PCMG Live 2020 Follow up Questions and Answers

Questions are a sign that a presenter has made comments that have resonated with their audience and inspired free thinking. People who are used to chairing meetings will know the requirement to have a few carefully prepared and choreographed questions "up your sleeve", just in case the audience have none of their own. Well, I am delighted to report that there were no such questions up sleeves at PCMG Live 2020 as each session had to be drawn to a close to keep to time amidst a flurry of typing as the audience tabled questions to each speaker. The event Steering Committee felt a lot of the questions were so good that they deserved addressing, even after the event. As a result, this article has been prepared for those of you who were there and those who couldn't make it, to consider the questions that were tabled and provide the answers from each of the presenters. We hope the following will be useful.

This article would not have been possible without the help of the presenters themselves, who have taken time after the event to address your questions. And to the PCMG Steering Committee who made it happen and in particular to Jean Edwards, PCMG Lifetime Achievement winner, who was tenacious in the task. And finally, thank you to all of you who asked the questions!

David Davies
(on behalf of the Steering Committee)

Jeremy Rassen, co-founder, president, and chief science officer at Aetion, a health care technology company that delivers real-world evidence for life sciences companies, payers, and regulatory agencies.

Have we been able to get more of a perspective/feedback from the patients who are at the centre of the trials about how technology is helping or has helped?

We frequently hear from patient groups who advocate for sponsors, regulators, and payers to consider real world evidence that provide insights on the patient experience outside of a clinical trial setting. This evidence can speed the development of life saving treatments, and help patients gain access to such treatments.

We partner with one such organization, *Friends of Cancer Research*, across a number of initiatives, including their Pilot 2.0, and most recently the COVID-19 Evidence Accelerator, hosted in partnership with the Reagan-Udall Foundation for the FDA, both of which are focused on advancing standards for the use of real-world evidence. They are a prime example of how patient advocacy groups can support the integration of technology into clinical research and can help drive alignment across regulators and industry.

What about investigator acceptance (or lack thereof) of technology? Will pharma push back more?

While investigator acceptance of new technologies may vary, we believe this will shift over time as they become comfortable with novel approaches. To help facilitate this, it's important that we present technology as an enabler and complementary to traditional approaches.

We saw an example of this with our work on the FDA demonstration project, RCT DUPLICATE, in which we're partnering with Brigham and Women's Hospital (BWH) on the replication of 30 clinical trials, and the prediction of 7 ongoing phase IV trials. An initial prediction study was completed as a pilot in 2019. Our partners at BWH shared results of the RWE analysis at the American Diabetes Association conference, just days before RCT results were shared in the same forum. When the RCT findings were shared, we were pleased to see the RCT investigators featured the RWE results alongside the traditional study. The RWE study provided an additional piece of evidence to further validate the RCT findings, and we believe this complementary relationship provides a path forward for collaboration with investigators as we expand the use of RWE in clinical research.

Speaking about clinical trial acceleration - where do you see the biggest areas of opportunity for concrete acceleration?

There are a number of opportunities for using real-world evidence to accelerate clinical trials — and nowhere has this been more apparent than in the current efforts to address the COVID-19 pandemic.

In recent years, we've seen a shift toward using external comparator arms to support drug development in the oncology and rare disease spaces, and now we're seeing a lot of interest in using external comparator arms to support the response to COVID-19, as sponsors face challenges with trial planning and patient recruitment. External comparator data can help us contextualize single-arm trials — and in the process, we can learn how to run trials more efficiently using real world data.

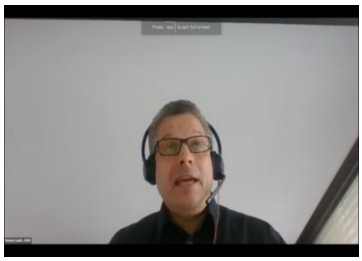
Vaccines, including COVID-19 vaccines, present another important opportunity for RWE. It's likely that efficacious COVID-19 vaccines will be quick to reach the market, making post-approval safety and effectiveness data over longer-term follow-up and in more diverse populations critical to the COVID-19 vaccine story. RWD provides the ability to monitor, in real-time, the effectiveness and safety of these vaccines post-market.

In your recent Covid experience, which technology did work?

At Aetion, we offer technology to help researchers turn real-world data into transparent and replicable real-world evidence. We're using Aetion Evidence Platform (AEP) in our COVID-19 research collaboration with FDA, and biopharma manufacturers use AEP to study the safety and efficacy of COVID-19 interventions and vaccines — as well as the commercial impact of the pandemic across their portfolio.

In April, we partnered with health data company, Health Verity to launch the first real-time, real world evidence system designed for biopharma manufacturers and regulators to assess treatment approaches for COVID-19. These research tools, which include the *Real-Time Evidence Platform*, employ Health Verity's real-time data — including medical and pharmacy claims, lab tests and results, hospital chargemaster data, and relevant EHR fields — to accelerate vital approvals of treatments and vaccines for COVID-19 and help fulfil the associated post marketing requirements.

In May, the FDA selected Aetion for its COVID-19 analyses because of its technology and team's ability to produce regulatory-grade analytics to inform the agency's response to the pandemic. We are also using the platform to participate in the parallel analysis workstream for the COVID-19 Evidence Accelerator, led by the Reagan Udall Foundation for the FDA and Friends of Cancer Research (FOCR).



Dennis Lauth, business development lead at Amazon Web Services described the impact of cloud-enabled advances that are set to transform the conduct of clinical trials

Dennis prefaced his comments with a disclaimer: "Opinions expressed below are solely my own and based on experience of my current and previous positions. They not necessarily reflect official Amazon Web Services (AWS) views or opinions".

How do we bring regulatory agencies along with us as we implement new digital innovation?

Developing cycles for digital health technologies are significantly shorter comparing to medical devices, diagnostics and pharmaceuticals which poses challenges to the traditional regulatory processes. To bring safe, secure and effective digital technologies into healthcare at a pace that matches the need of patients, providers and other stakeholders we need regulatory frameworks that accommodate the shorter timelines and unique agility of digital innovation. Regulatory agencies in the US and Europe have recognized the challenges and understand that digital health solutions require a new regulatory paradigm and have announced a series of reforms aimed at creating a regulatory pathway and building confidence in these tools.

The whole community (industry, patient advocacy groups, providers, payers, technology providers etc.) need to closely work and partner with regulatory bodies to ensure that digital health innovation is regulated under a framework that allows faster access to new technologies that help improved outcomes of patients at overall lower healthcare cost.

How will GDPR/Subject data privacy will be taken into account?

Compliance with data protection laws and commitment to protecting Personal Information is paramount on the journey to transform clinical trials and earning trust with patients and other involved stakeholders. AWS's extensive security technologies and rigorous attention to securing AWS's infrastructure and solutions are designed to provide customers with control over who has access to their data. AWS is vigilant about its customers' privacy and data security. AWS customers have always retained ownership and control of their content, along with the ability to encrypt it, protect it, move it, and delete it in alignment with their organization's security policies. Additionally, a large and growing number of healthcare providers, payers and IT professionals are using AWS's utility-based cloud services to process, store, and transmit Protected Health Information (PHI) and personally identifiable information (PII). AWS enables covered entities and their business associates subject to both the European Union's General Data Protection Regulation (GDPR)'s requirements, U.S. Health Insurance Portability and Accountability Act (HIPAA) and HITRUST to leverage the secure AWS environment to process, maintain, and store PHI.
New features are launched regularly, and AWS has 500+ features and services focused on security and compliance, thereof >120 HIPAA eligible services.

Is there experience from AWS on how big-data mining can create insights for protocol/trial planning?

Depending on the data quality, mining of big data can create important insights to create feasible, patient-centric clinical trials protocols. To share 2 examples:

- Knowledgent's Intelligent Trial Planning (ITP) application runs on the AWS cloud and uses AI/ML technologies like AWS SageMaker to mine multiple data sources (internal & external) and predict the feasibility of clinical trials. The tool helps biopharmaceutical organizations to do real time scenario planning to optimize study designs and run trial predictions including recommendation for trial sites. Clinical design teams can do the feasibility analysis in minutes vs. weeks. Greater accuracy for scenario planning also shortens timelines and reduces cost by -20%.

- Q^2 Solutions utilizes Amazon Textract and Amazon Comprehend Medical to quickly pull out important clinical details from complex clinical trial protocol documents to help reducing the risk of missing critical protocol information. Insights from those documents can be captured in just a matter of minutes vs. normally several human hours resulting in 50% reduction of workload.

What are we going to do with all of the data points that might be available to us with mobile technologies? If it does not form a part of an analysis dataset, should we even be collecting it?

The choice of physiological sensors for remote monitoring needs to be carefully considered as, despite the promise of continuous, longitudinal data (vs. site-based episodic), it is an invasion of the patient's privacy. Remote patient monitoring needs to rely on the right selection and standardized collection of high quality data to benefit patients and health systems. These benefits are contingent on devices, tools and analytics being valid, accurate and clinically use- and meaningful. Patients need to understand the use of their data, the limits to this use, and the inferences which can be made from it.

In addition, the size of the data streams from sensors and wearables can become a data tsunami – high volume, high velocity, high variety. Data management and data cleansing are paramount based on a secure, scalable enabling infrastructure which can support compute at scale, selection of the right database and data analytics powered by AI/ML.

Is the medical transcript of audio data only available in English or also in other languages?

Amazon Transcribe Medical is an automatic speech recognition (ASR) service that makes it easy to add medical speech-to-text capabilities to voice-enabled applications. Driven by state-of-the-art ML, the service accurately transcribes medical terminologies such as medicine names, procedures, and even conditions or diseases. Amazon Transcribe Medical can serve a diverse range of use cases, from transcribing physician-patient conversations that enhance clinical documentation, to capturing phone calls in pharmacovigilance, or even subtitling telemedicine consultations. The service is HIPAA eligible and prioritizes patient data privacy and security. Amazon Transcribe Medical launched end of 2019 and currently supports medical transcription in US English.

Richard Young, vice president, strategy at Vault CDMS, where Richard is responsible for defining strategy and direction, especially with respect to clinical data management.

Do we need a global 'conference on harmonisation' for digitisation or is there an agreement across many players already?

Yes, we absolutely do. There are some well documented initiators for harmonisation, such as CDISC and TransCelerate, but there remains a very real need to create a non-commercial alignment. Examples of potential outreach programs include Align Biopharma (https://www.alignbiopharma.org/) and Align Clinical CRO (https://www.alignclinicalcro.org/)

The missions of these two groups are;
- Align Biopharma is a life sciences industry standards group, established to make it easier for healthcare professionals (HCPs) to work with life sciences. Through open technology standards, industry can streamline how HCPs get the treatment information they need to deliver improved care to patients.
- Align Clinical CRO is a life sciences industry standards group, established to make clinical trials run by CROs on behalf of an industry sponsor more cost effective and efficient. Through open technology standards, the industry can streamline how they plan, execute, and manage trials with CROs and bring products to patients faster.

By way of example, both of these groups were formed to find industry best practice solutions to everyday problems, but to do so in way that is technology agnostic. It is important that any and indeed every vendor has the ability to ingest / use these standards. I believe that only by removing the commercial interest can this be readily attained.

To give you three examples:
1. Align Biopharma has defined an identification and authentication standard to enable single sign-on for HCPs to access online content – including websites, portals, virtual events, or webinars – across all companies.
2. Align Biopharma has sought to define standards for consent and preference management so that there is consistency in how HCPs specify communication preferences with each company.
3. Align Clinical CRO has defined an operational data exchange standard that will define the data and structure that technology companies can implement to consistently and easily exchange data between CROs and Sponsors in clinical trials.

This work is merely a starting point - driving real world, quick-win benefits across the board. By leaving the commercial focus behind, it creates a forum for real sharing, but the work is just a starting point. That is exactly why a forum will be of great value.

Natural History studies have been used for many years to build comparative data esp. in rare disease. Can we apply this in a broader manner?

Yes - this is something that could be and should be explored. There is a major focus on data transparency, and of course placebo arms. I firmly believe that these principles can - and should - be extended.

The key is to have access to complete and concurrent data, and data that we can attribute contextually. The definition / categorization of the data therefore is critical. Data used out of context will lead to poor results. The challenge for me again is set in a commercial World. Bring data together in a manner where all contributors and consumers can utilise simply, with the appropriate access privileges and without overt restriction is critical. The ethical and financial benefits to all are clear, but as an industry we must agree what the rules for using data really are. No one likes single use data, but paying twice for your data is even worse. This is where an extension of groups like Align BioPharma can come into their own

Steve Martindill, vice president clinical operations at Gilead Sciences, where he leads teams supporting Gilead's development trials and post-marketing studies outside of US.

In your recent Covid experience, which technology did work?

We had to run all our COVID studies 100% remotely for the first time at Gilead. We used no remote SDV or SDR as we currently do not allow that. We didn't utilise any particularly new technology for these studies and although our CROs offered patient management apps etc most of our sites didn't need them. We did make use of direct to patient IMP and home nursing services where permitted and this helped with patient retention. Internally we relied heavily on zoom. We also made use of real-world data to provide controls to our studies which were not PBO controlled.

Given the anticipated demise of onsite monitoring, are contracts going to migrate away from activity based and towards earned value?

I think it will take some time before on-site monitoring dies off completely, but we are certainly moving towards less SDV and more targeted data review which has been shown to be more effective from a data quality perspective. Our contracts are already based more on deliverables, rather than rewarding activity and I expect this will become the norm.