COVID-19 Rapid Response Working Group

Meeting Highlights

Topic: How to Adapt Clinical Studies That Must Continue Treatment and/or Recruitment Because of Limited Standard-of-Care Options

Meeting Date: April 23, 2020

Objective of the COVID-19 Rapid Response Working Group: To enable the continuity of clinical trials with strategies and practical support, ensuring that there is a focus on patient safety, data integrity, and regulatory compliance as the COVID-19 situation evolves.

Executive Summary: In the fifth session of the Rapid Response Working Group, a group of AQC Members representing over 40 Member companies gathered to discuss **How to Adapt Clinical Studies That Must Continue Treatment and/or Recruitment Because of Limited Standard-of-Care Options.** The approach to this topic is greatly influenced by therapeutic area and whether standard-of-care options are available. During the session, an executive leader representing an investigative site stated that, during this COVID-19 situation, he has used the definition of "essential trials" as being aligned to the need for the trial to maintain or provide for the health and well-being of participants, not the risk itself to the interpretability of the trial. In addition to the trial innovations that were discussed during the RRWG session, the use of Informatics and Analytics were shared during this session. These tools are used to carefully monitor the spread of disease at the community level so that specific site level decisions can be taken real time. Also, several speakers shared their thoughts on reopening sites and trials and outlined some of the criteria that they are using to take those decisions.

To date, over 80% of AQC Member companies have participated in our Rapid Response Working Group sessions and we have had 24 speakers representing 20 various organizations across large and mid-sized pharma, biotechs, CROs, and sites.

Below, please find a summary broken down into several key focus areas from the discussion:

1. **Defining Essential Trials**

   Trials considered to be essential provide for the health and well-being of participants. For some trials, it was acceptable to pause activities in the short-term, but now that several weeks have lapsed since the development of the pandemic, commencing those trial activities has become pertinent to the health and well-being of the participants, making the trial continuation now essential. Informatics and Analytics are being utilized to carefully monitor the spread of

disease at the community level so that specific site level decisions can be taken real time. To address the potential of losses to outcomes, including primary endpoints, sponsors may need to add additional trial participants. With regard to COVID-19 trials, some special considerations will need to be considered such as the use of eConsent, adequate PPE for site staff, and self-sampling by participants.

2. **Leveraging Technology/Informatics to Understand/Monitor Risk and Disease Spread**

   A discussion occurred around leveraging technology and informatics to better understand the spread of COVID-19 at the most discrete level in order to improve rapid decision making around trial activities. Identifying priority studies, using informatics, monitoring regulatory guidance, and conducting risk assessments are steps in the process that sponsors may want to consider in their plan for recovery from the COVID-19 interruption to research and trial activities.

3. **Criteria & Considerations for Reopening Sites**

   There are criteria and considerations in determining how to reopen sites to continue existing trials, start up new trials, and allow monitors on-site for site monitoring/source data review visits, etc. When deemed appropriate, monitors may be permitted on-site with some added precautions and patient enrollment could occur, perhaps away from the main hospital setting at off-site clinics. The approach to reopening in a large country such as China or the US will likely need to be done on a state-by-state basis as opposed to considering the full country active, as might be more appropriate for a smaller country. Operational, logistical, and procedural aspects will need to be considered.

4. **Innovations/Mitigations: Telemedicine, eConsent and Remote Consent, eBinder – A Follow-up from Last Week's Session**

   It was indicated that the quality management system may actually enable the use of innovations as opposed to acting as a barrier to it. As teams leverage these innovations as mitigations against COVID-19, they are realizing that what was once perceived as a risk may not be as substantial as previously thought. Sponsors are seeing more remote consent with a follow-up video conference/phone call with the patient, and some feel this is easier globally than eConsent; however, eConsent popularity has risen, as well. The utilization of telemedicine has drastically increased and is now being considered economically critical to sites. Patient consent for the use of telemedicine may be considered as implied since the patient is scheduling and willingly participating in the call/video conference. Leveraging the use of eBinders may reduce the necessity for monitors to travel to sites and this

current experience may change the equation around sustaining the cost of clinical site monitors.

5. **SDV/SDR: The Other Alternatives**

   One site indicated that they had increasingly shifted to a statistical risk assessment model to determine what needed to be source data verified. While this is something that the FDA has indicated as acceptable, companies have been reluctant to adopt based on perceived regulatory review risk. Historically, project teams tended to revert back to 100% SDV as the "safe" option when delivering a pivotal trial. This pandemic will give sponsors a reason to do verification in a more thoughtful and efficient way, performing risk-based monitoring by utilizing centralized monitoring and having it inform when and where on-site monitoring is required.

6. **Backend Processing**

   Sponsors who are looking at a database lock or interim lock may take on greater risk with regard to cleanliness of data, but may want to consider outreach on a 1-to-1 basis to sites for resolving key queries and will want to be mindful of the importance of documenting the decision and rationale for how interim locks were handled.

Links to COVID-19 Health Authority websites:

- World Health Organization (WHO) Coronavirus
- US Centers for Disease Control
- FDA Coronavirus
- European Medicines Agency
- European Centre for Disease Prevention and Control
- China National Medical Products Administration
- ProMED – International Society for Infectious Diseases
- ACRO COVID-19

If you are interested in learning more about the Avoca Quality Consortium (AQC) or the COVID-19 Rapid Response Working Group, please contact Dawn.Auerbach@theavocagroup.com.