PropSci

Modifying Clinical Trials: U.S. Regulatory, Liability & Insurance Webinar

March 2020

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Speakers Today

PropSci Co-Chair & Moderator

Andy Sucoff, Boston
Real Estate

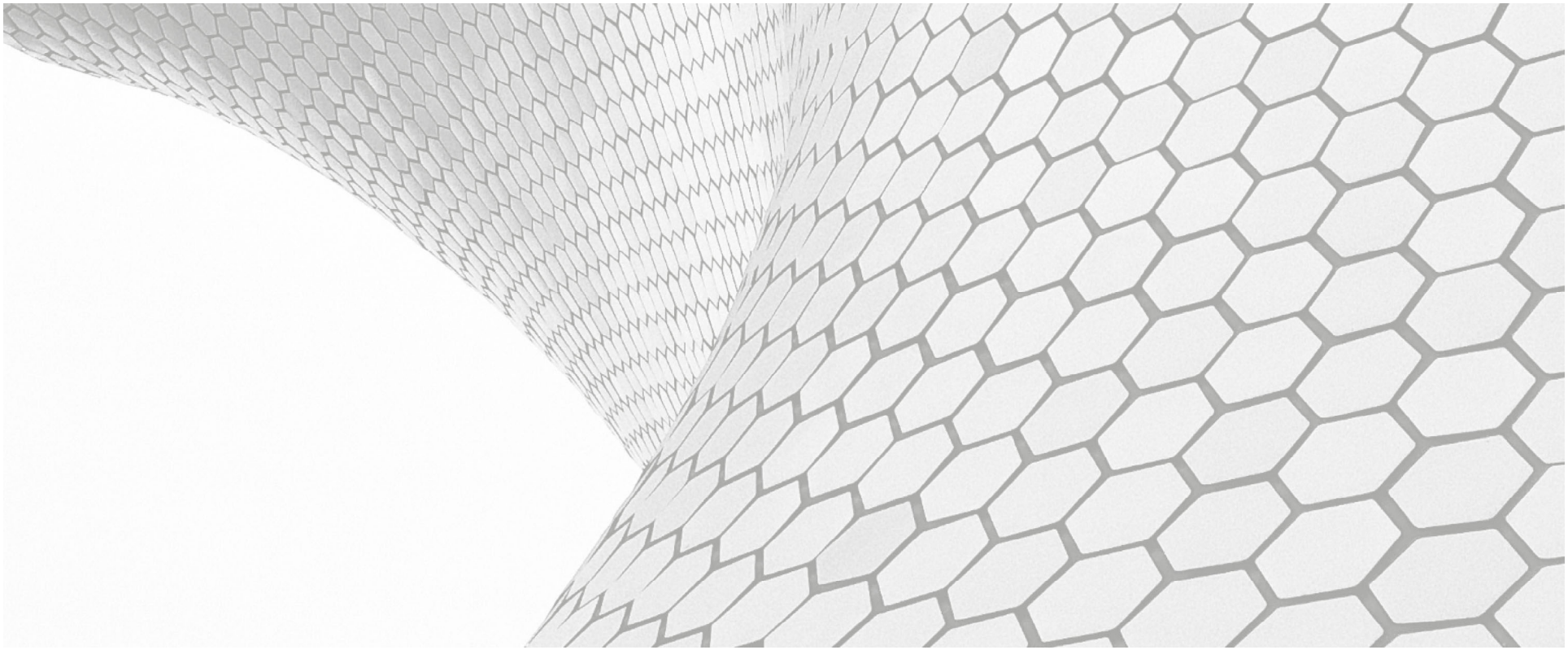
Julie Tibbets, Washington
FDA Regulatory Counseling

Roger Cohen, New York
Health Care Regulatory Counseling

Sarah Frederick, Boston
Products Litigation & Counseling

Carl Metzger, Boston
Risk Management & Insurance

FDA Regulatory Developments



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Key FDA Regulatory Developments

- March 18: FDA issued Guidance on Conducting Clinical Trials during the COVID-19 pandemic
  - Good Clinical Practice (GCP) requirements and Part 50 study subject protections, along with IRB review/approval requirements, generally remain in force with some flexibility
- March 19: FDA announced leveraging of compassionate use program for immediate expanded access to experimental drugs available
  - Subject to drug developer policies on expanded access
- FDA halted routine surveillance inspections
  - Foreign: “mission critical” inspections on case-by-case basis only (March 10)
  - Domestic: “for cause” inspections and “mission critical” only (March 18)
    - Site FDA audits still happening as recently as a few weeks ago but may slow down
    - March 25: IMMU announced “recently completed” pre-approval inspection
- March 27: FDA amended its Clinical Trials Guidance to add FAQs
- Clinical research sites following government shelter-in-place orders plus CDC interim guidance on “essential” vs. “non-essential” business functions and personnel
  - Room for interpretation → complicated web of site-adopted policies

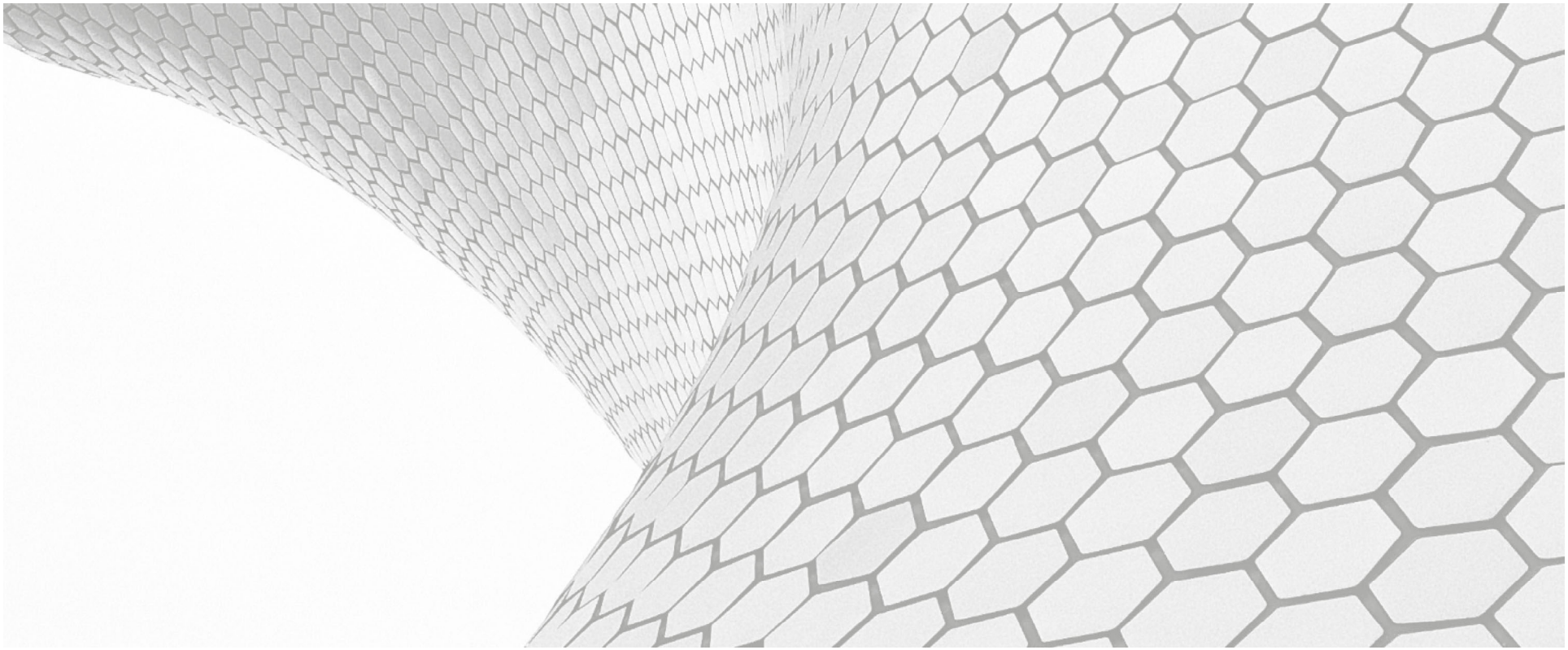
Key FDA Regulatory Developments (cont.)

- Guidance recommends sponsors:
  - Ensure subject safety and notify subjects of changes to the study or monitoring plan
  - Consult with IRBs regarding continuing subjects in trials per protocol (e.g., health system mandated COVID-19 screening implementation, protocol or informed consent form changes needed)
  - Consider alternative safety assessment methods (phone, virtual, other locations for conducting assessments) and consult FDA on alternative efficacy assessments (e.g., virtual assessments, delays, or alternative collection of research specimens)
  - Implement additional safety monitoring where site/product unavailable (e.g., withdrawal)
  - Document COVID-19 changes and how subjects were impacted, and note missing data on account of COVID-19 control measures
  - Talk to FDA if considering alternative administration/delivery (e.g., home nurse)
  - Talk to FDA about changes to data management/statistical analysis plans and address how COVID-19 protocol deviations will be handled before locking the database
  - Implement remote, if necessary, trial site monitoring programs

Key FDA Regulatory Developments (cont.)

- Practical takeaway from FDA's Clinical Trials Guidance: inventory your study design, consent, and site policies to identify the fewest *universal* changes needed to continue (avoid a patchwork across sites if possible)
  - Goal: take prudent measures while keeping the trial and (the majority of the) dataset as intact (and meaningful across subjects) as possible
- Clinical study reports (CSRs) for COVID-19 impacted trials should identify COVID-19 contingency measures and their impact on safety and efficacy results and include subject-level documentation regarding any study disruption
- Practical considerations:
  - Are all of your sites still up and running with site personnel and does the site consider your trial "essential" to continue?
  - If a Phase 1 or 2 study was underway, have you obtained enough data already to permit advancement to the next Phase?
    - Can you adjust your next planned study design to gather additional data missed due to COVID-19 disruption?
    - Could an open-label extension for those with apparent benefit be instituted in the interim under site policies?
    - What access is available via compassionate use – e.g., rare disease and third-line oncology patients?
  - Was the trial over-enrolled? How many patients could you lose without impacting the powering of the trial?
  - For planned trials, what adjustments can be made to still initiate on time? Are sites allowing non-COVID-19-focused healthy volunteer studies to initiate?

Clinical Site Investigation Developments



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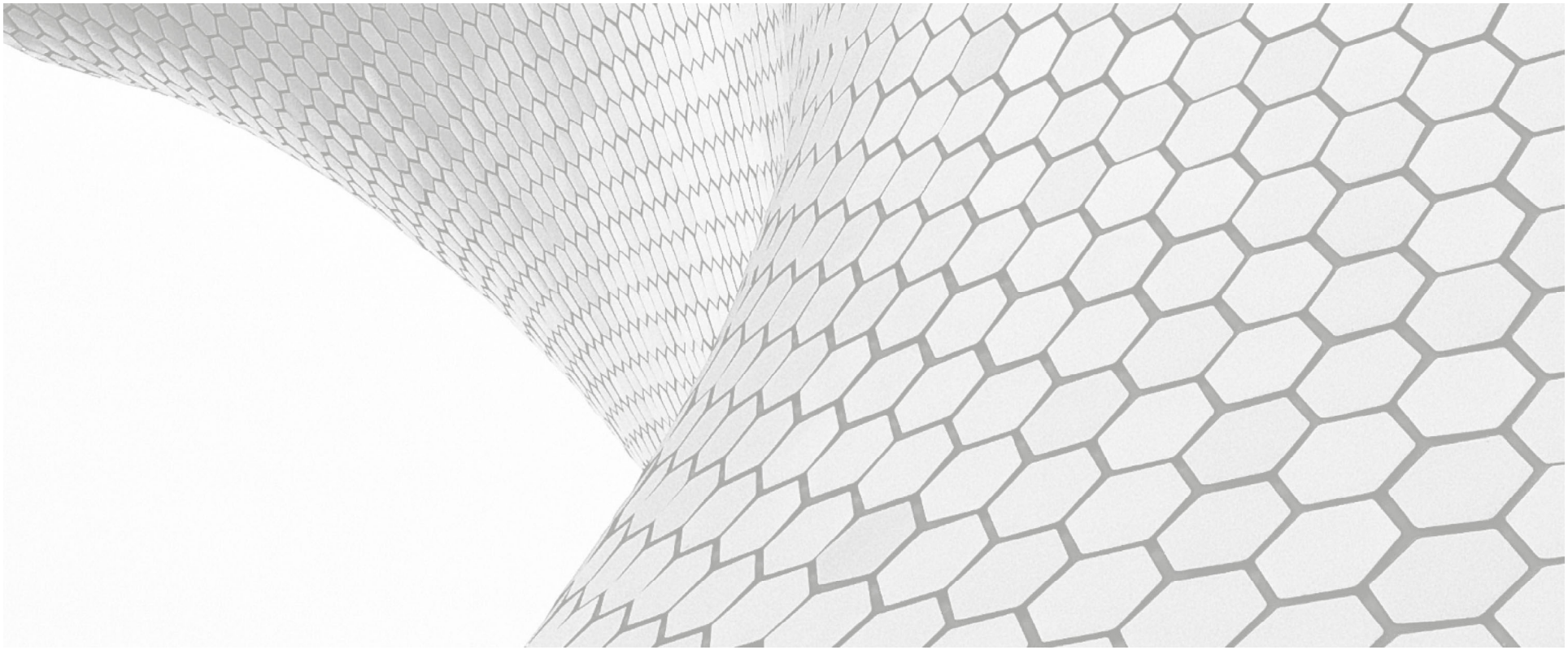
Clinical Site Investigation Developments

- No one-size-fits all clinical study site policies – adapted based on same government orders and guidelines but each is a bit different
  - Duke: policy appears to define Tiers 1-3 of clinical research where only Tier 1 can continue in person (i.e., protocols involving treatments for acute, life-threatening health conditions or where stopping the intervention could be harmful); Tiers 2 and 3 can continue if remote/virtual, otherwise must be suspended
  - Emory: announced non-essential research as determined by the school had to ramp-down by March 23; all new studies should be postponed; only critical and essential studies can continue; critical appears to be defined as where abandonment would cause irreversible and irreparable loss
- For ongoing clinical trials or future planned trials, what informed consent updates should be added?
  - Has the informed consent process changed?
  - Have the study risks changed? (e.g., increased COVID-19 exposure potential)
  - Have the study procedures/monitoring activities/data collection mechanisms changed resulting in new risks?
  - Have study personnel changed or is there a new study contact person at the site for adverse event reporting?

Informed Consent: FDA on Reconsenting Patients

- FDA March 2020 Clinical Trials Guidance FAQ 10 covers informed consent for subjects in isolation or under hospitalization:
  - Reconsents can be obtained electronically
  - When electronic means are not feasible or infection control policy prohibits removal of a signed consent from the study room, FDA allows:
    - 3-way call with the investigator, patient, and an impartial witness along with any other participants requested by patient
    - FDA recommends applying a consistent process (introduction of who is on call, reading of the informed consent, confirmation by witness that questions have been answered, confirmation by investigator that patient is willing to participate, and verbal patient consent plus signed consent to be maintained by patient)
    - If signed document cannot be transmitted to the site investigator, FDA allows other options, including: a photograph to be taken and transmitted, an attestation by the witness that consent was provided, a signed copy by the witness and investigator added to subject's trial record noting how consent was obtained (e.g., telephone), or written consent by a legal authorized representative
- Practical considerations:
  - may still have drop-outs
  - can consent modifications be aligned across site and IRB policies?

Liability Implications



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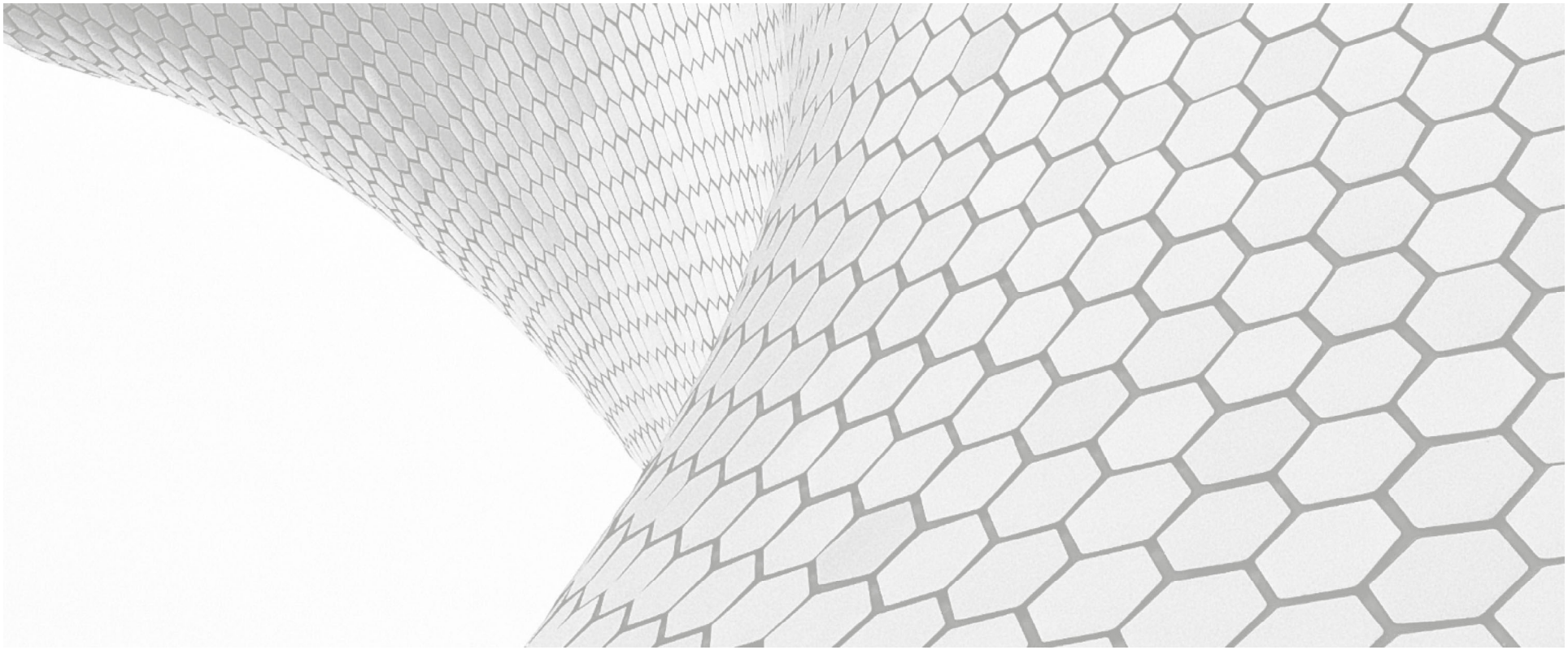
Liability Implications

- Liability Considerations When Pausing/Stopping Ongoing Clinical Trials
  - It is not unprecedented for study sponsors to face lawsuits, or the threat of lawsuits, from ending access to a study drug.
  - Considerations to guard against liability
    - Strong, clear informed consent language
    - Communicate decisionmaking and reasoning clearly to PIs and patient advocacy groups
  - Best practices for drafting informed consent documents
    - Use clear study termination language
    - Use clear language defining study time period
    - When offering expanded access, reaffirm sponsor's ability to end the study at any time, for any reason
- Liability Considerations When Continuing or Initiating Clinical Trials
  - Consider composition of data safety monitoring board
  - Update informed consent documents
  - If trial is related to COVID-19 response, make sure that compensation provision is aligned with PREP Act Declaration.
- PREP Act for COVID-19 Related Clinical Trials
  - Certain liability protections and immunity may be available for COVID-19 clinical trials
  - Liability protections are limited by federal law and the Secretary of Health and Human Services' Declaration.

Insurance Considerations



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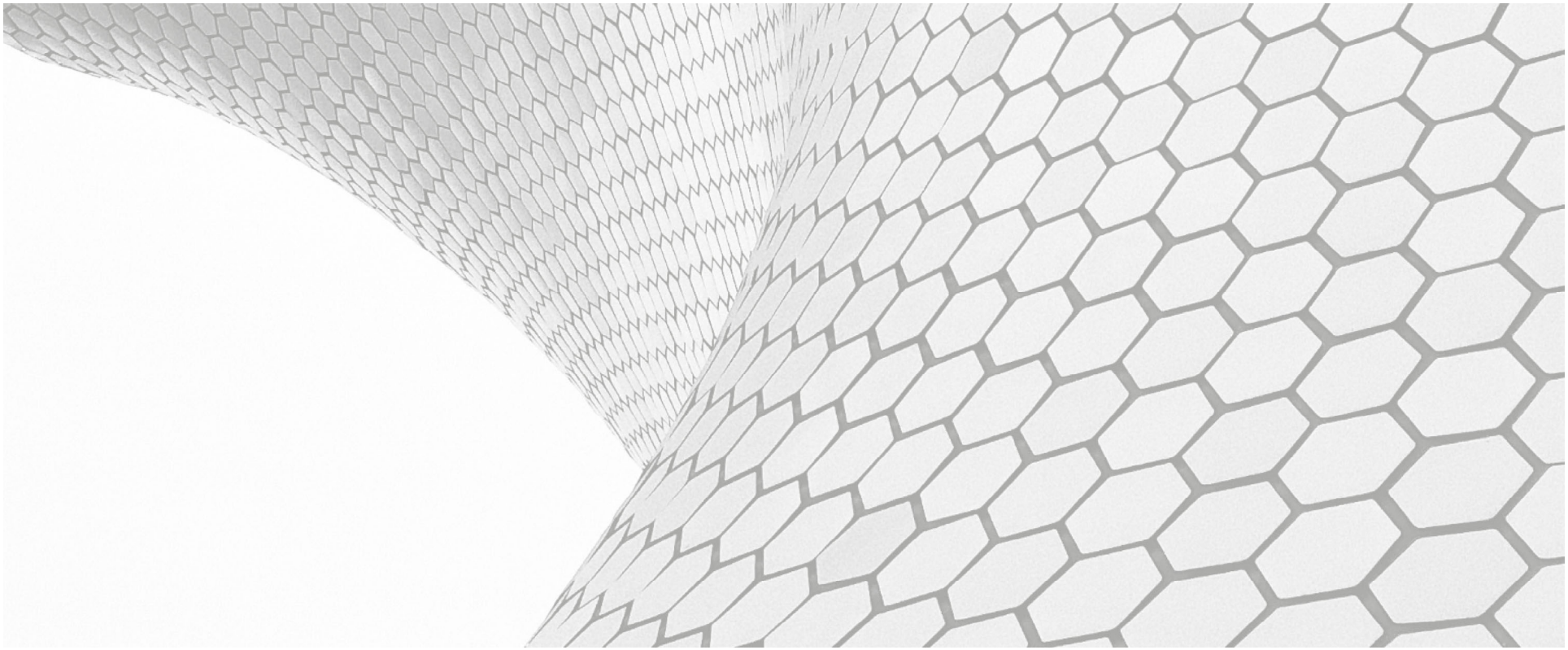
Insurance Considerations

- Coverage for Possible Losses Already Incurred
  - Existing programs – analyze wide and deep
  - Err on the side of notice, since coverage law will be evolving
- Proceeding with Studies in the Current Environment
  - Be proactive in assessing your coverage now
  - Adapt your practices, but be aware of the insurance coverage implications
- Planning for Commencing New Studies
  - Work with your insurance brokerage now about coverage questions and concerns
  - Be aware of your renewal dates and changes to your insurance programs – an evolving landscape

Current Work in the PropSci Space



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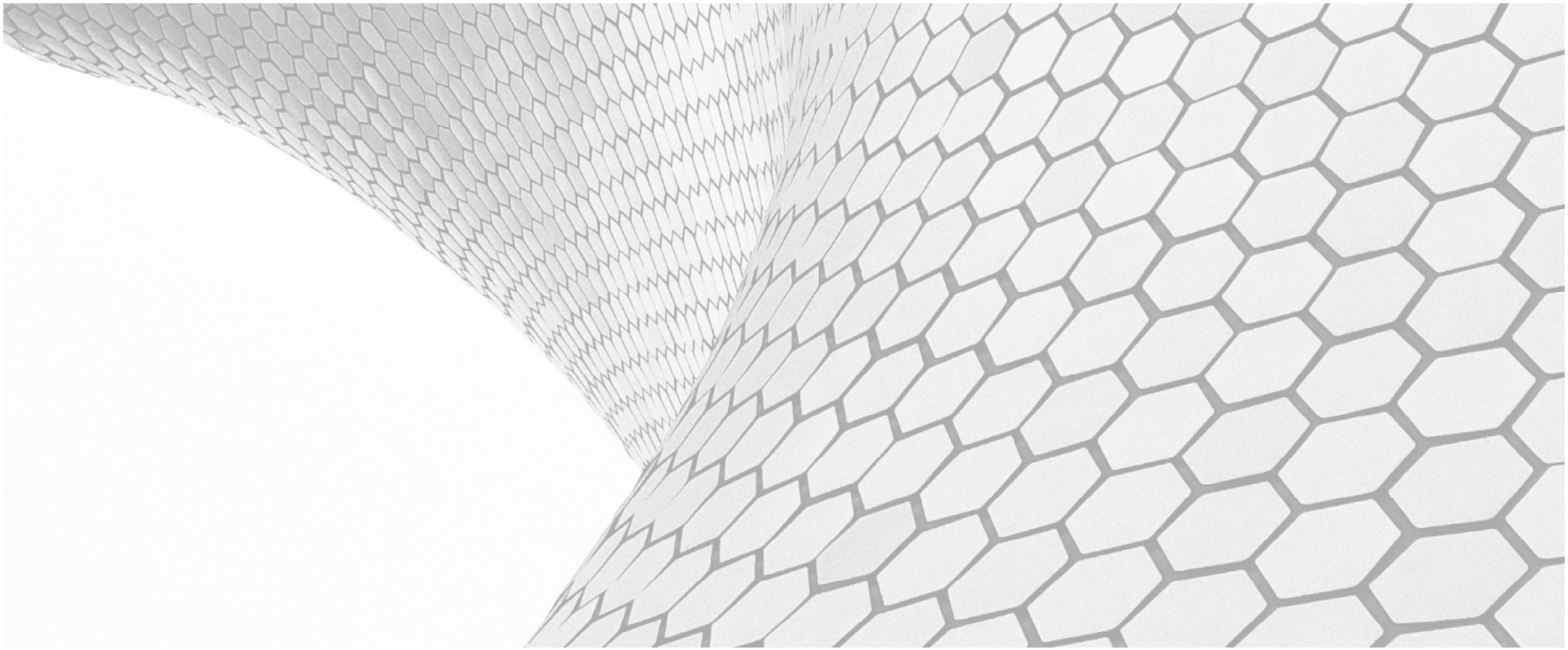
Open Forum | Questions or Comments?



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