The Latest

TransCelerate Advances Drug Safety Through New Initiatives

By José Vega, M.D., Executive Sponsor of the Pharmacovigilance Initiatives and Chief Safety Officer, Merck

Over the past 10 to 15 years, the importance of safety science and drug safety, or pharmacovigilance, have grown substantially across the biopharmaceutical industry. In parallel, local and regional pharmacovigilance regulations have continued to evolve, frequently in ways that are not harmonized globally, and which may not add value to patient safety efforts but require substantial resources to ensure compliance. In 2016, TransCelerate identified pharmacovigilance as a new potential area of focus for which the organization was uniquely suited to make important and pragmatic contributions. Two initial pharmacovigilance initiatives were launched in early 2017 and additional initiatives were launched the spring of 2018.

To find out the latest with TransCelerate’s pharmacovigilance efforts, we spoke with José Vega, M.D., Executive Sponsor of the Pharmacovigilance Initiatives and Chief Safety Officer at Merck about recent developments and the future pharmacovigilance roadmap.

José noted, “During our initial ideation process in the Fall of 2016, a number of important areas in the pharmacovigilance space were identified for which TransCelerate member companies could partner to make meaningful progress in a reasonably short timeframe.”

Hence, the creation of the first two pharmacovigilance initiatives:

- **Value of Safety Information Data Sources**
  aims to identify sources of safety information for single high value valid cases and develop a proposed method for aggregate reporting of lower value cases. This initiative has generated evidence to test the hypothesis that safety information from patient support programs, market research programs, and social media is of low informative value. The data generated has supported the conclusion that compared to unsolicited individual case safety reports Individual Case Safety Reports (ICSRs)

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cases from market research programs and social media are of lower informative value. In addition, the team has concluded that while patient support program cases were of no more informative value than spontaneous cases, not all patient support program are created equal in terms of the quality of safety data generated.

- **Interpretation of Pharmacovigilance Regulations** will share expertise to more efficiently and effectively meet the intent of ambiguous pharmacovigilance regulatory requirements. The initial focus was the Food Drug Administration (FDA) Investigational New Drug (IND) safety reporting guidance; the team subsequently moved on to interpret the EU Clinical Trial Facilitation Group’s Reference Safety Information (RSI) guidance. The team has most recently selected FDA’s post-marketing safety reporting for drug device combinations as the next regulatory guidance for focus. Over time, the Initiative hopes to work proactively with health authorities with the goal of modernized and internationally harmonized pharmacovigilance regulations.

José said that from the outset TransCelerate has proactively developed and implemented a comprehensive engagement plan with key regulatory authorities and with other industry groups. He went on to state, “Senior pharmacovigilance leaders from regulatory agencies have shared positive and supportive comments about the initial pharmacovigilance initiatives and their findings and have indicated their interest in remaining informed and engaged for TransCelerate pharmacovigilance efforts.”

In addition, TransCelerate recently announced two new pharmacovigilance Initiatives:

• **Intelligent Automation Opportunities in Pharmacovigilance:** Concentrating on identifying how intelligent automation technologies can be used to support execution of pharmacovigilance processes, limit errors commonly associated with manual data processing, and ultimately enhance patient safety. TransCelerate will deliver proposals that will initially help individual case adverse event identification, intake, processing and reporting.

• **Advancing Safety Analytics:** Aims to generate best practices and guidance around the improved implementation of interrogative methodologies for the assessment of aggregate safety data from various sources. At first, the initiative will focus on traditional sources of safety data, such as clinical trials, but will later plan to target data from large real-world sources.

José highlighted, “Having a strong, collaborative and committed group of safety/PV experts from 19 leading global biopharmaceutical companies provides a unique opportunity to successfully tackle and to make important and substantial progress in resolving pharmacovigilance challenges that we all face.”

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**Industry Lens**

**Data Sharing Collaboration Helps Science Break Through**

By Ülo Palm, MD, PhD, MBA, Senior Vice President, Drug Development Operations, Allergan, and Secretary & Oversight Committee Chair, TransCelerate

A new era of information sharing is emerging, transforming the way we aggregate, evaluate and analyze data. With this in mind, more and more pharmaceutical and biopharmaceutical companies are committing to greater transparency and sharing of clinical research data — acknowledging that, data sharing can be the catalyst to transforming the way clinical studies are designed and medicines are researched and developed.

Innovative clinical research and study designs will require a culture shift whereby open data sharing and transparency is the norm. Openly available shared data will enable researchers to further expand upon already developed data sets. Through the expansion of these data sets, the opportunity to discover new value through historical data will become available.

For example, the Human Genome Project in 2003 wouldn’t have been possible without hundreds of scientists and institutions around the world collectively sharing data in a centralized and efficient format. Data sharing also confirms the validity of existing research, while data transparency helps to streamline research making it easier to access and analyze data.

**Data Collaboration & Sharing Across the Ecosystem**

Though data sharing is a major component to the acceleration of research and development, sharing data in and of itself is not enough. Such acceleration will require a collaborative, universally accepted approach towards data sharing to enable the scientific community to successfully progress.

To get to a future state of collaborative, universally accepted data sharing, the lack of communication and appropriate context when relaying research findings will need to be addressed. For example, in 2013, The Economist reported on the inability for researchers to reproduce published clinical studies. According to The
Economist, a rule of thumb among biotechnology venture-capitalists is that half of published research cannot be replicated. In this current state, scientific researchers must spend much more time asking and answering questions to better understand the context and quality of the data than to fully understand the study’s findings. To quote The Economist again, “this squanders money and the efforts of some of the world’s best minds.”

In an ideal future state of data sharing and transparency, researchers would be able to fully understand the context and quality of the study results. They would also be able to continually pool and analyze said data thus building upon previous results. The continued pooling of data would allow researchers to better design their studies while also adding their own data to a continually growing data repository. The goal is to create the ultimate data sharing and knowledge vault.

TransCelerate, for example, is currently building an R&D data sharing platform that will provide participating member companies the ability to share de-identified preclinical and clinical data, and assimilate, aggregate and analyze those data, enabling them to draw on insights and conclusions from a large, continually expanding pool of shared data.

Initially, the platform will support BioCelerate’s first collaborative project, Toxicology & Background Control Data Sharing Initiative (note: BioCelerate is a wholly owned subsidiary of TransCelerate). This same platform will also support TransCelerate’s Placebo Standard of Care Data Sharing (PSoC) Initiative. This initiative aims to maximize the value of historical placebo clinical data collected during clinical trials, while protecting patient privacy. This reuse of data will expose less patients to study procedures, enable more patients to potentially benefit from novel life changing active treatments, and reduce the overall costs and time of clinical trials.

By being able to access and use de-identified data shared within this database, member companies will be able to design and develop novel approaches to clinical research – creating value by leveraging historical data that would otherwise simply be filed and stored. This initiative was the first cross-therapeutic, multi-sponsor clinical data sharing initiative of its kind designed to improve trial design and safety surveillance.

However, without the collective endorsement to ongoing data sharing and transparency efforts, scientifically valuable and impactful insights could be lost. Sharing data responsibly and collaboratively across the scientific research community will transform the current state of data collection and reporting, allow for faster medical and safety insights and, ultimately, lead to accelerated medical progress helping patients in need of new and better treatments worldwide.
Recent acceptance of data sharing and greater transparency in clinical trials is helping to propel efficiencies in research and development across the biopharma industry. In fact, there are valuable and impactful insights found in the data of past clinical trials and/or studies that could help clinical trial sponsors better design and execute studies. Specifically, acquiring and leveraging clean, historical data runs parallel to the industry’s ability to streamline clinical stage hurdles and more effectively improve patient recruitment and retention, and relieve patient burden.

In this edition of Accelerate to Innovate, we spotlight TransCelerate’s Placebo & Standard of Care (PSoC) Data Sharing Initiative leader, Jules Desmond, as he discusses the value and efficiencies created by this data sharing initiative.

Q. Could you share a little background on TransCelerate’s PSoC Data Sharing Initiative and why an Initiative like this is necessary?

A. As a research community, we spend an enormous amount of time and resources enrolling patients into clinical trials to receive a placebo or standard of care intervention. Data from these subjects are often only used once. The PSoC Data Sharing Initiative was established to develop a solution to enable the sharing of these datasets in order to maximize the value of clinical data collected in the control arms of clinical trials. We launched our database at the beginning of 2016 and it currently houses 120 clinical trial control arms representing over 82,000 patient’s data across a wide variety of disease areas. These de-identified, subject-level historical trial data are available for our 16 participating member companies to download and use to increase the efficiency of their clinical development programs.

Q. What are some of the benefits the PSoC Initiative provides to TransCelerate’s Member Companies?

A. Because of the quality and volume of industry-generated clinical trial data, there are many highly valuable use cases for these data.

The concept of data re-use remains a sensitive topic but is gaining traction across the clinical research ecosystem — whether it’s the investigator, the site staff or the patients who willingly give their time for clinical research.

TransCelerate Member Companies have used historical trial data to optimize the designs of their studies. The richness of the subject-level data has enabled companies to better interrogate key questions that teams frequently run up against in study and program design.

Often, we answer these questions using limited data, for example aggregate data reported in publications or real-world data, which may not report exactly what we want to measure in a clinical study or be reflective of the clinical trial patient. Using relevant historical trial data enables us to look at specific subsets of patients and can provide better insight into which types of patients may be best suited to be included in a trial.

Once a study is up and running, access to these data can also help us improve in-study management of patients. Site investigators and study researchers can be better equipped to answer questions around emergent safety signals. The existence of a large dataset can help provide context to observed safety event, or imbalances in events between investigational and control arms, especially when the number of patients in a trial is low and the events are seemingly rare.

Based on the available historical data, we may also streamline the trial by cutting down on specific assessments, given what we’ve seen in the past. This reduction in unnecessary burden to a patient and their caregivers is a huge focus for our industry.

There are also loftier, even higher impact potential uses for these data. The increasing acceptance of Bayesian statistical methodologies in clinical research is leading us to explore supplementing control arms in currently enrolling studies with appropriately matched historical trial data. For example, rather than recruit 200 patients into a placebo arm of a clinical trial, can may be able to instead recruit 150 patients and supplement this with historical trial data from 50 (or 100, or 200...) patients that was generated in similar studies from the recent past. These approaches are still being developed, but we are seeing successes. Since there are less patients enrolled, we can see huge value for our PSoC data in the minimization of patient burden through participation and in quicker delivery of medicines to patients by starting and completing trials faster.

The concept of data re-use remains a sensitive topic but is gaining traction across the clinical research ecosystem — whether it’s the investigator, the site staff or the patients who willingly give their time for clinical research. Plainly, the concept is that historical data should have a life and use beyond the original trial that produced it.

Q. What are some of the benefits the PSoC Initiative provides to TransCelerate’s Member Companies?

A. Because of the quality and volume of industry-generated clinical trial data, there are many highly valuable use cases for these data.
Q. What are some of the pain points experienced with accessing historical data?

A. The biggest pain points are usability of the data and having access to appropriate data.

Our initiative looks to increase usability by converting all incoming data into a unified format and data ‘language’ using CDISC standards. As part of the process, data is also de-identified. This drives consistency in the database, which is a huge benefit when it comes to use – we all know that the data is going to be a specific format, and that its conversion will have been quality controlled, whenever we delve into the PSoC database.

If we’re talking about substitution of data and/or optimizing protocol design especially, we need to look at data sets from studies that are very similar to the one that we want to design. This is where ‘appropriate’ data is important. We have various ways that we use to ensure studies shared to our database are as relevant as possible to the likely research areas of our member companies. These approaches have ensured that studies going into our database stand a very high chance of being used by other member companies. We don’t want a database full of data no one has any interest in using, so we work hard finding solutions for this as an initiative.

The industry is also experiencing a progressive shift in mindset when it comes to data sharing and reuse. Traditionally, companies may have been reluctant to share data with other companies for a variety of reasons. However, the community is seeing how data collaboration has positively helped companies move the needle. There’s a rising belief that sharing even de-identified control arm data can provide great benefit within minimal downside risk. An individual company having access to abundant historical data from TransCelerate’s Member Companies, will gain so much more than they’ll ‘lose’ by offering up some of their own data. It’s been inspiring to many of our members.

Q. What is next for the Placebo Standard of Care Initiative?

A. Both near and long-term, we look forward to expanding our database. With TransCelerate’s recent launch of DataCelerate, we will be able to share, search, and access the data much more efficiently than previously.

The objective is also to grow the data types and sources. There’s potential to move into the digital health space as well, with more and more companies collecting health and activity data from wearables.

Whether it’s with regulators, patient groups or academia, we will continue collaborating around the appropriate use of historical trial data to drive efficiency in clinical development. TransCelerate is in the business of maximizing efficiencies in research and development, and it is PSoC’s mission to make the industry aware that access to this data – control arm data – can change the trajectory of a clinical study and the life of a patient who needs new medicines now, not later.

To learn more about TransCelerate’s Placebo and Standard of Care Data Sharing Initiative, visit our website at: http://www.transceleratebiopharmainc.com/initiatives/placebo-standard-of-care/
Your Perspectives

Your curiosity is important to us. In this section, we’ll address questions from Academia, Sites, Technology Companies and CROs.

How do I participate and engage with TransCelerate Initiatives?

As a start, check out TransCelerate’s new webinar and roundtable series that aims to connect with stakeholders about new opportunities to improve the research and development process. These events are intended to assemble stakeholders from sponsors, sites, health authorities/regulators, consortia and CROs, to collaboratively evolve the conversation around various industry challenges.

Recently, the Placebo and Standard of Care Initiative held the first multi-stakeholder workshop with participation from over 60 attendees from the Food and Drug Administration, academia, patient advocates, and sponsors. This particular workshop centered around solving challenges regarding the use of historical controls in confirmatory trials and identifying how to address barriers for regulatory acceptance as well. As a result of the extremely positive feedback, the Initiative is actively exploring opportunities for future multi-stakeholder workshops around the world. Upcoming events will be on the TransCelerate Events page.

What is TransCelerate doing to impact change around data sharing?

A new era of information sharing is emerging, transforming the way we aggregate, evaluate and analyze data. Though data sharing is a major component to the acceleration of research and development, sharing data in and of itself is not enough. Such acceleration will require a collaborative, approach towards data sharing to enable the scientific community to successfully progress. That said, TransCelerate has recently launched a new platform, DataCelerate, which is a global technology platform that allows for multiple deidentified research and development data types to be voluntarily submitted, uploaded, converted, harmonized, and downloaded through an access controlled, secured environment by participating TransCelerate and BioCelerate Members.

Serving as a data lake solution, the robust development and scalable design of DataCelerate features a flexible single sign-on platform with an automated user interface to quickly develop translational insights across the research and development (R&D) continuum. The technology can support both structured and unstructured data and is built on the Accenture Insights Platform (AIP) to provide dynamic search, analytics, visualization and reporting.

Currently, BioCelerate member companies have access to the platform and are actively uploading and sharing toxicity study data in the system. In addition, TransCelerate’s Placebo and Standard of Care (PSoC) data repository will be migrated into DataCelerate, expanding the volume of data to include over 85,000 patients and in excess of 130 studies in nearly 20 therapeutic areas ranging from diabetes to rare conditions such as Duchenne muscular dystrophy.

DataCelerate is currently only available to TransCelerate and BioCelerate Member Companies. To inquire about joining these organizations, please contact membership@transceleratebiopharmainc.com or refer to our Membership Application.

I’m looking to find out more information about implementing eLabels within my organization. How can TransCelerate help?

TransCelerate is working to enable technological innovation through the eLabels Initiative which is helping clinical trial sponsors progress on the journey to digitally supported, patient-centric clinical supply chains. The main output is not an eLabeling system, specifications or a standard, but an eLabels proof of concept and an implementation toolkit to facilitate voluntary, modular adoption of eLabels and to assist in Health Authority engagement. The work of the eLabels initiative through the toolkit and the proof of concept show the ‘Art of the Possible,’ and could

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help relieve booklet label-related issues by providing patient-centric features such as text size modification, language selection, search functionality and the ability to quickly receive updates if the label content changes (i.e. expiry date, dosage modification and recall information). The patient could also have access to all information they need to aid them in adhering to the clinical trial regime and recording their information.

Check out this animation to learn more about the eLabels initiative and visit the TransCelerate website to access the Toolkit and other helpful information.

What benefits does the Protocol Deviations Initiative provide to sites and sponsors?

Within the biopharmaceutical industry, the topic of Protocol Deviations (PD) is met with a wince. Currently, clinical research sponsors and sites struggle to interpret certain elements of ICH E3 and the associated guidelines related to PD, particularly because there are some inconsistencies between the ICH and FDA guidance on this topic. This difficulty has led to questions on classification of “important” and “unimportant” deviations, and possible inaccurate or delayed reporting of deviations, or in some cases, overreporting. In turn, these inconsistencies have led to roadblocks for getting quality drugs to market more efficiently. We are working in close collaboration with the FDA to help push the PD Initiative so that it will create a sustainable framework for organizations to apply more consistent methods to interpret “important” deviations across all levels of an organization, leading to reduced burden for sites and sponsors, better reporting of issues that matter, and more efficient risk-based management of PD. TransCelerate’s PD experts are continuing meaningful engagement with FDA, a significant component of their work in developing a PD Management Toolkit.

To learn more, visit our Protocol Deviation Initiative’s webpage.
Check Out Our Top Hits from the last three months

@LillyTrials: Have you checked out @transcelerate’s eLabel initiative? Learn how using eLabels in clinical research holds potential to improve the patient, research site and sponsor experiences. http://bit.ly/2KanBwX

@CDISC: CDISC is proud to partner with @transcelerate on the innovative Digital Data Flow project. http://bit.ly/2KbQp5i

@transcelerate: #CRAIE update! We’ve added new communication templates to our webpage to help sponsors share information with #clinicaltrial participants. Visit our site to explore the new templates as well as our other tools & resources. bit.ly/2AeIKRD

@JanssenGlobal: Janssen is proud of our collaborative efforts as a member of @transcelerate to accelerate the development of new medicines. In honor of Clinical Trial Awareness Week, check out the initiative here: http://bit.ly/2IgdvFQ

@ACRP: Interesting perspectives on patient engagement from @transcelerate at #ACRP2018 http://bit.ly/2Ibo2Cm

@transcelerate: “Absent patients, and absent sites. Clinical Research simply doesn’t happen.” Great perspectives this morning from industry leaders! #ACRP2018 #ACRO pic.twitter.com/CLJtAeo5K

@transcelerate: Patient recruitment is a challenge for many companies performing clinical research. The @OnePersonCloser campaign is working to help #HCPs overcome this barrier. Learn how they’re making a difference. bit.ly/2H9SM6X #OnePersonCloser @ClinicalLeader1

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