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Article abstract

Paradoxically, the absence of HIV vaccine has been very structuring for global vaccine logics, and, more broadly, “global health” research. HIV vaccine research has oscillated between optimism and pessimism and has been central to the humanist justification for research in the South. From the attempt by the World Health Organization’s Vaccine Development Unit (VAD) on AIDS to become the centre of an “international” coordination effort to the diplomatic work involved with Thailand’s HIV research, I describe political contexts, and postcolonial power relations connected to HIV vaccine research. I argue that the failure of “international” coordination has paved the way for another politicization of global HIV vaccine research which led to a shift away from inter-state diplomacy to a “stateless” situation where the global vaccine logics contribute to the development of an experimental regime that relies on the capture of public resources and the availability of depoliticized biological subjects for the purposes of private valorization.

Politics of HIV Vaccine Research from International to Global Health

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Abstract: Paradoxically, the absence of HIV vaccine has been very structuring for global vaccine logics, and, more broadly, "global health" research. HIV vaccine research has oscillated between optimism and pessimism and has been central to the humanist justification for research in the South. From the attempt by the World Health Organization's Vaccine Development Unit (VAD) on AIDS to become the centre of an "international" coordination effort to the diplomatic work involved with Thailand's HIV research, I describe political contexts, and postcolonial power relations connected to HIV vaccine research. I argue that the failure of "international" coordination has paved the way for another politicization of global HIV vaccine research which led to a shift away from inter-state diplomacy to a "stateless" situation where the global vaccine logics contribute to the development of an experimental regime that relies on the capture of public resources and the availability of depoliticized biological subjects for the purposes of private valorization.

Keywords: HIV; Vaccine; Global health; World Health Organization; Aids; Research

Résumé : Paradoxalement, l'absence d'un vaccin contre le VIH a été très structurante pour les logiques vaccinales mondiales et la recherche sur la « santé mondiale », plus largement. La recherche sur un vaccin contre le VIH a oscillé entre optimisme et pessimisme, et se place au centre de la justification humaniste de la recherche dans les pays du Sud. Depuis la tentative de l'Unité de développement des vaccins (VAD) contre le sida de l'Organisation mondiale de la santé de devenir le centre d'un effort de coordination « international », jusqu'au travail diplomatique lié à la recherche sur le VIH en Thaïlande, je décris les contextes politiques et les relations de pouvoir postcoloniales liés à la recherche sur un vaccin contre le VIH. Je soutiens que l'échec de la coordination « internationale » a ouvert la voie à une nouvelle politisation de la

recherche mondiale sur le vaccin contre le VIH, qui a conduit à l'abandon de la diplomatie inter-étatique au profit d'une situation « sans État », dans laquelle les logiques vaccinales mondiales contribuent au développement d'un régime expérimental. Celui-ci repose sur la captation des ressources publiques et la disponibilité de sujets biologiques dépolitisés à des fins de valorisation privée.

Mots-clés : VIH ; vaccin ; santé globale ; Organisation mondiale de la santé ; aides ; recherche

Introduction

2020 was a pivotal year for global vaccines. The announcement of the COVID-19 pandemic sounded the alarm for the unprecedented biotechnological race for SARS-CoV-2 vaccines. For HIV vaccines, however, negative results released in February 2020, from what had been a promising longitudinal HIV vaccine trial, HVTN702, buried hopes for the proper development of a viable HIV vaccine. These hopes had been kept alive by clinical trials underway since the 1990s under the remit of the World Health Organization's (WHO) Vaccine Development Unit (VAD)[1] on AIDS, which I explore in this article. Despite this failure, the COVID19 vaccine fueled a new optimism towards the hope that HIV might finally be defeated using this mRNA technology. The extent to which any vaccine as a technology mobilizes past, present and future logics to become the object of research is indeed what Moulin (1996) describes as "an adventure," linked to the social, political and economic contexts that determine their stakes. These vaccine research dynamics reveal much about the historical and political context. In this article, I explore the WHO's coordination of HIV vaccine development in the 1990s and suggest that the current global health configuration of HIV vaccine research owes much to this history of HIV vaccine coordination, to how it was constructed materially, politically and ethically.

The HIV pandemic has played a central role in the advancement of medical biotechnologies that have improved the lives of those living with HIV and served as a marker in the context of the organization of global biotech development over the past 40 years. The development of antiretroviral drugs (ARVs) has been described as central in conceptualizing the new regime of "global health" (Packard 2016). Yet HIV research has largely failed to date in the promise of developing a preventative vaccine that could end the pandemic. Indeed, some see the advent of ARVs as contributing to the difficulty in advancing further need for an HIV vaccine since "highly effective" ARVs have made "partially

effective" vaccines less attractive and difficult to accept, from a public health perspective. The legacy of HIV vaccine discovery, however, even though it failed, is important not only in terms of its contribution to broader research on immunity and other diseases, but also in its advancement of institutional structures and programs. Indeed, HIV vaccine research cannot be reduced to an alleged graveyard of unsuccessful clinical trials. Too little research has documented the critical importance of failure and its productive effects in HIV research (Kingori and Sariola 2015). I suggest that the successes and failures constructed through the international organization of HIV vaccine research are the bearers of what would become a global vaccine logic.

HIV Vaccine Between International and Global Health Logics

Between 1990 and 1995, a specific Vaccine Development Unit on AIDS was set up within the WHO and its Global Program on AIDS (GPA) in a particular context. After establishing the Global Program on AIDS in 1986, Jonathan Mann resigned in 1990. The new Director General, Hiroshi Nakajima, who had limited Mann's budget and restricted his programs, introduced the AIDS Vaccine Development Unit to take control of the AIDS strategy and reposition the WHO at the centre of international research and governance networks. As a cornerstone of the globalization of HIV vaccine research, VAD contributed to the introduction of clinical trials in developing countries, thereby representing an important moment in the transition from "international" to "global" health, that is to say, from an inter-state governance of health to a global government of health, oriented towards global health problems or technologies offering solutions to these complex problems. In vaccine logics in general, and the HIV field in particular, this "global health" reconfiguration would later be exemplified by the "Global HIV Vaccine Enterprise" partnership established by the Bill and Melinda Gates Foundation in 2003, which owes much to the international attempts of the WHO, as I will describe below.

Innovative technical objects, such as HIV antiretroviral drugs, are presented as operators in the shift to global health (Packard 2016), as well as new regimes of triage and experimentality (Nguyen 2009). In this article, I pursue an alternative hypothesis, namely that the absence of an object, the search for a vaccine and its expectations, were the precipitating factors in the new configurations of health and ways of organizing research outside the large laboratories of the global North. Indeed, the absence of a vaccine seemed to be at first a failure of the WHO's VAD and a demonstration of the limits of its international coordination:

limited funding, partnerships that did not directly include all the stakeholders (in particular the pharmaceutical industry), and cumbersome bureaucracy, for example. The history, however, also shows the importance of these attempts in restructuring what would become global health through: a) the development of ethical reflections on the "necessity" of conducting clinical research in the South, b) practices of neutralization or redefinition of political and geostrategic interests, and c) linking of experts and expertise beyond national borders. One argument is that this international coordination may have represented a form of politicization of the epidemic and its research at a time when vaccine research was being "projectified" (Meinert and Whyte 2014), particularly under the impetus of privatization and private actors such as US biotech start-ups. On the other hand, we will see how this initiative was able to "depoliticize" HIV research, that is, to invisibilize the power relations that were constitutive of it, by contributing to the development of a new humanistic model favouring clinical trial experimentation in developing countries for humanitarian purposes based on a form of diplomatic work.

Investigating the Remains of International Vaccine Research

To better describe and understand the logics of HIV vaccine research, I explored with Muriel Mac-Seing the archives of a specific WHO program, the VAD, which remains largely undocumented in the vaccine and social science literatures. The archives are available upon request from WHO, chronicling the activities at the VAD that constructed an infrastructure of clinical trials. In total, this corpus represents 17,000 pages, revealing the rationale, the political stakes of the research, and the links between international organizations and local governments at the sites where the vaccine trials were to be deployed. These records reflect the work of the VAD in strengthening clinical research infrastructure and promoting research on virus characterization in the different contexts where the clinical trial sites were being prepared.

Thailand, selected by the VAD as a site to support its clinical research infrastructure, is particularly worthy of a case study to investigate global vaccine logics. Indeed, the Thai case, as the largest HIV vaccine trial in history, has often been taken as an example throughout the numerous Phase 1, 2 and 3 clinical trials conducted there. The RV 144 trial, known as the "Thai trial," is considered a milestone in vaccine research by reinvigorating hope from 2006 through to the negative results in 2020 from the South African HTVN072 trial. By exploring the logic and limits within which they were deployed, my research sheds light on the conditions of possibility created by these Thai trials. I augment these

archives with literature from the scientific clinical trials as well as the grey literature that discusses these trials. Little social science has been conducted on these clinical trials (Fordham 2014), or was subsumed in the epidemiological perspectives, rendering a historical anthropology of these experiments all the more relevant. Finally, I try, in this paper, to locate these archives and the remains of the international coordination of vaccine research they account for in dialogue with the emergence in the 1990s and beginning of the 2000s of public-private partnerships to coordinate HIV vaccine research through the Rockefeller and Gates' foundations. Central characters who were involved in international circles in the 1990s and later in global HIV vaccine partnerships will extend this reflection on the evolution of global HIV logics, although this paper is primarily focused on the WHO-VAD international coordination.

A Rush for Biotechnologies and Experiments

While HIV vaccine research oscillated between optimism and pessimism for almost 40 years, the formation of the VAD arrived at a time of particularly high expectations for a vaccine, when research on the envelope glycoprotein GP120 in the United States and the GP160 in France seemed most promising for inducing immunity. It was a time when the solution could (or should for some) be seen to come by "confronting reality." In describing the scientific spirit of the day, Jon Cohen quotes the vaccinologist Maurice Hilleman: "The AIDS problem is so devastating that what you want now is answers, and understanding later" (Cohen 2001). The epistemic and political stakes of the emergency favoured experimental trials and their deployment outside the laboratory.

Many candidates were in the pipeline by the early 1990s. Based on WHO (1992a) archival data, as of December 1991, 12 Phase 1 and 2 trials had been initiated by biotechnology companies offering recombinant synthetic stem peptides. Nine trials were initiated in the United States. There were high expectations that the studies would advance to Phase 3, and for this, the trials had to travel to where the epidemic would bring enough subjects. Phase 1 trials evaluating the safety and immunogenicity of vaccine candidates involve an average of 100 people, while Phase 2 trials define an optimal dose and schedules and require between 300 and 600 participants. The number of people needed for a Phase 3 trial varies depending on the objectives, the nature of the population, and the rate of transmission, but in general, the average is 2,500 to 10,000 people. The new experimental optimism had to be translated physically into a substantial research infrastructure to bring vaccine candidate drugs developed in the US into Phase 3 trials, along with a large number of

research subjects, especially in the "developing countries" which had the incidence and prevalence rates needed for Phase 3 trials. As a result, under the guise of humanitarian arguments, the global South had to be useful to the Northern vaccine development infrastructure. This is how WHO Director Nakajima astutely situated the aids vaccine unit.

One of the exemplary figures promoting this optimism and the experimental translation was the American epidemiologist, Donald Francis. In 1993, at the age of 50, after more than 20 years at the US Public Health Service, Francis retired and joined the biotech company Genentech, which was gaining an international reputation in the field of HIV vaccine development. He founded and chaired Genenvax, later renamed VaxGen, a spin-off company of Genentech, which aimed to develop and bring glycoprotein GP120 to clinical trials in the United States and Thailand. He was well known for his somewhat "crusader" (Martin 2003) spirit. His position towards vaccine development was clear: "If you can't risk failure, you should never do a vaccine trial" (Martin 2003), reflecting well the biotech industry ideology of the time. However, this experimental willingness came close to a stubbornness that was openly criticized by researchers in 1994 and 1995 (Martin 2003). Individuals "who joined VaxGen's team were often crusaders inflamed by Don Francis" and even though they knew the scientific community was skeptical, "they were too busy to care" (Thomas 2001).

Indeed, this strong desire to experiment grew in the early 1990s at the same time as the protective immunity produced by the vaccine was increasingly questioned when the geography of viral variants (that is, local subtypes) was emerging. This was a particular moment of figuration for postcolonial science (Rottenburg 2009), where an object or its expectation overturned the classical relationship between safety and use: "the relation between experimentally verified knowledge and its safe usage thus seem inverted in humanitarian interventions to save life" (Rottenburg 2009). This experimentality was reinforced by two important things: the nationalistic spirit of the time, and the development of the biotechnology sector. After the first episode of the Franco-American struggle over HIV discovery[2], vaccine research remained an important battleground for national research prestige. So too, the emergence of biotechnology companies driven by an emerging financialized capitalism boosted the sector and gave a structural voice to stakeholder and venture capitalists' profit expectations. It was a time when many public health researchers became executives or shareholders of companies directly involved in the development of the solutions they set out to evaluate. Optimism and

experimentality at the end of the 1980s were, therefore, the products of the particular socio-economic context of research privatization. The WHO's attempt to take over HIV vaccine research in 1990 was a strong gesture of international politicization of research in the context of a privatized rush for biotechnologies, national prestige, and profit.

The WHO and International Vaccine Logics, 1990 to 1995

The Vaccine Development Unit was created in 1990. With it, the WHO proposed to put its expertise back at the centre of vaccine research by: a) monitoring laboratory advances in animal models, b) promoting research for the development of "vaccines appropriate for the developing world", c) developing selection criteria for international clinical trial vaccine candidates, d) assisting in the implementation of field trials, and finally e) evaluating the results of these international trials (WHO 1991–1993, 415). The timing was rather strategic regarding the fragmentation of research and the need for research infrastructure, and specifically for the WHO as an organization. The Vaccine Development Steering Committee (VAD-SC) was set up after Jonathan Mann resigned from his position as director of the Global Program on Aids, which he had created a few years earlier. The new Director General of the WHO, Dr. Nakajima, was not sympathetic to Mann's way of operating, and the issue of human rights in relation to the fight against HIV was not unanimously supported by WHO member countries. The Director General decided to take over the fight against HIV from a more technical point of view by promoting vaccine development, where he was directly involved in appointing each member of the steering committee.

José Esparza, a 45-year-old Venezuelan-born physician and virologist, was established as head of the Vaccine Development Unit. His career is indicative of the predominant institutions in HIV vaccine research: first, as coordinator of the Vaccine Development Unit at the WHO, he would later become head of vaccine research at the Global HIV Vaccine Enterprise funded by the Bill and Melinda Gates Foundation. In 2016, Esparza still held a central position as president of the Global Virus Network, embodying the transition from "international" to "global" vaccine logics. During his time at the VAD, Patricia Thomas described him as someone with an influence that went far beyond "the small budget of his program" because of his "ability to synthesize and help people make deals and connections" (Thomas 2001, 203).

A Clinical Research Infrastructure in "Developing Countries"

The case for creating a research infrastructure in the South was strong from an international health perspective upheld by WHO and made clear by the VAD-SC (Heyward et al. 1994). First, most HIV infections occurred in "developing countries," where a vaccine would be used and have the most benefit. Second, Phase 3 trials require thousands of participants and must be conducted where the incidence is greatest, that is, in "developing countries." The plan was to develop a research infrastructure in these countries. The WHO VAD Steering Committee undertook an evaluation of 14 sites in developing countries deemed worthy of support to host a possible clinical trial, of which four were selected because of their infrastructure and potentialities: Uganda, Brazil, Rwanda, and Thailand. The process planned for Phase 3 efficacy trials to begin around 1997, that is, approximately five to six years after support of the sites was announced (WHO, 1992).

Less official arguments for the need to conduct vaccine trials in "developing countries" are also present in the archives, such as the costs and difficulties of recruiting research subjects in the North. The amount committed by WHO, with an annual budget for 1993 of about $1.7 million for each of the four sites (WHO, 1994), was well below the anticipated budgets for trials in the US, which would have required tens of millions of dollars. Furthermore, clinical trials in the US or in the North allowed for sufficient recruitment for Phase 1 and 2 trials but not necessarily for Phase 3 trials. As a result, developing clinical trials in the South was both an infrastructural need and an economical optimization.

It is in this context that the internationalization of clinical trials became necessary. While the "travel" of clinical trials in the 1990s has been well described (Petryna 2009; Rajan 2017), the key role played by the WHO's international coordination in the organization and argumentation for exporting clinical trials to countries in the South has been hardly evoked. Thus, the international coordination of HIV research was a particular moment of politicization of HIV research. On the one hand, it brought HIV vaccine research under the aegis of the WHO at a time when technological development was taking off in private companies; on the other hand, it was strategically helpful to take a humanitarian argument for developing research infrastructure in "developing countries" that would also benefit private interests. The WHO thereby appeared as a broker to advance the internationalization of clinical trials.

The Diplomatic Work to Advance Vaccine Trials in Thailand

Thai vaccine research is important because it would pave the way for two and a half decades of HIV clinical trials. Thailand was one of the four countries identified in 1991 as an HIV vaccine evaluation site (Heyward, Osmanov, and Esparza 1996). It had a strong medical and logistical infrastructure and a political commitment to prevention in general, and the vaccine in particular. Vaccine research was seen by the Thai government as an opportunity to strengthen its infrastructure (Excler 2003). With the support of WHO, a national plan for vaccine research was developed in 1992 specifying that before testing a vaccine in Thailand, human trials had to be done in the country where the vaccine was produced.

The WHO as an "Honest Broker" in a Long-Standing Military Relationship

The Thai case reveals the role of the WHO in the political construction of a vaccine trial field site that has longer social and political histories. In December 1990, the Royal Thai Army Medical Department and the US Army Medical Department informally agreed to collaborate on HIV research in the Thailand/ Phase 3 field efficacy trial that was to take place in 1994 and 1995. The Royal Thai Army and the US Army had a long history of collaboration starting in the 1960s in the context of US support of the Thai Royalty in the fight against communism. Founded in 1965, the Armed Forces Research Institute of Medical Sciences (AFRIMS) based in Bangkok brought together US and Royal Thai Army medical services.

Two VAD-SC members followed this collaboration closely. First, Prof. Natth Bhamarapravati of Mahidol University, Bangkok, who worked on the dengue vaccine, developed with Pasteur Mérieux and then Sanofi Pasteur and administered for the first time in 1992. Second, Dr. D. Burke, who was a colonel affiliated with the Walter Reed Army Institute of Research (WRAIR), located in Maryland, USA, and who founded the Department of Retroviral Research in 1998, had been aiming to control HIV/AIDS in the military population since 1990. At the time of the establishment of the committee, Burke was Director of the US Military HIV/AIDS Research Program, located in Rockville. Prior to that, he was Director of the Department of Virology at AFRIMS (Armed Forces Research Institute of Medical Sciences) in Bangkok, Thailand. Col. Burke and Lieutenant Pinyo, Surgeon General in the Royal Thai Army, had agreed that the Medical Department and the WRAIR would work together to strengthen the Thai Army's HIV testing capacity and develop a vaccine program. Through the

testing program, 50,000 to 60,000 recruits (men) from across the country were tested annually. These links helped in organizing the clinical trials research infrastructure in Thailand.

Three U.S. biotech companies involved in vaccine development were also part of these discussions. United Biomedical (UBI), Genentech and Chiron proposed vaccines based on GP120 and GP160 viral proteins. Biocine was the vaccine division of Chiron (the firm that developed the genetically engineered recombinant hepatitis B vaccine) between 1990 and 1997. Genentech was founded in 1976 in San Francisco, making its reputation by genetically developing hormones such as insulin or growth hormone. Attracted by the possibility of an HIV vaccine, Genentech created a spin-off company, Genenvax, and recruited Don Francis to develop and bring glycoprotein GP120 to clinical trials in the United States and Thailand. Genentech and Biocine-Chiron, the two northern California biotechs, were in the starting blocks for efficacy trials but their vaccine candidates only incorporated the most prevalent subtype in the United States and Europe, subtype B, whereas subtype E was the most prevalent in Thailand.

From an ethical and legal perspective, the VAD played a facilitating role in promoting trials; the development of clinical trials in the South had been part of José Esparza's rhetoric. The VAD-SC was well aware that these ethical issues were sensitive, as evidenced by archived files, including the acceptability of potential vaccines at the various sites selected. In addition, VAD was in conversation for legal opinions to frame the trials at both the international and local levels. Different scenarios were discussed with legal experts. The US State Department was also closely monitoring the situation: "if previous patterns hold, vaccines will probably be priced higher in the United States than elsewhere. This could lead to disputes over patents between US firms and their low-price competitors" (WHO, 1992). On the other hand, WHO was aware that the "issue of protecting patent rights of companies that might develop a successful vaccine would need to be addressed."

Global Vaccines, Local Variabilities

Despite the Royal Thai and US Army agreement, the deployment of a vaccine trial was not fully established in the early 1990s. On 4 September 1992, the Federal Coordinating Committee on Science, Engineering, and Technology (FCCSET) convened its Working Committee on Vaccine Development under the leadership of Daniel F. Hoth, then Director of the Division of AIDS National

Institute of Allergy and Infectious Diseases National Institutes of Health. At this meeting, the Thai Minister of Health explicitly stated his concerns and expectations of "least developed countries selected for vaccine trials", namely: a) respect for national sovereignty, b) adherence to national and international ethical standards, c) clear benefits to the population, and d) non-interference with national public health programs (WHO,1992). This statement was indicative of tensions in HIV vaccine research, occurring along two related fronts: one political, in relation to national sovereignty and the second, scientific, related to the local variants of the HIV epidemic. Indeed, the epidemics were very different in the US (mostly subtype B) and in Thailand (subtype E represented 80 to 93 percent of infections at that time) and the Americans from the National Institutes of Health (NIH) and the companies involved were pushing for trials to be launched with candidate vaccines incorporating only subtype B in the vaccine formula. The WHO's role was to make the American biotech companies Biocine and Genetech listen to public health and local national arguments and make those US companies integrate the variant most prevalent in Thailand in their vaccine candidates.

Indeed, the case of Thailand with its subtype E and the variability of subtypes in Central Africa resisted the global reasoning behind the international research at the time advocating the development of a universal vaccine. The WHO VAD reflected scientific and political tension between, on the one hand, the desire to know the efficacy of potentially universal vaccine candidates prepared in laboratories in the North, and on the other hand, the emergence of a new "viral cartography" (Crane 2011), precisely resulting from HIV characterization work produced, among others, on the sites financed by this same VAD and which were to host the vaccine candidates. WHO-VAD work was precisely to adapt vaccine research and cope with these tensions.

VAD played an important role in promoting a scientifically and politically favourable evaluation context. Indeed, these scientific and political issues were intimately linked. Some of these elements have been found in the archives, notably the discussions on vaccine subtypes. The reluctance of the Thai Minister of Health was made explicit, and the WHO facilitated discussions to change the position of the Americans and the companies involved. The national plan for vaccine research developed in 1992 with WHO support specified that before a vaccine could be tested in Thailand, human trials had to be conducted in the country where the vaccine was produced. This requirement was removed in 1994 by the National AIDS Prevention and Control Committee (NAC),

with the proviso that the vaccine should target the virus subtype present in Thailand (Excler 2003). Further studies showed that subtype B was the most prevalent among injecting drug users (about 60 percent) while the sexually transmitted population was infected with subtype E. This helped improve the scientific relevance of working on a vaccine for subtype B from a local perspective. Nevertheless, the controversy over the vaccines tested in Thailand was beginning to appear in the public press, and in 1993 the magazine *The New Scientist* pointed to the trials to test "controversial" vaccines and the underlying links between the American and Thai armies (Brown 1993).

The Diplomatic Work of the Aids Vaccine Unit

Another event made the WHO's intervention even more central. On 17 June 1994, the NIH, through its AIDS Research Advisory Committee, gathered at the Hyatt Regency hotel in Bethesda and made the decision to suspend Phase 3 clinical trials on the efficacy of GP120 on American territory. The reason for such a decision is not clear. The minutes from the NIAID council (NIAID 1994) indicate insufficient efficacy of vaccine candidates (definition of an acceptable efficacy level is discussed) and the "doubtful feasibility of recruiting 9 to 11,000 participants." Not mentioned is the cost associated with such trials (USD $20 to 80 million) and the pressure exerted by HIV activists for treatments rather than vaccines (Thomas 2001). The committee was careful not to close the door on research outside the United States: "In recognition of the difference in the dynamics of the epidemic throughout the world at the present time, these recommendations apply only to studies in the United States"(NIAID 1994). It left the door open for Thailand, as well as for Haiti, which would become a possible site in late 1994.

The decision not to go forward with GP120 candidates in Phase 3 trials in the US was a bitter disappointment for all those involved in vaccine research. For some Americans, especially those involved in these trials, the strategy was clearly to continue through the WHO to advance international vaccine trials. Don Francis said after the NIH decision, "They had no idea that what they did was kill vaccines"(Thomas 2001). But, as expected, he did not give up and sent a letter on 30 September 1994 addressed jointly to Peter Piot, then at the WHO's GPA, and Anthony Fauci of the NIH. Francis wrote in bold: "We must test a vaccine first, before we even contemplate the efficacy of the vaccine for a given population" (WHO,1994). Such initiatives indicate that biotech startups were determined to continue to find sites for vaccine experimentation.

For the WHO, the withdrawal of the NIH left the field open to pursue an international vaccine agenda and the VAD seized the opportunity. On 4 July 1994, Esparza lobbied within the WHO to regain control:

> The recent NIH decision not to proceed to efficacy trials of HIV vaccines in the United States was disappointing. It was obviously based on their own domestic pressures and needs and did not consider the global perspective. That decision indicates that NIH is not in the best position to lead a truly global agenda for HIV vaccine development. I believe that this should be the responsibility of WHO and that this decision gives us the opportunity to establish that much needed leadership (WHO 1994).

He proposed the organization of a special meeting in Geneva: "Thus, I would like to propose that GPA organizes a major consultation in Geneva, to discuss the Scientific and Public Health Rationale for Moving to HIV Vaccine Efficacy Trials"(WHO 1994). At the same time, Esparza also had to convince the Thai partners not to reject the trials. On 6 July 1994, he wrote to Natth Bhamarapravati, the Thai member of the VAD, arguing once again that the reasons for stopping the trials in the United States were primarily "domestic" and that the trials in Thailand should continue.

The WHO had to set limits to the pressures and demands of different partners. In April 1995, Esparza recalled the limits of the WHO's participation. "The role of WHO, which is to provide support to the national authorities, who are fully responsible for the decisions related to the conduct of HIV vaccine trials in their country. In this regard, WHO stands ready to advise the Thai Ministry of Health when requested" (WHO, 1995). Dr Esparza often reminded his NIH interlocutors of the WHO's role: "our role on HIV vaccine trials is to provide support to the host government, not to plan activities on their behalf." These ways of repositioning the WHO's role reflected the expectations of American colleagues regarding the roll-out of the trials in Thailand. Esparza also reminded WRAIR's John McNeil of the need for collaboration: "Thus, rather than being mutually and continuously suspicious of the intentions of other partners, we should be more open in our interactions, with the Thai Ministry of Public Health playing a leading role" (WHO, 1995). These elements confirm the political facilitator role played by the WHO to allow vaccine research fields to open up despite tense scientific and political situations. These elements also show strong expectations of the role of an institution such as the WHO -and its supposed neutrality- to bypass national institutions

to facilitate vaccine development. As a result, the WHO-VAD coordination appeared as an ambiguous politicization of HIV vaccine research by integrating national authorities in a more international framework on the one hand and contributing unwillingly to advance particular interests, those of research and the institutions and companies leading it from the global North, under the umbrella of its supposed scientific and political neutrality, on the other.

Structuring HIV Vaccine Research 1990 to 2021

The Thailand trials were paradoxically launched at the very moment when the evidence of the drug candidates' ineffectiveness was growing. Moore and Anderson's (Moore and Anderson 1994) questioning of the basis for those trials was part of the evidence considered by the SC-VAD that appears in the archive. Nevertheless, eight Phase 1 and 2 clinical trials were launched in Thailand from 1994 to 2002. Among these, the first three were for candidate vaccines targeting only subtype B. It was not until 1997 and the fourth clinical trial completed in 1997 that the non-B subtype was included, with Genetech's monomeric GP120 vaccine candidate (Excler 2003). These safety and immunogenicity trials paved the way for larger efficacy trials. The first efficacy trial in a developing country was initiated in 1999, combining subtypes B and E. It was completed in 2003. The second efficacy trial was the result of collaboration between the WRAIR and the Thai Armed Forces Research Institute of Medical Sciences (AFRIMS) based on various site collaborations forming the Thai AIDS Vaccine Evaluation Group (TAVEG).

Although these two trials were failures, a combined approach was nevertheless developed with some controversy on the merits of the trial (Burton et al. 2004; McNeil et al. 2004). The trial was started in 2003, combining two individually losing strategies, AIDSVAX and ALAVAC, which raised critical ethical and political issues (Fordham 2014). Nevertheless, this combination was advanced to the Phase 3 evaluation and tested on 16,000 people. This famous "RV144" trial, known as the "Thai trial" conducted between 2003 and 2006, was the largest HIV vaccine trial in history. Participants were vaccinated for 24 weeks starting in October 2003 and then tested for HIV until July 2006. The results of the study were released in September 2009. The initial report showed that the rate of HIV infection in volunteers who received the experimental vaccine was 31 percent lower than the rate of HIV infection in volunteers who received placebo. This reduction was not large enough for the Thai Ministry of Public Health to support licensing the vaccine; it would have licensed it if the reduction had been 50 percent or more[3]. Even though this trial might have diverted interest

towards other prevention strategies in Thailand (Fordham 2014), the trial's collaborators have stated that the results of this trial were the first evidence of the effectiveness of a vaccine in reducing the risk of HIV infection.

In the end, this trial, with its highly controversial interpretations (Cohen 2009) led to the only partially positive HIV vaccination result (Rerks-Ngarm et al, 2009), reinvigorating HIV vaccine research for the next decade. Indeed, it was on the basis of these partial results that the HVTN 702 HIV vaccine trial in South Africa began in 2017, testing a combination of two HIV vaccines that were slight modifications of those used in the RV 144 trial. This result might be indirectly credited to the VAD, despite the lengthy period between testing.

In 2023, "Thai Trial" remains the only one of the eight HIV vaccine trials conducted in history to have shown some efficacy. Even though the failure of HVTN 702 in 2020 points to the end of the road for this research initiated in Thailand, its history teaches us a lot about the present. More precisely, this history of HIV shows us the collusion of health, economic and diplomatic issues, and the role of business in the administration of proof, the articulation of various actors, and the political framework of anticipated positive results of such trials. The path thus traced by international vaccine logics sheds light on these issues that were emerging at the time of the VAD and that are still central today.

From International to Global HIV Vaccine Logics

The WHO-VAD: Not Global Enough?

The VAD concretely contributed to the building of a clinical trial infrastructure for vaccines which remains a relative success. The failures of the candidates considered, however, left the impression that this international coordination had failed. This failure became even more evident as other approaches were developed. A March 1994 meeting held by the Rockefeller Foundation at the foundation's Bellagio Center under the theme of "HIV Vaccines – Accelerating the development of preventive HIV vaccines for the world," made way for a global research configuration. The involvement of the Rockefeller Foundation signalled the end of "international coordination" by proposing new and more effective private partnerships for achieving health goals, as it had done for primary healthcare (Brown, Cueto, and Fee 2006). Esparza, as a good political strategist, told Seth Berkley, who would become the first director of IAVI, the International AIDS Vaccine Initiative (the organization that would follow this meeting), not to duplicate prevention efforts and that the WHO was already an "advocate for the

development of vaccines for developing countries" (WHO 1994b). On the other hand, at this meeting, blows to the WHO also came from some members of the SC-VAD. Don Burke argued that if the WHO "does not deliver what is needed, other organizations may have to do it" (WHO, 1994), providing an interesting look back at the WHO's diplomatic work. Indeed, this work allowed clinical trials to take place, but the precautions taken to respect national prerogatives in setting up such trials were not really appreciated by the supporters of an "acceleration" model who wanted their candidates in the pipeline.

In the end, this meeting would be seminal and bring about a shift towards a "global" rather than an "international" approach to research. The organizers of the meeting, supported by the Rockefeller Foundation, were already thinking big: an agenda was prepared for vaccine research over seven years and the budget of more than USD $600 million seemed to match those ambitions, in contrast with the USD $5 million budgeted by the VAD during its four years of existence. One way this ambition has been realized is through the creation of the IAVI, which would go on to benefit from massive philanthropic funding, including from the Bill and Melinda Gates Foundation. VAD and its international coordination were rendered obsolete by the emergence of what would become "global health" (Packard, 2016).

The Global HIV Vaccine Enterprise: The Last Vaccine Logic?

"It is not possible to plan for discovery, but we can indeed plan for the research" (Esparza, 2005), is one of the arguments made for the "need for a global Enterprise" (Klausner, 2003). This need is addressed in an article published in the journal *Science* by Richard Klausner, who has been an NIH researcher for more than 20 years and was a renowned director of the National Cancer Institute in the United States from 1995 to 2001. In 2002 he became executive director of the newly formed Bill and Melinda Gates Foundation, founded in 2000 and based on effective altruism. In his article in *Science*, Klausner proposed a vision of vaccine research acknowledged by almost all the actors mentioned so far in international coordination in their co-authorship of the paper: José Esparza, Anthony Fauci of the NIH, then director of IAVI, Seth Berkeley, Don Francis, and Peter Piot. This consensual vision, led by the Gates Foundation, was based on the urgent need to develop and evaluate more vaccine candidates: "the pace of development of HIV vaccine candidates needs to be accelerated" (Klausner et al., 2003). This acceleration was quantified: the paper estimated that it was necessary to extend the pipeline and enroll approximately 5,000 people in Phase 1 and 2 and 30,000 people in Phase 3, on an annual basis.

Cohorts of subjects ready for experimentation were needed to materialize this "acceleration" plan. This same issue was identified at the birth of the VAD, but with a very different scale of operations.

The solution was proposed in a surprising form, that of an "Enterprise," like a collaboration "which goes beyond the high quality but separate research projects that we have today." The work of organizations such as NIH, IAVI, ANRS and pharmaceutical companies was presented as an "enterprise." The focus was precisely on the fact that research was uncertain and costly and that "reliance on industry to carry the major load for discovery and development for HIV vaccines is unrealistic." The "Enterprise" thus exemplified the public-private partnership as an institutional necessity, but without the drawbacks of a bureaucratic organization such as the WHO-VAD. Indeed, the "Enterprise" intended to draw inspiration from the Human Genome Project, for which "no entity ran the project (...) We believe that the time is right for the major scientific and product-development leaders and the stakeholders involved in the global HIV vaccine development enterprise to come together in an analogous way" (Klausner et al. 2003).

This "Enterprise" vision for global vaccine logic showed both a global ambition beyond the national borders (that the VAD considered) and a profound grounding in values and ways of addressing empirical problems linked to entrepreneurial and tech capitalism. Anthropologist Tobias Rees (2014) has analyzed this form of global logic supported by vaccine technology. For Rees, this "Enterprise" proposed "a plan for humanity," and thus contributed to redefining a humanity conceived fore and foremost on a biological dimension. The Enterprise would be the appropriate form for a world context marked by what Rees designates as "state-less", that is, the political regime resulting from the destructuring of nation-states under the impetus of the neoliberal structural adjustment plans of the World Bank and the International Monetary Fund (IMF) in the 1990s. As a result, the Enterprise would have no need for diplomatic work between sovereign states, since precisely the individuals conceived in this humanity are depoliticized biological individuals. In contrast, the COVID-19 context has highlighted how large public-private partnerships have been set up to benefit from public research and to obtain guaranteed contracts from the richest nation-states who were seeking to ensure that their citizens, as political subjects, had access to several doses. As a result, the discourse of a depoliticized global humanity in global vaccine logics is not consistent with the practice; it is an artifact invisibilizing other key issues.

First, it is a discourse that allows the capture of public resources. Indeed, it is important to remember that while public-private partnerships are presented as central to the global vaccine logic, public research at the international level remains the main source of funding for HIV prevention, in the order of 88 percent (USD $935 million), far ahead of foundations' funding (10 percent)[4], which are also forms of public funding, as they mainly derive from tax exemptions. Presenting public-private partnerships as the driving force behind vaccine development also means that public research dollars are being channelled into an agenda, a "plan for the private," oriented towards the private economic development of vaccines for individuals and states that can afford them. Second, underneath the rhetoric of global biological humanity, there are issues of research infrastructure. The objectives are those of promoting a research pipeline through a regime of experimentation that allows for the availability of subjects (biological), even before the rational necessity of the research. This regime of experimentality is, however, far from obvious in many countries with which diplomatic relations remain fundamental to discussing the direction of research and the distribution of the possible fruits of discoveries. This discourse of a global biological humanity encapsulated in the global vaccine logics of the Enterprise, highlighted by Tobias Rees, thus contributes to the development of an experimental regime that relies on the capture of public resources and the availability of depoliticized subjects for the purposes of private valorization; materializing in the end a humanity for and foremost defined by the socio-political dimensions of biocapitalism (Rajan 2017).

Conclusion

The international coordination proposed and implemented by the VAD was maybe less obsolete than the global partnerships that succeeded it indirectly suggested, particularly when considering the place of diplomatic and political dimensions in the scientific coordination. However, by facilitating, through this diplomatic work, the supposedly political and scientific neutrality embodied by the WHO, the real political stakes of research and the redistribution of its discoveries have been greatly limited. Indeed, the experimental need formulated by the VAD on humanitarian grounds contributed to the development of an ambiguous biopolitical diplomacy: recognizing at the same time the states in which the research was carried out and trying to facilitate this research by promoting the scientific and economic interests of the countries of the North, while the political questions of the redistribution of the possible results of the

research were little discussed, especially in the midst of the emergence of the World Trade Organization and patent law in the mid-1990s. The VAD has been unable to put the issue of the vaccine as a common good on the table of HIV vaccine research.

The diplomatic work of the VAD contributed to taking local and national prerogatives seriously. However, this system also contributed to promoting "revolving door systems" by facilitating the movement of individuals between institutions with sometimes antagonistic interests, such as researchers from public research who became CEOs of biotech companies and organizers of clinical trials. This phenomenon taints the political takeover of research. In the same way, the promoters of this international research vision, such as Don Francis and José Esparza, who went through the revolving doors from the VAD to the Gates Foundation, were precisely those who implemented and legitimized the later global framework. The political diplomacy vision of research seems to have been lost in a vision of an "Enterprise" of research from which emerges an allegedly technicist and capitalist vision of the vaccine logics (diplomacy with non-humans or biological humans at best), to the detriment of their structural and economic stakes. In the end, international and then global vaccine logics characterize the political evolution of research and power relationships at the global level. The HIV vaccine, still an absent object, has thus revealed and contributed to structuring "global health" by profoundly influencing the political and social organization of research.

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Notes

1 These results were later followed by further negative results. The Imbokodo study stopped in August 2021 due to limited efficacy (around 25 percent) and the Mosaico trial, which was led by a global public-private partnership, including the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), the HIV Vaccine Trials Network (HVTN), the US Army Medical Research and Development Command (USAMRDC), and Janssen was stopped in January 2023 as it was not effective in HIV prevention.

2 This struggle was publicized by the Gallo-Montagnier controversy and resolved with the 31 March 1987 agreement between the United States Department of Health and the French Institut Pasteur on the distribution of royalties on diagnostic tests.

3 Another unexpected outcome from this "failure" might have been to seriously consider semi-effective vaccines. Even though less than 50 percent efficacy was not acceptable for HIV, it might have paved the way to start considering them as potential public health strategies, which happened a few years later with the RTSS malaria vaccine (efficacy around 30 percent). See Graham in this issue on "Leaky vaccines."

4 https://www.hivresourcetracking.org/, accessed 10 November 2022.

References

Brown, Phyllida. 1993. Controversial AIDS vaccine to be tested in China. *The New Scientist*, 29 May. https://www.newscientist.com/article/mg13818750-900-controversial-aids-vaccine-to-be-tested-in-china/.

Brown, Theodore M., Marcos Cueto, and Elizabeth Fee. 2006. "The World Health Organization and the Transition From 'International' to 'Global' Public Health." *American Journal of Public Health* 96 (1): 62–72. https://doi.org/10.2105/AJPH.2004.050831.

Burton, Dennis R., Ronald C. Desrosiers, Robert W. Doms, Mark B. Feinberg, Robert C. Gallo, Beatrice Hahn, James A. Hoxie, et al. 2004. "A Sound Rationale Needed for Phase III HIV-1 Vaccine Trials." *Science* 303 (5656): 316–316. https://doi.org/10.1126/science.1094620.

Cohen, Jon. 2009. "Unrevealed Analysis Weakens Claim of AIDS Vaccine." *Science* Vol. 5, 5 October. https://www.science.org/content/article/unrevealed-analysis-weakens-claim-aids-vaccine-success.

——. 2001. *Shots in the Dark: The Wayward Search for the AIDS Vaccine*. New York: WW Norton and Co.

Crane, Johanna T. 2011. "Viral Cartographies: Mapping the Molecular Politics of Global HIV." *BioSocieties* 6 (2): 142–166. https://doi.org/10.1057/biosoc.2010.37.

Excler, Jean-Louis. 2003. "HIV Vaccine Development in Asia." *Journal of Health Management* 5 (2): 327–41. https://doi.org/10.1177/097206340300500213.

Fordham, Graham. 2014. *HIV/AIDS and the Social Consequences of Untamed Biomedicine: Anthropological Complicities*. New York: Routledge.

Heyward, W. L., S. Osmanov, J. Saba, J. Esparza, E. Belsey, R. Stoneburner, J. Kaldor, and P.G. Smith. 1994. "Preparation for Phase III HIV Vaccine Efficacy Trials: Methods for the Determination of HIV Incidence." *AIDS (London, England)* 8 (9): 1285–1291. https://doi.org/10.1097/00002030-199409000-00011.

Heyward, William L., Saladin Osmanov, and Jose Esparza. 1996. "Establishment of WHO-Sponsored Field Sites for HIV Vaccine Evaluation in Developing Countries." *Development and Applications of Vaccines and Gene Therapy in AIDS* 48:139–144. https://doi.org/10.1159/000425169.

Kingori, Patricia, and Salla Sariola. 2015. "Museum of Failed HIV Research." *Anthropology and Medicine* 22 (3): 213–216. https://doi.org/10.1080/13648470.2015.1079302.

Klausner, Richard D., Anthony S. Fauci, Lawrence Corey, Gary J. Nabel, Helene Gayle, Seth Berkley, Barton F. Haynes, et al. 2003. "Enhanced: The Need for a Global HIV Vaccine Enterprise." *Science* 300 (5628): 2036–2039. https://doi.org/10.1126/science.1086916.

Martin, Richard. n.d. "Testing the First AIDS Vaccine." *Wired*, 1 January. https://www.wired.com/2003/01/aids/.

McNeil, John G., Margaret I. Johnston, Deborah L. Birx, and Edmund C. Tramont. 2004. "HIV Vaccine Trial Justified." *Science* 303 (5660): 961–961. https://doi.org/10.1126/science.1096161.

Meinert, Lotte, and Susan Reynolds Whyte. 2014. "Epidemic Projectification: AIDS Responses in Uganda as Event and Process." *The Cambridge Journal of Anthropology* 32 (1): 77–94. https://doi.org/10.3167/ca.2014.320107.

Moore, J., and R. Anderson. 1994. "The WHO and Why of HIV Vaccine Trials." *Nature* 372 (6504): 313–314. https://doi.org/10.1038/372313a0.

Moulin, A.-M. 1996. *L'aventure de la vaccination*. Paris: Fayard.

Nguyen, V K. 2009. "Government-by-Exception: Enrolment and Experimentality in Mass HIV Treatment Programmes in Africa." *Social Theory and Health* 7 (3): 196–217. https://doi.org/10.1057/sth.2009.12.

NIAID. 1994. "[Meeting Minutes, Meeting of the National Advisory Allergy and Infectious Diseases Council (1994: Bethesda, Maryland)]." http://name.umdl.umich.edu/5571095.0079.046.

Packard, Randall M. 2016. *A History of Global Health: Interventions Into the Lives of Other Peoples*. Baltimore: JHU Press.

Petryna, Adriana. 2009. *When Experiments Travel: Clinical Trials and the Global Search for Human Subjects*. Princeton: Princeton University Press.

Rajan, Kaushik Sunder. 2017. *Pharmocracy: Value, Politics, and Knowledge in Global Biomedicine*. Durham: Duke University Press.

Rees, T. 2014. Humanity/plan; or, on the" stateless" today (also being an anthropology of global health). *Cultural Anthropology*, 29(3), 457-478. https://doi.org/10.14506/ca29.3.02.

Rerks-Ngarm S, Pitisuttithum P, Nitayaphan S, Kaewkungwal J, Chiu J, Paris R, Premsri N, Namwat C, de Souza M, Adams E, Benenson M, Gurunathan S, Tartaglia J, McNeil JG, Francis DP, Stablein D, Birx DL, Chunsuttiwat S, Khamboonruang C, Thongcharoen P, Robb ML, Michael NL, Kunasol P, Kim JH; MOPH-TAVEG Investigators. 2009. Vaccination with ALVAC and AIDSVAX to prevent HIV-1 infection in Thailand. *New England Journal of Medicine*, 361(23), 2209-2220. https://www.nejm.org/doi/full/10.1056/NEJMoa0908492.

Rottenburg, Richard. 2009. "Social and Public Experiments and New Figurations of Science and Politics in Postcolonial Africa1." *Postcolonial Studies* 12 (4): 423–440. https://doi.org/10.1080/13688790903350666.

Thomas, Patricia. 2001. *Big Shot Passion, Politics, and the Struggle for an AIDS Vaccine*. New York: PublicAffairs.

WHO. 1992. "GPA Archive." GPA 698.

——. 1994. "GPA Archive." GPA 699.

——. 1995. "GPA Archive." GPA 697.