EMERGENCY PREPAREDNESS FOR INVESTIGATORS

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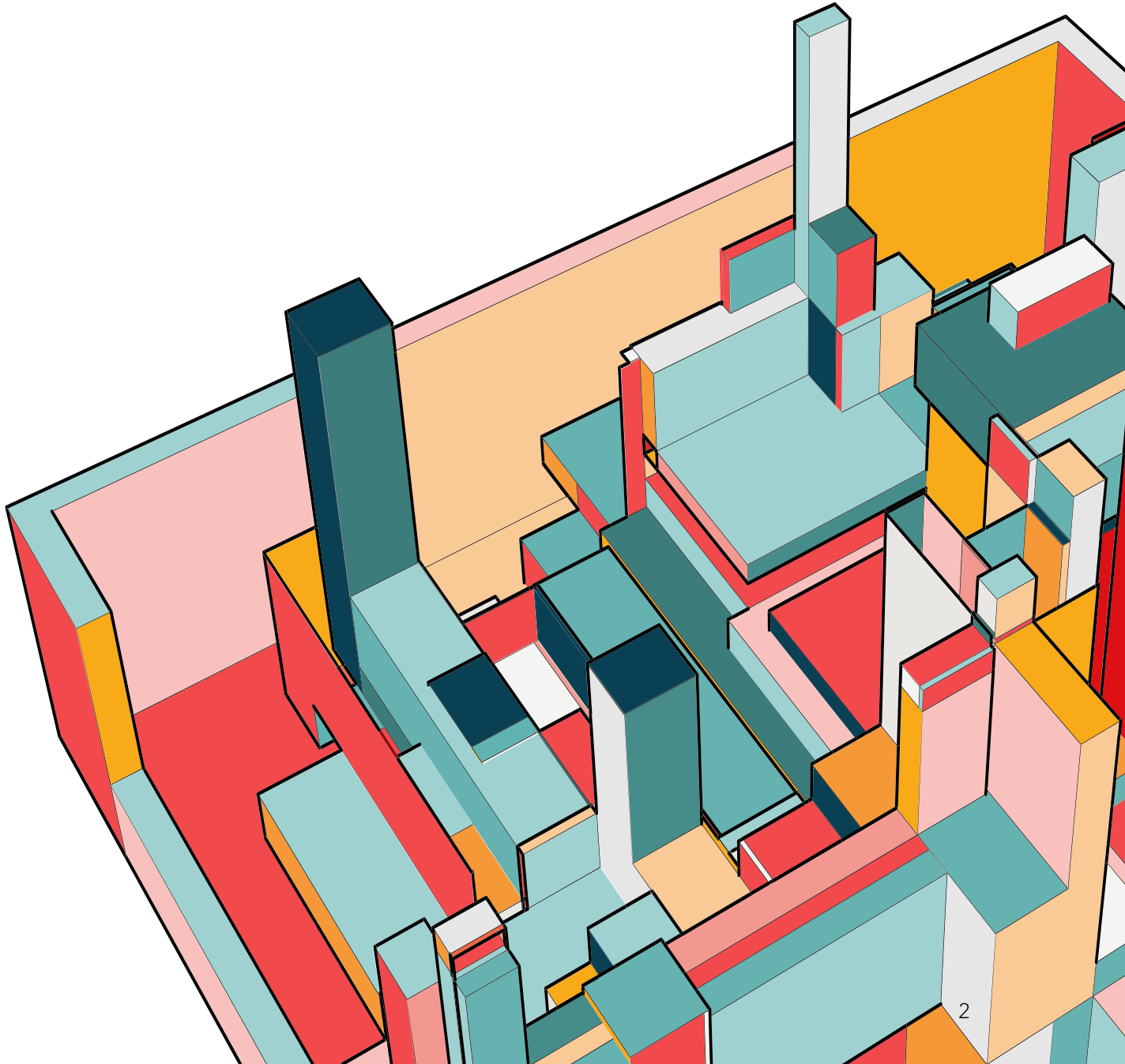
AGENDA

- What happens when there is an emergency?
- How Investigators can prepare for an emergency that impacts enrolled participants.
- What an Investigator should think about once an emergency has happened.
- How to work with the IRB during and immediately following an emergency



BEFORE THE EMERGENCY

- Multiple entities are involved in emergency preparedness and response (including Police, Fire, NIH Division of Emergency Management,& Institute Emergency Managers).
- Depending on the nature of the emergency and its impacts, different entities will take charge.
- There are plans in place to address emergencies such as Emergency Operations Plan (EOP), Occupant Emergency Plans (OEP), and Continuity of Operations (COOP) Plan.
- After a plan is created, it is important to participate in trainings and exercises to further your understanding of the plan.

THIS JUST HAPPENED!

- **What is our emergency?** – A category 4 hurricane has moved up the Chesapeake Bay and impacts the Baltimore/Washington region with sustained winds of 140 mph.
- **Who did it impact?** – Our PI/study team's ability to function and our research participants.
- **How did it impact them?** – Damaged a majority of the NIH Bethesda and Baltimore campuses, with minor impact to NIEHS. Many trees in Baltimore/Washington region where snapped or uprooted, bringing down powerlines. Power outages are expected to last weeks to possibly months.
- **What do we need to be thinking about next?** – The focus of this presentation.

YOU MIGHT BE THINKING…

We've Already Had Emergencies

- Yes, COVID-19, and PDS and we survived, however
- These and other emergencies have turned the spotlight on the need for better overall preparedness, and
- The ability to leverage important lessons that we've learned.

Why Does the IRB Care About This?

- New critical research cannot commence in response to an emergency without IRB approval (Think COVID-19).
- Any changes as a result of the emergency to ongoing research must reviewed by the IRB.
- Our accrediting body **requires**:
  - An emergency plan for the IRB and HRPP,
  - Education about the plan, and
  - Regular testing and evaluation of the plan.

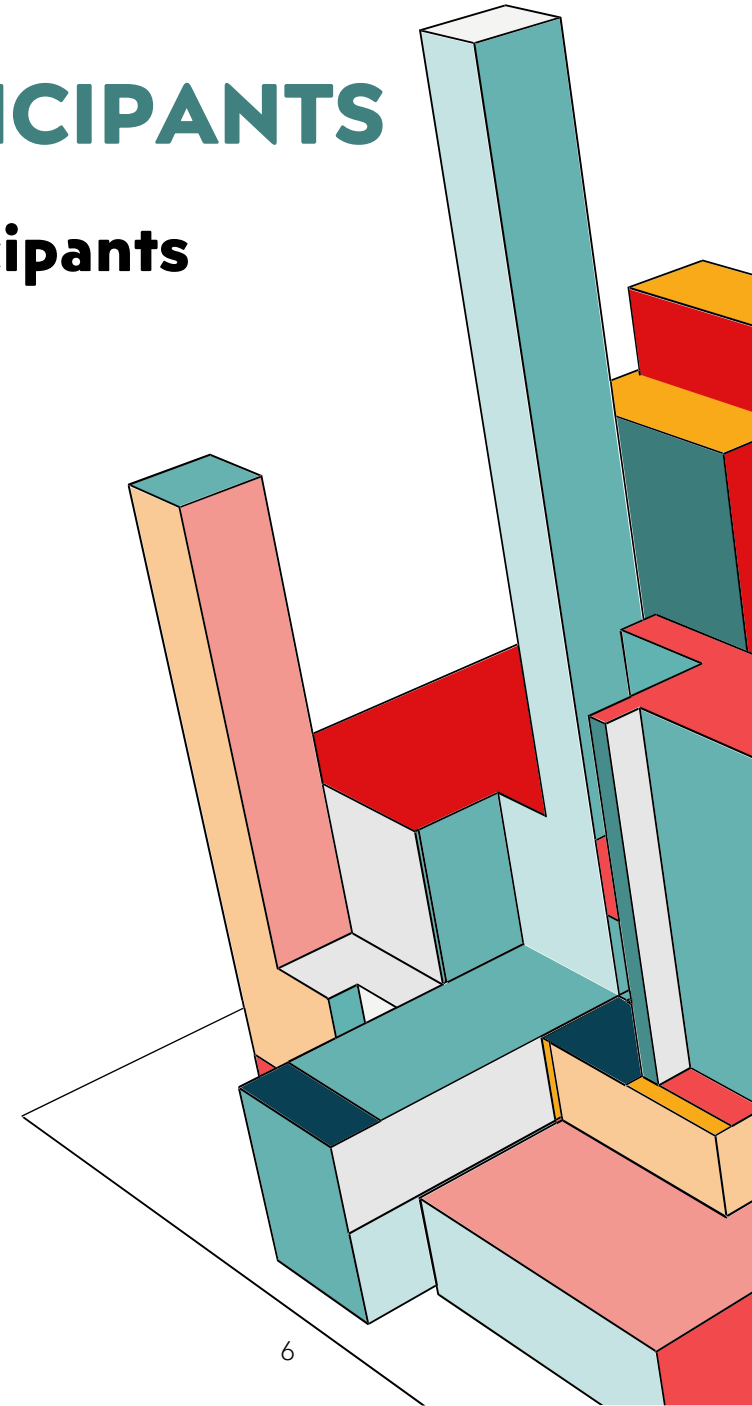
HOW YOU CAN PREPARE YOUR PARTICIPANTS

Collect Emergency Contact Information from Participants

- Maintain emergency contact information for your participants, including names, emails and phone numbers.
- Review and update this information annually.

Provide Study Contact Information to Participants

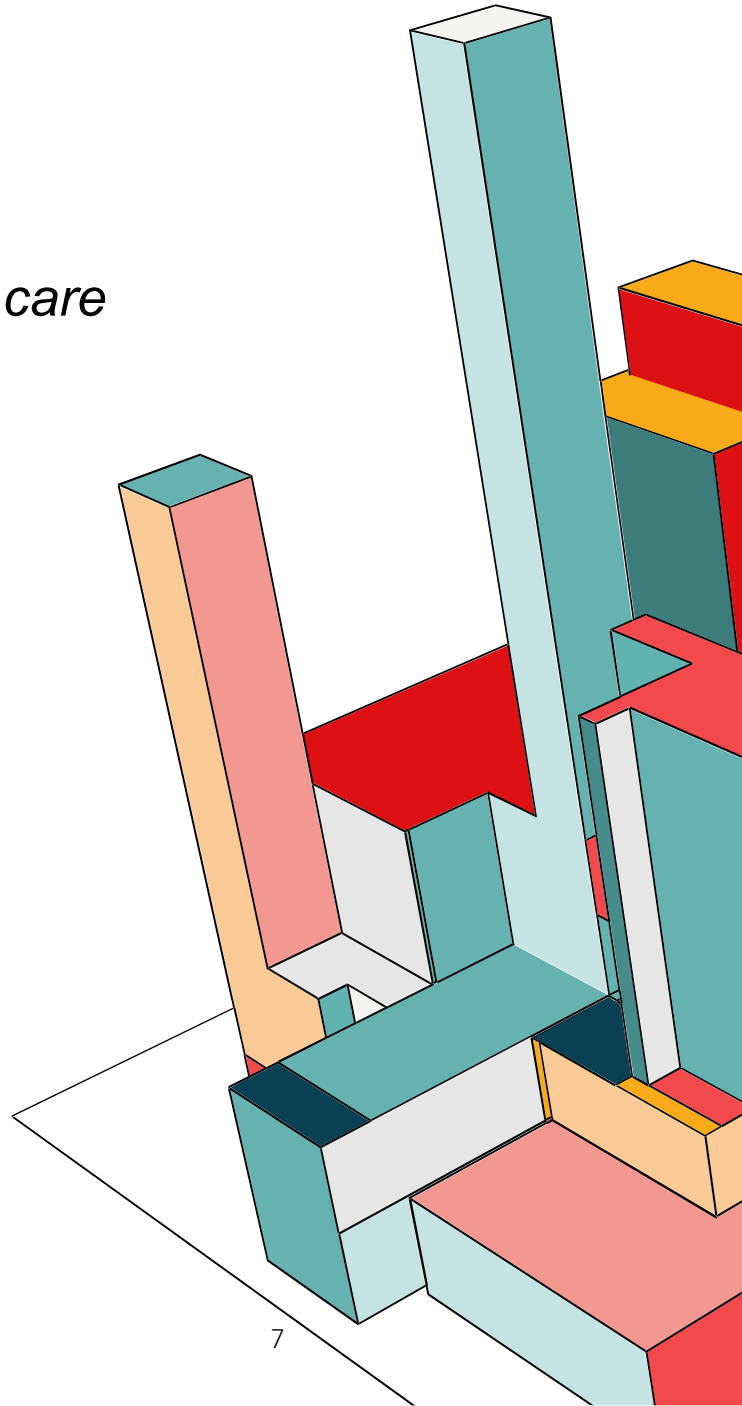
- Ensure that participants know how to contact the study team (usually in the informed consent).
- Be sure that participants know how to contact other study team members as a back up.
- Keep your own emergency contact information current in NED
- Review and update all of this information annually.



IF THE CC PHARMACY IS IMPACTED

Expect that tier one pharmacy will be focused on providing patient care during and immediately following the event.

- Pharmacy maintains strong supply chain & procurement.
  - Robust inventory on-hand,
  - Rapid access to pharmaceuticals via DLA/DOD,
  - ABC/PPV/open market suppliers,
  - Agreement with WRMC.
- Will anticipate patient needs for duration of event:
  - Identify and overstock, including chemo and pain.
- Downtime procedures.



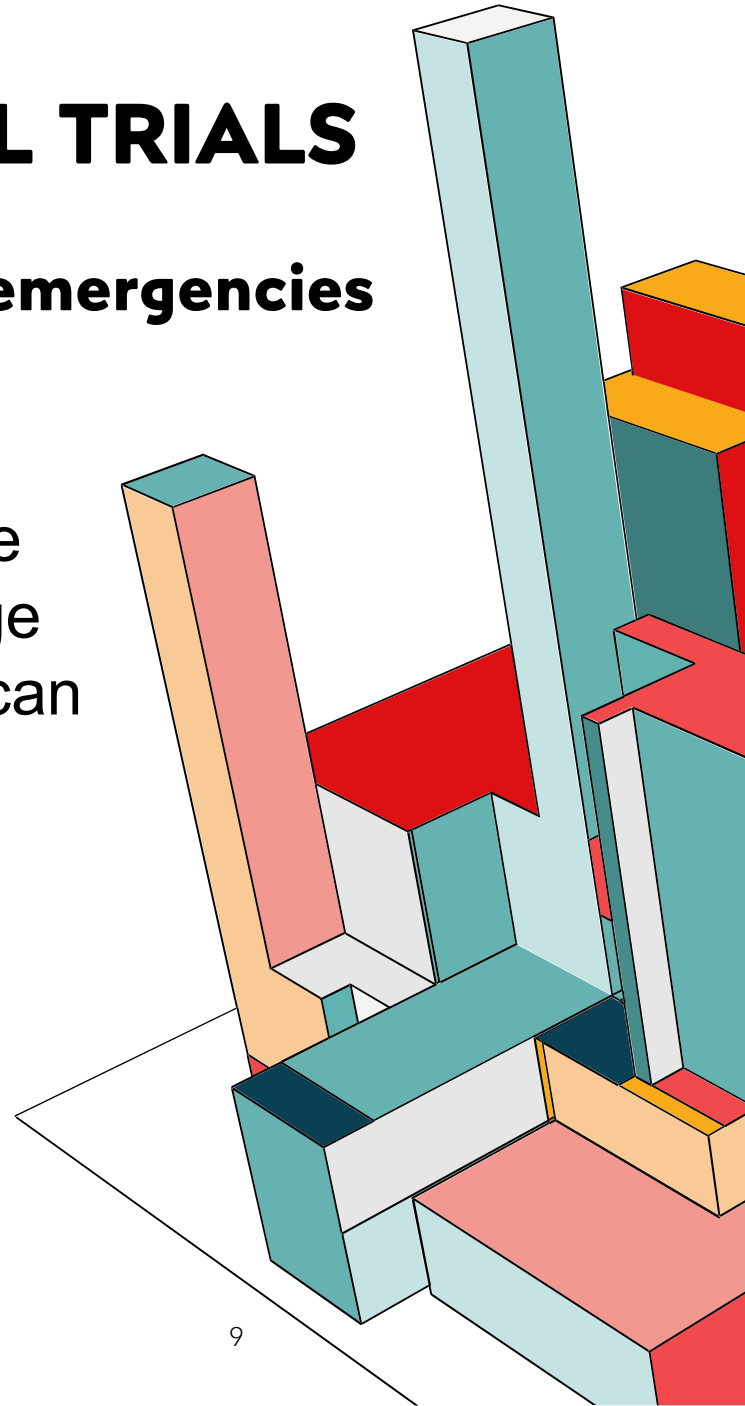
IF THE IDS PHARMACY IS IMPACTED

- If the NIH CC IDS Pharmacy is damaged but safely accessible.
  - Identify storage locations that are not impacted.
    - Assess amount of safe to use stock; inventory & secure.
  - Prioritize forward distribution where possible.
    - Ship IP via OP if available (to participant).
  - Reach out to sponsor(s) for emergency resupply if needed.
  - Downtime procedures for DARs if IDMS system is offline.
  - Management of CTUs.
- Other considerations:
  - Work with study team & IRB.
  - Provide logistical support of modifications e.g. shipping IP to other sites not impacted.

EMERGENCY PLANS FOR CLINICAL TRIALS

Flexible plans that define a process for responding to emergencies

- Patient safety comes first and foremost.
- Emergencies involve uncertainty, may require immediate decisions, and guidance may be inconsistent and change rapidly, and there are limits to how much organizations can prepare in advance.
- Making critical research decisions.
- Flexibility, Modification, Alternatives.
- Protocol Deviation and documentation.



CONSIDERATIONS FOR ONGOING TRIALS

Decisions short of stopping all research activities, Prioritizing patient safety

- Trials may continue or temporarily postpone.
- Recruitment or enrollment may be halted but research activities continue on existing participants.
- Studies that can continue via alternate mechanisms, such as remote study visits, video or conference calls.
- Sponsors in consultation with clinical investigators and IRB make the decision.

PROTOCOL MODIFICATIONS AND DEVIATIONS

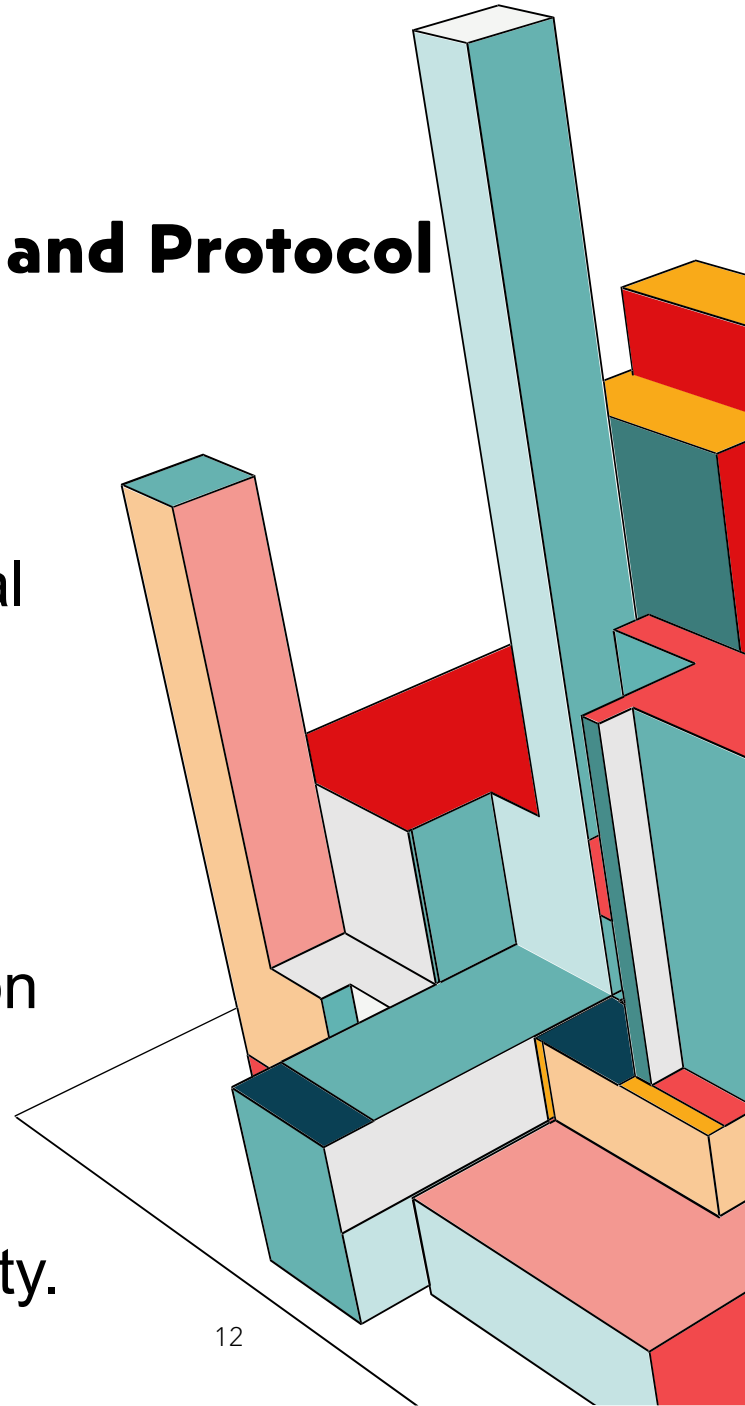
Necessary Changes, Including Protocol Deviations Can Be Unavoidable.

- Changes to a protocol usually require review and approval by the IRB and, in certain cases, the FDA.
- Modifications aimed at mitigating immediately hazards or safeguarding participants can be made without prior IRB approval but must be reported subsequently.
- Investigators must document any modifications as protocol deviations.
- Thorough records are essential for regulatory and sponsor audits.
- Protocol amendments that are not required to prevent imminent risks to patients can be implemented after submission to FDA and IRB approval.

DOCUMENTATION

Comprehensive Documentation of Emergencies and Protocol Deviations

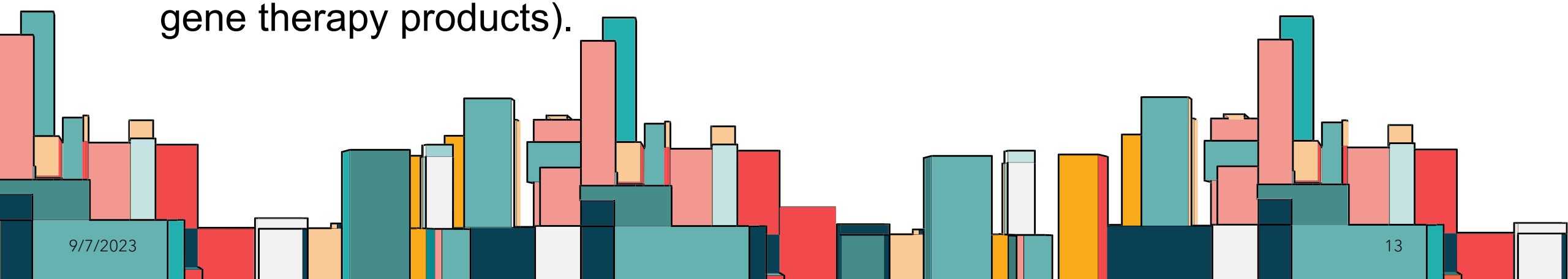
- Maintain comprehensive documentation for incident reports, emergency-related actions, decisions, and communications, as well as any modifications to the trial protocol.
- It is essential to report both emergencies and protocol deviations in trial documentation and final reports.
- Protocol deviations must be assessed for their impact on participant safety and data integrity.
- Sponsors and investigators collaborate with the IRB to prioritize reporting deviations impacting participant safety.



ALTERNATIVES TO PROTOCOL PROCEDURES

Maintaining Protocol Consistency and Patient Safety

- Alternative processes should be consistent with the protocol to the extent possible, and the rationale behind implementing any contingency measures must be documented.
- Alternative secure delivery methods or alternative administration, such as home nursing or utilizing trained non-study personnel at alternative sites.
- Modified storage and handling conditions could negatively impact product stability for complex investigational products (e.g., cellular therapy and gene therapy products).



PARTICIPANT SAFETY AND TRIAL INTEGRITY

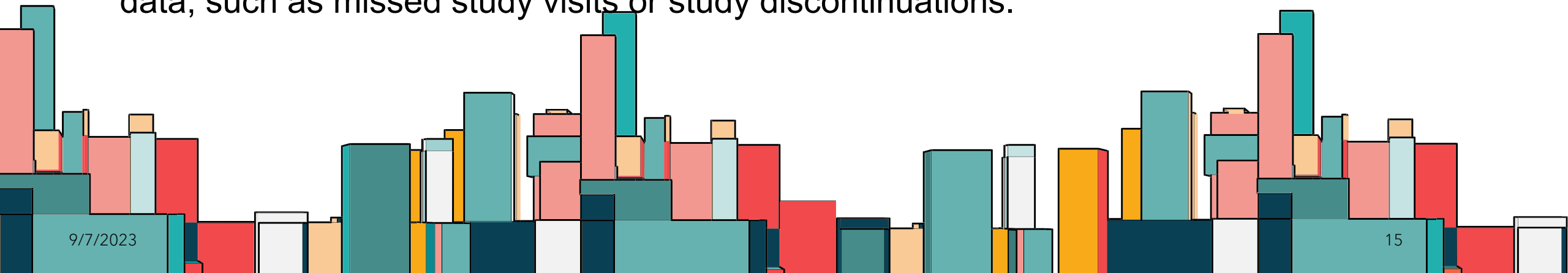
Evaluate impact and risk mitigation

- For alternative site infusions, all applicable requirements concerning IP maintenance, storage conditions, reconstitution specifications, and accountability remain and must be addressed and documented.
- For changes in protocol assessments (e.g., vital signs, visits, safety labs), document how the emergency caused changes, specifying the duration, affected participants, the impact, and how to mitigate risks to participants, including the need to discontinue IP.
- Specific procedures should be outlined for safeguarding biospecimens and data backups.

CRITICAL SAFETY AND EFFICACY DATA

Consult the Reviewing Division

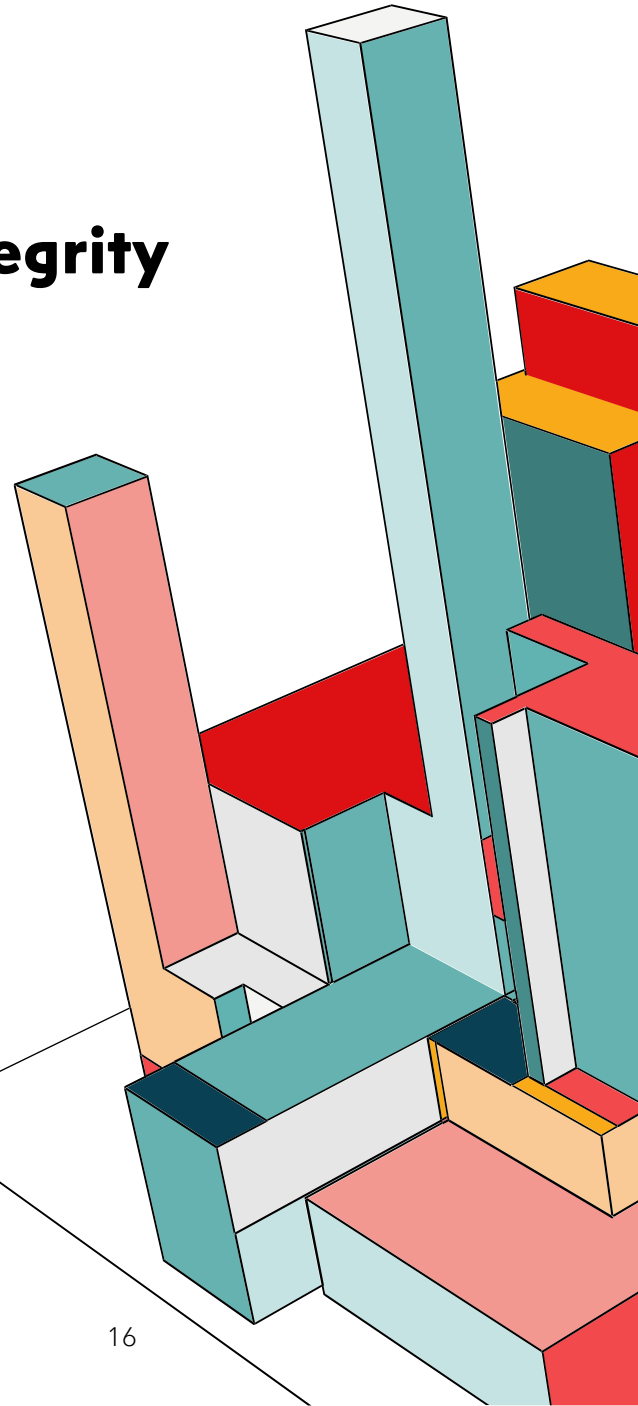
- Collection of efficacy endpoints assessments may be modified, such as use of virtual assessments, delays in assessments, and alternative sample collection.
- Uncollected and modified efficacy endpoints must be documented, detailing the reason and If the data management or statistical analysis plan changed.
- Changes should be addressed in the statistical analysis how protocol deviations related to emergency , such as IP and/or study discontinuation, alternative procedures used to collect critical safety/ efficacy data will be managed.
- Case Report Form should capture specific information explaining the basis of the missing data, such as missed study visits or study discontinuations.



MONITORING

Alternative Approaches To Ensure Data Quality And Integrity

- If on-site monitoring is not possible, central and remote monitoring or telephone contact with the sites to review study procedures, participant status and study progress.
- Communication plan for virtual data review meetings or regular updates.
- Delays in monitoring may result in delayed identification of protocol deviation including major deviations not due to the emergency.
- Document when monitors were unable to access, or had to delay monitoring and whether delayed identification was due to postponed monitoring.

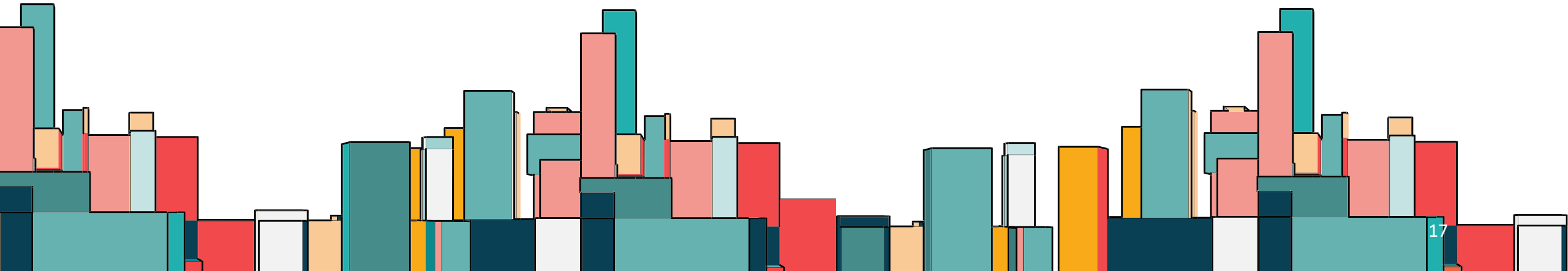


WORKING WITH THE SPONSOR

During the emergency, the Sponsor's response should assure the following:

- ✓ Safety of trial participants.
- ✓ Maintaining compliance with good clinical practice (GCP) and applicable regulations, if possible.
- ✓ Minimizing risks to trial integrity for the duration of the emergency.

For FDA-regulated clinical trials, active communication between Sponsor and FDA is essential.

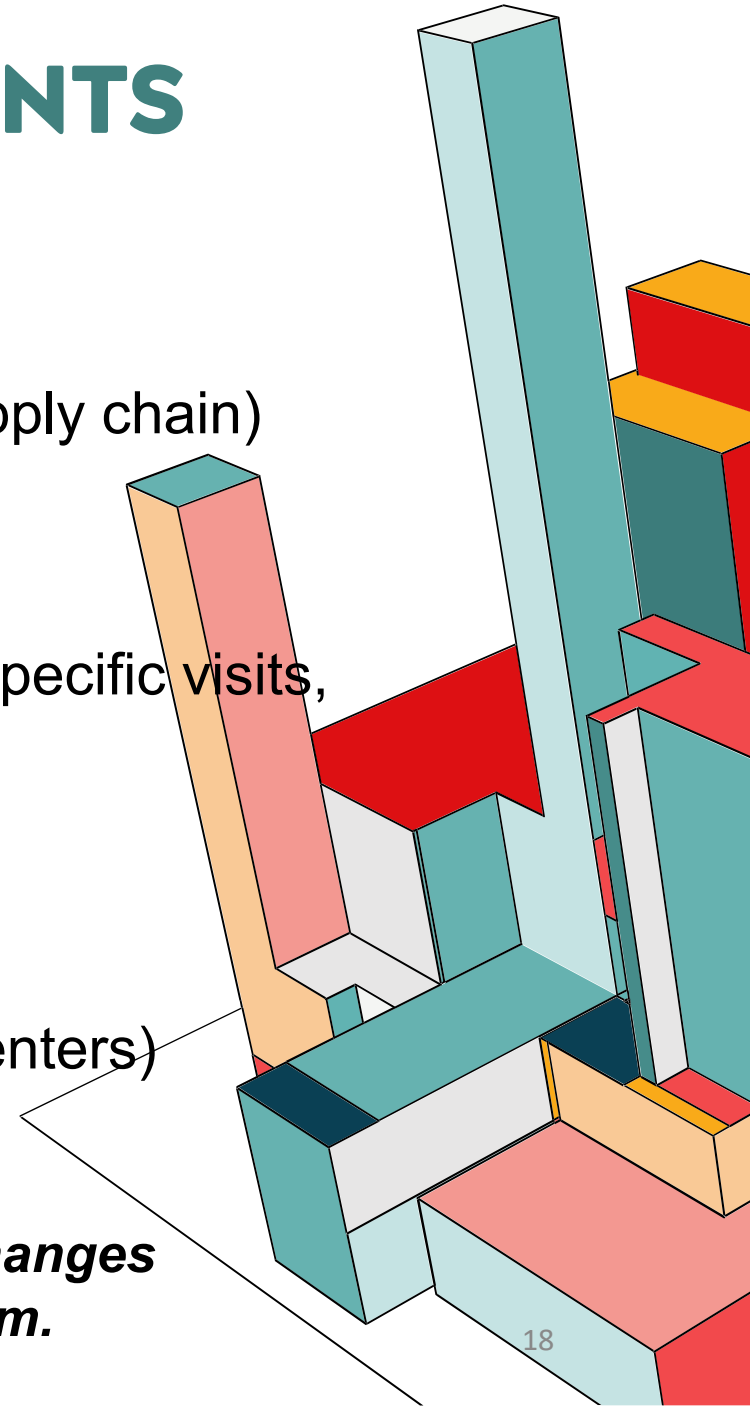


SAFETY OF THE TRIAL PARTICIPANTS

- Study decisions may include:
  - ✓ Continuing trial recruitment
  - ✓ Continuing use of the investigational product (impact on supply chain)
  - ✓ Changing the safety patient monitoring during the trial

- If trial participants are not able to come to the site for protocol-specific visits, sponsors should evaluate alternate methods:
  - phone contact
  - virtual visit
  - alternative location for assessment (local labs or imaging centers)

In all cases - trial participants should be kept informed of changes to the study and monitoring plans that could impact them.

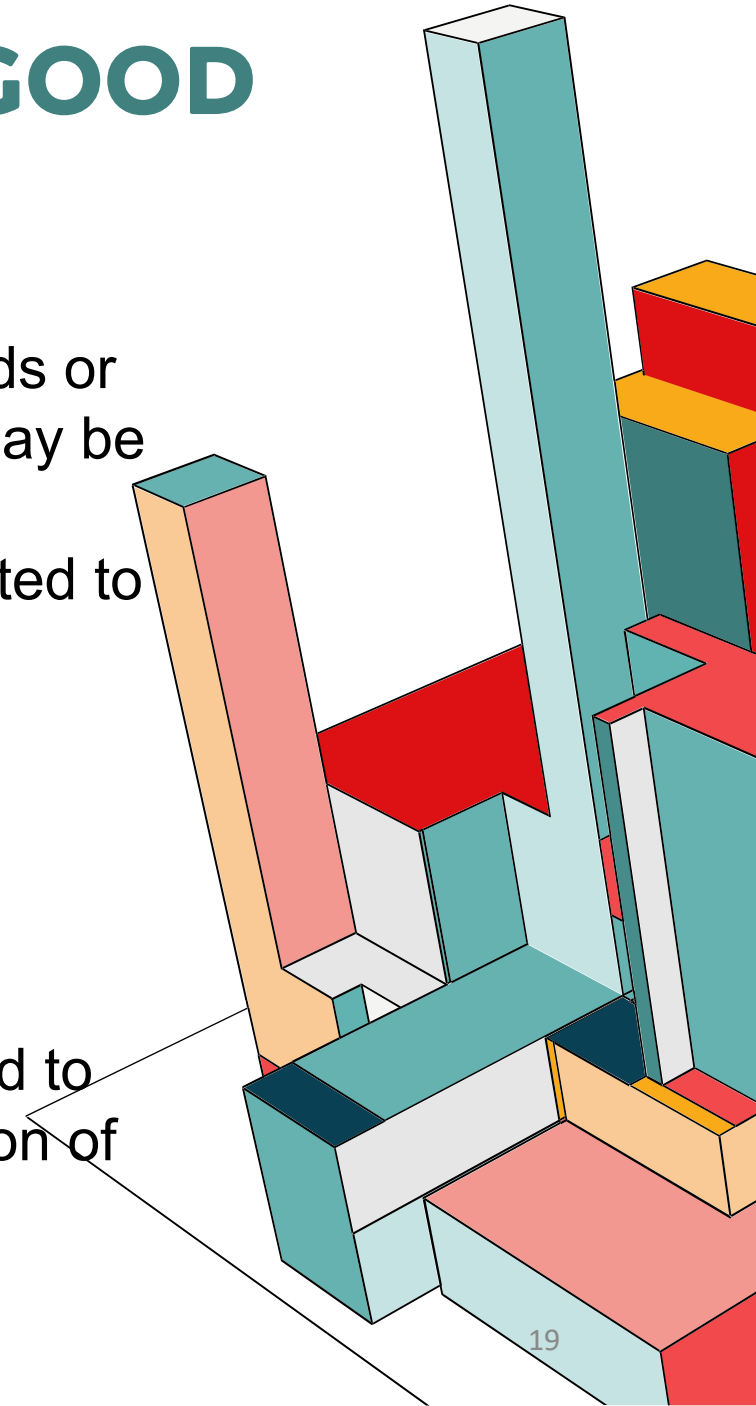


MAINTAINING COMPLIANCE WITH GOOD CLINICAL PRACTICE (GCP)

- **Protocol Changes**
  - ✓ Protocol changes focused on eliminating immediate hazards or to protect the life and well-being of research participants may be implemented without IRB approval or before filing an amendment to the IND or IDE **but** are required to be reported to the FDA and IRB afterwards.

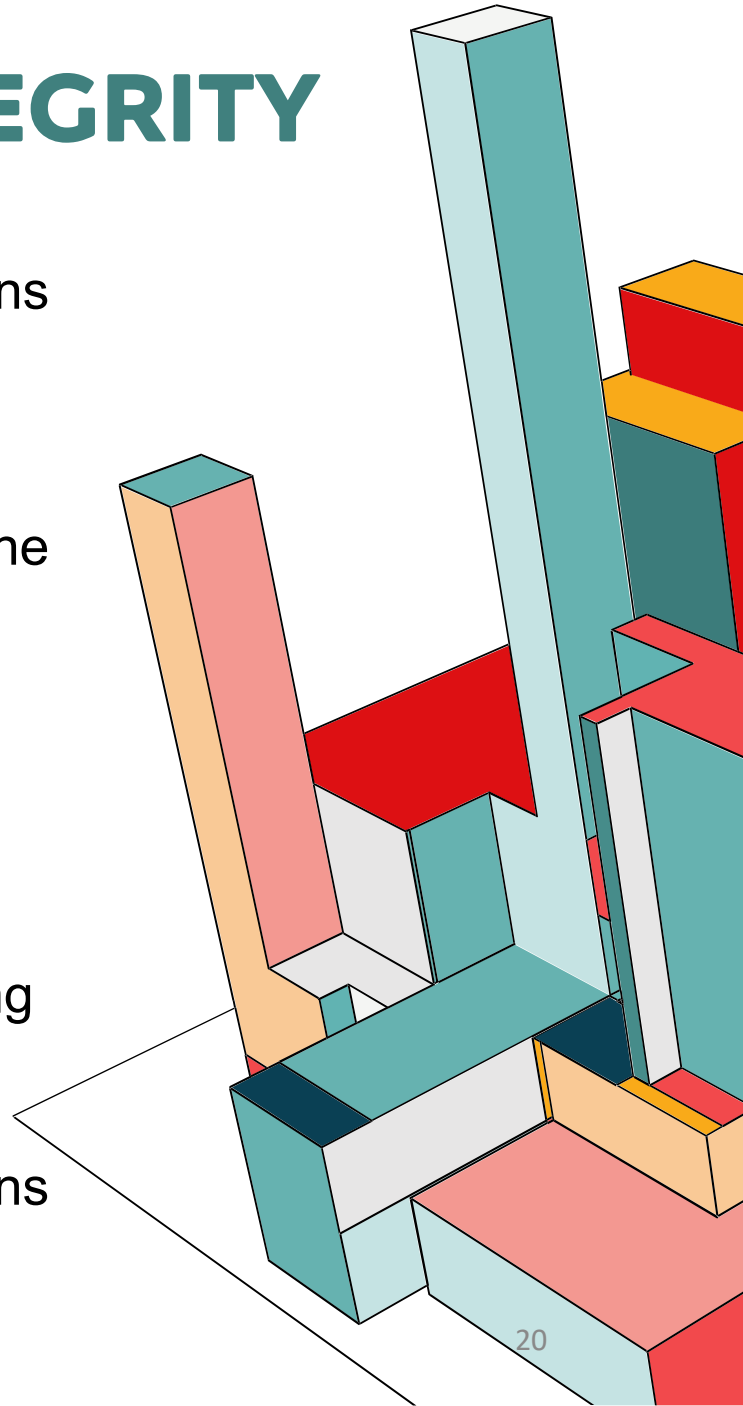
- **Documentation**
  - ✓ Sponsors and PIs should document the reason for any contingency measures implemented.

  - ✓ Sponsors and PIs should document how restrictions related to the emergency led to changes in study conduct and duration of those changes.



MINIMIZING RISKS TO TRIAL INTEGRITY

- Changes in study visit schedules, missed visits, or patient discontinuations may lead to missing information.
- It is recommended to capture specific information in the case report form that explains the basis of the missing data, including the relationship to the emergency for missing protocol-specified information.
- If changes in the protocol lead to amending data management and/or statistical analysis plans, the sponsor should consider consult with the FDA.
- It is understandable that protocol modifications may be required, including unavoidable protocol deviations during an emergency.
- Efforts to minimize impacts on trial integrity, and **to document** the reasons for protocol deviations, are important.



CAN'T FOLLOW THE IRB-APPROVED PROTOCOL? WORK WITH THE IRB

- Any modification to the research must be approved by the IRB before it may be implemented, unless it is necessary to eliminate an immediate hazard to a participant(s) and there is not enough time to get IRB approval.
- Avoid further delays – When submitting a modification, tell the IRB what it needs to know: explain the problem, how it impacts participants, your changes and any needed participant follow-up.
- If you must take an immediate action to protect a participant(s), report it to the IRB as Reportable New Information (RNI) within 7 days of the change.
- Single patient deviations/modifications may be submitted, if needed.
- Consult IRBO for how to submit temporary changes to the research as result of the emergency.
- If the change impacts more than 1 of your studies be sure to submit a modification for each affected study.

WHAT IF THE PROTOCOL IS HALTED OR STOPPED DUE TO THE EMERGENCY?

- If the PI, IC or Sponsor halts or stops the study unexpectedly as a result of the emergency, submit an RNI to the IRB within 7 calendar days (Manual Chapters 801 and 500), and
- Include a plan describing what actions, if any need to be taken to protect the rights, safety and welfare of any enrolled participants.
- Submit any modification(s) to support the actions proposed in the plan for review and approval by the IRB, and/or
- Submit deviations/RNIs per MC 801.
- If the research is temporarily halted, describe to the IRB, who will determine, and on what basis, the research will restart.

IF THE IRB IS IMPACTED BY THE EMERGENCY

- The IRB may have to temporarily change procedures, such as:
  - Alternate submission procedures, and/or
  - Alternate IRB meeting or review procedures.
  - The IRB may have to prioritize new research or suspend some research that is unsafe to conduct as result of the emergency.
- The IRB may have to add or change some procedures, or
- The Institutional Official may have to make temporary exceptions to policies.

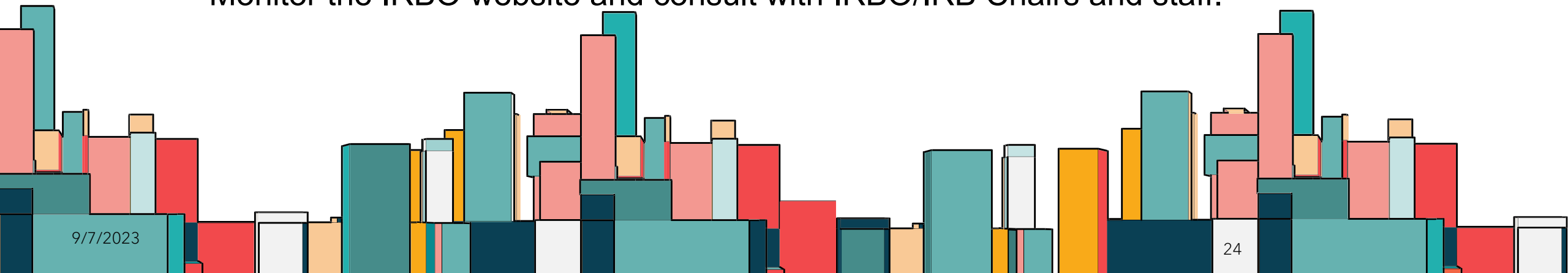
How will I know if things have changed?

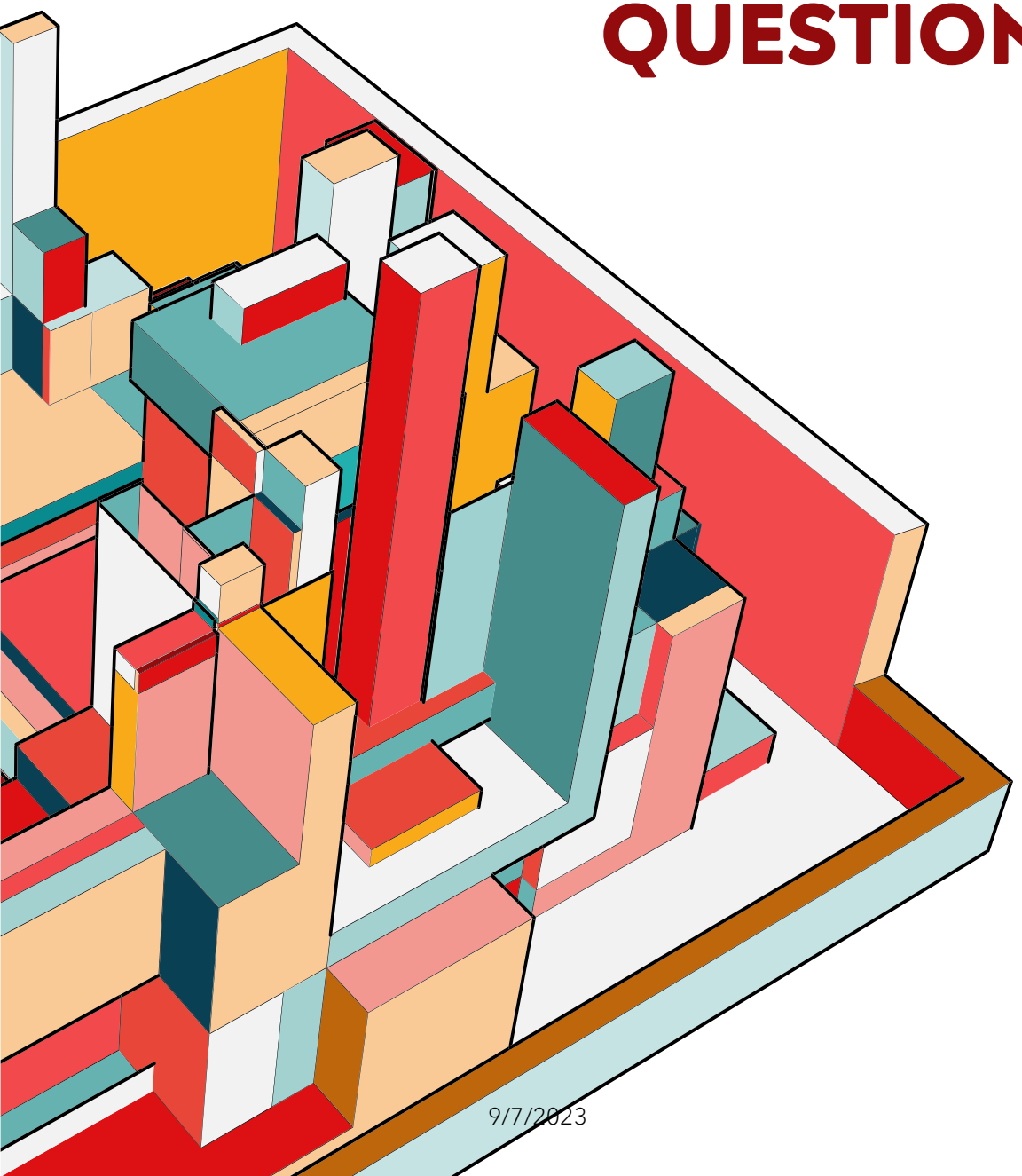
- Monitor the IRBO website for instructions and information (https://irbo.nih.gov/confluence/), and
- Look for email blasts or contact the IRB office.

FOLLOWING THE EMERGENCY

It will take time to return to normal

- For major emergencies, expect delays and prepare for things to be disrupted for 30 days or longer.
- It will take all of us working together to make the recovery/reconstitution period safe for our research participants.
- Expect regular communications from the OHSRP Director or designee and IRB.
- Expect temporary changes and sometimes multiple changes to procedures.
- Expect that the NIH or your IC to change priorities some of which may impact your research.
- Expect shortages that may impact your research.
- Monitor the IRBO website and consult with IRBO/IRB Chairs and staff.





QUESTIONS FOR THE PANEL?

RESOURCES

- IRBO website: https://irbo.nih.gov/confluence/
- IRBO email: irb@od.nih.gov
- IRBO number: 301-402-3713
- ORSC Regulatory Support Section email: REGSupportORSC@cc.nih.gov
- ORSC Clinical Monitoring email: ORSC_CRQM@cc.nih.gov
- Pharmacy (Main): 301-480-6337

THANK YOU