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Accumulus Synergy: modernizing interactions with and among regulators

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Biopharmaceutical companies push the boundaries of science to develop medicines, employ the most sophisticated techniques to visualize and analyze data, and then painstakingly transfer the results onto paper or PDFs to communicate data to regulators. It is like flying precious cargo halfway around the world on a jet plane and then piling it onto a donkey cart. The results are predictable: data are reviewed slowly and analyses are not as sophisticated as they could be, so patients get drugs later and at higher costs than they should.

Accumulus Synergy Inc., a non-profit organization backed by a dozen multinational pharmas, was created to bring interactions between drug sponsors and regulators, and among regulators, into the 21st century. If it is successful, drug development will become less expensive and faster. It will also be more democratized, as small biotechs and under-funded regulatory agencies will have access to capabilities that today are available only to large companies and a handful of leading regulators.

Accumulus aims to create a platform that will support two fundamental shifts in the ways drugs are developed and reviewed. It will facilitate moving from siloed interactions in which even different parts of the same regulatory agency find it difficult to share data toward fluid collaboration within agencies, and among agencies globally. The company also aims to move biopharma interactions with regulators from sporadic or sequential to continuous processes.

"Accumulus will make interactions with regulators, data flow and the whole process of submission review and approval of assets a lot faster. Exactly how much faster we don't know today," Jeremy Chadwick, SVP and head global development office, R&D at Takeda Pharmaceutical Co. Ltd. (Tokyo:4502; NYSE:TAK) told BioCentury. He serves as chairman of Accumulus Synergy's board.

Moving beyond 'PDFs and semi-antique' data formats

Janet Woodcock lit the spark that created Accumulus in April 2019 when she warned R&D heads of the world's largest pharmaceutical companies at a meeting of the Hever Group that progress in turning cutting-edge science into medicines was being slowed by regulators' reliance on "PDFs and other semi-antique" data formats. Woodcock, who at the time was

director of FDA's Center for Drug Evaluation and Research, urged the companies to collaborate among themselves and with governments to create a modern infrastructure that would allow sponsors to move from periodically shipping piles of static PDFs or pallets of paper to regulators to sharing data on a real-time basis.

Her comments, and the ensuing discussion at the Hever Group meeting, led to the creation of the Accumulus Project, which in 2020 became Accumulus Synergy Inc.

As the name suggests, the company is dedicated to using cloud computing to turn data into more than the sum of its parts. It is creating a platform that will allow medical product sponsors to share data with regulators securely, in near real time, and for regulators to communicate among themselves.

Woodcock, now principal deputy commissioner, told BioCentury recently that in addition to increasing the efficiency of reviews, she expects Accumulus to support knowledge management processes FDA is creating that are the key to increasing the consistency of its decisions, and also to lay the foundation for greater harmonization of regulatory requirements, especially those related to product quality and manufacturing.

Accumulus would complement FDA's attempts to create a modern, cloud-based knowledge management system, Woodcock said. "The goal is that we get a full dossier, a full picture, so when somebody submits an IND, we could go into our knowledge management system and find out all about that firm — its history, manufacturing sites, and inspection history. Right now, all of that is completely fragmented."

The move from static documents to data that can be manipulated will make it possible for reviewers to easily view how similar and related issues have been handled in the past, a prerequisite to making decisions less idiosyncratic. It will also make it possible to use machine learning and AI to improve the quality of reviews, and will facilitate meta-analyses and other types of cross-study comparisons, Woodcock said.

Subscription model

The dozen companies that are helping Accumulus Synergy get off the ground are each contributing about $3 million per year. They are also devoting time from staff who are helping develop the platform.

Accumulus Synergy's sponsors are Amgen Inc. (NASDAQ:AMGN), Astellas Pharma Inc. (Tokyo:4503), AstraZeneca plc (LSE:AZN; NASDAQ:AZN), Bristol Myers Squibb Co. (NYSE:BMY), GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), Johnson & Johnson (NYSE:JNJ), Eli Lilly and Co. (NYSE:LLY), Merck & Co. Inc. (NYSE:MRK), Pfizer Inc. (NYSE:PFE), Roche (SIX:ROG; OTCQX:RHHBY), Sanofi (Euronext:SAN; NASDAQ:SNY) and Takeda.

The companies sponsoring Accumulus are "completely clear that the benefit in terms of getting medicines to patients faster is such a strong benefit to everybody that the cost to get there will be acceptable," Takeda's Chadwick said.

Accumulus was established as a non-profit, a status that allows it to earn income to make it self-sustaining, and is intended to avoid concerns among drug sponsors and health agencies that it is exploiting its role as an intermediary to generate profits that could limit its use. "We wouldn't want the company sitting in this intersection between companies and sponsors and saying, 'If you use our tool, and you can file one month quicker or two months quicker, then we're going to charge you a certain amount of money,'" Chadwick said. "That wouldn't ultimately help patients."

The platform will be available on a subscription basis, Frank Nogueira, CEO of Accumulus Synergy, told BioCentury

Democratizing data

Accumulus is creating a secure cloud-based platform where drug sponsors will be able to place their data and provide access to health authorities.

It is also working to create a unified data model so sponsors will be able to create a single file that can be used globally.

In 2022, the ability to submit data electronically in a standard format may not sound revolutionary, but given where things stand today, it could be transformative.

"Typically, any developer of a new medicine over time ends up filing [for approvals] in something close to 150 countries over a seven- to 10-year time horizon," Nogueira said. Only 20 of those countries accept dossiers electronically, and none of them routinely accept all of the clinical, CMC or other data in a form that can be easily manipulated.

To be successful, a critical mass of drug developers must be willing to change their practices to make use of the platform and regulators must have sufficient trust in the platform to integrate it into their processes. One of the most attractive aspects of the new platform will be the capability to communicate a single dataset simultaneously to health authorities around the world.

The platform is intended to be multidirectional. Regulators will be able to use the Accumulus platform to send questions to sponsors, and to communicate with other regulatory agencies.

"Today, we primarily see interactions that are milestone-driven and involve one developer of a medicine communicating to one health authority," Nogueira said. "We envision, and I believe the ecosystem is envisioning, a world where the

communication is between one developer of new medicines and multiple health authorities, and then having the ability for those health authorities to collaborate amongst themselves. And that begins to create a chain of events that democratizes timelines across the world in terms of bringing medicine to patients more effectively, more quickly, but also by creating a much more collaborative effort around therapies and new treatments."

While the large companies sponsoring Accumulus will benefit from its work, the biggest beneficiaries could be small companies, especially those that haven't previously interacted with regulatory agencies.

Nogueira cited the example of a hypothetical Cambridge, Mass.-based start-up. "If you're trying to file your first IND, you probably don't have a technology team. You probably don't have a submissions tool. You probably don't even have a really good way to communicate with the agency. You certainly don't have a good way to communicate ex-U.S. We want to change all of that."

Supporting regulatory harmonization

Accumulus matches up with trends FDA and its peers around the world have been trying to accelerate, Woodcock told BioCentury. These include the ability for regulators to collaborate on reviews.

The biggest impact from Accumulus could be in removing roadblocks that prevent biopharmaceutical companies from updating manufacturing processes, and eventually by making harmonized product quality regulation possible, Woodcock said.

Drug companies, she said, "have to submit [applications] to every single country around the world that they have an approval in if they want to change their manufacturing process, and then they have to wait for the slowest to respond" before implementing changes. As a result, companies make as few manufacturing changes as possible.

Making it possible to create and provide access simultaneously to a single set of data about manufacturing processes would, Woodcock said, be a major improvement over the current situation in which there is tremendous duplication, with multiple regions and countries reviewing the same information repeatedly. "The first time you make a new drug," Woodcock said, "it may not be the right way to make it, so you need to innovate over time. If you have to send data to 50 different regulators and wait for each one of them to render an independent decision about what you should do, it's a nightmare."

The convergence could reduce the cost of drug manufacturing, Woodcock said. "If innovation is continually stifled because the smallest or slowest country takes years to approve changes, then nobody's going to invest" in processes that can make manufacturing more efficient.

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Ultimately, the Accumulus platform could make it possible for regulators to agree on a single manufacturing standard for each drug. "The goal is to go to a worldwide quality standard and a single approval for the quality side," Woodcock said. "I see this converging toward much more regulatory harmonization around the world, which can only help patients at the end of the day. And the manufacturing convergence in my mind will help innovation in manufacturing, which will help patients too, because we need to move toward modern manufacturing" to alleviate drug shortages.

Pilots in 2023, broad access in 2024

Accumulus will start rolling out pilot projects in 2023 and plans to have the platform broadly available in 2024.

One of its first pilots will involve Project Orbis, an initiative led by FDA's Oncology Center of Excellence that makes possible concurrent submissions and reviews of cancer drug applications in a number of countries. At present, regulatory agencies in eight countries participate in Project Orbis.

In addition to FDA, Project Orbis partners include the Australian Therapeutics Goods Administration (TGA), Brazil's National Health Surveillance Agency (Agência Nacional de Vigilância Sanitária [Anvisa]), Health Canada, Israel Ministry of Health (IMOH) Pharmaceutical Division, Singapore Health Sciences Authority (HSA), Switzerland's Swissmedic, and U.K.'s Medicines and Healthcare products Regulatory Agency (MHRA).

"We're working diligently with the agencies involved in Project Orbis to be able to first test submissions of synthetic data, and then do real data pilots in the next 12 to 18 months," Nogueira told BioCentury.

Accumulus is developing other pilot projects with these regulators, as well as with Japan's Pharmaceuticals and Medical Devices Agency.

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