Territorial Center for Independent Information and Pharmaceutical Advice - CHOLET HOSPITAL CENTER - Doctor Amine UMLIL

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Unpublished. Exclusive. Vaccines against Covid-19: uncertainties even about the intrinsic quality of products, their manufacturing processes, the batches marketed ... according to official documents published by the European Medicines Agency (EMA)

With the lighting of Madame Catherine FRADE, Doctor of Pharmacy, and former director of international regulatory affairs in the pharmaceutical industry.

Can we imagine the launch of a production line of cars, and the putting into circulation of these vehicles, despite the uncertainties raised in the official documents published? These uncertainties concern the quality of the parts making up the engine and the various other spare parts, including those relating to safety, the manufacturing process, the reproducibility of the batches sold, etc.

In the field of medicines (including vaccines), the pharmaceutical act of *"release"* of the finished product (authorized product intended for sale) constitutes the final control step which precedes the availability of these products to the population. . This key *"release" step is* the pharmaceutical responsibility of manufacturers, in particular.

In the continuity of its previous analyzes proposed, the CTIAP of the hospital center of Cholet therefore comes once again to reveal to the population, and undoubtedly in an unprecedented and exclusive way, new **capital** , vital **information** concerning **the 4 vaccines against Covid -19** following: that of the ***BioNTech / Pfizer*** laboratory ; that of the ***Moderna*** laboratory ; that of the ***Astra Zeneca*** laboratory ; that of the ***Janssen*** laboratory .

This work was made possible thanks to the invaluable contribution of Dr Catherine FRADE , pharmacist, and former director of international regulatory affairs in the pharmaceutical industry. Graciously, she sent us a documented written alert. In this document , it sheds ***light*** on data which is extracted, on March 22, 2021, from the Marketing Authorization (marketing authorization) itself; a marketing authorization qualified as *"conditional"* . She extracted ***"source data which is difficult to identify by someone who does not work in the field"*** . These data are therefore public and verifiable. Beforehand, it should be specified that the author of this document no longer works within the pharmaceutical industry; she says: *"First of all, I want to make it clear that I have no conflict of interest with the pharmaceutical industry"* . It is therefore with its agreement that the CTIAP intends to make available to the public, health professionals, decision-makers, etc. an analysis of some of these data that everyone should read carefully.

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everyone should read carefully.

This reflection first presents what a *"conditional"* marketing authorization is **(I)** . Then, she recalls that the studies concerning these vaccines are not finished since they extend from *"2021 to at least 2024"* **(II)** . Then, it reveals, undoubtedly unprecedented and exclusive, that the official documents, published by the European Medicines Agency (EMA), underline the insufficiency of the evidence also concerning the *"quality"* of the *"active substance"* and of the drugs. *"Excipients"* , *"manufacturing process"* , *"reproducibility of batches"* marketed, etc .; **(III)** . Finally, this analysis offers a **conclusion** .

I- First of all, it is important to understand what a *"conditional"* MA is

The AMM is for a drug what a gray card is for a car. Marketing Authorization is granted when a drug has proven its quality, efficacy and safety; with a positive benefit / risk ratio: that is, it presents more benefits than risks. Obtaining this Marketing Authorization is the essential condition for a pharmaceutical company to be able to sell a drug, including vaccines.

In this case, in the case of these vaccines against Covid-19, the 4 MAs issued are so-called ***"conditional"*** MAs . They are **temporary** . Their period of validity does not exceed **1 year** ; because they are obtained on the basis of ***"incomplete data"*** . To obtain a standard 5-year MA, the laboratories concerned must provide completed files for ***"studies in progress and studies planned for the years to come"*** . Throughout ***"this development"*** , close and coordinated surveillance between manufacturing laboratories and health authorities is organized through regular discussions. The *"conditional"* MA is ***"Reassessed annually"*** based on input and critical analysis of additional data provided and collected over a full year.

This *"conditional"* Marketing Authorization is a European Marketing Authorization. It was obtained by the accelerated centralized procedure. It allows simultaneous marketing in the following 30 countries (European Union and European Free Trade Association): Germany, Austria, Belgium, Bulgaria, Cyprus, Croatia, Denmark, Spain, Estonia, Finland, France, Greece, Hungary , Ireland, Iceland, Italy, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, Norway, Netherlands, Poland, Portugal, Romania, Slovakia, Slovenia, Sweden, Czech Republic.

Studies on these 4 vaccines are therefore still ongoing.

II- Secondly, the planned studies are still in progress and are spread over a period going from "2021 to at least 2024"

All the studies submitted during the MA application are summarized in the **EPAR** (European Public Assessment Report). The latter is **published** on the website of the European Medicines Agency (EMA). Planned studies, not yet carried out, are also included.

This schedule, which ***"runs from 2021 to at least 2024"*** depending on the vaccines against Covid-19, is defined in the ***"annexes"*** of the conditional MA and in the **published** EPARs .

For example, the *BioNTech / Pfizer* vaccine obtained this European conditional marketing authorization on December 21, 2020. And, the deadline for submitting

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"confirmation" of the efficacy, safety and tolerance of this vaccine is set at the month of *" December 2023 "* .

The *Moderna* vaccine obtained this Marketing Authorization on January 6, 2021. The deadline for submitting *"confirmation"* of efficacy, safety and tolerance of the vaccine is set for the month of *"December 2022"* , at least.

The *Astra Zeneca* vaccine obtained this Marketing Authorization on January 29, 2021. The deadline for submitting *"confirmation"* of efficacy, safety and tolerance of the vaccine is set for *"March 2024"* .

The *Janssen* vaccine obtained this conditional European Marketing Authorization on March 11, 2021. The deadline for submitting *"confirmation"* of efficacy, safety and tolerance of the vaccine is set for the month of *"December 2023"* .

But to date, and this is where the new and exclusive revelation is undoubtedly , another deadline has been set for these 4 vaccines. This time limit no longer only concerns the clinical trials in progress, but also the ***"quality evidence for the active substance and the finished product"*** , itself: that is to say the **intrinsic quality** (the heart) of the product sold. and administered to millions of people.

III- Thirdly, and this probably seems unprecedented, the official documents published also underline the incomplete nature of the evidence relating to the "quality" of the "active substance" and of the "excipients", of the "manufacturing process", of the the "reproducibility of the batches" marketed, etc .;

Thus, the deadline for submitting additional evidence concerning the *"quality"* of the *"active substance"* and of the *"finished product"* (that is to say the vaccine authorized and sold) is set at the months of:

"July 2021" for BioNTech / Pfizer;

"June 2021" for Moderna;

"June 2022" for Astra Zeneca;

"August 2021" for Janssen.

Indeed, for these 4 vaccines, the paragraph ***"E. Specific obligation relating to post-authorization measures concerning the conditional marketing authorization"*** , extract from Annex II of the Marketing Authorization, clearly mentions the following:

For the BioNTech / Pfizer vaccine (pages 18-19)

By *"March 2021"* , the laboratory must provide *"additional validation data"* in order to *"confirm the reproducibility of the manufacturing process of the finished product"* .

By *"July 2021"* , the laboratory must provide the missing information in order to:

"Complete the characterization of the active substance and the finished product" ;

"Strengthen the control strategy, including the specifications of the active substance and the finished product" with the aim of *"ensuring consistent product quality"* ;

"Provide additional information regarding its synthesis process and control strategy" in order to *"confirm the purity profile of the excipient ALC-0315"* and *"to ensure quality control and reproducibility between batches throughout the life cycle of the finished product "* ;

"Provide additional information regarding its synthesis process and control strategy" in order to *"confirm the purity profile of the excipient ALC-0159"* and *"to ensure quality control and reproducibility between batches throughout the life cycle of the finished product "* ;

And by *"December 2023"* , and *"in order to confirm the efficacy and safety"* of this vaccine, the laboratory *"will have to submit the final clinical study report for the randomized, placebo-controlled, observer study. blind (study C4591001) "* .

For the Moderna vaccine (page 15)

The laboratory must provide the missing information in order to:

"Complete the characterization of the manufacturing processes for the active substance and the finished product" (deadline *"January 2021"*);

"Confirm the reproducibility of the manufacturing process of the active substance and of the finished product (initial and final batch sizes) (deadline *" April 2021 "*);

"Provide additional information on the stability of the active substance and the finished product and review the specifications of the active substance and the finished product after longer industrial practice" with the aim of *"ensuring consistent product quality"* (deadline *"June 2021"*) ;

"Submit the final study report for the randomized, placebo-controlled, blinded clinical study for the observer mRNA-1273-P301" with the aim of *"confirming the efficacy and safety of COVID-19 Vaccine Moderna "* (Deadline *" December 2022 "*) .

For the Astra Zeneca vaccine (pages 14-15)

The laboratory must enter the missing information in order to:

"Provide additional validation and comparability data, and institute more in-depth tests" with the aim of *"confirming the reproducibility of the manufacturing processes of the active substance and the finished product"* (deadline *"December 2021"*);

"Provide the main analysis (based on the cut-off data of December 7 (post-database locking) and the final analysis of the combined pivotal studies" in order to *"confirm the efficacy and safety of COVID- 19 Vaccine AstraZeneca "* (deadline *" 5 March 2021 "* (for the main analysis) and *" 31 May 2022 "* (for the combined analysis));

"Submit the final reports of the randomized and controlled clinical studies COV001, COV002, COV003 and COV005" in order to *"confirm the efficacy and safety of COVID-19 Vaccine AstraZeneca"* (deadline *"May 31, 2022"*) ;

"Provide additional data concerning the stability of the active substance and the finished product and review the specifications of the finished product after long industrial practice" with a view to *"ensuring a constant quality of the product"* (deadline *"June 2022"*);

"Submit the synthesis and abstracts of the main analysis and the final clinical study report for study D8110C00001" with a view to *"confirming the efficacy and safety of COVID-19 Vaccine AstraZeneca in the elderly and subjects with underlying disease "* (deadline *" April 30, 2021 "* (for primary analysis) and *" March 31, 2024 "* (for final study report)).

For the Janssen vaccine (page 18)

The laboratory must transmit the missing information in order to:

"Provide additional comparability and validation data" in order to *"confirm the reproducibility of the manufacturing process of the finished product"* (deadline *"15 August 2021"*);

"File the final report of the randomized, placebo-controlled, single-blind clinical study VAC31518COV3001" in order to *"confirm the efficacy and safety of the COVID-19 Ad26.COV2.S vaccine"* (deadline *"December 31, 2023"*).

These facts allow us to propose a conclusion.

Conclusion

For these reasons, which are not exhaustive, it was therefore useful to find and read also and in particular the content of the said paragraph ***"E. Specific obligation relating to post-authorization measures concerning the conditional marketing authorization"*** , extract from the Annex II of the Marketing Authorization, corresponding to each of these 4 vaccines against Covid-19.

The insufficient evaluation therefore does not only concern clinical trials (studies carried out in humans (women and men)), but also the very quality of the active substance, of the excipients, some of which are new, of the manufacturing process, batches released and administered to humans in several countries around the world.

Moreover, these new excipients must be considered as new active ingredients; and thus be the subject of a complete evaluation file similar to that required for a new active principle.

The change of the trade name of one of these vaccines, as was recently announced for in particular the vaccine from the laboratory *Astra Zeneca* , could only be considered as a cosmetic arrangement of the product image for marketing purposes (conquest of 'new public confidence, boost in sales). It would not respond to questions raised regarding the quality, efficacy and safety of the product. It is one of the usual techniques used to make up (conceal) certain undesirable characteristics of the product concerned. A technique that has already been used to present other drugs in their best light.

As already mentioned previously, in the field of medicinal products (including

vaccines), the *"release"* of the finished product (intended for sale) is the final stage of control (of quality and therefore of safety) before *releasing.* available to the population these products.

This key step of *"release"* of the batches is the pharmaceutical responsibility of the manufacturers. **However, the responsibility of users (health establishments and professionals in particular) may also be engaged** .

In our opinion, these clinical studies should never have started before, at least, the total control of the intrinsic quality of the finished product and its manufacturing process; before stabilization of the formulas of these vaccines.

How could the results of these global clinical trials be compared if the vaccine administered varies from manufacture to production, from batch to batch, from region to region? other…?

These variabilities, which even impact the heart of the product, could even invalidate all the clinical trials carried out.

Even in a health emergency, it is therefore difficult for us to understand the foundations of these MAs (marketing authorization) which have been granted to these vaccines against Covid-19.

To the uncertainties linked to Covid-19, have been added the approximations linked to the use, and to the very intrinsic quality, of these vaccines. From now on, you would have to deal with two problems instead of one.

The maneuver seems subtle. The useful information is readily available in the official documents published within the framework of the AMM; but, these data are not made visible by the official discourse. The latter would only have sought to present these products as effective and safe, and without reservations; even though the formulas and manufacturing processes of these vaccines do not even seem to be fully stabilized yet.

These new revelations, undoubtedly unprecedented and exclusive, further sow doubt on the validity of consent (a fundamental freedom) which is supposed to be free and informed; and which would have been given by people vaccinated today.

Everyone has the right to clear, fair and appropriate information. This information is also permanent: in the event of new data being revealed, people who have already been vaccinated must be informed *a posteriori* (after the administration of a particular vaccine).

The vaccine ***"obligation"*** cannot therefore flourish ; even in disguised form, notably *via* a ***"vaccination passport"*** .

This new analysis further confirms our previous reflections such as the one entitled ***" Could the vaccine against Covid-19 (Tozinaméran; COMIRNATY °) be qualified as" defective "by the judge? "*** ; or those expressed in the two **open letters** which have already been sent in particular to the **Minister of Solidarity and Health** and to the **7 Professional Health Orders** .

The vulnerability does not spring solely on age and health status of people in particular. Not being able to access **independent** information on drugs (including

vaccines) is the primary source of poverty and inequality .

Moreover, concerning the uncertainties on the effectiveness of these vaccines, the Council of State noted, on March 3, 2021, in particular the **admission** of the Ministry of Solidarity and Health, itself, and the contradictions of the *French "administration"* . In this decision, and against the advice of this Ministry, the Council of State had taken a decision which seemed to tend towards the recognition of this effectiveness. But, a few days later, in a **new decision** (n ° 450413) rendered on March 11, 2021, the **Council of State** changed its position and admitted ***"the uncertainty which remains on the real effectiveness of the vaccine with regard to the spread of the disease. virus'***. It should also be recalled that, on February 18, 2021, the Minister of Solidarity and Health also recognized, and publicly, that no European country has been able to provide, either, the proof that these vaccines allow to prevent ***"serious"*** forms of Covid-19 (see **press conference** from *34min 44s*).

In its latest *"Update on COVID-19 vaccine surveillance - Period from 03/12/2021 to 03/18/2021"* published on March 26, 2021 - updated on March 29, 2021 -, the agency National Medicines Safety Authority (ANSM) reports in particular the **number of deaths that have** occurred in France after the administration of these vaccines. Deaths that are notified (reported) in pharmacovigilance (regardless of the certainty of the *"causal link"* between these vaccines and these deaths): ***"311 deaths"*** after the administration of the BioNTech / Pfizer vaccine; ***"4 deaths"*** after administration of Moderna vaccine; ***"20 deaths"***after administration of the Astra Zeneca vaccine; (no data for the moment concerning the last vaccine (Janssen) authorized). Knowing that in general for all drugs, there is a **strong under-notification** in pharmacovigilance despite the mandatory nature of these declarations.

Consequently, **prudence in** particular would even like that, in all the countries where these vaccines against Covid-19 have been marketed, all the batches thus *"released"* are withdrawn immediately ; and that these MAs which have been granted be suspended, or even canceled, as a matter of urgency until further notice . In any case, this is the meaning of the recommendations that we could suggest to the *ad hoc* authorities , and in particular to France . And, at *a minimum* , this information must be brought to the attention of everyone in a clear, fair and appropriate manner.

Especially since in the event **of serious adverse effects** , including **deaths** , and to establish said *"causal link"* with certainty, victims and their families are often helpless when faced with the requirement of ***" diabolical proof ".*** .

Posted by CTIAP center hospitalier de Cholet at 10:33

40 comments:

Anonymous April 2, 2021 at 2:12 PM

amazing !!
How then can one qualify as "informed" the consent which has been given by thousands of people without having been informed of this before their vaccination?
To be distributed widely. Thank you for your courage!