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ORIGINAL ARTICLE

The social shaping of biotechnological innovation. The case of Covid-19 protein vaccine in Cuba and the US

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Abstract

Like other technologies, vaccines are socially shaped by socio-economic, political and organisational factors. Property rights, value capture strategies and public innovation policies guide research teams in the biochemical design of vaccines, with inevitable consequences for their price and accessibility. The Covid-19 pandemic provided an opportunity to analyse this institutional shaping process and its consequences for global public health from a political economy perspective. Indeed, the same type of invention, a recombinant protein vaccine, was simultaneously and originally developed in the US and Cuban biopharmaceutical industries and in the field of philanthropic Open Innovation. The article shows, through empirical research that collected direct testimony from scientists and privileged observers of the vaccine development fields, how certain norms and values characteristic of the US industry (financialization, assetization and de-risk) created a path dependency in the use of proprietary and experimental biotechnologies that made the US vaccine Nuvaxovid more expensive and complex to produce, but no more effective and safe than Abdala, Soberana 02 and Corbevax. In addition, the institutional constraints of the US biopharmaceutical industry on radical innovation, even within a mature biotechnology platform such as protein vaccines, would have resulted in a competitive disadvantage for Nuvaxovid, which was as expensive as an mRNA vaccine but less rapid to market and less reliable in delivery. The case of protein vaccines against Covid-19 thus shows how the institutional architectures of techno-scientific capitalism create not only inequalities but also inefficiencies, and that an innovation path with excellent results is possible even in competition where the market is not the dominant order of worth.

Keywords Cuban Biotechnology · Financialisation · Open Innovation · Assetization · Covid-19 · Vaccine

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Introduction

During the Covid-19 pandemic access to vaccines between high-income countries and the rest of the world was so unequal to be referred to as apartheid (Brown and Rosier 2023).

The causes of this phenomenon have been described by several authors, who have identified the institutional conditions affecting the production, distribution and sale of anticovid vaccines. These include the maintenance of private intellectual property rights in a state of global health emergency (Dosi 2021; Stiglitz 2022), despite the fact that their development had been almost entirely covered by public funding (Graham 2019; Sampat and Shadlen 2021; Florio et al. 2023); the vulnerability of a "more than national but less than global" (Jensen et al. 2023) biochemical vaccine infrastructure characterised by manufacturing delays, supply chain disruptions and export restrictions; the weakness of international health actors such as the WHO in containing national protection efforts and commercial interests (Kelly et al. 2022; Geiger and McMahon 2023). Nevertheless, few studies have opened the 'black box' (Latour 1987) of vaccine formulations to demonstrate how the price and accessibility of vaccines are linked to their biochemical design, and how this, in turn, is shaped by socio-economic, political and organisational factors.

This paper offers an empirical study with these characteristics, analysing the trajectories of four protein vaccines against Covid-19, which were developed simultaneously and in an original form in capitalist and non-capitalist markets (Fligstein 2001a, b). In particular (see Table 1), Nuvaxovid was developed in the US bio-financialized industry (Glabau et al. 2017), Abdala and Soberana 02 in the state-led Cuban national innovation system, and Corbevax in a philanthropic open innovation platform.

The vaccines share the same technical frame (Bijker 1995), i.e. they use a common biotechnology platform and have a similar production process. However, only Nuvaxovid is based on proprietary (patented) and experimental (never marketed) biotechnology. As shown by the data from the third phase clinical trials (Heath et al.2021; Thuluva et al. 2022; Hernandez-Bernal et al. 2023) this peculiarity would not have had any particular advantages in terms of efficacy and safety, but it would have made Nuvaxovid more expensive and difficult to produce than the other vaccines (cf. data on Table 4).

The main argument of this article is that the biochemical content of these vaccines was socially shaped (MacKenzie and Wajcman 1985; Bijker and Law 1992). Research teams explored different development paths for the same type of invention and were not exclusively guided by a problem-solving approach aimed at efficiency or product safety. Rather, they selected technologies and components according to formal and informal rules of conduct (DiMaggio and Powell 1983; Fligstein 2001a, b) that were dominant in their organisational field. These rules reflected two different ways of producing innovations. On the one hand, Abadala, Soberana 02 and Corbevax have been developed in fields where companies are not-for-profit, relationships between actors are based on the free transfer of

Table 1 Protein vaccines, enterprises and institutional context of reference

Vaccines	Nationality	Enterprise	Institutional field
Abdala, Soberana 02	Cuba	Centro de Immunologia Genetica y Biotecnologica (CIGB) // Finlay de Vacunas Institute (IFV)	State-led biotechnology
Nuvaxovid	US	Novavax Inc	US bio-financilized Industry
Corbevax	US/India	Texas Children's Hospital Center for Vaccine Development/Biological E	Pharmaceutical Open Innovation supported by philanthropic funding

technology and knowledge (Reid-Henry 2018; Ibata-Arens 2021), and the right to health prevails over market interests (Mazzucato et al. 2020). These three vaccines have significant incremental innovations, aimed in particular at making the formulations accessible and safe for children and people with immune fragility. However, they have predominantly been designed using off-patent components, exploring the therapeutic potential of molecules readily available on the market, and adhering to a mode of innovation largely, though not entirely, inspired by *drug repurposing* (Conti et al. 2020). Nuvaxovid, on the other hand, was developed in a field where companies are publicly traded, relations between companies are competitive and based on the exclusive ownership of patents and knowledge (Belloc and Pagano 2012; Birch 2017), and public actors protect the right to health by promoting private research and development (R&D) (Florio 2022; Sampat and Shadlen 2021). This institutional architecture has shaped an innovation model based on the use of proprietary and experimental biotechnologies. Scannell et al. (2012) have defined this approach as "better than the Beatles", because it aims to achieve extraordinary therapeutic advances through rare, expansive, and also for this reasons patentable chemical compounds, within markets where very good solutions already exist.

Both the "better-than-the-Beatles" approach and drug repurposing have produced excellent results in the fight against Covid-19, but not within the same technical frame. The mRNA vaccines, which can be considered as the culmination of the first approach, proved to be the fastest to develop in the world, conferring a significant advantage to countries with the financial resources to afford it. However, as it will be discussed in the empirical findings of this study, applying the same recipe to the technical frame of protein vaccines was *path dependent* (Mahoney 2000; Pierson 2000). This is a phenomenon that has been studied extensively in the fields of economics and technology (David 1985; Arthur 1994) and that occurs when certain norms are reinforced by their adoption, making it difficult to deviate from the "path" they have established. Novavax used proprietary and experimental biotechnologies because, in the biofinancialised field, it would have been economically unattractive but also technically impossible to develop a vaccine without them. These institutional constraints made Nuvaxvoid too slow to reach the market in high-income countries and too expensive for the rest of the world. With much lower development costs and more technologically traditional formulations, Abdala, Soberana 02 and Corbevax have performed well in terms of efficacy and safety, with tens of millions of people vaccinated.

In this introduction, we have introduced two concepts—organisational field and path dependency—which guide the theoretical framework with which we shall analyse the characteristics of the institutional contexts of vaccines ("Organisational Field and Path Dependency" and "Norms and values of the institutional fields" sections). After describing the sources used and the logical design of the comparison ("Method and sources" section), we will explore in depth the four vaccines, analysing their main components ("Into the tube" section) and their different socio-health impacts ("The social shaping of Covid-19 protein vaccines" section). We then identify which distinctive institutional factors of the bio-financialized field would create path dependencies on the use of proprietary biotechnologies ("The failure

of Nuvaxovid" section). This part of the article reports data and information gathered not only by analysing scientific papers and literature, but also by conducting in-depth interviews with the scientists who developed Abadla, Soberana 02 and Corbevax, and with experts of the bio-financilized industry. Finally, in "Why trying to be better than the Beatles can be a problem" section, we compare the research findings with those of the literature that has already critically observed the limitations and contradictions of the ways in which innovations are produced in techno-scientific capitalism, and we highlight which elements of innovation are suggested by the case study on protein vaccines.

Organisational field and path dependency

Between the behaviour of a company that develops a vaccine (micro level), and the set of variables that intervene to condition its actions (macro level), there lies a 'meso' level consisting of the internal dynamics and organisational principles that characterise that company's reference market (Fligstein and McAdam 2012). Several authors (Di Maggio and Powell 1983; Bourdieu 1993) have framed this level within the concept of 'field', applying it to various empirical contexts, including capitalist markets (Fligstein 2001a, b, p. 2).

A 'field' is a social arena in which a group of actors *(incumbents)* tries to reproduce a system of domination through the production of a local culture that defines social relations with other actors *(challengers*). In the case of markets, the production of local culture depends on the different configurations with which public authorities, firms and other types of actors, in an often conflictual dynamic, have structured different apparatuses of rules and norms over time.

Vaccines are undoubtedly products of ingenuity, but they are also commodities. The institutional contexts in which they are generated can be regarded as fields/markets in which actors with different kinds of capital (Bourdieu 1993) preside over the production and exchange of basic goods such as drugs and vaccines. In order to understand the functioning of these kinds of fields, it is crucial to observe how institutional schemes are distributed within them. In particular, property rights, which determine who is entitled to distribute profits; governance structures, i.e. the principles that regulate collaborative and/or competitive relations; and the conception of control, i.e. the social representations that reify and justify status hierarchies, in particular the models of state intervention to support or replace the market.[1]

As Fligstein (2001a, b, p. 2) notes, fields tend towards stability. The content of their normative apparatuses is the product of a historical process whereby agreements established at the time of a field's creation conditioned future ones: *early events matter* (Mahoney 2000). Although field theory does not explicitly

[1] For reasons of space, but also of relevance to the aims of this article, we do not include description of the level in Fligstein's (2001a, b) model concerning the "rules of exchange", which would require further investigation of the manufacturing and validation standards of clinical trials as boundaries of the respective markets.

refer to the concept of path dependency (Arthur 1994; David 1985), this notion can be effective in describing the condition that occurs in those fields where certain norms create *increasing returns* (Pierson 2000), i.e. the more they spread, the more irreversible their adoption becomes, even in the presence of better alternatives.

Although there is not a shared theory of path dependency (Mahoney 2000), Pierson (2000) proposes the attribution of specific characteristics to the social processes affected by this phenomenon. Among these characteristics, particularly relevant to the protein vaccines case study are those of inertia and potential inefficiency: by reiterating crystallised patterns of action, path dependency can freeze actors in their choices even if potentially better alternatives exist (Barnes et al. 2004).

Pierson (2000) identifies some conditions that would facilitate the establishment of path dependency, particularly in processes of adoption of emerging technologies. Firstly, high investment costs would tend to bind acquirers to the valuation of their assets until the depreciation or expected return is satisfied (*large set-up*). Furthermore, the risk associated with the *large set-up of* the investment would push buyers to develop quasi-statistical competence i.e. to adjust their purchasing behaviour on the basis of their perceptions of the future market (*adaptive expectations*).

Large set-up is a condition recurrent throughout the vaccine industry because of the characteristics of the technologies used in it. Particularly in the case of the protein vaccine value chain, the cost of equipment is on average higher than in other biopharmaceutical sectors. Moreover, many of the production processes are not scalable, so that companies are compelled to use the manufacturing equipment in which they have invested in the past (Douglas and Samant 2018). However, in the case of bio-finance, investments are not limited to manufacturing infrastructure. Much higher costs may be involved for a company that has to acquire a licence or have its own distinctive innovation approved by patent offices and regulators (Bourgeron and Geiger 2022).

Adaptive expectations are recurrent in a market, like the bio-financialized one, where financial players are dominant. Shareholders have an interest in investing their resources in emerging biotechnologies that, in the not too distant future, may become *disruptive* and engender profitable drugs or vaccines in a monopoly regime (Dosi and Stiglitz 2014). The process of allocating such resources depends on several factors, but one of the most important is the ability of companies to provide evidence about the reliability and application potential of their proprietary biotechnologies. This reinforces the application of such biotechnologies to different objects and fields, and it accordingly shapes the internal organisation of companies, from the procurement of know-how to the type of production infrastructure.

In conclusion, a theoretical framework integrating field theory and path dependency is useful for establishing a comparative grid comprising the markets where the four vaccines were generated, and for identifying which organisational principles made the bio-financialized market more constrained to the use of proprietary and experimental biotechnologies, even when they entail disadvantages.

Norms and values of the institutional fields

As we briefly introduced in the first section, vaccines have been created through two different modes of innovation: "better than the Beatles" and drug repurposing. The first, which dominates the bio-financialized field, directed R&D towards patentable solutions using rare, expensive chemical compounds. The second, which dominates the other two fields, pushed for the creative reuse and recombination of existing molecules. These modes of innovation are not simply expressions of human ingenuity, but are the product of norms and values of different organisational fields. In this section, we use the scheme proposed by Fligstein (2001a, b), which we have outlined in "Organisational field and path dependency" section, to reconstruct how these norms and values were generated and how they operate (Table 2).

The US bio-financialised field

In this field, property rights are predominantly the prerogative of financial actors. Most pharmaceutical companies are publicly traded, as are academic spin-offs and start-ups that hold patents on inventions with commercial potential (Lazonick and Tulum 2018). Legally, property rights are linked to intellectual property regulatory models (Coriat and Weinstein 2012), in particular the Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS). TRIPS was approved by almost all countries in the world in 1994 and extended US regulations on IPR globally (Belloc and Pagano 2012). Patents apply not only to finished products, but also to the components, technologies and processes by which they are produced (Mazzucato and Li 2021). They last for 20 years, and only in very rare cases can be 'suspended' by states through compulsory licenses in health emergencies (t'Hoen 2016). These measures have facilitated the creation of monopolies in a market where demand is structurally non-elastic (Dosi and Stiglitz 2014), attracting venture capitalists interested in "betting" on the winning patent.

In the field of bio-financialisation, competition is primarily concentrated on the generative phase of the innovation process. The individual who patents first is the winner. This governance structure also creates the conditions for a value capture strategy based on self-valorisation (Gaudilliere 2021), which is not only to sell

Table 2 Interviews with scientist, manager and academics

	Cuban national innovation system	Us biofinancilized industry	Open innovation platform
Scientist involved in the vaccine development	6	–	2
Manager and industrial experts	4	2	2
Academics	1	3	2

The table divides each respondent according to the organizational field for which they were interviewed. However, as on almost every occasion, scientist, academics and managers provided insights and information about all vaccines

commodities, but to generate value through expectations. As Birch (2017) notes, most biotech companies do not generate profits for their shareholders by selling drugs, but rather by "assetization". This process involves the transformation of scientific knowledge into an asset that generates profits without being sold. This happens with the financial value of patents and other intangibles, which can rise or fall sharply on news or rumour about their future applicability.

Public innovation agencies, such as the US National Institutes of Health (NIH), play a key role in controlling this market. Many of the patents commercialised by biotech companies relate to discoveries and inventions determined by government-funded research projects (Mazzucato 2016). This is particularly the case for mRNA vaccines (Roy 2023). During the Covid-19 vaccine race, the role of the state was further extended to cover the costs of clinical evaluation and industrial scale-up of vaccines (Sampat and Shadlen 2021), which are conventionally borne by private capital. In particular, the US government has funded the development of seven vaccine candidates, including Novavax, with a total contribution of around $18 billion through an innovation policy called Operation Warp Speed (Sowels 2021). The European Union, on the other hand, supported the acceleration of these vaccines through Advanced Purchase Agreements (APAs), a procedure that involved an upfront payment to the supplier with no obligation to return the money if the product did not prove effective and safe (Florio et al. 2023).

The Cuban biotech field

In Cuban biotechnology, property rights are wholly owned by the state (Cardenas-O'Farril 2021), which controls a network of 32 biopharmaceutical companies. The integrator of the system is a government agency, Biocubafarma, which facilitates collaboration between companies and the internationalisation of their products (Yaffe 2019; Gonzalez and Fernandez 2020).

In this organisational field, there is no private intellectual property, but inventing scientists are recognised with a share of about 1 percent of the profits generated by their patents. Cuba acceded to the Trade-Related Aspects of Intellectual Property Rights (TRIPS) Agreement in 1995, having previously strongly contested the General Agreement on Tariffs and Trade (GATT), which in 1986 had initiated the creation of a global model of intellectual property regulation. As outlined by Plahte and Reid-Henry (2013), the Cuban government has adopted a less restrictive stance regarding patents, at least in part, due to the success achieved by its domestic biotechnological field in developing original drugs and vaccines.

The governance structure of this market is based on the concept of a "closed cycle" (Sabharwal 2018). The governance structure of this market is based on the concept of a 'closed cycle' (Sabharwal 2018). It involves a vertically integrated organisational model in which all stages of the innovation process are carried out either within a single company or through partnerships between companies in a national network (Zamora Rodríguez et al. 2021). Indeed, in the Cuban sector, there are no clear incumbents and challengers. Domestic demand is met through cooperative rather than competitive relationships. Moreover, prices are not freely set by

companies, but are agreed with Biocubafarma, based on production costs and a fixed profit of around 10 per cent. This is not the case for exports. Some Cuban companies sell their medicines and vaccines in Africa and Asia (Gonzalez and Fernandez 2020) and act as "challengers" in these markets, where the products offered by the bio-financed companies are too expensive or do not have sufficient margins to justify investment in R&D.

The concept of control of the Cuban field confronts two theses on the "public" role of the economic system. The first is that of *consagracion*, an internal organisational culture based on a shared political-ideological background in line with the values of the Cuban revolution (Reid-Henry 2018), in which companies are first and foremost a political tool at the disposal of the government (Núñez Jover and López Cerezo 2008). This view contrasts with another standpoint which aims instead to integrate Cuban companies into the world capitalist market. In the short term, this implies a revision of certain norms in the Cuban sector, including directing R&D towards products that are primarily patentable and that intercept health priorities in the global North, where most of the global added value is concentrated.

Open innovation field

The concept of open innovation (OI) originated in the for-profit pharmaceutical sector and refers to initiatives aimed at facilitating the exchange of knowledge between companies, for example by sharing patents that have not yet been successful (Chesborough 2003; Hunter and Stephens 2010). Nevertheless, there are instances where the market fails to function effectively (Trouiller et al. 2002). This occurs when companies have capabilities to find solutions, but there is a lack of profit incentive, or when market solutions result in prices that are unaffordable for countries with low and middle incomes (Mazzucato and Li 2021). In this context, OI became a set of initiatives designed to facilitate the formation of alliances between different actors (universities, enterprises, non-profit organisations) based on different kinds of incentives: accumulation of reputations, the fulfilment of a social mission, but also the penetration of a market (Lezaun and Montgomery 2015).

One of the most common initiatives of OI are the partnership development products (PDPs), an example of which is Texas' Children, which developed Corbevax. PDPs exemplify the diverse motivations that inspire OI. They can facilitate the exploratory phase of innovations with limited market appeal, as evidenced by the case of the Medicine for Malaria Venture (Burrows et al. 2013), encourage voluntary licensing as exemplified by the Medicine Patent Pool (Bermudez and t'Hoen 2010), or, like the Texas's Children, establish research infrastructures capable of developing drugs and vaccines with a design tailored to the economic and technological possibilities of low-income countries. PDPs have different motivations but share common traits (Kelly et al. 2022). The companies in question lack the requisite manufacturing infrastructure for mass production. In order to facilitate collaboration, they share know-how, information, and encourage the sharing of patents.

Even in its most radical versions, OI does not position itself as an alternative to the market or to public forms of R&D for biopharmaceutical innovation. Its purpose

is to fill the gaps left by the market and the state, and to try to address their shortcomings through organisational innovations based on the search for positive-sum games (Barbera and Negri 2021) between market, not for profit and public actors.

Method and sources

This research adopts the comparative case study approach (Skocpol 1979; Goldthorpe 2000; Anckar 2008), in particular the most similar system design (MSSD). This technique aims to identify the factors that explain a divergence of outcomes between similar cases. Following the MSSD's logical scheme, institutional field factors serve as independent variables of the biochemical content of vaccines. In particular, financialisation (property rights), strong IPR (governance structure) and de-risk (conception of control), would act as incentives and constraints for the adoption of proprietary and experimental biotechnologies in Nuvaxovid. The absence of these peculiar factors in the other two institutional fields would explain their more traditional and cheaper formulation. At the same time, the biochemical content of vaccines can be considered an "independent variable" (not the only one, but a significant one) of their socio-health impact. In fact, the use of components influences the cost of production, the approval and timing of doses, and thus their administration. In this case too, therefore, one of the features of Nuvaxovid that was absent in the other three cases, namely the use of rare and expensive adjuvants, would explain the overpricing and under-utilisation of Nuvaxovid.

The research in the field was conducted through the combined use of documentary analysis and semi-structured qualitative interviews. The analysis of the formulations and socio-health impact was carried out by inspecting technical documentation produced by the manufacturing companies when publishing the results of clinical trials in scientific journals (Dunkle et al. 2021; Heath et al. 2021; Hernandez-Bernal et al. 2023; Thuluva et al. 2022; Toledo-Romani et al. 2024), as well as by consulting institutional databases on the progress of national vaccination campaigns, and surveys and news items published in the international press. With regard to the structure of the entrepreneurial and intellectual property of companies, besides consultation of their websites, analysis was conducted of documents filed with the relevant patent office.

A total of twenty two semi-structured interviews were conducted, which can be divided into two groups (Table 3): interviews with scientists who led or participated in vaccine development (8), and interviews with experts and academics from the vaccine industry and the three different areas of vaccine development (12). It should be noted that the first group of interviews covered in detail the development processes of Abdala (3), Soberana 02 (3) and Cobrevax (2). Unfortunately, it was not possible to conduct interviews with the research team that developed Nuvaxovid, as the manufacturer explicitly refused to do so. This gap was filled by interviewing scientists from the other three organisations about the characteristics of Nuvaxovid, and by consulting surveys published in peer-reviewed journals that focused on the generation process (Tinari and Riva 2021; Wadman 2021; Johnson 2021). For the second group, interviews were conducted with executives from Biocubafarma, an

Table 3 Characteristics of the biotechnological institutional context following Fligstein's framework (Fligstein 2001a, b)

Institutional fields	Property rights	Governance structures	Conception of control
US bio-financialised Industry	Financialization of enterprises' property	Monopoly and assetization through strong IPR	De-Risk strategy
Cuban 'state-led' biotechnology	Public ownership of enterprises and patents	Biocubafarma as integrator of National Innovation System	State entrepreneur
Transnational open innovation	Preference for off-patent formulations	Trans-national platform of knowledge interchange	Both market and state failure

agency that coordinates Cuba's national biopharmaceutical innovation system (4), with experts of biopharmaceutical industry of advanced capitalist countries (4), and with scientist and academic experts in vaccine development and production (6).

The interviews with the Cuban scientists were held in person, at the beginning of 2023, at the headquarters of the two manufacturing companies (CIGB and IFV). The interviews with Corbevax scientists and all the others were conducted online. The interviews focused on the characteristics of each vaccine solution, the presence of product/process innovations, the role of public and non-profit clients in the co-design of the vaccine solutions, the presence of partnerships and collaborations outside the corporate structure that marketed the vaccines, and the type of agreement established. The interviews with the experts were conducted online and focused on the characteristics of the development areas, the innovation policies that drove the acceleration of the four vaccines, the empirical evidence available to date on efficacy, safety and comparisons between different adjuvants, the opportunities and limitations of drug repurposing and the better-than-the-Beatles approach.

In the following paragraphs, quotes from interviews are reported with the name and role of the interviewers who agreed to be mentioned.

Results

This section sets out the results of the empirical research. It is divided into three subsections: analysis of the biochemical design of the four vaccines, with an in-depth look at the main features of Nuvaxovid's divergence ("Into the tube" section); identification of the institutional factors in the bio-financed field that shaped the peculiar formulation of Nuvaxovid ("The social shaping of Covid-19 protein vaccines" section) and the consequences of this design on their socio-health impact in terms of the available data on efficacy, administration and production cost ("The failure of Nuvaxovid" section).

Into the tube

Protein subunit vaccines have been used for decades to fight serious infections such as tetanus, hepatitis B, meningitis or diphtheria (NIH 2019). They are called 'protein-based' because their main characteristic is that they train the immune system by using only part of the pathogen responsible for the infection, usually a protein (Pulendran et al. 2021). These types of proteins, when included in vaccine solutions, are called 'antigens' because they have the function of training the immune system to reproduce antibodies.

Although protein subunit vaccines are very heterogeneous, the biotechnology platform is unique, and its core elements recur in any formulation. According to Fabrizio Chiodo, a researcher at the National Research Council (CNR) in Italy and an international partner of the IFV research team, there are three main components to the formulation process:

> In the production of a protein vaccine, the first step is the composition of the amino acid sequence from which the protein or peptide of the virus, i.e. the antigen, is made. The second step is the expression system, i.e. the technology that allows the antigen to be replicated in cells that act as incubators. Finally, the third step is the choice of an adjuvant to boost the immune response.

These three levels (antigen, expression system, and adjuvants) structure a comparison grid between the biochemical formulations of the four vaccines (Table 1).

Abdala and Corbevax are essentially the same vaccine. They both sequence only one part of the Spike (S.) protein, the receptor binding domain (RBD), which is used by the virus to bind to human cell receptors. The two vaccines also express the antigen in a yeast cell, a technology known for decades in the vaccine industry and used for several mass formulations, including that against hepatitis B. This is the cheapest replication technology available on the market, but it also has important immunological advantages, explains Gerardo Guillen, director of biomedical research at CIGB:

> Pichia pastoris is a yeast that glycosylates, i.e. adds sugars to the antigen as it replicates in the cell. These 'added' sugars are long chain sugars and 80% of them are D-mannose, a sugar that is naturally present in our body and in the cells that expose the viral antigen to our immune system to produce antibodies against it. This produces a good immune response.

Another common element between Abdala and Corbevax is the use of aluminium hydroxide as an adjuvant. It was first developed by British immunologist Thomas Glenny in 1920 and has since become the most widely used adjuvant in the world, off-patent and affordable. The only difference is the use of CpG, which Corbevax scientists have added to the formulation because they believe it strengthens immune memory in the long term. This is a proprietary adjuvant, which makes Corbevax's branding by some press journals as a completely 'off-patent' vaccine questionable. However, the scientists at Texas' Children's Hospital assured that this component remains affordable on the market.

Although they are both derived from the same field of research, Abdala and Soberana 02 are distinct vaccines. The latter is the sole conjugate vaccine against SARS-CoV-2 in the world: the RBD antigen of the S protein is "docked" to an inactivated *tetanus toxoid*, which enhances the immune response. This solution has been employed in the past for numerous paediatric vaccines, including that against haemophilus B, which was developed independently by the Cuban national innovation system in the mid-1990s. Furthermore, Soberana 02 contains antigens developed in mammalian cells, which represents one of the most complex and expensive technologies on the expression system market. These antigens have previously been used by Cuban scientists for the development and production of monoclonal antibodies against various tumour types.

The most significant divergences can be observed in the composition of Nuvaxovid. In all three levels, the US vaccine has exceptions. Firstly, the vaccine employs the entire S protein, rather than a partial component. Secondly, the vaccine employs an innovative expression technology, such as that utilised in baculovirus

cells, which confers significant advantages during the manufacturing phase. Nevertheless, the most pertinent discrepancy pertains to the level of adjuvants, in particular the use of PS-Core 80 and Matrix-M.

These two biotechnologies are patented by Novavax. The PS-Core 80 which is not technically an adjuvant but still performs an immunopotentiating function, is Polysorbate 80 core (PS80 core), a nanoparticle that binds S. trimers up to 14 copies, making the vaccine molecule similar in size to Sars Cov II (Wadman 2021). The second is Matrix-M, an adjuvant consisting of nanoparticles containing a saponin extracted from the Quillaja saponaria Molina tree (QS-21), a rare oak tree. Although this adjuvant shows significant evidence of efficacy, and is among the few to have received authorisation from important market regulators such as the US Food and Drugs Administration (FDA), it also presents several vulnerabilities. This substance, indeed, is subject to very strict protection by state authorities because it is already used in the food and beverage industry.Without stringent regulations on its extraction, there is a risk of it being endangered (Borrell 2020). Moreover, It was estimated that the maximum amount that can be extracted for the vaccine industry is equivalent to 6 million doses (Ragupathi et al. 2011), while only for the US, Novavax should have provided the equivalent of 100 million doses. A huge demand, such as the Covid-19 vaccines one, could replicate what happened to the Pacific yew tree, which almost became extinct in the 1980s, when its bark was discovered to contain an active ingredient useful for a chemotherapeutic drug, pactlitaxel (Gersmann and Aldler 2011). In addition to environmental vulnerability, there are also economic factors to consider: the cost of QS-21 is considerable, estimated at approximately USD 100,000 per gram. The equivalent in one dose would amount to approximately USD 5 (Borrell 2020), which raises production costs to levels only accessible to high-income countries.

The social shaping of Covid-19 protein vaccines

In the previous section, important differences were noted in the biochemical content of the four vaccines, even though they are an expression of the same technical frame. Our thesis is that it is not the free ingenuity of the research teams that explains these 'divergences between similar cases', but the constraints and incentives established by the norms and values characteristic of the respective organisational fields.

In relation to antigen sequencing, the difference between those who, like Novavax, developed the whole protein, and the others who opted for RBD, seems to be explained by looking at the economic factor. This is according to Sonsire Fernandez, one of the IFV scientists who supervised the development of Soberana 02:

> Novavax mimics the trimeric structure of S., which means that the immune system sees something more similar to the real virus, and in principle this is an advantage. However, already at the beginning of the pandemic, it was realised that about 90% of the neutralising antibodies were formed predominantly against a single region of S., the RBD. Moreover, targeting the RBD had objective operational advantages, because sequencing it is easier, quicker and cheaper than sequencing the entire S-protein.

However, Novavax was not isolated when it made the decision to develop the whole S. as antigen. In fact, all vaccines developed in its field, including those with MRNA, have been constructed with this feature. A case of *mimetic isomorphism* can therefore be assumed (Di Maggio and Powell 1983). Novavax, of all the companies involved the smallest and most inexperienced, may have preferred to follow its more established competitors at a time of high uncertainty. Moreover, in the bio-financed field, cost savings were not a priority value, whereas it was for the Cuban companies and the entity that developed Corbevax.

The need to develop formulations that are cheap to manufacture and easy to scale up explains the strong similarities between Abdala and Corbevax, but not the differences between the first and most widely used Cuban vaccine and its "compatriot" Soberana 02, particularly in the field of expression technologies. This element appears to contradict our hypothesis, as similar institutional norms often result in disparate biochemical outcomes. However, isomorphism is not always the strategy that organisations adopt when subjected to the same pressures. In certain instances, including the highly challenging context in which Cuba confronted the pandemic, heterarchy, or the maintenance of distinct evaluation principles within a single field, may be a viable approach (Stark 2009).

The closed circle logic, which entails the concentration of the entire value chain of vaccines within the inter-organisational network of BioCubaFarma, prompted Cuban scientists to focus on biochemical designs that could utilise all the fermenters in the country, which could alternatively express antigens in yeast or mammalian cells. Abdala and Soberana 02 are, therefore, different not only because IFV and CIGB follow different immunological schools, but also—and perhaps above all—because their different design made it possible to optimise existing resources and speed up industrial scale-up. As Rolando Perez, Biocubafarma's scientific director, explains:

> Given the uncertainty of the results, we decided to focus on several designs based on different immune strategies and production technologies. This gave us two advantages: we increased the probability that at least one formulation would work and, if we had more than one, we could start industrial-scale production in parallel, using several facilities that would not be suitable for a single formulation.

This interdependence is reflected in other decisions made by Cuban scientists in formulating their vaccines. For example, the reason Soberana is called '02' and not '01' is that the first version of the vaccine had a not optimal formulation and an error in the antigen assay. This information, which is extremely sensitive because it refers to a failure, was not hidden but shared by the IFV with the CIGB, the permanent table coordinated by the Cuban government to organise the country's response to Covid-19. Dagmar Garcia Rivera, deputy director of the IFV, tells the story:

> The initial dose of antigen we put in Soberana 01 proved to be insufficient, so we increased it. The team developing Abdala, which was still preparing the formulation at the time, also learned from this experience. There was constant

communication between the companies developing the vaccines and there was never any competition between us.

Finally, Cuban enterprises that developed the vaccines were public. This aspect, according to Shoenfeld (2020), is of greater relevance than merely operational considerations. The fact that vaccines were produced and distributed by public organisations contributed to a 'caretaker' role for the country's political authorities. This was not the case of the US, which merely covers the full costs of vaccine development and industrial scale-up but does not claim any role in the legal ownership of their use, nor in their biochemical configuration.

The main differences between the four vaccines are in the adjuvants, in particular the use of Matrix-M and PS-Core 80 in Nuvaxovid. Novavax relies heavily on these two biotechnologies, for which it has exclusive commercial rights and strong technical and scientific expertise. It has used them for malaria and respiratory syncytial virus (RSV) vaccine candidates, and the company's website repeatedly references these two biotechnologies, defining Novavax's position in the vaccine industry. In other words, Matrix-M and PS-Core 80 are Novavax's strategic assets, which defines its value in terms of its organisational field. Whether or not they were convinced that the use of these biotechnologies was necessary to achieve an effective formulation against Covid-19, the scientists who developed Nuvaxovid could hardly have taken a different path. Novavax would have been economically uninterested and probably technically incapable of developing a 'simpler' vaccine candidate.

This restriction on the use of proprietary and experimental biotechnology was determined by the rules of the biofinance field. Novavax's ownership is held by 600 different financial institutions, including Blackrock and Vanguard, which also own shares in Moderna, Pfizer and many other companies in the sector. These large shareholders have chosen to back Novavax because Matrix-M and PS-Core 80 allow them to formulate an innovative offer in a market such as that of protein vaccines, where it is not easy to stand out after 40 years of use. These two biotechnologies make the company potentially attractive in terms of the sector's governance structures, monopoly and assetisation. On the one hand, their presence gives Novavax full control of the product value chain. On the other hand, even if they do not reach the market, the accumulation of evidence on the application potential of the two biotechnologies would increase the value of Novavax's shares and, indirectly, its patents. Lastly, the uncertainty about the efficacy and safety of experimental biotechnologies, which might suggest caution in their use, is offset by the concept of field control, which is based on the internalisation of the industrial costs of trial failure into the public purse. Indeed, "de-risking" has been the watchword guiding the United States and other advanced capitalist countries in the incubation of vaccine candidates, by fully bearing not only the costs of development, but also of testing and industrial scale-up (Sampat and Shadlen 2021), without affecting the property rights of the companies.

Financialisation of corporate ownership, value capture through assetization and de-risking are the norms that have shaped the biochemical content of Nuvaxovid, like that of all other vaccines developed in the same organisational field. These norms, in place long before the appearance of SARS-CoV II, dictated the type of

response that the technoscientific and industrial players in the field would be able to implement (Birch and Muniesa 2020). In this "world", an effective and safe vaccine against Covid-19 could only have come about through the better-than-the-Beatles approach: only through the use of proprietary and experimental biotechnologies. However, in the case of protein vaccines in particular, this constraint has become entrenched as a path dependency: i.e. it has been a harbinger of inefficiency, leading Novavax to develop a vaccine that is unnecessarily expensive, slow and complicated to produce.

The failure of Nuvaxovid

The use of proprietary and experimental biotechnology only in Nuvaxovid had negative consequences on the vaccine's socio-health impact. According to scientist Maria Elena Bottazzi, who coordinated the Corbevax development, Novavax has completely failed in its public mission:

> Novavax has not been able to go beyond "formally perfect" clinical trials. However, the amount of vaccine reaching the population, after 1 year of distribution, is less than one million doses. This is also due to the fact that the vaccine is very complex to produce, the costs are high, and it is not easy to make it replicable and scalable. If one considers the public investment that went into developing it, the doses used, and if one makes the same comparison with our vaccine or the Cuban ones, one wonders how much it really cost.

The following table reconstructs the socio-health impact of the four vaccines. It does so by using three variables: efficacy, doses administered, and public and philanthropic investments made for the vaccine's development (Table 4).

Comparative studies on the efficacy of the four vaccines have never been carried out. Of the four vaccines, the only one to have received WHO pre-qualification is Nuvaxovid, while the other three are, as of September 2023, still under review. However, this procedure, which is very onerous for manufacturers and is based on the good manufacturing practices (GMPs) of high-income countries, refers—in the opinion of the Cuban scientists interviewed—mainly to the characteristics of the equipment used for the individual batches, and does not replace the validation activity carried out by the individual national regulators.

Table 4 Comparison among vaccine formulations

	Antigen	Expression System	Adjuvants and Immunopote
Abdala	Spike Protein (RBD)	Yeast (*Pichia pastoris)*	Alum
Soberana 02	Spike Protein (RBD)	Mammalian (*CHO cells*)	Alum
Corbevax	Spike Protein (RBD)	Yeast (*Pichia pastoris*)	Alum + CpG
Nuvaxovid	Spike Protein (Whole Trimeric Protein)	Insect (*Baculovirus*)	Matrix-M

If, therefore, one considers the data from phase III trials published in various scientific journals and approved in the countries where they were administered, it can be argued that all four formulations, after a full course of doses (two or three depending on the vaccine concerned), are effective in combating symptomatic Covid-19 disease and are safe in terms of side effects (Toledo-Romanì et al. 2022; Heath et al. 2021). In the case of Soberana 02, there are also efficacy data collected in the Cuban paediatric population (Toledo Romanì et al. 2024), who were vaccinated from the age of two onwards, which confirm the efficacy data, and also show excellent results from the point of view of the safety of the formulation even for children (Table 5).

The doses administered exhibit a first major difference, with a clear under-utilisation of Novavax compared to the other three vaccines. As of September 2023, in the countries of the European Union, where Novavax has been authorised since January 2022, 225,000 doses of the vaccine had been administered (European Commission 2023). On the same date, in the United States, where it has been authorised since July 2022, the doses administered amounted to around 80,000 (US Government 2023). In Cuba alone, as of September 2023, more than 45 million doses of the two Cuban vaccines had been administered (Minsap 2023). Unfortunately, due to the ongoing trade war with the USA, the Cuban managers interviewed refused to state exactly how many doses had been exported to foreign countries. On the same date, Corbevax was reported to have been administered to 73 million Indians (Indian Government 2023).

Several factors were responsible for the under-utilisation of Nuvaxovid. One of them was the lack of experience on the part of the manufacturing company, which had never produced any other product before the Nuvaxovid vaccine. This was admitted by Novavax's scientific director, Gregory M. Glenn, in a statement reported by an investigation published in the *British Medical Journal* (Tinari and Riva 2021):

> If I can be a little bit defensive, about two years ago we were a very small company, we didn't have manufacturing. It's also somewhat artsy, it takes people with a lot of skills. You can't just get people off the streets to do it.

The difficulty of industrial scale-up resulted in delays in deliveries, as happened with GAVI, which decided to terminate a supply contract worth around USD 700 million (Nolen and Robins 2023).

However, the problems experienced by Novavax were not caused solely by a lack of material infrastructure. As early as September 2020, Novavax could count on the support of the world's largest vaccine manufacturer, the Serum Institute of India (Tinari and Riva 2021). What was decisive was the experimental formulation of the vaccine, in particular the use of a rare adjuvant, namely Matrix-M, subject to severe supply constraints. This component raised the price of the vaccine to the same level as that of mRNA vaccines and complicated the technology transfer to manufacturing companies in the Global South, thus excluding users in middle- and low-income countries. It also slowed down the authorisation process at most important regulators in high-income countries, such as Food and Drugs Administration (FDA)- and European Medical Agency (EMA) (Johnson 2021). Nuvaxovid did not arrive in the EU until February 2022, when the third-dose campaign had already been completed

Table 5 Socio-health impact of the 4 protein vaccines

	Full vaccination efficacy	Administered doses (Sept. 2023)	Public and not for profit funds	Countries
Abdala/Soberana 02	> 90% (Toledo-Romanì et al. 2022; Bermejo et al. 2022)	> 45 mln (Minsap of Cuba 2023)	< 50 mln $	Cuba, Belarus, Iran, Mexico, Nicaragua, Saint Vincent and Grenadine, Venezuela, Vietnam
Nuvaxovid	> 90% (Heath et al.2021)	< 1 mln (ECDC, 2023; CDC 2023)	> 2 mld $ (Florio et al.2023)	Australia, Canada, EU, UK, US et al. (41 countries in total)
Corbevax	> 90% (Thuluva et al. 2022)	> 70 mln (India Gov.)	< 12 mln di $	Botswana, India

in almost all countries, and in the USA, which had also incubated the vaccine with public funds. It was only authorised in July 2022, when demand had already been exhausted by mRNA vaccines. The use of an experimental formulation also slowed down the extension of the vaccine as a booster for heterologous vaccination (i.e. conducted with different vaccines), and for paediatric vaccination, in contrast to the other three vaccines, in particular Soberana 02, which was immediately made available for children aged two and above. which was still in its infancy in 2022.

A further indicator of Nuvaxovid's disappointing performance is the financial market's reception of its sales. Between 2020 and 2022, the stock value of Novavax rose by more than 200% on the news of US public funding of its vaccine candidate, and the publication of the first clinical efficacy data. The collapse of the market-cap to pre-pandemic levels, and thus to the brink of delisting on the Nasdaq, began immediately after the vaccine went on the market, in early 2022. By November 2023, Novavax's stock was worth less than before the pandemic.

On the development cost side, Nuvaxovid received $1.6bn (Congressional Research Service 2021) by the US Government, with a commitment to deliver 100 millions of doses within the end of 2021, in the event of effectiveness. It also received around $700 m from GAVI for the delivery of doses to low-income countries (Nolen and Robins 2023). These figures cannot be compared with those used in Cuba, although, as Rolando Perez of Biocubafarma points out, the 'tens of millions' invested by the Caribbean state was a huge sacrifice:

> We had to make some imports, but these can be counted in the order of a few tens of millions of dollars. For us, however, it was a colossal effort. Making vaccines cost us sacrifices and money that was invested in this and could perhaps have been spent on something else, electricity, food.

In the case of Corbevax, the development investment amounted to only a few million dollars, and derived almost entirely from philanthropic funds (Salam 2022).

Why trying to be better than the Beatles can be a problem

One of the most important results of the empirical research on protein vaccines is to show some limits and controversial "side-effects" of the "better than the Beatles" approach to biopharmaceutical innovation. This is an argument backed by empirical evidence which goes beyond this case study. In particular, the bio-financialized field, amid increased resources for R&D, would find it increasingly difficult to develop novel active ingredients, and to make them sufficiently effective and safe to be placed on the market (Kapczynski 2023). This is argued by both Scannell et al. (2012) and Pammolli et al. (2011) in two separate papers published in *Nature*. In the first, the authors propose the concept of Eroom's Law, which is the opposite of Moore's Law in electronics, whereby the number of New Molecules Entities (NMEs) would halve every nine years per billion dollars invested in R&D. In the second, the authors describe a 20 to 60% increase in the drop-out rate for more than 28,000 patented chemical compounds in OECD countries from 1990 to 2010.

According to both of the above-mentioned studies, the main explanation for these numbers is the "better-than-the-Beatles" problem (Scannell et al. 2012), that is, the tendency to search for molecules able to generate radical innovations in markets that are profitable but already saturated with solutions. This, on the one hand, would induce R&D to search for rare and expensive chemical compounds (Ibata-Arens 2021), with ambitious therapeutic targets, but which for this very reason are more prone to failure. On the other hand, it would make research teams underestimate the therapeutic potential of *drug repurposing* (Conti et al. 2020). Both patterns can be observed in the case of protein vaccines. On the one hand, a "better-than-the-Beatles" vaccine like Nuvaxovid, which makes use of rare and expensive adjuvants and nanoparticles, invented within a mature biotechnology platform and with ambitious therapeutic goals, proved to be too expensive and of little use. On the other hand, Abdala, Soberana 02 and Corbevax represent the *drug repurposing* therapeutic potential, which is cheaper and more scalable, but not less efficient or safe.

However, neither Scannell et al. (2012) nor Pammolli et al. (2011) set out to identify the institutional factors that determine the "better-than-the-Beatles" problem. The empirical analysis of protein vaccines presented here seeks to interpret the phenomenon as a path dependency created by specific norms of the bio-financialised field. The most important of these would be the financialisation of corporate ownership, the prevalence of value capture strategies based on assetisation, and de-risked public innovation policies. In particular, these processes would make conditions such as large set-up and adaptive expectations more widespread and recurrent. They would also link their business model and technical-productive capabilities to the exploitation of a specific intangible.

Path dependency does not always result from radical innovation. Moderna and BioNTech were also subject to the same institutional pressures as Novavax. Yet their path did not prove inefficient. In the case of Novavax, the path dependency lies in the fact that it applied the principles of the Better than the Beatles approach to a mature biotechnology platform such as protein vaccines—out of economic interest, but also because it could not do otherwise. This created a series of competitive disadvantages for Nuvaxovid that devalued it and pushed it out of the market. A patent-free and low-cost protein vaccine had relevant competitive advantages over mRNA vaccines: lower development costs, ease of technology transfer, fewer side effects and no need for special coolers to store batches. These advantages were lost with the adoption of an experimentalist approach, which increased the cost of developing Nuvaxovid and the uncertainty about rare side effects at the level of an mRNA vaccine, but without the same speed of production and commercialization. With regard to the most prevalent vaccines in middle- and low-income countries, Nuvaxovid's distinctive and intricate biochemical composition rendered it too expensive.

A large body of critical literature (Lave et al. 2010; Gaudilliere 2021; Torreele et al. 2021), agrees in associating markets characterised by financialisation and strong IPR with dysfunctional effects on the quality and direction of biopharmaceutical R&D. However, what does not emerge in these studies is what can be inferred from the case study on protein vaccines. The first inference is that the game can be a negative-sum one even for companies that own innovations: this is what has been described by research in regard to Novavax. Yet GSK-Sanofi and Merck, which have

developed protein vaccines in the same field and with experimental characteristics similar to those of Nuvaxovid, have performed even worse. The second inference is that organisations with fewer resources but which are unconstrained by the bio-financilezed institutional architecture can do better—and this is what emerges from the Cuban case in particular.

Several studies have documented episodes of successful innovation generation in the Global South (Cassier and Correa 2007, 2010; Ibata-Arens 2021). However, the cases collected in these studies concern examples of generic drugs, which, although they involve incremental innovations relating to the production process and the use of certain components, remain 'copies' of original inventions developed in advanced capitalist countries. This is not the case, in particular, of Abdala and Soberana 02: the two Cuban vaccines are completely original, and their development has led their manufacturing companies to register patents on process innovations.

Although in favour of the patent waiver dispute during the pandemic, Cuba has not exposed itself to the same extent as other countries, such as South Africa or India (Plahte and Reid-Henry 2013). The distinctive feature of Cuba's innovation system is that it is competitive in the generative (Lage 2012), and not the implementation, phase of the innovation process, as is the case of other developing countries (Cassier and Correa 2007, 2010). The objective of Cuban biotechnology, immediately after the development of drugs for its population, is to export its inventions. This objective is perfectly consistent with the political-ideological doctrine that inspires the entire Cuban experience. Exporting drugs means bringing dollars into the country, i.e. valuable currency which Cuba, due to the US embargo, desperately needs. Highlighting the strategic value of generative know-how in the Cuban entrepreneurial experience is also the case of mixed companies abroad, in which Cuban companies participate together with foreign, often private, industrial and scientific partners, contributing their own patents as capital. A significant case is that of the cancer vaccine Cimavax, developed by the Centro de Immunologia Molecular (CIM) and in an advanced stage of clinical evaluation at the Rosewell Park Cancer Center in New York.. The Cuban case should therefore be related, not to the strand of literature on biopharmaceutical innovation in the Global South, but to the one that has updated reflection on the role of the state in the vaccine industry, and on the need to extend its functions, powers and responsibilities in the conduct of innovation processes.

This strand of studies did not originate with the advent of the Covid-19 pandemic. Graham (2019) observed that the anti-Ebola vaccine, ERVEBO, developed by Merck, was created by Canadian scientists affiliated with state laboratories. He further noted that the transfer of knowledge from public technoscientific actors to private industrial companies is a sort of path dependence, for which the public sector cannot be efficient in manufacturing scale-up and sales. Blume and Mezza (2021) observed that in several Northern European countries, the presence of public research and production infrastructures effectively met the domestic demand for vaccines. They further noted that the dismantling of these infrastructures after 1990 was one of the main causes of these countries' vulnerability to the Covid-19 pandemic. Others, notably Sampat and Shadlen (2021), instead pointed out that, during the pandemic, the state's role in co-constructing biotechnology markets expanded beyond

covering the costs of molecule exploration, as in the past. According to Mazzucato and Li (2021), never before had there been such recognition of the public value generated by state investment as in the case of anti-Covid vaccines. Although the two economists argued against an entirely public control of the pharmaceutical industry, they proposed a 'nationalisation' of the sector, i.e. the state should own the patents generated with its own funds, and it should create infrastructural 'commons' for the sectors, such as gene therapies, most exposed to market failure. In a study submitted to the European Parliament, Florio et al. (2023) proposed that the EU should establish a public infrastructure for pharmaceuticals and vaccines on a par with CERN for atomic energy. The new public institution would consist of a network of existing pharmaceutical R&D laboratories in universities and public research centres in the member states. However, a manufacturing infrastructure would also be added to the network, which, at least in the case of vaccines, would enable the sale of products on the market, and increased competition with big pharma.

In none of these studies, however, is the Cuban case considered, if not as good practice, then at least as a case study for further investigation. Instead, the evidence from the study on protein vaccines suggests that the governance of Cuba's national innovation system could be an inspiration for the development of a public research infrastructure. Particularly interesting to study, due to their marked difference from those institutionalised in capitalist countries, are the institutional mechanisms that incentivise collaboration between companies, protect public ownership of inventions, and place the industrial sector in the role of an operational arm of the national health system, rather than in a counterpart role.

Conclusions

The development of a safe and effective protein vaccine against Covid-19 was possible without resorting to molecules that, trying to be "better than the Beatles", led to economic failure and low social impact. In the case of Nuvaxovid, this dysfunctionality was informed by a path dependency induced by the institutional systems of the bio-financialized field, within a technical framework where the most competitive solution was the drug repurposing approach implemented by Abdala, Soberana 02 and Corbevax.

Radical innovation has rewarded mRNA vaccines, which, unlike protein vaccines, do not require medium- to long-term production processes. However, as Maria Elena Bottazzi of the Corbevax development team argues, the rest of the world needed a different kind of innovation, which the protein vaccine framework made possible:

> To make an effective vaccine, there was no need for complicated technology or proprietary adjuvants that cost so much money. In the emergency created by Covid-19, innovation meant using existing resources and scaling them up at an impressive rate, because the priority was not to make a profit but to save as many lives as possible.

Novavax would not and could not have developed simpler vaccines even if it had wanted to. Its shareholders were not economically interested and, probably, the

company was also technically unable to do so. However, the same cannot be said for other entrepreneurial players that received the same funding from governments and non-profit organisations. Giant companies such as GSK, Merck and Sanofi, which, together with Pfizer, were "the big four" in the vaccine industry before Covid-19 (Douglas and Samant 2018), had a sufficiently diverse infrastructure and know-how to attempt a solution like the Cuban or Corbevax vaccines. If they did not even try, it is simply because they had no interest in doing so, nor did they have any incentive or sanction from the public to test a path other than experimental vaccines.

The price of this failure was paid not only by the companies that failed in their trials or in the sale of their vaccines. Most of the bill was paid by states and public–private organisations such as GAVI, which invested billions of dollars in doses that were either never delivered or arrived too late to be of any use. In all advanced capitalist countries, no vaccine that, like Abdala, Soberana 02 and Corbevax, relied predominantly on off patent and low-cost components was commercialised. Even in the second phase of the pandemic, drug repurposing was not considered as a possible strategy by the companies or the governments that funded them.

Finally, the "side-effects" of the "better-than-the-Beatles" approach arguably are also caused by the lack of policy guidance for innovation. The key to path dependency is useful to reconstruct the sequence of events and decisions that, well before Covid-19, limited the scope for action not only of firms but also of governments, making it too costly, risky or even technically impossible to act without recourse to the market. Tracing in detail the aforementioned events and decisions falls outside the scope of this article. Yet, possible insights could be made into the regulations that legalised the privatisation of knowledge generated with public funds, dismantled public research institutes that had designed and produced vaccines, and extended to drugs and vaccines the same kind of regulations in force for other technological innovation products. The topicality of this analysis concerns both future strategies to combat Covid-19, which still is a threat to global public health, and measures to be undertaken if new pandemic viruses emerge (Pryanka et al. 2024). The use of the bio-financialized market has entailed costs and inefficiencies that were not sufficiently highlighted during the acute phase of the pandemic. Understanding and debating these shortcomings can support policy actions aimed at changing the framework conditions for a future response to these global challenges.

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