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Pharma Firms Spend 'Billions' On Failing: More Collaboration Needed On Innovation

by Ian Schofield

Speakers at a DIA EuroMeeting session on the challenges and opportunities facing regulators in the years to come discussed several options including more proactive engagement by regulators, more sharing by drug sponsors, and being innovative across the whole of the regulatory landscape.

Pharmaceutical companies across the world have spent "billions and billions of euros on failing", regulators need to be "in front of innovation" rather than catching up with it, and patient organizations are not that interested in getting involved in the regulatory aspects of drug development.

These were some of the more provocative views expressed at the DIA EuroMeeting in Glasgow, UK, earlier this month, during a "town hall" session on the scientific and regulatory challenges and opportunities facing agencies across Europe.

The tenor of the session was set by an audience poll which found that almost 60% of those present did not think that Europeans are "getting the innovation that society wants."

Panelists outlined what they saw as the progress made so far in encouraging innovation, the key obstacles to innovation, and some possible ways forward, including more proactive engagement by regulators and more sharing amongst pharmaceutical companies in the "precompetitive space."

Pierre Meulien, executive director of Europe's public-private Innovative Medicines Initiative, said "huge technological breakthroughs" had allowed scientists to understand the pathogenesis of many diseases at the molecular level" and elucidate much more about the genome and about how proteins work in both health and disease. That, he said, was "driving a big shift in medicine" from an approach based on anatomical issues to one based on pathway biology medicine that would "drive a completely different taxonomy of diseases."

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"Pharmaceutical companies across the world have spent an awful lot of money on failing" – Pierre Meulien, IMI director

But, said Meulien, everyone was aware that there was an "innovation gap" at global level. "If you look at just one disease, Alzheimer's disease, it is a huge burden, a complex thing," and "pharmaceutical companies across the world have failed, and have spent an awful lot of money, billions and billions of euros, on failing, essentially."

He said more collaborative ways of working were needed "where we can really try and understand the failures and build upon the new knowledge and try things out in different ways. If we cannot find another way of approaching things like Alzheimer's disease or introducing pharmacological prevention to catch people early on and prevent locked-in dementia, we have a bigger problem than we think we have," he declared.

This need for more collaboration was also voiced by Thomas Senderovitz, director general of the Danish medicines agency, who said that "in the precompetitive area, whatever that means, we need to have sponsors less afraid of sharing. One of the reasons we fail is that 10 or 15 companies work on the same target, nine of them fail, and the other five or six continue on the same development path. Maybe that's not the wisest ways of using our resources."

The regulators too have their part to play in making sure innovation goes in the right direction. Guido Rasi, executive director of the European Medicines Agency, said the agency had "for many years" promoted early multistakeholder engagement in order to reduce development risks and ensure "we know as soon as possible what innovation is coming."

Senderovitz said it was important to think of innovative ways for regulators to "interact with stakeholders, academia, patients, other users, looking at things like advanced therapies, companion diagnostics – it is the whole [thing] that we as regulators have to be very ready to face." Regulators, he said, had to be "in front of innovation, not running behind it. We must be much more advanced and much more prepared for this, and not wait until the avalanche hits us."

He suggested it was up to the regulators to "change our mentality. We should not lean back and say 'bring this drug to us and we will evaluate it'." It was "not just being the bad regulators that put up obstacles and say yes or no, but actually taking part in this process."

Appearing to refer to the debate over earlier drug approval through the likes of adaptive

pathways, he said regulators had a responsibility to help bring better treatments to patients "in due time." This did not necessarily mean in the fastest possible time, though. "Due time is the time when we know enough so that the benefits are clear and the harm is acceptable, and I think that is an interesting debate."

For Christa Wirthumer-Hoche, chair of the EMA management board and head of the Austrian regulatory agency AGES, regulatory authority assessors needed better training in how to evaluate the new kinds of drugs coming through pipelines. It was for this reason, she said, that the EU network training center had been set up, "so that assessors are really state of the art and they have the knowledge to be able to assess the dossiers of these new innovative products."

She also suggested that regulators engage early with academia to "ask them about the latest developments" and "train them in regulatory affairs" – something that Rasi also addressed when he mentioned the recently announced framework agreement between the EMA and academia. (Also see "*EMA Tightens Links With Academia To Boost Innovation And Regulatory Science*" - Pink Sheet, 6 Apr, 2017.)

Data, Data, And More Data

Education of physicians should also not be left out of the equation, according to Meulien, who said medical doctors needed training "so that they can work more closely with informatics experts to really try and understand how to analyze the massive amounts of data that will be produced. We will have millions if not billions of datapoints to look at in some of these complex diseases – who will analyze these data, who will decide which patients get into a clinical trial or gets a particular medication?" he asked.

The topic turned to the kind of data regulators will really need to arrive at their decisions, and how far real world data (RWD) play a role in the regulatory process. "What kind of decisions do we have to make, and what information do we need to make those decisions?" Senderovitz asked. "For example, should this particular molecule be approved at this time, and can we rely only on randomized clinical trials and can real world data be supportive?"

He expressed some doubts over the utility of RWD, at least at the present time, noting that "I don't really like that term, what does it cover?" Questions had to be asked: "Were these data prospectively generated, are they randomly generated, are they fit for decision-making? There is a lot of mapping [to be done] before you can say, 'oh let's use RWD as part of the approval process'."

Before RWD could be used meaningfully, Senderovitz said, technical obstacles had to be overcome, such as the lack of harmonization of electronic health records "within, never mind among, countries… and making sure that legislation does not stop us from making sensible collaborations across borders."

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It would take some time, he said, before we reached a point where RWD was part of the approval process. However, "as we move the approval process up earlier, with PRIME [the EMA's priority medicines scheme] for instance, we are bound to use post-approval data that are not RCT to continuously monitor the risk benefit. So I think we need to be more open as regulators, we need to get our heads around these types of data, and we need to be very clear about which kind of decisions we want to make and when the data can be used."

The role of the patient in ensuring innovation was properly targeted was also discussed at the session, with some expressing doubts over how far patients were willing to get involved. Wirthumer-Hoche said patients needed to be "trained in regulatory topics so that they can really participate in discussions."

However, she was skeptical as to their enthusiasm for such involvement. "To be honest, what we realized in Austria was we tried to involve patients in different committees, to inform them about our regulatory activities, what is put in the patient leaflet, about patients' expectations, and we recognized that they are not really interested." While the agency had "really tried to get in touch with them," pretty much the only organized patient groups were those for rare diseases. She said the agency was continuing to involve and inform them "but I have to say it is not an easy task."

Improving Predictability

Asked how they would improve the predictability of the R&D process overall, panelists suggested various ways forward, including more cooperation among regulators and health technology assessment bodies to maximize eventual market access.

Rasi said fostering more robust evidence, "hopefully with some other stakeholders like payers and health technology assessment bodies," would "certainly increase predictability." He said the EMA could not discuss price "but we certainly contribute to the value, or comparative value" of new drugs.

For Senderovitz it was a question of making sure innovation stretched across the whole landscape, "not only high-level super molecules or biomarkers" but also making continuous improvements in areas like clinical trials, assessments, and how to use data more effectively.

He also outlined other challenges facing the sector, such as the increasing complexity of pharmaceutical supply chains, outsourcing of active pharmaceutical ingredient manufacture, packaging, clinical trials and so on. "It is enormously complex, and that complexity is not decreasing. That can actually tilt the whole thing – we have unfortunately several recent examples of medicines withdrawn from the market for poor quality or falsified data." Such things, he said, could "destroy patient and public trust in medicines, which would be disastrous. I think there are ways to further strengthen and simplify how we do that, but I don't have the full

answer."

"Maybe one of the biggest challenges is the speed with which this all happens," he observed. For example, new guidelines take a long time to draft and consult on, "and by the time the guideline is finished the world has changed again."

From the editors of Scrip Regulatory Affairs.