MAGI’s Clinical Research Cloud Conference 2020: Week 1 Recap

It was a busy week at MAGI’s Clinical Research Cloud Conference 2020. Ace reporter Martin Berman-Gorvine could not attend all the sessions, but the following are his take-aways for the week.

Monday, June 22
Clinical Trial Agreements

“I think one of the byproducts of COVID is really more awareness of clinical research and also its impacts on new treatments and potentially vaccines. Previously when I’d been talking to friends or family about my role, it was really difficult to explain what I did,” Megan Trost, vice president for study startup and administration at WCG Clinical, said during the session “COVID-19 Changed Everything—What This Means for the Future of Clinical Research.” The much higher profile for clinical research is an historic opportunity, she said. “People are really desperate for a cure, and this is making them really hungry for information on how we get there,” added Lindsay McCarthy, Vice President of WCG Clinical’s PharmaSeek & PatientWise. A study conducted in April by the Center for Information and Study on Clinical Research Participation showed that 27 percent of respondents had heard about COVID-19 trials through traditional media, as opposed to just 12 percent who heard about such trials through social media, so it may be worthwhile for those in clinical research to rethink the value of the former method despite its cost, she said. Sites and sponsors will have to recalibrate everything after the pandemic passes, McCarthy said.

Simply figuring out which subject injuries are caused by a clinical trial is tricky, according to the session “Into the Abyss: Subject Injury and Indemnification.” “Subject injury” definitions in both clinical trial agreements and research informed consent forms usually exclude symptoms of underlying disease or its progression,” Jonathan Walland, senior corporate counsel at Pfizer, said. The drug manufacturer fulfills its duty by disclosing known risks in the investigator brochure and trial protocol, and the principal investigator in turn discloses these risks to the research subject via the informed consent process, he said. “At least theoretically, there’s this strong public policy against holding anyone liable for unforeseen or unknowable risks because, otherwise, no one would want to test new vaccines or new medicines,” Walland added. However, significant gray areas remain. For example, he said, “There is a lot of discretionary control for the [principal investigator] and the research staff in the hospital in pronouncing research injury causation.” Other topics covered in the session included how to word the informed consent form and indemnification and insurance clauses.

If you’d like to avoid “a decade-long legal battle,” it’s important to clarify the rights to ownership and use of discoveries in clinical research when drafting a clinical trial agreement, according to Tiffany Yancey, contracts manager for United Therapeutics Corp., who spoke at the session “Intellectual Property (IP) Provisions in CTAs.” Ancillary agreements, such as consulting agreements or joint development agreements, may also spell this out, Yancey said. IP ownership can be based on either creation or payment, so it must be decided in advance who, the investigator or the sponsor, gets the rights if, for example, the investigator identifies a patentable alternative use for the sponsor’s study drug. For sponsors, market exclusivity is important to offset R&D costs, and the research sites have...
interests, too—not just revenue but also noncommercial purposes, such as their educational mission and institutional policies.

If you’re involved in drafting a clinical trial agreement and terms like “study data” and “confidential information” don’t give you pause, you need to pay closer attention.

Study data is nonidentifiable information resulting from or developed in the course of clinical research and is owned by the sponsor or the investigator in an investigator-initiated trial, said Conor Flynn, Contracts Manager at the State University of New York at Buffalo during the session “Those Devilish Details: Key Words & Phrases in Clinical Trial Agreements.” Often research sites are allowed to make internal or non-commercial use of study data, he added. Sponsors want to keep control of confidential information as much as possible, so investigators must be careful in drafting CTAs or “you could inadvertently lose the right to publish the study data,” said Michael Powers, general counsel of the academic research organization GOG Foundation.

Certain nuances apply when drafting an agreement for clinical research where the researcher is the sponsor, according to the session “CTAs for Investigator-Initiated Trials.” Among several other considerations, research institutions should take into account institutional review board deadlines; goal dates; regulatory and serious adverse event reporting periods; signatory schedules; whether a clinical research organization is to be included; and whether multiple pharmaceutical companies are supplying the study drugs, which could complicate intellectual property negotiations, according to Rikki-Quinn James-Renz, director of contracts and supplier services, supply chain at Temple University Hospital.

For industry partners, matters to keep in mind include the rights of other funding entities, if any; what the company is expecting from the agreement; whether there is an expectation to get study data from the sites; whether the study data is expected to be used for registrational purposes; and what is required from the site or investigator to ensure that the data can be filed with a regulatory agency, said Shobita John, counsel, R&D transactions at Bristol Myers Squibb.

**Tuesday, June 23**

**Budgets & Billing**

Having a win-win philosophy is important, Tiffany Yancey, contracts manager at United Therapeutics Corp., said in the session “Constructive Tactics for Effective Budget Negotiation,” since “we all want to make sure that our respective companies are profitable, but the real goal is to help save and improve lives, period.” Tips that she and Marshall Morris, a partner at DelRicht Research, offered include “ask for what you need,” which requires defining your goals; support your request with documentation; bill for the “little” things that add up, such as fixed fees, the pharmacy startup fee, ad-hoc fees and the protocol amendment fee; standardize nonprocedural or conditional fees based on the specific therapeutic indication; and use your leverage. Sponsors and CROs appreciate it when sites have an expedited startup process in place, Yancy and Morris said.

Both sponsors and sites must determine their definition of fair market value, which has to be documented, justified and time-tested, Susan Adler, director of clinical research operations at Hackensack Meridian Health Network, said during the session “Fair Market Value in Clinical Research.” Sites negotiating fair market value with a sponsor should be sure to ask how the proposed amount was calculated and be prepared to back up requests for more money than the sponsor initially offers, she said. Sponsors negotiating with sites, on the other hand, can take advantage of a number of customary financial tools used in industry-sponsored clinical research to help document fair market value, said Elizabeth Frey.
Miller, an associate at Rawle & Henderson. Both speakers said sites should not claim overhead fees as a catch-all for fair market value, but only for true overhead costs like the often-underbudgeted research administration office.

From the sponsor perspective, vital considerations when it comes to budgets include data entry, monitoring, the consenting process, and how much time the principal investigator has to spend with the subjects, Jane Jacob, vice president of clinical research at Orthofix, said at the session “Hidden Costs.” Things for the sites to consider, she said, include realistic costs; the need to operate in the black; the standard of care in the field; and costs for treatment that exceeds the standard of care in the study, which the site should ask the sponsor to provide additional funding for. The goal should be to avoid renegotiating the budget, she added.

Roughly 72 percent of clinical sites are paid on time per the contract payment terms, and roughly 70 percent of patient payments are paid correctly, Nicolas Cindric, CEO of WCG Clinical Services, said during the session, “Making and Collecting Site Payments.” He said the figures come from PFS Clinical, a subsidiary of WCG. Some of the factors involved in the large number of sites that are paid late or incorrectly are confusing contract terms; strict formatting, data and milestone parameters for invoices; poorly trained payables and site staff; and lack of accountability by clinical research organizations and sponsor staff. To negotiate profitable study budgets, sites should appreciate their value, apply lessons learned from previous studies, document local costs and fees, weigh payment difficulties when considering whether to do a new study, and ask for what they want and need, said Shaun Williams, vice president of investigator management solutions at Syneos Health.

In order for Medicare to cover "routine costs" in a non-device clinical trial, the investigational item or service must belong to a Medicare benefit category and the trial must both have "therapeutic intent" and enroll patients with a diagnosed disease, Deborah Suarez, director of research administration at Baptist Health South Florida, said during the session “Medicare Reimbursement for Clinical Trials.” Suarez also said Medicare automatically covers routine costs in clinical trials funded by the National Institutes of Health, the Centers for Disease Control and Prevention, the Agency for Healthcare Research and Quality, the Center for Medicare and Medicaid Services, the Defense Department, and the Department of Veterans Affairs as well as trials supported by centers or cooperative groups that are funded by those agencies. Medicare also automatically funds routine costs in trials conducted under an investigational new drug application reviewed by the FDA and drug trials that are exempt from having an IND under 21 CFR 312.2(b)(1). The clinical trials policy under the Social Security Act states that best practice is to conduct one’s own analysis to confirm the trial’s qualifying status, Suarez said.

**Wednesday, June 24**

**Regulatory Compliance**

“Continue to use the regulations as the floor, not the ceiling” when doing clinical research during the current pandemic, Quincy Byrdsong, associate vice president for research administration at the WellStar Research Institute, said in the session, “How Will COVID-19 Change Regulations & Compliance?” For example, while expanded access to investigational drugs has always been available and research sites knew all about it, many healthcare institutions had to “dust this off” with regard to possible COVID-19 treatments, David Vulcano, vice president for clinical research compliance and integrity at HCA, said. Everyone involved must exercise their best judgment, Byrdsong said. Lasting regulatory change may be coming, but for now “temporary allowances to get us through this pandemic” are the order of the day, he added.
Clinical researchers should adopt the data protection requirements for clinical investigations from the perspective of the European Union’s 2016 General Data Protection Regulation (GDPR) and its 2014 Clinical Trials Regulation, according to information presented in the session "Recent Developments in Subject Data Privacy & Security." They should also establish appropriate consent procedures for secondary use of personal data and check for any new documents published by the European Data Protection Board at https://edpb.europa.eu/edpb_en.

Norbert Clemens, senior manager for science and clinical affairs at Kaneka Pharma Europe, said that there are many nuances and unsettled areas; for example, earlier this year the European Data Protection Supervisor said in a preliminary opinion that sometimes standard clinical research informed consent may not be “the most suitable legal basis for data processing and that other lawful grounds” should be found under the GDPR. Norbert Clemens, senior manager for science and clinical affairs at Kaneka Pharma Europe, said.

A new requirement since 2018 in clinical research that involves more than minimal risk and lengthy informed consent forms is that those forms must begin with a concise and focused presentation of the key information and must be organized and presented in a way that helps understanding, a requirement that came out of standard practice in high-risk studies and those with vulnerable subjects, George Gasparis, president of the PEER Consulting Group, said in the session, "Informed Consent Under the Revised Common Rule." Elements that should be considered for inclusion in this concise summary are the research’s purpose, procedures, risks, benefits and voluntary participation, he added. This key information section should be one-half to three pages long, Heather Kim, quality assurance manager at WCG Clinical Services, advised.

A tip for clinical researchers developing COVID-19 trials is that they should propose protocol modifications if the IRB defers approval, Lindsay Abraham, IRB chair and regulatory lead at WIRB, said in the session, "Would You Approve This COVID-19 Study? Study Approvals at the Edge.”

This recommendation arose from the first of three case studies presented in the session, all of which are “right on the edge of approval,” according to Abraham. The proposed study involved an investigational COVID-19 outpatient treatment protocol to help adult patients avoid hospitalization. There was to be a single investigator, and the study drugs were approved for different indications but did not have an FDA investigational new drug application for COVID-19. Also proposed for use in the study was a dietary supplement that was dropped when the institutional review board objected. When the board reviewed the protocol in March 2020, it deferred its decision to address a number of additional concerns, Abraham said. "One of the issues that presses IRBs and the research industry as a whole possibly to the edge during this time of a worldwide pandemic is the need for research that both looks at possible treatments and vaccines and also gives subjects access through research to experimental drugs and experimental treatments, possibly expanded access, or otherwise,” she added.

The FDA tends to select research sites for good clinical practice inspections in certain circumstancess: if the sites are high-volume enrollers, “for cause” instances or previous unfavorable inspections or other “red flags exist, or the FDA has new investigators,” consultant Janet Holwell said in the session, “GCP and Inspection Readiness.”

Sites with a high volume of patients and/or data have a greater impact and may pose more risk with regard to overall study results, she explained. For-cause inspections are those that result from a complaint, a report or some other information that flags the site, and the FDA does the inspection without warning, she said. However, most inspections are routine and not considered for cause; and so, advance notice is given, although it may not be much. Inspections may occur pre- or post-approval. Inspections vary in duration and to varying
degrees, inspectors will take copies of documentation and may follow up for more information. Last year, 72 percent of clinical sites inspected by the FDA had no action indicated, Holwell said, “so I think we’re in pretty good shape.”

**Thursday, June 25**

**Clinical Operations, Project Management & Risk Management**

The tremendous push to develop new COVID-19-specific treatments and vaccines has led to “the rapid relative growth of collaborative sharing co-development arrangements,” Kenneth Getz, deputy director and professor at the Tufts Center for the Study of Drug Development (CSDD), said in the session, “How Well Will Our Response to COVID-19 Transform Clinical Operations Long-Term?” The total number of co-development arrangements announced publicly in the past four months is greater than the total of such arrangements in the three preceding years, Getz said, according to figures compiled by the CSDD, which has been monitoring public announcements by the top 50 clinical trial sponsors since March 16. Of these sponsors, 34 percent were engaged in independent development of treatments and vaccines and 42 percent were engaged in collaborative development as of March 30, rising to 46 percent and 56 percent, respectively, as of May 8.

“You need to think about the project tasks and deliverables and communicate them” when setting priorities in clinical research, Dawn Sauro, chief development officer at Clinipace, said in the session, “Setting and Managing Priorities in a Clinical Project Schedule.” Researchers should also identify items that need cross-functional or client review and that challenge people’s assumptions, she said. “Think about data management throughout the trial; it does save your backend timelines and deliverables,” she advised.

Subject recruitment is one of many areas of clinical research being affected by the current COVID-19 pandemic. “At some sponsors, recruitment was halted” when the pandemic broke out, Rosanne Petros, associate director, global clinical trials management at Merck, said in the session, "Bringing Studies Back Online After COVID-19." She added that Merck did not stop recruiting into ongoing trials, “but many of our sites did halt recruitment, or they had a really hard time recruiting patients” due to such problems as staffing difficulties and trouble securing personal protective equipment. To mitigate these problems, she suggested asking such questions as whether study procedures or consenting can be done remotely; continuously assessing whether you need additional sites, including rescue sites; amending the protocol; and rescreening subjects who were reluctant to come into sites earlier but may be more willing now that some pandemic-related restrictions are easing.

“The new normal” in clinical research as a result of the COVID-19 pandemic will “hopefully” feature “new existing policies, procedures, work instructions, systems, tools, training” and more, Shanley Curran, an attorney with Boston Scientific, said in the session, “How Will COVID-19 Change Clinical Project Risk Management?” She said that options for remote consent are likely to become more common, as well as things like “study-specific disaster risk assessment as part of our readiness plan.” The goal, she added, is “so that we can have in place processes that support the kind of flexibility in our practices that enable us to be resilient and responsive to unexpected disaster on the worst side, but to flexibility on the most thoughtful side.”

For continuous risk management in clinical research, “key components of the core team” should be included throughout the process, not as a “one-and-done” action, Dawn Niccum, senior director, quality assurance and compliance, at inSeption Group, said at the session, "Assessing and Characterizing Risk in Clinical Research." To help guarantee success, ensure that actions are assigned to individuals, consider data over the life of the study, assess internal and external data, and identify trends, she said.