The precautionary principle and the authorisation of Covid-19 vaccines under EU law

by Alessandra Donati

No value judgments on the efficacy of the Covid-19 vaccination

This post does not contain any value judgement on the efficacy of the Covid-19 vaccination, nor should it be interpreted as intending to discredit the important role played by the producers of vaccines, the European Medicine Agency (EMA) and the European Commission in the vaccination campaign. Focusing only on an assessment of the legal implications of the decision of the Commission to grant conditional marketing authorisation (CMA) to Covid-19 vaccines, its purpose is to nurture the legal discussion of the conditions and effects of public health measures taken in an atmosphere of risk and uncertainty. It applies the legislation, case law and scholarship on the precautionary principle to evaluate the granting of CMA to Covid-19 vaccines.

The accelerated procedure for the authorisation of Covid-19 vaccines

Due to the emergency and the need to quickly find something to inhibit the spread of Covid-19, the development and the authorisation procedure of Covid-19 vaccines have been accelerated. The greatest gain in acceleration of the production process was possible because of the contraction of the standard procedure for the development of vaccines and the

combination of different phases of their development. Clinical trials started before the completion of the *in vitro* and *in vivo* tests and the EMA began to evaluate the vaccine before the standard laboratory checks had been completed. Some manufacturers started producing their vaccines before obtaining EU marketing authorisation. As a result, vaccines were distributed across the EU and available for use before the standard procedure for their development was complete.

Regarding the authorisation procedure, several arrangements allowed for a faster decision by the EU Commission that allowed for the authorisation of the first vaccine (Comirnaty developed by BioNTech and Pfizer) only 9 months after the pandemic was declared.

First, under Article 14(7) of Regulation 726/2004 and the provisions of Regulation 507/2006, the Commission and Member states agreed to activate the CMA procedure to expedite the approval of Covid-19 vaccines. Under the framework of the CMA, a marketing authorisation is granted on less comprehensive clinical data than normally required, relying on robust post-authorisation safeguards and controls. Under Article 4 of Regulation 507/2006, a CMA may be obtained where the EMA's Committee on Human Medicines finds that, although comprehensive clinical data referring to the safety and efficacy of the medicinal product have not been supplied, all the following requirements are met:

(a) the risk-benefit balance of the medicinal products is positive;
(b) it is likely that the applicant will be able to provide the comprehensive clinical data;
(c) the medicine will allow fulfilling unmet medical needs; and
(d) the benefit to public health of the immediate availability on the market of the medicinal product concerned outweighs the risk inherent in the fact that additional data are still required.

CMA are valid for one year and can be renewed annually.

Second, to support the granting of a CMA, the EMA conducted a rolling review of scientific data provided by vaccine developers. This allowed the EMA to evaluate the quality, efficacy and safety of the vaccines continuously as data become available instead of waiting until all the trials were completed.

Third, the EU Commission also ensured that the process leading to vaccines' marketing authorisation took place as quickly as possible by shortening administrative steps, such as the period for consulting the Member states through comitology.

Fourth, in July 2020, the EU Parliament and the Council adopted Regulation 2020/1043 concerning Covid-19 vaccines as all of them are classified as genetically modified organisms (GMOs). Under Article 2, all operations related to the conduct of clinical trials of Covid-19 vaccines containing or consisting of GMOs shall not require a prior environmental risk assessment or the consent of national authorities in derogation of Articles 6 to 11 of Directive 2001/18/EC and Articles 4 to 13 of Directive 2009/41/EC (GMO Directives). Producers of the vaccine were to implement measures to minimise any environmental impact resulting from the intended or unintended release of the GMO into the environment, and the manufacture of the vaccine was to be subject to the terms of the GMO Directives. The Regulation will remain in place until Covid-19 is considered as a pandemic. Its purpose is to facilitate production and reduce the time taken to execute the clinical trials. Under the GMO Directives, an environmental risk assessment was a precondition for consent to carry out clinical trials involving GMOs. However, there is considerable variation between Member states in the

requirements for evaluation of the environmental risks for such trials. If all these requirements had to be respected in all Member states where clinical trials were to be implemented, this would have caused enormous delays in the deployment of the vaccines.

The CMA: a precautionary measure

This post analyses the decision of the Commission to grant a CMA. Its core claim is that the decision of the Commission should be qualified as a precautionary measure. Indeed, according to the established case law of the CJEU, the conditions for the application of this principle are met. We are facing a serious risk to public health linked both to the continuous spread of Covid-19 and the large-scale use of new vaccines, which still need to prove their efficacy to contain the diffusion of the virus, especially in the long term. However, this risk is uncertain since the scientific data supporting the authorisation of vaccines are incomplete and require further investigation. In these circumstances of risk and uncertainty, the precautionary principle should apply. Provided for by Article 191 § 2 of the Treaty on the Functioning of the European Union (TFUE), the precautionary principle is a key principle of the European environmental policy. Since *National Farmers' Union and the United Kingdom v. Commission* in 1998, the CJEU has repeatedly applied the precautionary principle in the field of public health. As a principle of anticipated action, precaution requests the decision-makers to anticipate the time of action when there is an uncertain risk affecting the environment and public health. Therefore, if traditionally public action was conditional on the proof of a certain risk, the precautionary principle obliges the authorities to anticipate the time of action at the stage of uncertainty.

As a precautionary measure, the legality of the decision of the Commission should be assessed accordingly and decision-makers (EU institutions and Member states) enjoy a wide discretionary power because of the complexity of the issues before them. However, the discretionary power of the decision-makers is not unlimited because they must comply with a set of procedural obligations aimed at ensuring that even under scientific uncertainty, the use of the precautionary principle is backed by scientific data and it is not arbitrary. To assess the legality of the decision of the Commission to grant a CMA to Covid-19 vaccines, I will examine whether these procedural obligations were complied with.

The risk assessment of Covid-19 vaccines

According to established case law, the risk assessment must be based on the best and most reliable scientific data, and the most recent results of international research. The CJEU does not specify the meaning to be attributed to these terms, nor does it indicate which types of studies meet these criteria. However, by granting the experts the discretion to choose the scientific sources of their expertise, the Court stresses the importance of selecting the highest quality data. The risk assessment must also be transparent and carried out by independent experts separated from the political decision-makers and who do not have a conflict of interests with third parties potentially affected by their decision.

The analysis of this discharge of this obligation, in this case, raises several concerns. These are, of course, only preliminary concerns that will be reassessed in the coming months as further details emerge.

First, one may wonder if the decision by the EMA to implement a rolling review of the scientific data is compatible with the idea of grounding the risk assessment with the best

scientific data, or simply the most available data. The question arises since the rolling review is an *ad hoc* procedure that can be activated by EMA in an emergency to speed up the risk evaluation by assessing the data for an upcoming highly promising application as they become available, but preceding the formal submission of a complete application for marketing authorisation. Therefore, by definition, the scientific information submitted has not been selected to identify the best, but rather is all that is available when the application is filed.

Second, if the EMA stressed its strong commitment to ensuring the transparency of its evaluation procedure of Covid-19 vaccines by shortening its standard publishing timeframes and publishing information it does not normally publish for other medicines, it is more difficult to assess its compliance with its obligation to ensure independent expertise. Following an inquiry of the European Ombudsman, the EMA took measures to ensure separation between the experts involved in providing advice on the development of Covid-19 vaccines and those in charge of their evaluation. It is also true that when establishing the mandate, objectives and rules of procedure of the Covid-Etf that played a key role in the evaluation of Covid-19 vaccines, the EMA clearly stated that the members of the committee:

> shall not have any direct interests in the pharmaceutical industry, which could affect their impartiality. They shall undertake to act in the public interest and an independent manner and shall make a declaration of their financial and other interests at least on an annual basis or when new interests arise […] Members of the Covid-Etf and experts shall refrain from involvement in any purchase procedure under the EU Advance Purchasing Agreement for Covid-19 vaccines. If involved in such purchase procedure, restrictions on involvement in ETF activities are applicable to Covid-Etf and experts.

However, to ensure the independence of that expertise, it will be necessary over the coming months to assess whether the EMA has been able to avoid interference with vaccine developers that might have jeopardised that independence. If this aspect is particularly difficult to check under normal circumstances, it will be even more challenging for Covid-19 vaccines. Not only the urgency of the authorisation procedure but also the necessary dialogue and exchanges with private companies applying for Covid-19 vaccines that characterised the EMA's risk assessment are all elements that will require a further investigation to assess the compliance with the principle of independence of the expertise.

Third, the adoption of Regulation 2020/1043 derogating for the duration of the pandemic the requirement for an environmental risk assessment as a condition for obtaining consent for clinical trials raises a question of compatibility with the precautionary principle. The application of this principle is conditional on the execution of a risk assessment as complete and exhaustive as possible. The purpose of this assessment is to confirm that, despite the existence of scientific uncertainty, the risk is sufficiently grounded and is not hypothetical. Considering the obligation to execute a risk assessment before implementing the precautionary principle, the decision to lift this obligation for clinical trials of the vaccines containing GMOs might cause some surprise. This measure is justified by the objective of protecting public health 'in the unprecedented situation of public health emergency created by the Covid-19 pandemic' (Regulation (EU) 2020/1043, whereas 17) and the need to quickly approve the vaccines by avoiding the bureaucracy linked to the environmental risk assessment before the clinical trials. However, if the need to protect public health by rapidly deploying vaccines is undeniable, it is also important to guarantee the legality of their authorisation in compliance with the precautionary principle. A risk assessment is a guarantee of the sound use of the precautionary

principle and is intended to avoid arbitrary measures that are not backed up by scientific evidence.

The risk management of Covid-19 vaccines

The risk management of the precautionary measures by EU political decision-makers involves two procedural obligations.

First, the decision-makers must consider the results of the risk assessment conducted by the EMA. This obligation gives rise to a duty of care. They must examine, carefully and impartially, the scientific assessment made by experts before the adoption of a precautionary measure to show that, although uncertain, the risk is sufficiently likely to require the implementation of a protective measure. They must also consider any new scientific knowledge arising after the expert assessment was carried out which could change the evaluation. According to the CJEU in *French Republic v. Commission* and by the General Court in *Solvay Pharmaceuticals v. Council*, the production of new scientific knowledge may require a re-examination of the measure taken under the precautionary principle.

Second, decision-makers must consider the other pros and cons of the action. In *Basf Agro BV v. European Commission*, the General Court explicitly recognised the binding nature of the pros and cons analysis and the obligation on decision-makers to carry it out before adopting a precautionary measure. However, the Court did not specify how it should be done, which leaves decision-makers with a wide margin of discretion. For the Commission, this analysis is generally carried out with the implementation of a cost and benefit analysis. The obligation to analyse the costs and benefits of the action responds to the need to broaden the spectrum of elements considered before the adoption of a precautionary measure to include non-scientific considerations.

The risk management by the Commission before granting a CMA raises several concerns. Again, these are only preliminary and will need to be reassessed in the coming months.

First, considering the lack of comprehensive scientific data that supported the granting of the CMA, it is important to verify compliance with the obligation to consider new scientific evidence that might have emerged after the granting of the CMA. This will be possible with the implementation of an efficient monitoring system. This is important because exceptionally large numbers of people received Covid-19 vaccines, many more than the large numbers involved in the clinical trials. Therefore, it is only after the authorisation that the quality, safety and efficacy of Covid-19 vaccines will be tested on a significant scale and under real-life use. The manufacturers have been entrusted by the framework of the CMA to provide the EMA and the Commission with the results from the main trials of the vaccines, which are ongoing. These trials and the additional studies conducted by vaccines developers will provide further information on the quality, safety and efficacy of the vaccines. The EMA and the national authorities have also prepared a safety monitoring plan for the vaccines which outlines how relevant new information emerging after the authorisation and uptake of the vaccines will be collected and reviewed. The plan requires the EMA to monitor suspected side effects reported by individuals and healthcare professionals posted to an EU database called EudraVigilance.

Second, one might wonder if the need to speed up the authorisation of Covid-19 vaccines fully justifies the decision of the Commission to reduce the consultation period of the Member states through the comitology procedure. This procedure is important in ensuring that, besides the

scientific findings, the precautionary measure is grounded by the consideration of other non-scientific factors such as the social, economic or political implications. Given that the decision to grant a CMA had enormous consequences in the social, political and economic arenas, it was important to be sure that the effect of these non-scientific factors was properly considered.

Conclusion

'In the biggest global health crisis for a century, we chose to go it together so that every part of Europe got the same access to a life-saving vaccine'. With these words, taken from the 2021 speech on the State of the Union, the President of the EU Commission, Ursula Von der Leyen highlighted the significant efforts made by the EU institutions and Member states to ensure access to Covid-19 vaccines for the European population. However, as she recognised, 'the speed of events and the enormity of the challenges are sometimes difficult to grasp'. One of the biggest challenges lies in the trade-off between the need to quickly deliver vaccines by speeding up their development and authorisation and the obligation to ensure their quality, safety and efficacy in compliance with EU law. As a response to this trade-off, the EU Commission granted – on positive advice from the EMA – a CMA to those Covid-19 vaccines that meet the criteria set out by the applicable regulations.

Against this backdrop, the core claim of this post is that the decision of the Commission should be qualified as a precautionary measure. With the qualification of the decision of the Commission as a precautionary measure, its legality was assessed to determine if the Commission had complied with the procedural obligations that surround the implementation of the precautionary principle under EU law. As a result of this analysis, some issues have been identified concerning the risk assessment conducted by the EMA and the risk management by the Commission. This analysis does not contain any value judgement on the opportunity or efficacy of the Covid-19 vaccination. By pointing out and assessing some elements of concern of the CMA under the precautionary principle, the post offers a reflection on the conditions and effects of public health measures taken in a condition of risk and uncertainty. This might be relevant given the current revision of the health regulations being undertaken by the EU institutions to better reconcile the need to act quickly in an emergency with the obligation to comply with the procedural requirements of the precautionary principle under EU law.

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