Anatomy of a health scandal – Dengvaxia Sanofi's dengue fever vaccine

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When I saw the pictures of these Filipino families demonstrating against Sanofi and its dengue vaccine Dengvaxia, shouting "Filipino children are not guinea pigs", it reminded me of the title of a book published in 2015 by a world-renowned Danish professor of medicine, Professor Peter C. Gøtzsche: Deadly Medecines and Organized Crime. How the pharmaceutical industry has corrupted health services! The scene was set. And as a French doctor and activist, I had to share information about Sanofi, a French multinational pharmaceutical company! But before we talk about the vaccine, let's take a look at the dengue virus and its history, which teaches us a lot about liberal globalization.

Even viruses have a history! Four dengue fever viruses and globalization, or the re-emergence of dengue fever in a hemorrhagic form!

Long a benign disease, dengue fever is experiencing an exceptional expansion, with the recent appearance of severe haemorrhagic forms. Dengue fever has been known since the end of the 18th century, when it caused, during the rainy season, epidemics in ports, tropical regions and the Mediterranean, most often benign and simply very painful. It was called breakbone fever, dandy fever... This disease is spreading worldwide. The number of cases more than doubles every ten years. 8.3 million apparent cases in 1990, now between 80 and 100 million. Overall, 2.5 billion people are potentially exposed to the disease in more than 100 countries. The limits of its spread are still far from being reached, as the spread area of aedes aegypti and aedes albopictus, the mosquitoes that transmit dengue fever viruses, is widening with global warming.

Global warming, international freight transport (Aedes albopictus arrived in the USA in 1985, on a boat carrying old tires from Asia, the shape of which is ideal for collecting some water and mosquito larvae), the appearance of huge urban concentrations where the water is stagnant, the road network failing and gigantic daily transports (Mumbai-Bombay, 7 million people use the train every day between the centre and the periphery), the cessation of mosquito control programmes (common vector for dengue and yellow fever, aedes aegyptii had been eliminated from the South American continent in the 1950s to 1960s when yellow fever was controlled, it has since reappeared), have promoted a high population density, and a high density of biting vectors, and thus the expansion of

dengue fever, and other arboviroses, such as zika, chikungunyia, yellow fever...

Not only is dengue fever developing, but since the 1950s, in the Philippines, in Thailand, a new form of dengue fever has appeared. Dengue hemorrhagic fever with shock syndrome, sometimes fatal. This form of hemorrhagic dengue fever is also in the process of globalization. Today there are nearly 500,000 cases of dengue hemorrhagic fever every year with just over 10,000 deaths per year.

Since the 1990s (Chastel 1992, Grubler 1997), the main hypothesis adopted by the majority of researchers to explain the emergence of the hemorrhagic form of dengue fever has been the parallel circulation of the four types of dengue virus. Indeed, according to the hypothesis of Halstaed's immunological facilitation, not only does infection with a first dengue fever virus not create immunity for the other three viruses, but it also promotes the penetration of the virus into the cells, with explosive production of cytokines, bleeding and shocks. Globalization is making the four types of viruses circulate faster and faster everywhere at the same time, thus multiplying the number of haemorrhagic forms. Let us remember that for more than 25 years this problem, which will be that of Denvaxia, has been known by researchers!

Sanofi's Dengvaxia, at financial risk!

In September 2008, Sanofi acquired $230 million from Acambis, a small Anglo-American bio-technology company with a dengue vaccine candidate. If this vaccine becomes the first dengue fever vaccine on the market, before Takeda and Merck's vaccines, it can become a blockbuster, i.e. a product that brings in more than $1 billion to Sanofi each year! But developing a vaccine takes an average of 12 years, involves a lot of money and requires the agreement of the public authorities at all times. Has Sanofi taken the necessary steps to ensure that its vaccine arrives on the market first, before all its competitors, and that its return on investment is as rapid as possible?

On November 29, 2017, Sanofi must announce that, after reviewing the 5-6 year results of its clinical trials, vaccinated people who had never been in contact with dengue fever suffer more than others from serious forms of the disease! Dengvaxia is accused of causing the deaths of 14 people in the Philippines in December 2017, and 65 as of July 2018. Families demonstrate, accuse Sanofi of treating Filipino children as guinea pigs and health officials as corrupt. It must be said that the vaccination campaign for the 870,000 Filipino children cost $70 million, more than any other vaccination program in the country. The new Philippine government is asking for a refund. Vaccination is stopped. Prosecution is ongoing. The plant that manufactures the vaccine in France is shut down, with several years of stocks. Chronicle of a health scandal!

Sanofi acquired Acambis and its vaccine candidate in September 2008. But it was in May 2009 that he began building a plant in France for his future vaccine Dengvaxia in Neuville-sur-Saône. An investment of 350 million euros, for an announced production of 100 million doses each year from the end of 2013. An incredible bet on time, but above all a financial bet, because at that moment, Sanofi has just launched phase two clinical trials in Thailand, with 4000 participants aged 4 to 11. And the results will not be available until September 2012!

"When Sanofi launched the human clinical trials, we alerted him to various potential risks, such as possible interference between different strains of dengue fever, but especially a specific immune response that allows the virus to enter target cells even more easily after initial exposure. This is what Fréderic Tangy, head of the viral genomics and vaccination unit at the Pasteur Institute, told journalists Lise Barnéoud and Chloé Heketsweiler of the leading French daily newspaper, Le Monde, who produced an excellent report on Dengvaxia on 6 March 2018 entitled"Vaccination against dengue fever: the Sanofi fiasco". A file from which we get a lot of information.

The first results of these phase two trials are disappointing and surprising. The protection is only 30%. And even almost zero against the dengue strain 2 of the virus, despite the highest antibody levels! There are many questions about this vaccine for which Sanofi is already building its plant for millions of dollars.

To big to fall! This applies to banks and the 2008 financial crisis, but it also seems to apply to the fastest possible introduction of Dengvaxia. While questions are being asked about the first results of phase two, without even waiting for the full results, which will only be known in September 2012, Sanofi is moving on to phase three in 2011, involving 30,000 children in 12 countries. And incredible, while the entire scientific community knows the links between primary infection and severe form of the disease when re-infected with another strain, only 10% of the children included in the trials will be tested to see if they have been previously exposed to the dengue virus. The answer falls. Only 20% of the 10% tested have never been in contact with the dengue virus. Sanofi researchers have done the calculation since 2015. Only 2% (20% of 10%) of the sample will be analysable to calculate the risks involved in vaccinating children who are never in contact with dengue fever! Unconsciousness or a desire to save? Have the authorities validated the incredible protocol of these clinical trials?

In September 2015, the results of the first three years of monitoring are made public. They show that in the Asian trial, vaccinated children aged 2 to 5 years have a 7.5 times higher risk of hospitalization for severe dengue fever than unvaccinated children! And in this group of 2 to 5 year olds, half of the children tested had never been in contact with dengue fever before.

Not listening to these alarms, to save its investments, Sanofi simply decided to change the minimum age for vaccination. In its September 2015 publication, it advances for the first time the minimum age of 9 years. Simply hoping that from this age onwards, the benefit/risk balance will become favourable.

This is a risky gamble, contested by many researchers, including those at the WHO, when you remember that it can only be based on a sample of 2% of those tested! But a winning financial bet hopes Sanofi, which wants to save the blockbuster Dengvaxia at all costs.

Despite these alerts, Sanofi was granted a first marketing authorization for Dengvaxia by Mexico in December 2015. Yet Mexico is the country where, according to Sanofi’s publication, the effectiveness of the vaccine is the lowest, with only 30% of people protected. But in fact, it was in April 2014, during a trip by the French President François Hollande, that Mexico’s decision was taken. A commitment was signed in July 2015 by the Mexican Deputy Minister of Health, a certain Pablo Kuri Morales. Sanofi knows the minister well. He was its Scientific Director in Mexico from 2009 to 2011.

A few days after Mexico, it is the Philippines’ turn to authorize Dengvaxia on December 22, 2015, while the Phase 3 trial is still ongoing! This is what the newspaper Le Monde writes: “On two occasions, on May 14, 2015 and December 2, 2015, the Philippine Minister of Health, Janette Loreto-Garin, meets with Sanofi’s management. There are also suspicions of a conflict of interest. For example, one of the biggest supporters of the vaccine is Kenneth Hartigan-Go, Under-Secretary of Health from 2015 to 2016, former head of the Philippine Public Health Agency from 2010 to 2014, but also founder and director, from 2001 to 2009, of the Zuellig Family Foundation, whose pharmaceutical branch is the exclusive distributor of the vaccine in the Philippines. When Philippine dengue specialists alert authorities, such as Lenila Dans, an epidemiologist at the University of Manila,”the dean of his university received a letter from Sanofi asking that the statements on the risks of Dengvaxia be withdrawn".

Dengvaxia, no authorization in France and Europe!

Mexico, the Philippines and Brazil very quickly grant marketing authorization. While the French territories of Martinique, French Guiana, Guadeloupe and Reunion Island are also affected by the disease, the vaccine from the French laboratory Sanofi is not authorised. The High Council of Public Health, in a statement dated 7/10/2016, "does not support the early use of this vaccine in the French American Territories. Some co-morbidities, mainly sickle cell disease, could lead to the development of severe forms of dengue fever. And it was only in April 2016 that Sanofi filed an application for marketing authorization in Europe. While the European Medicines Agency takes an average of two hundred and seventy-seven days for an authorisation, today, almost 900 days later, there is still no European authorisation for Dengvaxia!

In April 2016, on the recommendation of its SAGE Strategic Expert Group, WHO gave the green light to vaccination. This decision was highly criticized, especially since WHO experts had previously criticized the vaccine. We remember the accusations of the British Medical Journal and the Council of Europe about the links between WHO experts and those in the pharmaceutical industry during the H1N1 flu season.

Sanofi and corruption...

On December 11, 2017, on CNN Philippines, former Health Minister Garin declared "No corruption in Dengvaxia's purchases". However, Sanofi's current situation with regard to corruption is serious.

In December 2012, Sanofi agreed to pay $109 million to the US courts to settle charges of bribery against US doctors for prescribing its treatment for joint diseases. In 2014, Diane Ponte, a former Sanofi legal assistant in the United States, filed a complaint for being fired after reporting a $34 million bribe fraud paid to doctors, pharmacists and hospitals in the United States to promote her diabetes treatments, which account for one fifth of her sales. In 2018, the SEC, the US Securities and Markets Authority, forced Sanofi to pay $25 million to stop its corruption investigations into bids in Kazakhstan and the Middle East. According to the SEC order, these programs "involved bribes to public procurement officials and health care providers to obtain tenders and increase prescriptions for Sanofi products.

Drugs are not commodities, health is not a financial product.
Sanofric (it means Sanimoney) , billions of profits, thousands of job cuts

It was behind this banner that the collective of employees in anti-Sanofric struggle demonstrated. Like the unions SUD and the CGT, they denounced the stock market redundancies of the French pharmaceutical giant, which had become the first capitalization of the CAC 40 ("the French Stock Exchange"), ranked among the top five pharmaceutical giants in the world. Sanofi has already eliminated 5000 jobs in France since 2008, particularly in Research and Development. "40% of research programs are cut", which, according to CEO Chris Viehbacher, should allow the group to focus on "high value projects and reallocate resources to external partnerships". Four thousand research positions are being sacrificed worldwide, a third of the workforce.

To continue to maintain a profit rate of 20%, as in 2013, Sanofi is buying back drug or vaccine candidates. And it is multiplying R&D partnerships with public university laboratories, capturing innovations without having to bear the costs. The only beneficiaries of Sanofi's ?7.4 billion profit in 2015 were shareholders, who received 51%, or ?3.8 billion. Employees, on the other hand, had to be satisfied with a new plan to cut 600 jobs, 2% of the workforce. In 2013, Sanofi received 137 million

euros of research tax credit and tax credit for competitiveness from the French government, while it paid only 600 million euros in taxes. The employment of the 230 employees of the Dengvaxia plant in Neuville-sur-Saone is in danger. Some of them will have to go to other factories.

Vaccines and medicines victims of capitalism…

The Dengvaxia scandal is not isolated. Sanofi markets a useful and effective drug against epilepsy, valproic acid, under the name Depakine, Depakote or Micropakine. But since at least the 1980s, it has been known that this drug is dangerous for pregnant women's future children. Despite this, it continued to be prescribed en masse to pregnant women. The French National Drug Safety Agency estimates that "between 16,600 and 30,400 children are estimated to have early neurodevelopmental disorders, including autism, because their pregnant mother continued to take Depakine. And it was reported in spring 2018 that Sanofi de Mourenx's French plant, which produces this valproic acid, was releasing a carcinogenic substance into the environment at rates 190,000 times higher than the maximum allowed. And it's been at least three years!

Pristinamycin, manufactured by Sanofi, is an excellent antibiotic against skin infections, but the market is very small. In his book La Stratégie de la Bactérie, Quentin Raveli shows how Sanofi has succeeded in positioning it in lung infections, which are much more frequent, but where it is not very effective!

I introduced this presentation by talking to you about the book Deadly Medecines and Organized Crime. How the pharmaceutical industry has corrupted health services. This is no coincidence. A few days ago Professor Peter Gøtzsche was expelled from the governance council of the Cochante coalition. Too anti Big Pharma! To pay tribute to him, this is what this world-renowned specialist, who paved the way for Evidence Based Medicine, explained in this book: "After asking what drugs we need and at what price," he concluded that the for-profit model is the wrong model. It calls for the nationalisation of the pharmaceutical industry, the abolition of its patents, full disclosure of all data used for marketing authorisations, full independence of regulatory authorities and the evaluation of medicines by public sector bodies".

After many other examples, the history of Dengvaxia shows that only a powerful social movement, which knows how to attach itself to independent experts, can bring these demands around the world. So let's build it together!

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