proposals for specific target audiences (*Ibid.*). Therefore, decisions about vaccine development must be made considering its use in vaccination policies: application scenarios; possible target audiences and priority age groups; and adverse effects to be avoided (*Ibid.*) – which reveals the importance of investments in vaccine research that comprise multiple vaccination strategies, sensitive to the context (Lacey, 2014).

Chart 2. Vaccine platforms

Platforms	Classical designs		New technologies	
	Inactivated virus (IV)	Live attenuated (LA)	Viral vector	Genetic (DNA and RNA) (G)
Advantages	Safer than LA	Generally safe	Generally safe	As vacinas de mRNA não se integram no genoma, sendo consideradas geralmente seguras
	Economical	Economical		
	Studies show induction of an empirical immune response greater than G	They generally induce a more potent immune response than IV	They induce potente imune responses	They can induce potente imune responses, but studies showed empirical immunogenicity lower than IV
		They can produce long-term protection. Many vaccines require only a single dose with long-lasting immunity	No adjuvants required	No adjuvants required
	They offer a greater chance of use by priority groups such as pregnant women		They offer a greater chance of use by priority groups such as pregnant women	
		Production outputs can be increased with high yields of attenuated viruses, which can benefit mass public health campaigns	Vaccines that are easy to update in the case of a viral mutation	Theoretical advantage of rapid development and production and rapid adaptation to new and emerging infectious agents

continue...

Platforms	Classical designs		New technologies	
	Inactivated virus (IV)	Live attenuated (LA)	Viral vector	Genetic (DNA and RNA) (G)
Disadvantages			They are not economical	They are not economical
	Inactivation may alter its immunogenicity	Not recommended for individuals with a weakened immune system and pregnant women	May induce anti-vector immunity, potentially reducing the immunogenicity of subsequent inoculations using the same viral vector	Limited efficiency of cellular uptake of nucleic acids
	They generally require the use of adjuvants to stimulate robust immune responses and may require multiple doses		May require multiple doses	There may be requirements for new delivery systems or immunization routes that require staff training. May require multiple doses
		The association of neurological complications with a direct viral attack may affect the design of neurovirulence tests		DNA vaccines pose a hypothetical risk of integration into the genome
				There is less experience than VA and VI with commercial-scale production Há experiência menor que LA e IV com produção em escala comercial

Source: WHO (2016a); Garg, Mehmetoglu-Gurbuz & Joshi (2018); Fiocruz (2021); Castanha & Marques (2020).

Other technical-social problems are relevant in terms of the ethical dimension. Poland *et al.* (2018) revealed barriers to prioritizing pregnant women and women of childbearing age as the ideal target audience: lack of ethical consensus, gaps in knowledge about the pathogenesis of Zika during pregnancy, lack of standardization of results, difficulties in evaluating safety in research. Poland, Ovsyannikova and Kennedy (2019) argued about the difficulty of including certain populations in clinical trials, such as: pregnant women, children and others.

Barret (2018a) showed that the durability of immunity induced by vaccine candidates had not yet been answered, affecting the number of doses needed to avoid possible outcomes. A problem with important implications, given the challenge posed by Poland, Ovsyannikova and Kennedy (2019): the supply of vaccines to poor countries, given the cost history of newer platforms, and the issues involving prioritization of supply, in contexts delimitation. From this perspective, Castanha and Marques (2020) raised the challenge of maintaining public and private financing to support phase III research, and developing business models to attract investments that enable the maintenance of clinical studies and sustained production of vaccines. Both stress the possibility of a new outbreak of SCVZ and the time needed to resolve complex development problems.

The suggestion made by Barrett (2018b) regarding financing – reducing phase III costs, keeping trials and study sites pre-designed, so that they can be resumed during new outbreaks – clashes with the current scenario of vaccine development. Furthermore, what would be the implications for poor countries and populations, in the event of a new SCVZ epidemic and the demand to accelerate the industrial production of vaccines?

Current implications of the zika epidemic in Brazil

We carried out interviews with a group of people involved with the research and the public cause: 2 representatives of associations of mothers and families; 2 public health professionals and 1 education professional; 2 vaccinologists. A mix of technical-scientific knowledge with values and knowledge from life experiences. Affects managed through questioning, consensus and contradictions.

The first consensus is to prioritize the protection of future mothers. Among those who work in public health, there is also concern about the impact of SCVZ

outbreaks on the country's health system and economy. These meanings engender a consistent guideline that the main role of the vaccine is the prevention of new cases of the syndrome. Its development, according to a vaccinologist, would bring the "benefit of leaving pregnant women at ease that they could get pregnant, without running the risk of becoming infected with Zika and affecting their children".

There is dissonance about the time needed to develop the vaccine. The urgency in preparation is evident in the mothers' speeches: "the vaccine could have been launched a long time ago, but, unfortunately, we [...] only hear that there is a study that has a vaccine project being developed, but in the population it is still did not arrive". For vaccinologists, the development and production process are a temporal challenge, as this cycle is complex and time-consuming. However, both groups agree that the country should not wait for a new outbreak to be "prepared".

According to experts, it is a financial investment and political effort. In the first case, funding for research and production industrial complexes. Political will would translate into demand for the vaccine through the National Immunization Program. Once various age groups were addressed, the circulation of the virus would decrease, affecting the incidence of SCVZ. According to one of these narratives: "if you think about serious diseases [...], that you have production of strategic vaccines, I think that, at the very least, Zika would be a vaccine [...] considered a strategic vaccine".

This scenario creates challenges for the research process and for the institution of vaccination. According to vaccinologists, the first is to assess whether the candidate product is really effective. To demonstrate that the virus is not circulating in a vaccinated population, compared to an unvaccinated one, it is essential to differentiate cases of Zika from other diseases transmitted by the *Aedes* mosquito. The accuracy of serological diagnostic methods and the fact that most cases are asymptomatic impose difficulties and can prolong the time of studies.

The next one is reaching phase III of a seasonal disease. The issue is aggravated by the demand for volunteers for this stage, which increases research costs, especially with the reduction in the incidence of the disease. Another challenge is to define reliable serological markers of protection, or correlates of protection, to assess efficacy. The question involves the amount of antibodies needed to generate protection and the time they would remain in the vaccinated individual. Depending on the platform developed, immunity can be more robust and long-lasting (Table 2). According

to an expert, the target audience determined by the TPP brings to research the problem of determining the vaccination cycle of a woman of childbearing age, to keep her protected against SCVZ. The interviewee also argues that it would be ideal for vaccination processes to develop different platforms.

Questions about efficacy and safety give rise to the fourth challenge: defining animal models for clinical testing. As ZIKV only makes humans sick, measurements of other living beings are impaired. The next challenge is to create a standard for comparison between studies, as different institutions and companies have developed specific ways of evaluating their results.

The sixth challenge is to develop a multivalent vaccine for dengue, zika and chikungunya – strategic for public health, as it would simultaneously solve important problems in areas endemic for diseases transmitted by mosquitoes. The last is to maintain research in the scenario of project cancellation, due to the end of the health emergency and a rationality focused on the market. In this sense, the decrease in interest in the disease, with repercussions for care and research, and the uncertainty about their stay in the country are narrative intercessions of the group.

Respondents agree that zika control goes beyond the limits of biotechnological devices. In the speech of the association representatives, the challenges of implementing basic rights are part of the process, mainly because children are growing up and demanding more from the State apparatus. They report facing barriers to accessing public transport, leisure, the care network, accessibility – issues that include social protection and the inclusion of people with disabilities in society.

A common concern is the uncertainty of an imminent epidemic, given the lack of solutions to the problem of *Aedes* proliferation. The fundamental importance of basic sanitation policies for preventing mosquito-borne diseases is a consensus. A vaccinologist highlighted the persistence of the problem in Brazil for more than 30 years and his lack of belief in the existence of a single and efficient measure to eliminate it.

The convergence of experts on vaccine development and vaccination as societal projects has put public institutes in the spotlight. According to a vaccinologist, these institutions play a fundamental role, as zika can be considered a neglected disease, as it currently attracts little interest in other institutions in producing its vaccine.

An ontological policy

Data from the epidemiological update on zika, published in February 2022, once again brought global uncertainties to light. Of the 6 demarcated regions, 5 showed evidence of autochthonous vector transmission of ZIKV, in 89 countries and territories. The Americas continued to report the most new cases and India had faced epidemics in 2019 and 2021 (WHO, 2022).

The sanction of the emergency scenario by the WHO involved negotiations and technical-scientific exercises that involved framing problems, designing paths and modeling lives in action. Weavings that Mol (1999) and Law (2004) call ontological politics. Practices guided by scientific evidence, capable of avoiding primary rejections of their ideas and methods, thus capable of shaping existences (Mol, 1999).

The standards resulting from the TPP and technical regulation focused efforts on mitigating the occurrence of SCVZ. However, distinct purposes and tactics can be highlighted. The experience of vaccination against rubella, since the introduction of the live attenuated virus vaccine in 1969, helps to illuminate other dimensions of the issue. Hinman (2007), in an analysis of American and English cases, concluded that the ideal strategy to maximize the prevention of congenital rubella syndrome (CRS) would be to initially prioritize the vaccination of women of reproductive age and then interrupt the circulation of rubella for vaccinating children.

In 2015, Brazil received the Rubella Elimination Certificate, a territory free from SRC. The controls took place due to the successive combination of vaccination strategies (mass, campaigns and routine), with different purposes and coverage of different target audiences: male/female, children/adolescents and adults (Fiocruz, 2015). A different scenario from that designed for zika, in which the ideal prevention of SCVZ would be the responsibility of the female population, between 15 and 49 years old.

Considering the challenges that permeate the research and production processes of a vaccine, the restriction of the target audience to women of reproductive age presents fragile support, in addition to implying ethical aspects that require further discussion. The exclusive adoption of decontextualizing and market-oriented strategies ignores: the heterogeneity of demand; under-investigation of the effects on the lives of the target population; the failure to produce long-term responses to socioeconomic risks; the dubious scope, neutrality and impartiality of research (Lacey, 2014).

The inconsistencies are relativized in view of the vaccine's targeting of an audience restricted in number and gender. In this power game, making women exclusively responsible for preventing SCVZ leads to hypervulnerability, which occurred in the first epidemic of the syndrome in Brazil. The affected population – made up mostly of young, black, northeastern people, living in a situation of lack of sanitation – was recruited for the “combat mosquito” campaign, which stated microcephaly as a result of a lack of self-protection (Lopes; Reis-Castro, 2019). By making them visible, we argue that intersections of race and social class are fundamental for analyzing the consequences of the application of knowledge production. In this sense, holding women responsible seems to cover up a much greater damage: the disability produced in the wake of the congenital syndrome and its relationship with social lack of protection. This calls on us to reflect on the way in which racism, ableism and CIS heterosexism are made invisible by scientific and technological enterprises, being reiterated by these same buildings as logics and guidelines for social ordering.

We also wonder about the implications for vulnerable populations and territories of the modeling of life promoted by the WHO in major emergencies. Above all because its regulations highlight the existential threat of the epidemic, hiding the necessary political action to promote social protection. Thus, in addition to becoming justified targets of data collection, these actors face much greater barriers to the production of rights.

Another notable device for building vaccination strategies, which led to the control of rubella and CRS, was epidemiological surveillance. WHO (2022) highlighted the challenge of Zika surveillance, even in places with good laboratory capacity, due to the restricted availability of diagnostic tests and the impairment of ZIKV detection capacity in several countries, in the scenario of the COVID-19 pandemic. (*Ibid.*). Such perspectives leave doubts about a greater presence of Zika in the world, creating barriers to the regular production of public health policies, surveillance and prevention measures, including the maintenance of vaccine studies (Poland; Ovsyannikova; Kennedy, 2019).

Thus, we argue that the agency of the TPP reinforces research practices that ignore the heterogeneity of demand contexts, making invisible the need to develop products suitable for vaccinations in endemic conditions. Furthermore, it increases the space for acceptance of certain platforms in national regulatory processes, an aspect of fundamental interest to biotechnology research institutions, which

were even part of the groups brought together by the WHO (2016a; 2016b). The maintenance assumption for many of the studies is the profitability of the vaccine – which makes it part of a profitable business model. Design constituted from the perspective of market value and technological progress, producing research practices that are not involved with the dimensions of life events and the uncertainties arising from techno-scientific innovations (Lacey, 2014).

Thus, the TPP was created to contain the likelihood of potential harm linked to the production of a new vaccine, not to raise doubts about the process (WHO, 2016b). We emphasize that only one clinical trial in Chart 1 completed phase II: a ZIKV DNA vaccine, developed by the National Institute of Allergy and Infectious Diseases (NIAID) in the United States, administered by an innovative needle-free device. Although there are doubts about the incorporation of vaccine genetic material into the human genome, the platform has two expectations: rapid adaptation to new and emerging infectious agents; ready development and production. As a possibility, the product becomes more attractive, even if the vaccine will require multiple doses and the application device, staff training.

Resolving concerns about potential damage aims to increase the space for acceptance of products in certain markets and is linked to the possibility of mobilizing the EUAL. According to the document, in the context of emergency, “the community may be more willing to tolerate less certainty about the efficacy and safety of products, given the morbidity and/or mortality of the disease and the deficiency of treatment and/or prevention options” (WHO, 2015). This rationality seems to emphasize that “the legal responsibility to compensate the harm caused by the use of an innovation will generally be considered satisfied, as long as the innovation was introduced in accordance with the decisions of the commissions” (Lacey, 2014, p. 686). Developments with implications for scientific institutions and their professionals: prioritization of objects and promotions, ways of evaluating results and productions, values defended by both. Consequences that produce divergences between commercial and scientific interests (*Ibid.*), especially in contexts of greater demand, such as health emergencies.

According to Lacey (*Ibid.*), the search for technoscientific innovations occurs due to the expectation of their benefits, on the part of certain groups. From this perspective, the experience of the COVID-19 pandemic exemplifies even greater effects. For Yamey (2021), by February 2021, rich nations, which represented 16%

of the world's population, had purchased more than half of the vaccine doses on the market. A recurring practice, as it had happened during the 2009 swine flu, and produced global inequalities. This occurred because these nations had the capital to purchase products directly from vaccine companies, to the detriment of committing to the collective purchasing consortium (COVAX), which guaranteed greater equality for other poor countries.

Final considerations

As the WHO defined the TPP for emergency use only, it determined the social universe in which it must operate, its ontological policy and a specific socio-technical project. It is a project that stands out for focusing on mitigating the occurrence of SCVZ, implying: exposure, accountability and blaming of women for prevention; institution of certain vaccination strategies; making other possible scenarios invisible; greater space for acceptance of certain platforms; expansion of global inequalities.

Addressing the barriers listed for the development of the Zika vaccine requires a reflection on the organization's ontological policy, so that it engenders better adaptation to the multiplicity of global scenarios: diversification of control options; ways of distinguishing less vulnerable populations; contextual adequacy of ways of coping; review of models of institutional policies and society participation.

The rubella experience showed the possibility of different vaccination strategies, carried out with classic technologies, without the idealization of vaccine scenarios. Furthermore, control efforts were undertaken to eliminate both the disease and SCR. Because it is transmitted in different ways, mainly by mosquitoes, Zika prevention involves more than vaccines. However, maximizing SCVZ control necessarily includes its development and vaccination policies. According to Fernandes *et al.* (2012, p. 12), "it is not vaccines that save lives, but vaccination". In this sense, we consider that the ontological policy established by the WHO engendered a powerful emergency rationality that distinguished the vaccine from the social need for vaccination, pushing the latter towards invisibility.¹

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Note

¹ L. N. da Silva and F. de S. Dias: conception and design, article writing, critical review, final approval of the version to be published.

Resumo

Vacina contra zika: desenvolvimento, agenciamentos e controvérsias sociotécnicas

O ensaio teórico discute as controvérsias sobre o desenvolvimento da vacina contra a zika, evidenciando as negociações que envolvem as escolhas técnico-científicas e os efeitos da definição do “perfil do produto alvo da vacina” (TPP) para uso somente no cenário emergencial. São propostas três perspectivas de análise em diálogo com os Estudos Sociais da Ciência: os fluxos de estabelecimento de normativas pela Organização Mundial da Saúde (OMS), as narrativas publicadas em revistas especializadas e de um grupo de entrevistados. Concluímos que os termos de definição do TPP ajudaram a constituir a política ontológica da OMS, implicando: exposição, responsabilização e culpabilização de mulheres pela prevenção da síndrome congênita da zika; instituição de certas estratégias de vacinação; invisibilização de outros cenários possíveis; maior espaço de aceitação de determinadas plataformas; ampliação das desigualdades globais. Tal política ontológica engendrou uma potente racionalidade emergencial que distinguiu a vacina da necessidade social da vacinação, empurrando a última para a invisibilidade.

► **Palavras-chave:** Zika vírus. Síndrome congênita de zika. Vacinas. Vacinação. Estratégias de saúde globais.

