Highlights and Summary of Part 6 Webinar:

Going Remote During COVID-19: Considerations When Moving Studies Out of the Clinic Setting

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What does informed consent mean when a trial is remote? Where does eConsent come into play? And how are IRBs and FDAs viewing these changes? These are just some of the issues tackled in a series of WCG webinars that address the coronavirus-related challenges facing the clinical trial industry.

Featured speakers:

1 **Dawn Furey**
Vice President, Head of Portfolio Delivery Operations, The Janssen Pharmaceutical Companies of Johnson & Johnson

2 **David A. Borasky, MPH, CIP**
Vice President of IRB Compliance, WIRB-Copernicus IRB Group

Lindsay McNair, MD, MPH, MSB, *Chief Medical Officer, WCG,* moderated.

You can find links to this webinar and an array of COVID-19 resources on our **WCG Insights Program page.**

Direct-To-Patient Home Healthcare and the Influence of COVID on Our Portfolios

1 **Dawn Furey**
Vice President, Head of Portfolio Delivery Operations,
The Janssen Pharmaceutical Companies of Johnson & Johnson

Foundations for Any Trial

Patients: Patients are the bedrock of our clinical trials. Whether patients can get to the clinic, and whether they want drugs shipped directly to their home, and whether patients are comfortable with having their private information shared with third-party vendors are always the number one concerns.

Sites: Making sure we stay in touch with our sites and listen to them, because there's not a one-size-fits-all approach for patients or sites in this global pandemic environment.

Country regulators: Are they allowing direct-to-patient shipments? Are they allowing home healthcare? What are the adaptations that have been made to privacy regulations that allow information to be given out that, under normal circumstances, would not have been given out?

Creating an Objective Decision Framework

Based on available data, science of the compound and patient journey.

Understanding the Patient Journey

Consider the following questions:

- Is there a greater benefit than risk to the patient with the path you've proposed? In some cases, patients desperately need to get to the clinic. They will be in a far worse situation if we tell them to stay home.
- What are the risks that you can anticipate? How will you mitigate them?
- What risks are you prepared to take? What can you be prepared to assume as a sponsor or as a site when you're looking at those risks? How are you going to mitigate those risks?
- How are you going to look at the ever-evolving regulatory guidance?
- Regardless of which path you decide to take, how can patients' safety be overseen? How can your obligation, as the sponsor, be fulfilled and documented?

Evaluate the Science

How much data do you really need? As Ken Getz likes to say, we collect much more data these days than we did 10 years ago, because we can. It's so much easier to collect data. But what is the bare minimum that you

need to ensure that these patients have care? What does that look like?

- What visits could be eliminated?
- What visits could be done through telemedicine?
- What visits could be postponed? How long can patients go between visits?
- How will the medication be delivered?
- How do you handle lab draws?
    - Can some be pushed out?
    - If lab draws are essential within a particular window, can they be done remotely? If not, how will patients get to a lab?

Exploring the Option of Home Healthcare

Is home healthcare right for your trial? Among the considerations:

- Will patient safety be jeopardized?
- How much of your trial can be managed via home health care or via telemedicine?
- Are you doing it because you want to keep your visit schedule as close as possible to the original schedule? If so, would it be better to skip some visits and have patients come to a central location?
- What are home health providers allowed (or able) to do?
    - What will home health care providers be asked to do by the sponsor or by the site, versus what will they be allowed to do?
    - What happens if a patient asks a home health care provider to go beyond what they've been contracted to do? What's the guidance the sponsor or the PI wants to give to that home health care provider as to how they should respond to that?
    - Will a doctor be available to answer the questions from the home health care provider? Is there a guidance document that you want them to refer to?
- How can the drug be safely provided to patients? If it's shipped directly to them or to a local distributor…
    - What instructions do patients need?
    - Will home health care providers be a component of the drug delivery or the drug supervision?
    - How do you ensure patients are being instructed appropriately? Do we need to have a telemedicine component coupled with that direct-to-patient shipment?
    - What supervision do Private Investigators (PIs) or the study staff need to continue to provide?
- What options will you provide to the patients?
    - Where do you need them to sign off on having home healthcare?
    - What if they are pleased with the site but dislike the home healthcare provider?

Keeping Patient Care at the Forefront

Other questions to ask include the following:

- How will you establish liability for the home health care provider?
- Is the PI getting their data and driving oversight on a continuous basis? How often is that PI able to look at that data?
- Is a sponsor getting data and driving oversight? Data entry may be suffering during this pandemic.

- What do you do when there are gaps in the data?
- Do you have a risk-based monitoring system set up? How can you utilize that data along with maybe IVRS data or IWRS data?

- How will the home health care staff be trained and managed? Who will do the training?
- How will you manage requests throughout the trial to bring on new home health care staff? To support new locations?
- What if patients are unhappy with the home healthcare provider? They choose their doctor; can they choose their home healthcare provider?
- What if patients need to consult with their PI? What type of provisions for telemedicine are available to those patients? Is there a study nurse on call?

There are more questions than answers. But thinking through the questions is essential.

The IRB Perspective

2 **David A. Borasky, MPH, CIP**
Vice President of IRB Compliance, WIRB-Copernicus IRB Group

These webinars have been going on for more than six weeks, and in that time we've learned quite a bit.

First, the COVID-19 pandemic has affected nearly every study that was in planning or underway. All facets of the research enterprise have had to be agile and react quickly.

Second, we see that regulators have been very responsive. As an example, the FDA quickly launched their COVID guidance for ongoing trials in that last week of March. It's already been updated three times. And OHRP also issued guidance on April 9. They're truly moving fast to provide us with the answers we're all searching for.

And third, as the work continues, we see that everyone in the industry has become more adept at managing in this context. It's certainly not

WCG IRB Philosophy

This is the philosophy of the WCG IRBs -- and we

hope, the philosophy of IRBs everywhere -- is that the regulations do provide us with a great deal of latitude and now is not a time for IRBs to be afraid of using that latitude and to hold the reins of the decision-making that have been given to IRBs by the regulations and by the regulators.

Regulations provide IRBs with a great deal of latitude, and WCG IRBs are committed to embracing the flexibility allowed by regs.

An IRB should not be a roadblock to making changes that are essential to maintaining research that is:

- Ethically appropriate and maximizes safety of study participants, research teams and the general public
- Scientifically valid
- Compliant with the regulations

The last thing any IRB should be is a roadblock to making changes that are essential to keeping research going forward.

Research, COVID and IRBs

So there is obviously a very large volume of change and that continues. Patterns are emerging.

Most frequent questions and issues: The most frequent questions and issues haven't shifted significantly, although they have become more nuanced. They relate to:

- Reducing the number of protocol-mandated study visits
- Use of alternatives--e.g., home visits / telemedicine, shifting commercial or consumer laboratories to get things done
- Shipping investigational products directly to research subjects

Embedded in all these questions is another one: "How do we convey that information to the participants in our trials?"

New trends in questions / issues: New question and topics have emerged over time, including:

- Adjustments to compensation
- Options for consent process including e-consent
- Should protocols in development include provisions for similar scenarios? What will these provisions look like?

Implicit in all these questions is this: "Where do we stand in terms of what kind of IRB review is going to be required?"

What Needs IRB Approval?

In this context, we're talking about changes in previously approved research.

- **Changes in study procedures that may impact participant safety or the integrity of the research.** They're not all going to affect participants' safety or the integrity of the research. But depending again on the type of visits or the type of labs we're talking about, there could be some.
- **Changes in provision of investigational product (e.g., ship directly to participants).** We're still

getting a lot of questions about that. And again, it's typically not something the IRB is going to get in the way of. Impact of federal and state laws. Local pharmacy boards may have restrictions that are in place around this and of course those need to be accounted for. Of course, all this presumes that self-administration is appropriate or that mechanisms are being put in place along with the direct provision of product to ensure that dosing can happen in a safe manner with appropriately licensed professionals when that is necessary.

Regulatory Guidance

If we look at the regulations, it's pretty clear in the IRB regulations in part 56 [21 CFR 56.108(a)(4)]: *"Each IRB shall … (a) Follow written procedures for ensuring that changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval…"*

But what if implementation can't wait for IRB review? The regulations cover that: "*…except where necessary to eliminate apparent immediate hazards to the human subjects.*"

Immediate changes may be needed for the best interest of those involved in the research. Changes made without IRB approval should be submitted as soon as possible. The typical WCG standard is five days, but of course these are extraordinary times and we are being flexible.

Compensation When Patients Don't Visit Sites

WCG has received a lot of questions about compensation. What happens when there are research studies that offer compensation, but they were based on in-person visits and people showing up?

- Can we continue paying subjects if visits are remote? **Yes, you can.**
- Can we reduce or eliminate payments to subjects that reflect a decreased burden of participation? **Yes, you can.**

An IRB's role is to protect against undue inducement--maintaining or reducing approved amounts should not affect that analysis.

Informed Consent

We've also had lots of questions around informed consent.

- **Regulations require initial consent.** They also require consent when there are applicable significant new findings that may relate to the subject's willingness to continue participation. (This is typically called "re-consent," but that is not a regulatory term.)
- **New information can be presented in different formats.**
  - Revised consent document
  - Addendum to consent
  - Memo or other communication to subjects
  - Orally by phone or in person
- **Documentation can also be achieved in several ways.** "Unless we are having people go through a whole new consent process with a totally new or revised consent form, documentation no longer has to fit that regulatory criteria that we'd see in a new consent, a new enrollment into a research study."
- **Goal: Keep burden minimal.** According to the

Secretary's Advisory Committee on Human Research Protections (SACHRP), "When there is a need to present participants with new information, IRBs should encourage use of the least burdensome approach for the participant."

FDA guidance has evolved. One of the first revisions to their guidance was to add a series of FAQs; two address informed consent challenges.

Q10: *How do I obtain signed informed consent from a patient who is in isolation when a COVID-19 infection control policy prevents us from entering the patient's room to collect a signed informed consent form?*

Q11: *How do I obtain informed consent from a patient unable to travel to a clinical trial site where electronic informed consent is not an option?*

- Consider electronic informed consent; it allows you to reach out to participants who are otherwise isolated
- Utilize other technology to enhance the process
- Ask subjects to return signed documents by mail
- If unable to document in real time, use witnesses to confirm that the consent process was completed
- Document everything!
  - How it was confirmed that the patient signed the consent form (e.g., attestation by the witness and investigator or the photograph of the signed consent)
  - Statement of why the informed consent document signed by the patient was not retained (e.g., due to potential contamination of the document)

More Flexibility, But Regulations Still Stand

The FDA is working hard to give creative solutions to research sites and partners. "We've had a lot of people reach out to us and say, we understand that the FDA has relaxed their requirements or has backed off from the regulations. I just want to affirm that that is not the case at all."

Take advantage of that flexibility to be bold and come up with creative solutions to make the research go forward and maintain regulatory compliance.

Electronic Consent and Electronic Signatures

One frequent question that we've now seen popping up as sponsors and sites are contemplating moving to

electronic formats: *Does 21 CFR Part 11 apply and will it be enforced?*

Part 11 is the FDA regulation that covers electronic signatures, electronic records, and it applies to those records or signatures that are being done for FDA-regulated research.

- **Applies to FDA-regulated research:** If you're outside the FDA guidelines, you may have some more flexibility in terms of what you can do or use in an electronic sense.
- **Not all e-signature and eConsent tools comply.** Not all commercially available eConsent solutions are Part 11-compliant off the shelf. Adobe, DocuSign and similar e-signature products have both Part 11- and non-Part 11-compliant versions.
- **No extra flexibility:** FDA has not indicated whether they will allow flexibility for electronic signatures.

Looking to the Future

Should future protocols have provisions for pandemic management? This is a question that's difficult to forecast now because what we're experiencing is unprecedented.

Continuity Plans

Sponsors and sites should consider having ready-to-implement continuity plans. But including those plans in protocols may be challenging. One size may not fit all. It's good to have plans, but it may be difficult to write them into protocols in a meaningful way.

More Attention to eConsent, Virtual Trials

The challenges posed by the pandemic may stimulate renewed consideration of eConsent and virtual clinical trials, which are both things that have been around for a while but for a variety of reasons haven't had a tremendous amount of uptake up to this point.

Moving Forward

Some final piece of advice:

- **Stay in touch.** Sponsors and sites should remain in close contact with each other and with the IRB.
- **When in doubt, err on the side of patient safety.** That certainly goes along with the idea that you can implement certain changes without prospective IRB approval; that is rooted in subject safety and that should be an overriding concern for everybody.
- **Document everything.** The FDA is very clear in their guidance that they understand there will be numerous deviations to ongoing research, but they expect to see those recorded and managed.

Questions from Audience

Questions for Furey

Dawn Furey
Vice President, Head of Portfolio Delivery Operations, The Janssen Pharmaceutical Companies of Johnson & Johnson

&

Questions for Borasky

David A. Borasky, MPH, CIP
Vice President of IRB Compliance
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Q **Dawn, is there anything that vendors or service providers, who are working with sponsors on the conduct of the study, could be doing to support their sponsor partners right now that would be helpful while sponsors are struggling with these COVID-related issues?**

A **Furey:** I think right now the most important thing that a vendor or service provider can do is to be very transparent and communicative with sponsors about what they're thinking. Everyone is dealing with unique challenges that were mostly unanticipated. By liaising with the sponsor, we can understand what your business strategy is. That's because when you change your business strategy or make a deviation in order to deal with your particular COVID situation, it may actually impact the sponsor's business. There may be some concessions a sponsor can make to help you with your business continuity because we are so intertwined, and your success is our success. And so, having those conversations, and not assuming that we have to do the best we can unilaterally, are the most important things that, I think, a vendor, or a service provider can do in helping to support us through these difficult times.

Q **Some of these changes are happening in studies with shifts to telemedicine visits, changes to lab draws, things like that. If we need to communicate those things to the study participants and we**

want to do that, either a sponsor wants to do that or a site wants to do that, by sending out a letter to the study participants to let them know what's changing in the study and what they should expect, does that letter, does the written communication to the participants need to be approved by the IRB?

A

Borasky: That's a good question. We are being asked that a lot, so I'm not surprised that it came in through our audience as well. The WCG IRB approach has been to say that we think, consistent with the ICH guidelines and with the expectations of the regulators, that these things need to be reviewed as part of the consent process, and the ongoing nature of the consent process. So yes, we have been asking to have those submitted for review.

Q

How would you handle resumption of a study if it's in a multicenter trial when the benefit-risk assessment may differ between the sites?

A

Furey: We have to recognize that we need to be flexible. And sometimes we need to build more flexibility into our documentation, so we can have sites or countries that are moving in one direction while others are moving in a different direction. That we have the flexibility to do either one.

For example, let's say, psychiatric clinics that are within hospitals: You don't want patients coming in for those visits to the hospital where the COVID infection is being treated and you feel that that presents an undue risk to the patients. In other cases where that center is completely removed from the hospital setting, and there's very little risk to patients who come in. Having that patient come in (rather than turning to home healthcare or telemedicine) might be the best for that site and that patient. I really encourage you to think creatively around how you can be flexible, so you can accommodate those multicenter trials and geographic and patient-centered needs.

Q

Would home healthcare providers, if they are performing study assessments or collecting study data, need to have human subject protection training?

A

Borasky: It depends. I think, it may be unrealistic to suggest that all of these people would go through a complete human subjects training program.

I do think that, to the extent possible, we want people who are interacting with study participants to understand that what they're doing is for research purposes, what that means and what the limits of their role are, and so forth. They've got to be appropriately trained to do what they're being asked to do. And it is probably worth having some component of understanding what research is.

But I don't think it's realistic to say, now, we're going to sit down and do a three-hour training on things like the Belmont report, or the ethical underpinnings of human subjects' research when the role is going to be fairly limited to collecting some well-defined specific amount of data.

Q **So, it sounds like this is one of those questions where perhaps talking to the IRB about what their role will be will help you get the best information in advance?**

A **Borasky:** That's correct. Talking about that goes across more than just ethics training. What are the expectations for how they're trained and the data they're collecting, do they have to be listed in delegation logs and so forth? I mean, I think there's going to be a lot of "it depends" in there.

Q **Again, with regard to home healthcare providers, what would the sponsor's expectations be of them with regard to adverse event reporting, and the collection of adverse event data while they are interacting with study participants?**

A **Furey:** We would expect is a certain amount of adverse-experience reporting training is provided as part of contracting with home healthcare providers. And once the right expectations are set up, at what point the home healthcare provider would be reaching out to a specified person at the site, and how the sponsor is going to be getting that information fed back.

So, once again, there are going to be differences in who they contact at the site, and what set up is available for consultation. But it's important that especially in these COVID response periods we are not leaving the PI out of the equation when we're developing these home healthcare solutions, that we are making sure they are getting that information, and they are still providing that liaison for the patient even if there's a home healthcare provider retained.

Q **Does the FDA form 1572 need to be changed, if visits are moving from plans to be in the clinic to telemedicine, or if participants are now going to a commercial or local lab instead of getting blood drawn at the clinical site as was originally planned?**

A **Borasky:** We have had a number of people also reaching out with some 1572 questions in this context. There is a previously published FDA guidance on 1572s, and they have a question in there about when it has to be updated, and completed, and signed due to new circumstances. And, in that, the FDA notes that there are two instances when it's necessary: when an investigator's participating in a new protocol that's been added to an IND, and that new investigators added to the study. Other changes to an IND do not require it be revised and signed in these circumstances. And I don't believe it's in the current FDA guidance and in the COVID materials by the FDA. But the FDA has been clear that they're not expecting 1572s to be updated with this information.

Sites should keep documentation locally about what they're using and for how, but they don't need to change the 1572.

The OHRP and FDA guidances around doing research and COVID are all linked from the WCG FAQ page on our COVID resource website, **www.wcgclinical.com/covid-19/faqs/.**