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04.05.2023

Tags:

Europe, EMA, European Medicines Agency, Regulator, Exclusive

In conversation at DIA Europe 2023 in Basel, European Medicines Agency Executive Director Emer Cooke looks back at the lessons EMA has taken from the COVID-19 pandemic response, outlines the Agencyâ??s approach to antimicrobial resistance, and highlights how it hopes to contribute to a stronger European clinical trials ecosystem.

Pharmaceutical industry leaders have spoken glowingly of the open dialogue and rapid regulatory decision making that characterised the COVID-19 pandemic response and are hoping that this can continue moving forward. What lessons from this unprecedented period do you hope to build on at EMA moving forward?

Starting with the successes of Europeâ??s pandemic response, EMA authorised eight vaccines and eight therapeutics within two and a half years, provided 1.4 billion vaccine doses across the 30 EEA countries, and was responsible for the export of 2.4 billion vaccines to 160 countries. It was a remarkable achievement based on close collaboration between developers, regulators, wholesalers, distributors, and policymakers.

This happened because all stakeholders were facing the same challenges and became united behind a common purpose. In the early stages of the pandemic, before joining EMA, I was working at the World Health Organisation (WHO), where the urgent need for therapeutics and vaccines against COVID was felt particularly strongly. However, ensuring that these products were safe, effective, and of high quality was non-negotiable, meaning that the same standards as any other marketing authorisation needed to be applied. It is a big responsibility to give a vaccine to a population of 500 million.

A lot of work went into streamlining the regulatory process, and the fact that there were so many willing clinical trial volunteers was a success factor. Our first data sets were in the region of 30,000 subjects, compared to around 2,000 for a standard vaccine trial. We also moved towards allowing the conduct of studies â?? such as in animals and in humans, when the risks allowed â?? in parallel rather than sequentially to further speed up the process. Thirdly, EMA â?? together with experts around the world â?? identified the probable side effects of these sorts of vaccines and monitored these products more intensively than others. Additionally, while EMAâ??s mandate is drug evaluation, there was a lot of work involved in procurement, logistics, and distribution that needed to come together to make such a massive process happen.

The Agency was well prepared and the Health Threats Plan that we activated in February 2020 allowed us to offer rapid scientific advice to developers, introduce the concept of rolling reviews, and set up our Pandemic Task Force which concentrated expertise. EMA is also Chair of the International Coalition of Medicines Regulatory Authorities (ICMRA) and has been committed to working on the wider international stage. This was a collective, rather than a competitive, effort.

There was a level of frustration that many of the trials being conducted, particularly for therapeutics, were small and not statistically significant, so as ICMRA we put out a statement to encourage people to conduct trials that would be meaningful. This bore fruit on the vaccines side, but did not in therapeutics where almost no new or repurposed products â?? bar dexamethasone in the early days of the pandemic â?? came to fruition.

How applicable can the COVID experience be to reviewing products in other therapeutic areas and regulatory activities?

We must admit that the pandemic presented a unique set of circumstances. However, it did foreground the importance of a collective approach, bringing together different stakeholders to engage in open dialogue in what was effectively a non-competitive space. From a regulatory perspective, we see opportunities to continue some of these discussions in the ICMRA setting. We also now have a new legal mandate that allows us to do a lot more work on preparedness and anticipating possible future pandemics.

Elsewhere, COVID restrictions prevented on-site inspections, leading to the introduction of virtual distant inspections as well as hybrid inspections whereby some national regulators could be on the ground while others participated remotely. Guidance for all of this now exists. There are, of course, pros and cons for all of these measures; they are quite resource intensive, meaning that these measures should be reserved for exceptional circumstances. In addition, it is important that industry submits mature dossiers. Rapid authorisations are facilitated by a combination of large datasets, quality dossiers, and agile regulators.

Some industry sponsors have talked to us about â??educatingâ?• regulators in new areas like mRNA technology. While this may be an overstatement, how challenging is it as a regulatory body to stay on top of the cornucopia of therapeutic approaches and technological platforms being brought forward today?

EMA has different fora to ensure we know what is to come. The first is our horizon scanning service, which attempts to anticipate which parts of the development pipeline we need to get ready for. We also hold regular pipeline meetings with companies to discuss the projects that have almost reached proof of concept stage and which, if successful, we might be dealing with in three to four yearsâ?? time.

In addition, EMA has an Innovation Task Force (ITF) which helps companies with an innovative idea to navigate the regulatory pathways. This Task Force also helps EMA in terms of building future capacity by identifying the areas in which we need to strengthen our expertise.

Overall, EMA aims to remain at the pulse of scientific advances and anticipate future regulatory needs. One example of this is the conference we organised in February this year on RNA-based medicines, where we discussed with industry and academia the scientific and regulatory opportunities and challenges for these medicines.

Antimicrobial resistance (AMR) has been described as a â??silent pandemicâ?• and a major threat to the health of Europe. How is EMA working with industry and academia to combat this looming issue?

EMA has been doing a huge amount of work around AMR for a long time, and in a concerted manner since at least 2010. However, the regulatory aspects will only be one part of the solution. If a promising product emerges, as happened during COVID, EMA will bring regulators together and make sure that it is reviewed.

In the context of the pandemic, EMA piloted the â??OPENâ?? initiative to increase international collaboration on the evaluation of vaccines and therapeutics, which saw regulators from outside the EU participate as members in our scientific meetings. This led, for example, to the AstraZeneca vaccine that we authorised achieving WHO pre-qualification and then authorisation in 160 countries within two weeks; a process could take between two to eight years in normal circumstances. OPEN has now been launched as a full programme, with a focus on AMR-related products and medicines that target an unmet medical need via our â??PRIMEâ?? pathway. The idea is to move towards more collaborative reviews and common inspections.

Should the right AMR-related product be presented to EMA, there are a number of opportunities that we are ready to push the button on. Up until that moment, our role is to be prepared and support the developers. A lot of work is going on. The OPEN procedure allows for the involvement of regulators from other jurisdictions, we provide guidance to developers, we interact with international regulators, and our work within the ICMRA is helping us raise awareness of the threat of AMR among both patients and healthcare professionals globally. On the veterinary side, we monitor the sales and prescriptions of antimicrobials in animals. While we have seen a 47 percent decrease in the use of antimicrobials in animals in recent years, and an 80 percent decrease in the use of polymyxins, there is still a lot of work to be done. For example, last winter saw shortages of certain antimicrobials in Europe due to a supply-demand mismatch, but most of the unanticipated respiratory infections were actually viral rather than bacterial, meaning that antibiotics were not the solution. There is still a lot of inappropriate use of antibiotics and the need for better diagnosis.

The EU Clinical Trials Regulation entered into force in January 2022 with the aim of ensuring that the EU offers an attractive and favourable environment for carrying out clinical research on a large scale, with high standards of public transparency and safety for clinical trial participants. While EMA does not have a clinical trials mandate, what role will the Agency have in promoting the overall clinical trials ecosystem in Europe?

EMA does not have a specific mandate to authorise clinical trials, but I like to see the agency as something of a â??fairy godmotherâ?? that does a huge amount to improve the environment for clinical trials. To this end, along with the European Commission and the heads of national medicines agencies which approve trials within their countriesâ?? borders, we launched the Accelerating Clinical Trials in the EU (ACT EU) initiative last year. This initiative aims to relaunch the EU further as a competitive centre for innovative clinical research.

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ACT EU was borne out of the realisation that there is huge complexity in the system and has been designed around ten priority areas. Some major wins have already been secured, including guidance on complex clinical trials as well as decentralised clinical trials, which COVID helped promote the acceptability and importance of. Moving forward, we are focusing on the implementation of the Clinical Trial Regulation, as EMA holds responsibility for the management of the Clinical Trials Information System (CTIS), a game-changing initiative which allows for a single submission and supports the flow of information between clinical trial sponsors, EU Member States, European Economic Area (EEA) countries, and the European Commission.

We feel a strong responsibility to create an enabling environment as part of this collective effort. The wider EU area represents 500 million people; a huge population that companies should not be running away from. What we are working towards will not happen overnight, but the foundations are in place for a sea change in how clinical trials are regulated across Europe.

One can assume that because of the single-payer nature of European healthcare systems and the unified real world data they generate, the continent has a golden opportunity to make use of data and artificial intelligence for drug development. What is your take, and how is EMA involving itself in this process?

EMAâ??s Data Analysis and Real World Interrogation Network (DARWIN EU) â?? a coordination centre to provide timely and reliable evidence on the use, safety and effectiveness of medicines from real world healthcare databases across the EU â?? recently celebrated its first anniversary. DARWIN EU brings together a federated network of data providers but also has regulators, patients, health technology assessment (HTA) bodies, and payers on its advisory board to help determine its work programme. While DARWIN EU only completed four studies in 2022, we are planning between ten to 15 in 2023, and around 150 per year from 2025. We have a huge opportunity to ensure that we are asking the right questions of our healthcare systems to optimise patient treatment.

Companies need to be more engaged in collaboration with HTA bodies; currently, only 50 percent are considering the HTA perspective at the early development stage, for example, which is not enough. There needs to be a move beyond pure regulatory questions to a consideration of what

HTA bodies and payers might need. EMA has already engaged in 62 parallel joint scientific consultations with the European Network for Health Technology Assessment (EUnetHTA) consortium, in the recent years.

What are the key items on your priority list up to the end of your term as executive director of EMA in 2025?

As regulators, we have a great opportunity to build on the COVID experience and make sure that we are part of an ecosystem that brings new products which can make a difference for patients. We saw we could help make that happen, and the ongoing work on HTA will contribute to it.

EMA has identified three focus impact areas. The first is ensuring that our evaluations are high quality, rapid, and robust. The tools and lessons from COVID can be translated into other areas, particularly oncology. 45 percent of the products that go through EMA are oncology-related, and especially in the context of the EUâ??s Europeâ??s Beating Cancer plan, this is a field where we can really make a difference.

Secondly, we are looking at how we can improve evidence generation to support innovation for example through the ACT EU initiative and (DARWIN EU), but also through the engagement with stakeholders such as HTAs.

Thirdly, all these tasks should be underpinned by transparency and communication. COVID effectively made us innovate on the fly, but it also changed the way we work. We must use simpler language, be more impactful in our communication, and everything we do has to be accompanied by full transparency.

As a final message, I am absolutely committed to ensuring the sustainability of the European network. We have seen some challenges with expertise and resources. This means we need to become more efficient and ensure we have enough expertise to deal with both routine and surge capacity. I am personally working very closely on this area with our tactical group on resourcing, which is looking at streamlining, capacity building, and effectively building the regulators of the future, across the EU.

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