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Momentum Builds In Europe To Push Biosimilars Forwards

Medicines For Europe Biosimilars Leaders Discuss Latest Industry Developments

by David Wallace

With Europe's biosimilars industry bolstered by a recent statement from the EMA and HMA, as well as the prospect of a more streamlined regulatory pathway in future, Medicines for Europe's biosimilars chair Isabell Remus and director of biosimilars policy and science Julie Maréchal-Jamil spoke to *Generics Bulletin* to discuss the path forward.

There was an air of positivity at Medicines for Europe's 18th Biosimilar Medicines Conference held in Brussels, Belgium, in early October, especially given that the region's biosimilars industry had recently been bolstered by a statement from the European Medicines Agency and Heads of Medicines Agencies setting out the scientific rationale supporting the interchangeability of biosimilars in the EU (*see sidebar*).

Topics of discussions at the conference ranged from the place of biosimilars in the EU's pharma strategy, the varying levels of access to biologics across Europe and procurement best practices to changes in the regulatory landscape and international harmonization.

And while there was an acknowledgement of the challenges faced by the industry, there were also hints of progress in areas such as the potential for reducing the

EMA And HMA Speak Out In Favor Of Biosimilar Interchangeability

By Chloe Kent

22 Sep 2022

Stakeholders in Europe have been hesitant to allow interchangeable substitution of biological products, prompting the European

clinical data burden for developers filing biosimilars with the EMA.

Against this backdrop, on the sidelines of the conference *Generics Bulletin* spoke to the chair of Medicines for Europe's biosimilar medicines group and Sandoz Europe's head of biosimilars and specialty, Isabell Remus, along with the association's director of biosimilars policy and science, Julie Maréchal-Jamil, about the latest developments in European biosimilars.

Medicines Agency to clarify its stance on the issue.

Read the full article here

EMA-HMA Statement Offers A Bridge To Those With Hesitancy

Asked first about the EMA-HMA statement supporting the interchangeability of biosimilars, Remus emphasized "the trust that this can bring and the confidence that this will continue to instil, because it's coming from a very credible body, it's got the scientific base to it."

"We believe that it will continue to build trust and have especially importance in countries that are not using biosimilars that much," Remus suggested.

"The hope would be that [for] those that are more sceptical and hesitant, a statement like this would give them assurance and confidence and drive the usage of biosimilars moving forward."

Maréchal-Jamil characterized the statement as "a consolidation of what already existed and an opportunity to address the gap" in access and information from member state regulators.

EMA-HMA Biosimilar Interchangeability Statement Offers 'Unity And Clarity' For Europe

By David Wallace

11 Oct 2022

The recent statement by the EMA and HMA affirming the interchangeability of biologics and biosimilars has given a boost to Europe's biosimilars industry ahead of key legislative reforms, heard delegates to Medicines for Europe's 18th Biosimilar Medicines Conference in Brussels.

Read the full article here

"We counted 40% of agencies having no information on biosimilar medicines; not a single piece of information on biosimilar medicines," Maréchal-Jamil pointed out. The statement would therefore help to bring "equal footing on seizing the opportunity of biosimilar competition, where the lack of information may have meant the trust could not be reached," with the statement acting as a "bridge" to those with remaining hesitancy on biosimilars, where "basically the opportunity was within reach, but not really seized."

With Remus pointing to comments made from conference panelists about the need to restart education and rebuild trust every time biosimilars entered new therapeutic areas, she said that the EMA-HMA statement would also help here "as we expand into further therapeutic areas where people might be exposed to the usage of biosimilars the first time. Again, it is something that gives assurance and clarifies."

This included areas such as ophthalmology "or multiple sclerosis, another area that I think is worth mentioning," Remus said. "So there are several areas that are going to be new to biosimilars and the first biosimilar launches in these therapeutic areas moving forward."

Even within certain therapeutic categories, Maréchal-Jamil noted, new areas needed to be opened up. "Sometimes even when we say oncology, we're being very generalist about this therapy area when in fact there are a lot of sub-specialties within oncology and where we know, it's not because the breast cancer specialist has been very familiar with [biosimilar medicines use] that it will be readily extrapolated by oncologists, colleagues outside breast cancer."

"We can target entirely new [therapeutic areas], but the cancer community is also not monolithic. And they're going to have to expand a little bit the base of familiarity."

Asked about how easily learnings from one therapeutic area could be translated into another, Remus said there was a degree of a "positive halo effect over into other therapeutic areas" but this could not be taken for granted. "You still need to make sure that everyone is on board, the different stakeholders. You still have to do it. But there's a better base."

And Maréchal-Jamil suggested that "that cumulative effect will definitely be of benefit when we have more new cancer medicines, even if different types of cancers. Even if there are sub-specialties, information, dialogue will be needed but it's closer to home than a completely new therapy area. Same will apply in immunology. In both cases, we expect that experience will be more easily relatable and translatable."

Overall, "the statement has been really well received," Maréchal-Jamil summarized, even among "stakeholders that have not yet been very engaged in biosimilar medicines, like the orphan disease community, that is welcoming the statement as one way to start building the future competition in a very difficult space. So, I would say feedback is rather positive."

Ultimately, the statement represents "a great resource in that it puts all the science and experience in one place," she concluded. And despite some concerns expressed by the brand industry (Also see "*R&D Industry Finds Biosimilar Interchangeability Statement By EU Regulators 'Concerning'*" - Pink Sheet, 22 Sep, 2022.) "when you read the statement in its entirety, I don't think there's a lot of ambiguity about what it talks about. It's science and how it is translated in practice."

"What it talks about is evidence, experience with physician and patients at the center. And the rest is practice, and for doctors, patients to design as part of national frameworks. It's very unambiguous, in my opinion."

Rising Costs Add To Competitive Pressures

Asked about the competitive and cost pressures faced by the European biosimilars industry, Remus said that as the market reached "a more mature stage," it was "expected from a more mature stage that there is more price competition."

"I think what we have to watch out for, though, is that in light of the current energy and inflation situation, from a cost perspective, there's increasing pressure on this industry, on the off-patent industry as a whole. And so, I think that is something to really watch out for."

"When we had the COVID crisis, we were realizing how important it is to have European manufacturing, in order to make sure that we have access to health care, access to medicines moving forward," Remus recalled. "And I would say that, in light of the current cost pressures and the price pressures, I think we really have to watch out for our European manufacturing footprint, and really make sure that what was called out by Europe as a whole, to preserve that, look at that, and really make that a focus."

"Some of the other geographies are not equally impacted as Europe currently is," Remus acknowledged. "And so that is something that I think is important, not just for biosimilars, but in a wider scope, when we look at this industry that within Europe, I think plays an utterly critical part to sustainable healthcare, sustainable access to medicine."

Still 'Enormous Potential' To Improve Access

Discussing the potential for biosimilars to not only reduce costs but also increase access, Remus and Maréchal-Jamil were asked whether this aspect of the industry's offering was sufficiently recognized in Europe.

"I think there's still huge disparities," Remus acknowledged. "And it's not because the diseases are less prevalent in one country versus the other, but it's about the adequate treatment that's provided or not."

Referring to data presented at the conference that illustrated disparities in access across Europe, Remus observed that "even in a country like Italy, that we would say is a wealthy country that has good medical care, even there we saw that a large number of eligible patients are not getting access to biologics. And that was on the higher ranks of biologics use within Europe."

"If you go further down that line, and you look at countries that have less per capita use, like Poland has, there's an enormous potential to further increase access and give patients access to

biologic medicines."

Source: Julie Maréchal-Jamil

Maréchal-Jamil said one issue was that "you don't have the metrics to look at the lack of access. I think we're forming our policy frameworks without a full grasp of what this gap means."

"Until very recently, it was a tough conversation to be openly having because it was recognizing that no, we're not doing the best we could for European patients," she indicated. But "I think times are changing and that's opening up, because COVID forced a reality check on healthcare systems and revealed both the gaps or the tension we have in the system."

"Now, I think it's a conversation we can more openly have with policy makers and budget owners. Governments are recognizing the need to invest in health in a different way."

Then a second aspect of the issue, Maréchal-Jamil suggested, was "more about how you envision off-patent biosimilar competition as a tool, not for savings which is very short-term, but as a tool in the bigger picture – how you, as a public service provider, can deliver better care."

"And I think that shift, that pivot is also quite led by COVID lessons learnt. Because we saw it's not just about medicines A and B reaching patients – it's about having a systems approach. So I see both the need for better metrics to describe the issued and the focus on doing better for patients in how we design policies as really important aspects for us to get better at."

"There's a dynamic effect to it," she continued, as "the biosimilar opportunity we have today will keep evolving as we go on. We're going to get new therapeutic agents [opening up] to competition. This is going to move, it's all dynamic."

"And the next challenge here is probably the policy tempo, and the action tempo. Currently, policy making and translating it into action are definitely not fully matching the rhythm of how opportunities or options are becoming available."

Ultimately, Remus pointed out, "I think the generics and the biosimilar providers are actually part of the solution. And I think that's really important to recognize."

With many markets operating clawback mechanisms "that we are equally affected by as an

industry," Remus said "the question is, you know, if you have a solution that you want to actually leverage and optimize and maximize, is that the right mechanism? I think that's one important consideration."

And "the second point I want to make sure we don't miss is about smart procurement," Remus said. "That becomes really important in the current situation where I think we need to look at multi-winner frameworks. What are the criteria? You know, what are the criteria that determine value overall?"

"I just want to make sure that as we talk pricing and sustainability, we don't leave those two things out, because I think they're very, very important for our industry, and for us to ensure that we have a sustainable business moving forward."

European Guidance Will Help Advance Procurement Solutions

Expanding on issues around procurement – and the need for a joined-up approach to procurement principles across Europe (*see sidebar*) – Maréchal-Jamil said "I think it's sort of a basic principle that any complexity that you add in the system, in an industry like ours, is again, a challenge to delivering on the opportunity."

Generally, she said, "the focus on the solutions or general principles Isabell was pointing out are quite harmonized."

Industry was expecting a European Commission study on the topic to be published soon, she noted, "and that this will drive quick adoption of good practice by member states."

The focus of the current discussion was not on the goals, Maréchal-Jamil suggested, "how do we actually do this, operationally?"

Remus indicated that European-level guidance on the subject would be key here.

Joined-Up Approach Must Underpin European Biosimilar Procurement

By David Wallace

17 Oct 2022

A more joined-up approach is needed on European procurement if the biosimilars market is to remain sustainable in the face of pricing and cost pressures, according to a discussion by industry stakeholders at Medicines for Europe's 18th Biosimilar Medicines Conference.

Read the full article here

"If there is a central guidance, then the countries are obliged to implement it," she observed. "Whereas if you leave it up to the country, you know, it depends, it will prolong things enormously, and might then also lead to different outcomes."

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Regulators Have Overcome Hesitation As Science Advances

Finally, Remus and Maréchal-Jamil addressed the question of moving towards a more streamlined regulatory pathway for European biosimilars – potentially removing the need for comparative efficacy clinical trials – that could make it financially feasible for the industry to provide competition to smaller-value biologic brands as well as blockbuster biologics.

"I think in Europe anyway, the option has always been there to waive comparable efficacy trials," Maréchal-Jamil noted.

But now, "the EMA has invited applicants to proactively come talk to the agency, asking to bring new ideas and approaches forward" (*see sidebar*).

They clearly stated 'We're open to your strategies to solve what could be an unnecessary hurdle'."

Remus agreed that it was now "a very different dialogue. It was about, how can we now make it happen? And what are some of the considerations that we now have to talk about? Whereas there was much more hesitation a few years back."

Streamlined European Pathway Needed For Biosimilars To Hit Smaller Targets

By David Wallace

14 Oct 2022

A more streamlined European regulatory pathway for biosimilars – potentially removing the requirement for confirmatory efficacy trials – is needed for the industry to be able to feasibly offer competition to smaller-value biologic brands, heard delegates to Medicines for Europe's 18th Biosimilar Medicines Conference.

Read the full article here

"So I think it has really moved far. And I think there's broad alignment that [waiving confirmatory trials] is a possibility. And it's okay, because science has advanced our understanding, what critical criteria is, it has evolved."

"And so I think it's now about, how do we implement it, and how do we make it happen? That's where the discussion now is."

> *"Europe has been the front leader in biosimilars, right? And so maybe now it's about time to go into that area."*

Asked whether Europe could move ahead in this way without global regulators such as the US Food and Drug Administration also making similar moves at the same time – given the global nature of biosimilar development – Maréchal-Jamil noted that "when we published our *first scientific paper,* two years ago, on this issue, with the International Generic and Biosimilars medicines Association, we worked on a *companion policy paper* where we said exactly this: there's now consensus around the science, there's consensus around the experience, and the possibility to move the needle; to operationalize this and make an impact for patient access to biologics, we need a global implementation roadmap." (Also see "*IGBA Calls For 'Streamlining' Of Global Biosimilars Process*" - Generics Bulletin, 30 Sep, 2020.)

"Without this evolution, or if it takes 10 years and multiple divergent requirements for major regulatory jurisdictions to move in that direction, or make it a principle… then operators in the system – biosimilar developers – will face massive complexity, even more than today, defeating the promise of faster development, of possible, or broader access to more regions earlier."

"All that is hanging on: are we able to coordinate implementation?"

Remus agreed. And addressing the question of whether Europe would move forward even without other regulators moving in tandem, she replied "I will say yes, because I think, you know, this is a new area. I think we need to move forward, gain experience, learn along the way. And, you know, Europe has been the front leader in biosimilars, right? And so maybe now it's about time to go into that area."

Referring to the UK Medicines & Healthcare products Regulatory Agency having already removed the assumption that comparative efficacy trial data is needed for biosimilar registration (Also see "*UK Lays Out Reduced-Data Pathway For Biosimilars*" - Generics Bulletin, 9 Oct, 2020.), Remus said "it was a bold move on their side. And I think it's sort of opened the eyes of many to say, okay, it is possible, because the MHRA is a very credible body."

"So it's actually opened a window to say, alright, you know, someone's moving here. Why can others not go in the same direction?" (Also see "*UK Could Become 'World Leader' On Biosimilar Regulation*" - Generics Bulletin, 29 Apr, 2021.) But, she said "it's going to be a process and a lot of dialogue, and a lot of change to go this new way on more complex molecules."

And Maréchal-Jamil concluded by pointing out that the World Health Organization's own biosimilars guideline, revised earlier this year, "opens that door as well." (Also see "*Clinical Efficacy And Safety Studies 'Redundant' For Most Biosimilars*" - Generics Bulletin, 7 Sep, 2022.)

"WHO will probably undertake efforts in training regulators around the globe," she predicted. "This is needed to socialize that concept and other state-of-the-art approaches brought forward in the revised WHO guideline."

“We are certainly not expecting that overnight we’re going to get many regulators implement streamlined biosimilar development,” she acknowledged. “However, realistically, having a roadmap from regulators on the implementation of this important concept is a key enabler for global biosimilar access.”