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COVID-19 Shakes Up Real-World Data Studies

by Sarah Karlin-Smith

US FDA hopes COVID-19 may finally spur data coding changes that will make real-world evidence projects proceed faster. The pandemic is now part of five real-world data projects using FDA's Sentinel system, but some other real-world data projects are paused due to the health crisis. The private sector is also changing the way it conducts real-world data work due to COVID-19.

COVID-19 is leading to a plethora of real-world data projects at both the US Food and Drug Administration and in the private sector, ranging from research to try and anticipate oncoming shortages to studies of what approved treatments might be helping patients. Beyond the immediate utility of the research, FDA is also hopeful the urgent nature of the pandemic may finally be the push needed to encourage the adoption of interoperable data coding standards throughout the country.

FDA is relying on real-world data projects to elucidate COVID-19's natural history, to track drug shortages during the crisis, and to understand how drugs being used to treat infected patients may be impacting their outcomes. It is conducting many of these through its Sentinel system. (*See table at the end of the story.*)

HHS is also partnering with Oracle to utilize the company's therapeutic learning system, a secure web portal that is designed to collect real-time medical data from healthcare providers about how patients are responding to COVID-19 treatments. It is capable of breaking down patients by age, underlying health conditions and symptoms.

FDA believes the current crisis might finally lead to fixes to long-standing problems that slow down real-world evidence development. Up first: data interoperability.

“The COVID-19 pandemic has highlighted the problem created by lack of uniformity in coding our data nationally. The urgency of the pandemic may create an eagerness across the country to move to a national system,” Greg Pappas, associate director for national surveillance in the Center for Biologics Evaluation and Research, and Michael Waters, who works on a number of data interoperability efforts at FDA, told the *Pink Sheet*. “Use of standard coding will make RWD more accurate, less costly, and more rapidly available.”

That standard coding may come about through the work of the SHIELD (Systemic Harmonization and Interoperability Enhancement for Laboratory Data) collaborative, a two-year-old multiagency, public-private partnership to make laboratory data from in vitro diagnostics interoperable is focusing its efforts on COVID-19 and SARS-COV-2.

SHIELD has developed a tool to guide uniform collection of data, and FDA and the Centers for Disease Control and Prevention are looking at ways to circulate and promote use of these uniform approaches to coding.

Without consistent coding standards, it can take months to manually curate data, Pappas and Waters explained. “If codes for specific SARS-COV-2 laboratory tests are not used the same in different clinical centers, when the data is aggregated across a city, the state, or the nation, that data cannot be analyzed. If the coding of different studies are not collected in the same way, it will be very difficult to combine studies.”

Use of the standard terminology developed by SHIELD could help health care institutions across the US manage shortages and put infrastructure in place to expedite clinical evaluations of therapeutics, they said.

“This is a critical need to make RWE more relevant to fighting the pandemic and a major step for the future of RWE interoperability,” Pappas and Waters said.

Overall, agency leaders have said the pandemic is forcing FDA to step outside its comfort zone and use RWE rapidly inform regulatory decisions and clinical trial designs. (Also see "*Real-World Evidence On COVID-19: US FDA Approaching With 'Sense Of Urgency'*" - Pink Sheet, 21 Apr, 2020.)

Some Work Put on Hold

While some real-world data work is getting a boost under COVID, other work is being stalled due to the virus.

FDA said screening and enrollment is on hold for two of its real world evidence demonstration studies that are being conducted per the 21st Century Cures Act (Also see "*Real-World Evidence Demo Projects From US FDA To Include New Mobile App*" - Pink Sheet, 6 Nov, 2018.).

The Cures Act required FDA to establish a program to evaluate the potential use of RWE to support approval of new indications for approved drugs and to satisfy-post approval study requirements. The studies on hold are:

- RELIANCE, a randomized controlled "real-world" trial comparing long-term use of roflumilast and azithromycin to prevent chronic obstructive pulmonary disease exacerbations, and

- Limit-JIA, a randomized "real-world" trial in patients with limited juvenile idiopathic arthritis comparing abatacept plus usual care with nonsteroidal anti-inflammatories and intra-articular glucocorticoids versus usual care alone.

Missed Opportunities?

There are also opportunities for real-world data to help sponsors who have had to rethink ongoing traditional clinical research during COIVD-19, but so far it doesn't seem like companies are going this route.

FDA's Jaqueline Corrigan-Curay, director of the Center for Drug Evaluation and Research's Office of Medical Policy told the *Pink Sheet* that trial sponsors could consider whether real-world data, particularly data gathered using digital health technologies or decentralized trial approaches, could be used during the COVID-19 pandemic.

The Center for Drug Evaluation's RWE team said they are not aware of new RWE studies "intended to fill gaps from traditional clinical trials that have been disrupted."

COVID Spurs Changes In Data Sources, Study Speed

Outside of FDA, private sector players also say the unique circumstances of COVID is spurring changes in the field, from what people want to study, to how they are studying it.

"It's changed our view on which real-world data sources can be most informative for the questions that we have ahead of us," said Jeremy Rassen, president and chief science officer of Aetion, a healthcare technology company that works on real-world evidence projects with regulatory agencies, drug companies and payers.

For example, when Aetion is working with insurance claims for a real-world data study they are typically using claims that are at least six-to-nine months old. Now during COIVD, they are looking at claims in real-time. "These are well understood data elements, but by and large we weren't in the practice of using them for these kinds of studies for safety and effectiveness. But I think they can be readily used if you analyze them properly," Rassen said.

Aetion has partnered with HealthVerity to establish a real-world evidence system designed for

drug companies and regulators to assess treatment approaches for COVID and generate evidence on the impact of the pandemic on broader treatment use. They also created a tool to help companies and regulators understanding the overall impact of COVID-19 and how COVID and non-COVID patients are accessing health care resources.

The crisis has caused people to start thinking more about using real-world data for external control arms. Prior to COVID these control arms drawn from real-world data were largely used in oncology, but Aetion's Rassen thinks COVID may make people more comfortable using them in other spaces where it is not feasible or ethical to randomize.

COVID-19 has also led to new real-world evidence research that is indirectly linked to the crisis, Andrew Kress, CEO of HealthVerity said. For example, he said there is now a lot of focus on the impacts of patients potentially missing health care or medication treatment due to canceled health appointments or the need to stay at home because of the virus.

"We are seeing a kind of reshaping of the research priorities to try and account for the very rapid changes in patient behavior even outside of COVID." And people want that work done fast, Kress added. "The traditional model of the way that people plan out research has sort of been upended. … Most of our clients are calling us about research needs they want answered in six days instead of six months."

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