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How a year of coronavirus activity unfolded at the EU's medicines regulator

The speed with which coronavirus vaccines have been developed surprised everyone and could transform public health into the future, says Dr Fergus Sweeney, head of the clinical studies and manufacturing taskforce at the European Medicines Agency (EMA). Here he gives us a glimpse at the work of the regulator over the past year as part of the fight against Covid-19.

07 April 2021 - By RICHARD GRAY

We have people who follow health threats all over the world as they develop. In late 2019, they started to see reports from China of an unusual respiratory disease and they were trying to understand what it might potentially be.

The first meeting I remember about Covid-19 was in early January 2020. My colleagues had previously been looking at what happened with the coronaviruses that cause MERS and SARS. While these hadn't spread to a great extent, we were very aware something like this could emerge as a potential problem.

At this stage it wasn't clear how far this would spread, but we could see what was happening inside China with their lockdowns. Even if the disease had not spread outside China, this was something we were paying attention to because a lot of the active pharmaceutical ingredients for medicines used in Europe come from manufacturers in China. There was the possibility the lockdowns would have an impact on the global supply chain for medicines.

So, the first steps I took in early January were to contact pharmaceutical industry associations so they could start preparing for that disruption. At the same time we were preparing for the possibility the virus would spread.

The EMA has an established public health threat plan that we revamped significantly following the lessons we learned in 2009 with the H1N1 flu pandemic. This meant we had significant planning in place and we very quickly launched the EMA's Task Force (ETF) on Covid-19. This brought together experts on vaccines and therapeutics drugs from all over Europe.

I don't think many of us expected vaccines to advance so soon. At the beginning of the pandemic it seemed more likely it would be therapeutics – the medicines to treat the viral infection – that we would be seeing first.

As a regulatory body, we need specific answers to a range of questions about safety and how effective a medicine or vaccine is before we can authorise them.

We wanted to help developers to build clinical trials that would give us the answers we needed and offered scientific advice very early to help do that. This included what size of clinical trials we might need, what levels of efficacy we would be looking for and what clinical endpoints would be relevant – (for therapeutics this can involve) things like levels of hospitalisation, time spent in hospital, time spent on oxygen, mortality rates.

It's not just the 900 or so EMA staff in Amsterdam who are evaluating the medicines, but we are working with about 4,500 experts from the European Medicines Network. We were also reaching out to other international regulators like the FDA in the US, Health Canada, SwissMedic, MHRA UK and the PMDA in Japan. Covid-19 is a global problem so it was important we were giving the same advice compared to these regulators otherwise it would create confusion and make consistent clinical trials and manufacturing very difficult.

There were a lot of researchers who started small clinical trials with medicines that were already available to see if anything could work to dampen the acute respiratory distress caused by the virus. Often these were not big enough to deliver a result on their own and led to a lot of controversial discussions about hydroxychloroquine, for example.

'There is a huge sense of pride within the EMA and among the experts who we have worked with that we are all contributing to something that is making a difference on a global scale. And the

work done during the pandemic will have long lasting impacts too', underlines Dr Fergus Sweeney, EMA. Image credit - European Medicines Agency

It was really important that these were tested as part of large, randomised trials capable of giving definitive evidence. In the case of hydroxychloroquine, it turned out it didn't work. But there were others such as dexamethasone (where large clinical trials showed it as effective in treating severe Covid-19) where we quickly reviewed the information so we could deliver a position that could help guide clinical practice in Europe.

But contrary to what the initial expectation was, by the last quarter of 2020 we started to see clinical trial results of vaccines that were showing some really high level of efficacy. Vaccine development had been accelerated to squeeze into less than a year what would normally take 5-15 years of development, but without diminishing the standards.

There were a number of reasons for this: the clinical trials themselves were very large and since the disease itself was so prevalent, they got the numbers needed in a short period of time. Manufacturers also built factories and developed facilities ahead of when they would have normally – there was a large investment at risk, as typically they would wait for the trials to finish.

Once there was a sufficient level of evidence that a vaccine was looking promising, we switched into what we call 'rolling review'. Normally developers wait until they have a complete dossier on all the trials and manufacturing. It comes to us in a big package on what we call day zero, and we start the evaluation process that lasts a year or more.

With rolling review, however, as results from clinical studies, manufacturing data or non-clinical results become available, we ask questions and get them to resolve issues – such as asking them to do different tests or changing things in the manufacturing process. It means by the time we reach what would normally be day zero of the process, we have all the information needed for it to become a formal marketing application, which then only requires a few weeks to a couple of months to finalise.

I'm not sure we can maintain this pace of work long-term as we have people working around the clock, but there are definitely lessons about how we work remotely, share information and collaborate that could help us in the future.

For all of us involved in this work, we have been very aware that the timeframes we have been working to are very important. The public health need is enormous and unwavering. We would see numbers of cases and deaths come out day after day, and we naturally want that to change. But at the same time we need to make sure that any of the vaccines and medicines we approve to try to change the situation are safe and that people can trust those medicines. It had to be a careful scientific evaluation.

There is a huge sense of pride within the EMA and among the experts who we have worked with that we are all contributing to something that is making a difference on a global scale. And the work done during the pandemic will have long lasting impacts too.

There has been a major step forward in public health in terms of our understanding of vaccines and developing new types of vaccines such as the mRNA vaccines. It has shown (the different vaccine platform technologies) can be quickly adapted, which will be important not only for dealing with new Covid-19 variants we are starting to see emerging, but also for whatever the next pandemic might be. They could be useful in the annual influenza vaccination campaign or for other diseases.

The pandemic has also generated a large amount of information about manufacturing and the efficacy and safety of these vaccine technologies. It has opened up enormous opportunities for public health which would have taken years under normal circumstances.

In the meantime we have other vaccines coming through that we are continuing to assess. We also have a very big job as the various vaccines are given to millions and tens of millions of people to make sure that they

continue to be safe – if there are rare events we are picking them up and monitoring for safety. This is something we do for all medicines and vaccines but the scale is very different here.

We also need to understand whether vaccinated people can transmit the virus or not. We are working to (authorise manufacturing sites to) increase vaccine production. At the same time we are also seeing some therapeutics now coming through such as monoclonal antibodies – antibodies produced in the laboratory – that can be used to protect and treat people who've already got an infection. We are still evaluating antiviral medicines and immune system modulators that can help to treat the later phases of serious disease.

We are now just entering a phase where the medical community is trying to understand what the long-term consequences will be for people who have been infected with Covid-19 and are now suffering what is often referred to as long Covid. There seem to be different symptoms in different people and how those people are going to be treated will be a growing issue in the coming years.

There is a lot still to be done and the pandemic is far from finished.

As told to Richard Gray.

This interview has been edited for length and clarity.

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