EURACTIV

FROM VACCINE RACE TO MARATHON: WHAT'S NEXT FOR COPING WITH COVID?

SPECIAL REPORT | JULY - OCTOBER 2021

https://eurac.tv/9TCT

With the support of HIPRA

EURACTIV

FROM VACCINE RACE TO MARATHON: WHAT'S NEXT FOR COPING WITH COVID?

SPECIAL REPORT | JULY - OCTOBER 2021

https://eurac.tv/9TCT

The COVID-19 virus is not going anywhere any time soon and, as new variants keep cropping up across the globe, vaccine development cannot afford to stand still.

There are currently just over 100 vaccines in clinical development worldwide but only four authorised vaccines in the EU, of which mRNA vaccines dominate.

As the initial vaccine race has started to subside, discussion have started focusing on the need for booster shots and a longer-term vaccination strategy.

How can the EU strengthen its vaccine autonomy? What kind of booster vaccines will be needed? And what will the strategies for coping with COVID look like in the near future?

In this Special Report, EURACTIV looks at what we should expect in this ongoing vaccination marathon.

Contents

INTERVIEW

Spanish firm finetunes 'second generation' COVID-19 vaccine for EU's booster campaign

By Gerardo Fortuna and Giedre Peseckyte | EURACTIV.com

Spanish company HIPRA expect to deliver between 600 to 980 million doses of its COVID-19 vaccine candidate for 2022 and up to 1.2 billion in 2023. [HIPRA]

A Spanish company active in animal health stands ready to start clinical trials and get the EU's regulatory go-ahead for a 'deadline-proof' recombinant protein vaccine. EURACTIV spoke with the company's chief of the vaccine programme.

Toni Maneu is the human health director of Hipra, a Spanish company developing a COVID-19 vaccine candidate. He spoke to EURACTIV's journalists Gerardo Fortuna and Giedre Peseckyte.

HIPRA is a veterinary pharmaceutical company and it is specialised in the production of animal vaccines. Why did you decide to join the COVID vaccine 'marathon'?

One year ago, our R&D department did a proof of a concept with a recombinant protein platform against the SARS-CoV-2 virus due to our experience in vaccines. And the results were very good, so it was a matter of responsibility to share the results with the national health authorities, the Spanish agency of medicines and medical devices (AEMPS), who told us to continue with the project.

This close cooperation with the Spanish medicine agency was the real starting point because we did not have regulatory experience in the field of human health and we wanted to follow all the guidelines needed.

This was the beginning, but what point are you at now?

We have pre-clinical results showing that our recombinant vaccine

Continued on Page 5

Continued from Page 4

is effective against the Wuhan, UK, South Africa and Brazil variants, while we are now waiting for the results against the Indian variant, which probably will come this week.

In August, we are going to start phase one of the clinical trials followed by phase two in September in public hospitals. The rest of the clinical trials are scheduled throughout autumn in some public hospitals we have contacted in Spain, Italy, Portugal, and Malaysia – if they accept to do so.

So far, four vaccines have been authorised in Europe – two adenovirus-based, two messenger RNA (mRNA). How is this recombinant protein vaccine different?

It takes longer to develop recombinant protein vaccines but their advantage is the versatility and the capacity to adapt to new variants. That means that in a short period of time, we can adapt this second-generation vaccine to potential new variants that can lower its effectiveness.

Another advantage is that this recombinant platform is already known and used in human health. So, we are confident that we are going to launch a vaccine as safe as other recombinant proteins vaccines.

The third benefit concerns logistics as the ideal temperature for its storage is between +2 and +8 degrees Celsius, which is a significant difference compared to mRNA vaccines.

Lastly, the price will be much lower than the one of mRNA vaccines but keeping the same level of effectiveness, versatility, with the addition of a more manageable logistic. This is why some health authorities and the scientific community foresee the recombinant protein vaccines as ideal for the booster strategy.

Why so?

When we started, we didn't think about a booster strategy. The scientific community, the Spanish agency of medicines, and the hospitals told us that the most interesting thing from a research perspective would have been to conduct clinical trials with a view of entering the booster phase of the vaccine race. They told us to continue on this because, for sure, we are going to have COVID with us for a while.

At the same time, if Europe is interested in booster, other countries in the world are interested in the full vaccination programme as they have many people who have not been vaccinated yet. I recently had a conversation with Vietnam's ministry of health and only 4% of their population is vaccinated, so they are in a very delicate situation.

How would 'booster trials' work?

We are starting clinical tryouts in Europe with the booster strategy. That means that the volunteers will come from being vaccinated with existing vaccines. We need two groups of people vaccinated with mRNA and adenovirus vaccines or people that have been infected previously. This will depend on the European medicines agency (EMA) or the Spanish medicine agency's decision.

How many vaccines are you planning to produce in the following years as they are planned to be used for both: booster strategy and full vaccination?

So, by the end of September/ beginning of October, we are starting the production. We expect to deliver from October to December, between 50 to 75 million doses. Depending on the demand we aim to deliver between 600 million to 980 million doses of vaccines for 2022. And in 2023, it will be up to 1.2 billion.

And how are you going to ensure that there are no shortages in the pipeline and that vaccines are delivered on time – like others? Is the vaccine you are developing 'deadline-proof'?

I think we have learned from the experience that other vaccines had. Secondly, we already have experience with vaccine production. This amount of doses for an animal health company is not complicated: right now we are producing 24 billion doses a year in our facilities – and this number can show you our capacity.

Regarding the delivery, we have the stock already because we learned from the experience of other companies that had problems with delivery. We have a stock in advance for 2021 and 2022 and the essential materials are in our facilities in order to ensure the delivery.

Protein subunit and inactivated vaccines line up to join vaccination campaigns

By Giedre Peseckyte | EURACTIV.com

Worldwide vaccines developed under other platforms are lining up, with recombinant proteins and whole virion inactivated vaccines leading the way. [EPA-EFE/ROBERT GHEMENT]

The EU seems to be comfortable with betting on mRNA COVID vaccines for now. But just around the corner, vaccines developed under other platforms are lining up, with recombinant proteins and the whole virion-inactivated vaccines leading the way.

There are four COVID vaccines authorised in the EU at the moment: mRNA vaccines such as Comirnaty or Spikevax, developed, respectively, by Pfizer/BioNTech and Moderna, and adenoviral vector vaccines – Oxford's Vaxzevria and the single-shot Janssen by Johnson&Johnson.

The EU vaccination strategy is heavily relying on mRNA vaccines. The Commission recently signed the world's largest contract for COVID-19 vaccines contract with Pfizer/BioNTech, which foresees the delivery of 1.8 billion doses of vaccines between the end of the year and 2023.

Contacted by EURACTIV, a European Commission spokesperson explained that the focus should be on technologies that have proven their worth and mRNA vaccines are a clear case in point.

But vaccine developers are already working with new vaccine platforms.

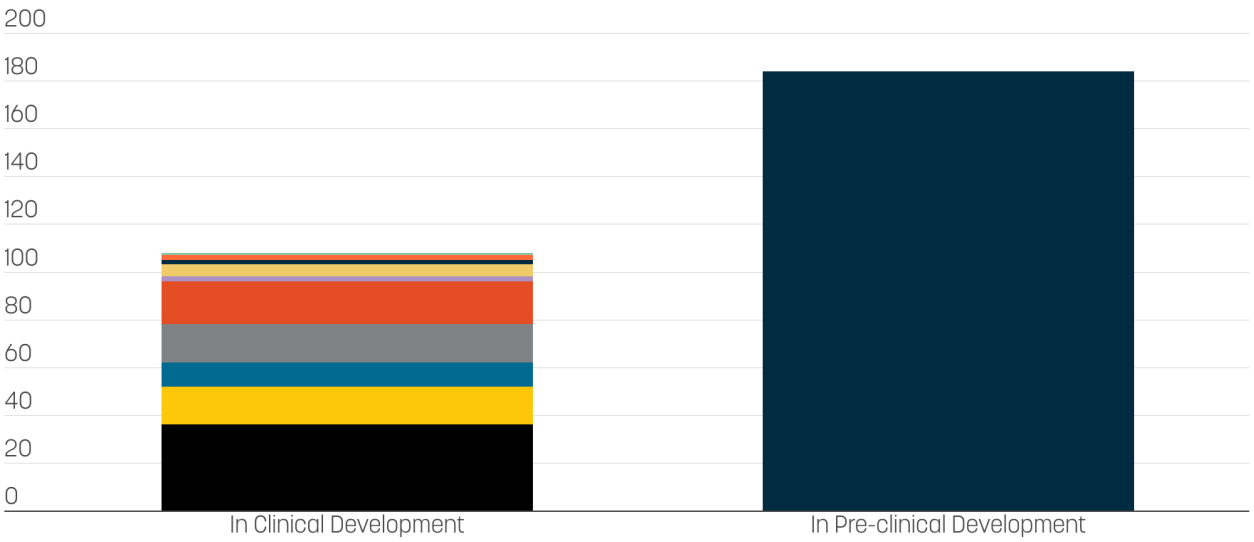
The EU European Medicines Agency (EMA) is in contact with slightly over 30 developers of potential COVID-19 vaccines and running a rolling review of four potential COVID-19 vaccines.

Based on the World Health

Continued on Page 7

Continued from Page 6

Vaccines in clinical and pre-clinical development worldwide



Source: WHO

Organisation landscape of candidate vaccine development, there are more than 100 vaccines in clinical development worldwide, dominated by protein-based subunit vaccines.

"The main types of vaccine we're going to see coming through next are these recombinant proteins and the whole virion inactivated vaccines," Adam Finn of the European Technical Advisory Group of Experts on Immunisation (ETAGE), who is also chair of paediatrics at the University of Bristol, told EURACTIV.

These two platforms, he added, "are much more traditional" and might be entering the vaccination campaigns already in the upcoming months.

"There are a whole lot of other more experimental platforms. And it's quite hard to get information about those because very often the developers are quite secretive about what they're doing," said Finn.

PROTEIN-BASED SUBUNIT VACCINES GETTING READY FOR VACCINATION MARATHON

The Commission spokesperson said that protein-based subunit vaccines were also recommended for use by scientific experts, in addition to mRNA vaccines.

These vaccines should be cheaper as they can be transported at higher temperatures than mRNA vaccines.

"It's a very well-established technology now. It's been around for about 30 years. The most prominent example of this technique is the hepatitis B vaccine," said ETAGE's Finn.

"In principle, it ought to be a much easier, more straightforward way to make vaccines than either of the new technologies where the manufacturing bases have to be set up from zero," he said.

The cheaper price and large quantities, together with emerging evidence of their effectiveness, should boost the popularity of this type of vaccine. Another factor is the safety of the new platforms used for COVID-19 vaccines.

"There are emerging rare but serious, or potentially serious, safety signals with new platforms, which is interfering with the political will to use them," Finn said.

'MIX AND MATCH' COULD KEEP THE VACCINATION ROLLING

These new COVID-19 vaccines might be the ones that join the 'mix and match' or heterologous vaccination strategy already seen in some member states.

Continued on Page 8

Continued from Page 7

In a joint update released on Wednesday (14 July), the EMA and the European infectious disease agency (ECDC) noted that experts responsible for the vaccination programmes in more than a half of member states have decided, with a view to their national situations, to use different vaccines for the second dose from the ones used for the first.

In a heterologous vaccination strategy, which has already been applied for some other vaccines, a different vaccine is given for the second dose in a recommended 2-dose schedule. This may allow quicker vaccination strategy rollouts.

"Perhaps the most compelling reason for mixing and matching is that it gives you flexibility in terms of supply," explained Finn, pointing to situations where health authorities have been giving a particular vaccine to the population and then cannot get any more of it.

While preliminary results from studies in Spain, Germany, and the UK suggest a satisfactory immune response and few safety concerns, EMA and ECDC are still refraining from issuing a definitive recommendation to use different COVID-19 vaccines for the two doses.

In Finn's opinion, using different vaccines is a "quite good idea".

"The positive side is that there may be an advantage to presenting the same antigen to the immune system in a different way, in the sense that that may stimulate either a bigger response or a broader response than just using the same hit all the time," he said adding, however, that it is not yet clear how those better responses turn into better protection.

Some vaccine platforms can be easier adapted to new COVID-19 variants

By Giedre Peseckyte | EURACTIV.com

As new variants might occur the vaccines might need to be adapted to fight the new strains. [felipe caparros/SHUTTERSTOCK]

For now, vaccines are capable of dealing with SARS-CoV-2 virus variants circulating in the world. But as new variants potentially emerge vaccines might need to be adapted to fight the new strains.

Scientists warn that vaccine developers and authorities need to be prepared to adjust their vaccines but also the regulatory framework needs to be set to allow fast decisions.

All viruses, including SARS-CoV-2, the virus that causes COVID-19, change over time.

While most changes have little to no impact on the virus' properties some changes may affect the virus's properties, such as how easily it spreads, the associated disease severity, or the performance of vaccines.

COVID vaccines currently authorised in the EU were developed under two platforms: mRNA and adenoviral vector vaccines.

So far the vaccines authorised in the EU seem to be managing to protect people from circulating variants.

"We can see that vaccines are still working against variants, but we have reduced efficacy against, for example, the Delta variant," Camilla Foged, professor at the University of Copenhagen, told EURACTIV. Foged is leading a research group on Vaccine Design and Delivery at the Department of Pharmacy. She added that all the vaccines show slightly reduced efficacy, but are still very good at protecting against hospitalizations and deaths.

A Lancet study published on Monday (13 September) showed that

Continued on Page 10

Continued from Page 9

vaccines remain highly effective against severe disease, including that from all the main viral variants.

Averaging the results reported from the observational studies, vaccinations had 95% efficacy against severe disease both from the delta variant and from the alpha variant, and over 80% efficacy at protecting against any infection from these variants.

"The virus can still mutate, we can have more variants in the future, that's very likely," said Foged. This, according to her, might result in lower vaccine protection.

HOW EASILY CAN THEY BE ADJUSTED?

Foged also said that for mRNA vaccines it is "relatively easy" to adapt to new variants. "I know that Pfizer is testing a vaccine against the Delta variant. But it won't be approved in the near future," she said.

There are other vaccine platforms lining up and the traditional ones – recombinant proteins and the whole virion inactivated vaccines – might be approved in the coming weeks and months.

However, it might take slightly longer to adjust them to new variants, if needed, said Adam Finn of the European Technical Advisory Group of Experts on Immunisation (ETAGE), who is also chair of paediatrics at the University of Bristol.

He told EURACTIV that mRNA and adenoviral vector vaccines "reformulated slightly quicker, all you need is the genetic sequence to start doing that".

For Professor Foged, too, it will take longer to adapt protein-based vaccines to new various virus strains, "because you have to express a new protein".

But adjustability is only one side of the coin. Another issue is how to deliver newly adjusted vaccines.

ETAGE's Finn said that despite being able to make the first steps of reformulation faster when it comes to mRNA and adenoviral vector vaccines, since they are "new platforms" there still might be "some challenges of producing millions of billions of doses reliably, as they are less experienced of doing it".

Foged pointed out that procedures to respond rapidly to changes in virus mutations need to be prepared. "It's important for the authorities to make procedures so we can rapidly respond to new virus variants. And also for the companies to be able to quickly test vaccines against new areas," she said.

Finn also pointed to how developers focused on the Beta variant in the spring while in summer everyone was concerned about Delta.

"So everyone was making the wrong variant vaccine, they've gone off in the wrong direction. And coming back around, and getting in the right direction, takes quite a lot of time. So it's more strategic thinking than the practical aspects of making the new vaccine that is challenging at the moment," Finn concluded.

VACCINES ADAPTED TO NEW STRAINS MIGHT BE A BETTER BOOSTER

The Lancet study also highlighted that a booster vaccine developed to fight new strains of the virus might be a better option than using one of those already available.

"Even if new variants that can escape the current vaccines are going to evolve, they are most likely to do so from strains that have already become widely prevalent. Therefore, the effectiveness of boosters developed specifically to match potential newer variants could be greater and longer-lived than boosters using current vaccines," stated a Lancet press release.

It added that a similar strategy is used for influenza vaccines, for which each annual vaccine is based on the most current data about circulating strains, increasing the likelihood that the vaccine will remain effective even if there is further strain evolution.

'Mix and match' approach to COVID-19 vaccines could help boost effectiveness

By Giedre Peseckyte | EURACTIV.com

The effectiveness of boosters developed specifically to match potential newer variants could be greater and longer lived than boosters using current vaccines. [HangermanCnx_Thailand/SHUTTERSTOCK]

Scientists are divided on whether 'mix and match' or heterologous vaccination strategies can work against COVID-19. These strategies include using different combinations of vaccine types and brands to boost immunity. While some argue that this would increase the protection, others say that more evidence is needed.

A heterologous vaccination strategy is where a different vaccine is given for the second dose in a recommended 2-dose schedule.

Experts responsible for the vaccination programs in more than half of member states have decided, with a view to their national situations, to opt for this 'mix and match' approach, as was noted by the EU's medicine agency (EMA) and the European Centre for Disease Prevention and Control (ECDC) in a joint update.

The EU-funded project 'European Corona Vaccine Trial Accelerator Platform' (VACCELERATE) supported a study in Germany that tested the immune response of people receiving heterologous vaccination and demonstrated encouraging results.

The study found that matching the first dose of an adenoviral vector-based vaccine with a booster mRNA shot could be "an interesting option if the thrombosis risk posed by adenoviral vector-based vaccines is a concern, and it increases flexibility in a setting of a vaccine shortage."

However, further studies are needed to address the safety and clinical efficacy of heterologous vaccination regimens, the study reads.

Continued on Page 12

Continued from Page 11

While other preliminary results from studies in Spain and the UK suggest a satisfactory immune response and few safety concerns, EMA and ECDC are still refraining from issuing a definitive recommendation to use different COVID-19 vaccines for the two doses.

VACCINE DEVELOPERS NOT TOO SUPPORTIVE

In Lithuania, health authorities allowed the 'mix and match' approach in the national vaccine strategy. Aurelija Žvirblienė, head of the department of immunology and cell biology at Vilnius University's Institute of biotechnology, was among the chief research scientists who supported using different vaccine shots.

"Scientifically, this should be useful because different vaccines differently stimulate the immune response. Most importantly, all vaccines authorised in the EU target the same coronavirus proton," she told EURACTIV.

In fact, 'mix and match' would not make sense if vaccines targeted different antigens, Žvirblienė added.

Despite the views of many scientists, vaccine producers do not seem to be particularly in favour of mixing shots.

Žvirblienė explained that "this is understandable: one producer will never say that a different producer's vaccine is better for the second shot," she said.

'MIX AND MATCH' COULD RESULT IN STRONGER IMMUNE RESPONSES.

Adam Finn of the European Technical Advisory Group of Experts on Immunisation (ETAGE) at WHO told EURACTIV that using different vaccines is a "quite good idea" firstly, as it may allow quicker vaccination strategy rollouts.

"Perhaps the most compelling reason for mixing and matching is that it gives you flexibility in terms of supply," explained Finn, pointing to situations where health authorities have been giving a particular vaccine to the population and then cannot get any more of it.

"The positive side is that there may be an advantage to presenting the same antigen to the immune system in a different way, in the sense that that may stimulate either a bigger response or a broader response than just using the same hit all the time," he said.

However, he added that it is not yet clear how those better responses turn into better protection.

'MIX AND MATCH' FOR BOOSTERS WITH NEW VACCINE PLAYERS COMING IN

'Mix and match' technology can also be used when giving the booster dose. This is highly important as the countries are preparing their booster strategies and giving additional shots for older and immunosuppressed people.

Žvirblienė gave an example, that for a person who received the first two doses of adenoviral vector vaccines, "it would be beneficial" to use either mRNA or protein-based subunit vaccine, once EMA authorises them.

She added that protein-based vaccine developers "are actively preparing" their vaccines to be used as a booster. "Protein-based vaccines are being tried out with other vaccines, mRNA and vector vaccines as second or third dose," she said.

Camilla Foged, professor at the University of Copenhagen, told EURACTIV that people might trust protein-based vaccines more and be more positive, as "the reactions after the injection might be milder and we have more experience with protein-based vaccines, that's more traditional vaccine technology".

"Because we have a lot of people that are very sceptical about these new mRNA vaccines and would prefer more traditional technologies," Foged added.

She pointed out that despite the pros of mixing vaccines from the immunological point of view, there is "a challenge from a regulatory perspective because most companies are taking the boost with their own vaccine," she said, adding that heterologous vaccine strategy is currently looked at in more academic settings.

PROMOTED CONTENT

DISCLAIMER: All opinions in this column reflect the views of the author(s), not of EURACTIV Media network.

The vaccination race: a public health view

By Antoni Trilla

[Shutterstock/BaLL LunLa]

Marathon runners say that the real difficulties, what they call "the wall", appear between km 30 and 35. At this point, physical and mental exhaustion forces some runners to withdraw. We have reached this point with COVID-19. We must find the tools and the strength to keep on running. Finishing this race is critical for all of us. It is critical to the entire world.

Antoni Trilla, MD, PhD is an Epidemiologist at Hospital Clínic of Barcelona, Professor and Dean of Medical and Health Sciences School at the University of Barcelona, and Research Professor at ISGlobal.

By October 1st, the EU stands at a 63% level of full vaccination, meaning that 63% of the EU population has received a full course of vaccines, either one or two doses, depending on the vaccine used. By contrast, the UK stands at 70% and the USA at 55%. Among the most populated countries in the EU, Spain reaches the 77% level, followed by Italy (69%), France and Germany (65%) and Poland (51%).

Are these high statistics enough?

With the Delta variant of concern (VOC) dominating the field in the EU and elsewhere, we need more population to reach the immune status. The level of immunity is not equal to the level of vaccination: some people are immune because they have overcome COVID-19 or because they have a certain degree of cross-immunity against other coronaviruses. Others do not respond well enough to vaccines, especially the elderly and the immunosuppressed patients. Not all people can still get vaccinated (eg: children under 12 years of age). Finally, and pitifully, not all

Continued on Page 14

Continued from Page 13

people agree to be vaccinated. Much work remains to be done to reach the so-called herd immunity.

The technical definition of group or herd immunity is that of an adequate level of immunity, able to keep the basic reproductive number (R0) of a disease below 1 in a specific population in the absence of other control measures. The Delta VOC is more transmissible than the original virus and than the Alpha VOC: its R0 ranges between 4 and 8.

The theoretical level of group immunity for Delta (calculated as 1- 1/R0) would lie down around the 85% level of a fully immunized population. Vaccinating 85% of the entire population, adding perhaps 5-10% more due to the likely absence of a good immune response in some individuals, is a very hard goal to achieve.

The key issue now that we are coming closer to the end of the race is how to reach that 85% or 90% of the vaccinated population. Why are there people still not vaccinated in Europe?

Three necessary but not sufficient conditions must always be met for a successful vaccination campaign: 1) to have safe and effective vaccines, 2) to have the ability to administer them quickly and in a handy way, and 3) that most of the population agree to get them.

In the EU we fulfil the first two quite well. We are also investing heavily in new vaccines research and development. We need safe and effective vaccines against current and likely VOC that could appear in the future. Vaccines that are also easy to store and deliver.

However, the third condition is now what worries us the most and the hardest to overcome. The theory explains that there are people radically opposed to vaccination (the deniers or "anti-vaxxers"), people who are reluctant to vaccination and are primarily concerned about the safety of vaccines and their possible adverse effects (the "vaccine-hesitant"), and a third group who do not seem to be interested in vaccination, which we classify as "apathetic" or unconcerned.

Some business and marketing theories show that communication strategies must necessarily be different to address vaccine hesitancy and vaccine apathy. In the case of hesitant people, whose response is emotional and cognitive but with a high involvement, adequate technical and scientific information is required. We need to establish a useful dialogue: listen to them, answer their questions and address their concerns, showing empathy towards them. In the case of the apathetic, indifference is the norm.

They do not get involved and do not even make the psychological effort to worry about the disease or the vaccine. Apathetic people can be persuaded by simple, quick, and emotional arguments. New messages are conveyed by unusual, non-formal, channels. The source of the communication may be more important for them than the evidence or arguments used. These sources can be people they know, have high regard for, and/or have provided them with good information in the past. They should be people who are relatively similar to the group they are addressing.

For a 25-year-old apathetic unvaccinated citizen, a famous and respected sports star or a successful artist is far better than an expert scientist or physician. Better use Instagram or Facebook than newspapers, radio or television for reaching these apathetic people.

Identifying the best channels and messages to reach those who still need convincing may be the single most effective action to increase our vaccination rate.

It is likely that in the future we will live with COVID-19 in an endemic situation. There will be infections and sick people, some of them with severe forms that will need to be admitted in a hospital, and also deaths, but hopefully in low and manageable numbers, as happens and have happened with many other infectious diseases (pneumonia, diphtheria, measles).

Vaccines are not perfect, but they are by far the best option, and together with new treatments they are our tools to get out of this nightmare. We must continue to inform people and persuade them to be vaccinated. It will get harder and harder, but we can do it. We are only a few kilometres away from the finish line.

For information on
***EURACTIV** Special Reports...*

Contact us

Gerardo FORTUNA
Agriculture & Health Editor
gerardo.fortuna@euractiv.com
tel. +32 (0) 2 788 36 69

Teresa DOMINGUEZ
EU Affairs Senior Manager
teresa.dominguez@euractiv.com
tel. +32 (0) 47 601 78 26