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EU Regulator Raises Possibility Of Shorter Drug Approval Timelines

26 Mar 2021 | **NEWS**

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Executive Summary

With the EU pharmaceutical legislation due to undergo a radical shake-up to create a future-proof regulatory system, the time is ripe for industry to engage with efforts to make the European drug approval process more agile.

A PROPOSAL TO REVISE THE EU PHARMACEUTICAL LEGISLATION IS EXPECTED IN 2022 *Source: Shutterstock*

The upcoming review of the EU pharmaceutical legislation is the ideal opportunity for drug companies to address any concerns they might have about the pace of medicine approvals in Europe compared with other jurisdictions, a senior EU regulatory official has suggested.

While the real-time assessment of COVID-19 vaccines and treatments by regulators worldwide has raised industry expectations, Anthony Humphreys of the European Medicines Agency says that rolling reviews cannot be the new normal as they are very resource intensive.

Nevertheless, industry may be in a position to influence changes to the 210-day period that is currently enshrined in the EU legislation as the maximum time (in addition to clock stops) allowed to review a new marketing authorization application, suggested Humphreys, who heads the EMA's Regulatory Science and Innovation Task Force.

"The famous 210 days in Europe with the one clock stop opportunity… although we tend to do multiple [clock stops]… has got at least a 25-year history, if not longer," Humphreys said at the Drug Information Association's virtual Europe 2021 conference on 19 March.

"I believe it… [was in place] in the '70s and the '80s and it is even a feature of the national licencing system in Europe," Humphreys said during a session on what the "EMA of the future" should look like. The last time the 210-day timeframe was looked into was in 2004, when the pharmaceutical legislation was revised to pave way for the "accelerated assessment" of new medicines of major public health interest, he recalled. (Also see "Accelerated Assessment" - Pink Sheet, 6 Jan, 2006.)

With the pharmaceutical legislation set to begin another review this year – primarily to implement the many ambitious changes outlined in the EU pharmaceutical strategy adopted last year – "maybe now is the time… to really have a discussion" on the 210-day review timeframe, Humphreys said. (Also see "Radical Shake-Up In Store For Entire EU Pharma Legislation" - Pink Sheet, 25 Nov, 2020.)

On whether the EU should change its 210-day timeframe for reviewing all drugs or whether it should introduce some more flexible mechanisms, he said that "now is the time to engage in that and influence the pharma strategy and [see] where it lands with regard to the [revised pharmaceutical] legislation."

Humphreys' comments were in response to Alan Morrison of Merck Sharp & Dohme pitching for "more dynamic regulatory assessments," "more agile authorization" and other changes that drug companies think are needed for the EU to remain a global leader in the biopharmaceutical field in the future.

EU Decision-Making On Drug Applications

Another aspect of the EU's centralized drug approval process is that the final marketing authorization decision rests with the European Commission, which has up to 67 days to take a decision after a drug is recommended for EU-wide approval by the EMA.

Humphreys recalled that during the H1N1 pandemic, "we were amazed" the decision-making process "could be done in one to two days" and "prior to that it was accelerated for protease inhibitors in the mid-90s. But it was done in hours this time [for COVID-19 vaccines]. And of course, people are then saying, well, if

something can be done in hours, why then does it need to take 67 days?"

The EMA executive said he could not comment on the commission's decision-making process, "but if there is an opportunity to amend that specifically for the pharma area - and there is an if - then this will be the time to have that dialog indeed" in the context of the pharmaceutical legislation review.

When contacted by *Pink Sheet*, the commission declined to comment on the scope of the review of the general pharmaceutical legislation, but said that the roadmap and inception impact assessment for the revision would be published for four weeks of feedback in the second quarter of 2021. There will also be a public consultation in the second half of the year. "The Commission intends to make a legislative proposal to revise the legislation end of next year," a spokesperson said.

The legislation is to be reviewed to help implement the changes envisaged in the pharmaceutical strategy to create a future-proof regulatory system and to harmonize and streamline many of the existing processes and procedures.

"We've actually heard much of this before" and "have had myriad examples" of legislative changes to harmonize and simplify processes, said Morrison, who is vice president of regulatory affairs international at MSD. Examples include the EU Clinical Trials Directive and the EU pediatric and pharmacovigilance legislation.

These changes have had a diametrically opposite effect and "created greater level of regulatory complexity, more bureaucracy and increased costs. And certainly, that is something we have to guard against in the future," said Morrison, who represented the European pharmaceutical federation EFPIA at the conference session.

Do All EU States Need A Seat At The Table?

Another topic raised by Morrison was whether the EU's centralized approach to medicines evaluation should be re-examined to make better use of available expertise within the network.

He noted that while several agencies had created "centers of excellence" for certain therapeutics or technologies, the EU in contrast follows the "rapporteur system, where there is a more generalist overview."

"When you develop any kind of process, you want to minimize handoffs," Morrison said. He suggested that creating centers of excellence within the EU network, to whom decision making could be devolved, would help to streamline the system. Having more expertise-driven committees and advisory groups could help the EU to deliver on agile assessments of medicines, he added.

Humphreys agreed that it was a "fair question" to ask whether all the seven scientific committees at the EMA "still need to have a member state model… 25 years into the system." And given that the EU would eventually get back to pursuing its "enlargement agenda," these committees would get even larger as representatives from new member states were added.

However, Humphreys noted that the "element of representation" and the "sovereignty issue," especially in relation to pharmacovigilance, were quite important and a unique feature of the EU system. "It's not just a [question of conducting] scientific assessments," he said.

He argued that it was not fair to generalize too much as all drug evaluation systems were created to serve the political ecosystems they existed in. “The FDA is set up to license for the [United] States and we’re set up for Europe.”

As to making the drug evaluation process more agile, Humphreys said the EMA was currently going through a “working party revision exercise… and we've already identified the need to have an agile and dynamic turnover of experts in emerging fields like real-world evidence, artificial intelligence, modelling and simulation - you know the topics.” The need for dynamic, adaptable expertise was absolutely recognized, he said.

Mobilizing Expertise In The EU Model

The EU’s centralized drug assessment model, Humphreys explained, is designed to mobilize the best expertise from all EU member states big or small. “That is one of its great features,” he said.

Over the last few years, the EMA has been trying to “blend in” quality, non-clinical, clinical, pharmacovigilance and other expertise available across member states into its pre- and post-authorization procedures through Multi-National Assessment Teams or MNATs. (Also see "EMA Multinational Assessment Teams Move Into Post-Authorization After Delay" - Pink Sheet, 22 Aug, 2017.)

It is a way of getting some of the smaller EU national competent authorities (NCAs) involved in the system. Some of these experts – depending on how the NCAs are structured - work in university hospitals close to cutting-edge research and have first-hand clinical experience, Humphreys explained. “I would expect that approach to continue.”

In the future, Humphreys believes the EMA’s ability to mobilize expertise will be enhanced even further, supported by remote ways of working. “I think the old model of flying everybody to a fixed location… has had its day. Nobody is saying it's a 100% flip over to virtual, but certainly everybody's talking hybrid models.”

As for access to top-level scientific experts, he said these were “very busy guys” working in university hospitals, who may find it easier to participate in virtual meetings. “They might be able to give us an hour or two for a critical discussion, but they're not going to give us a day or two.”