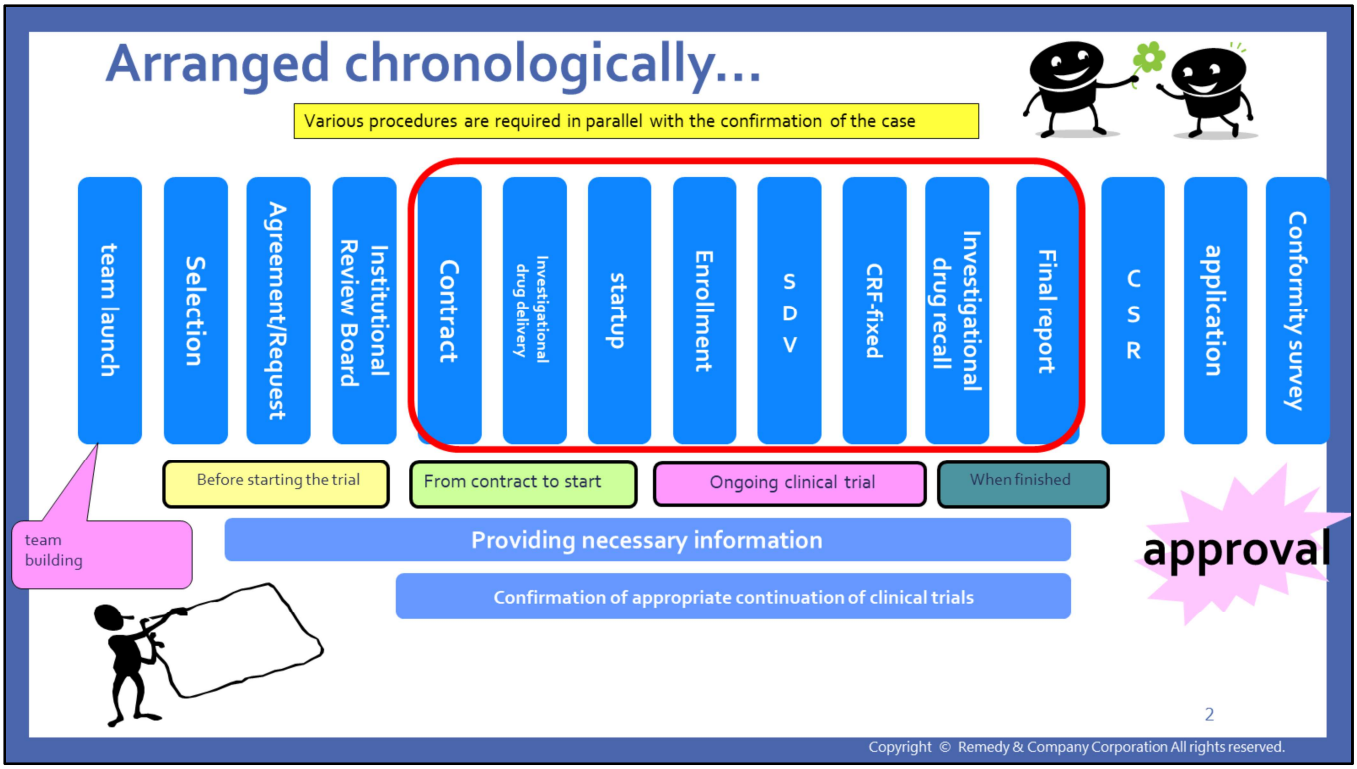
【 Procedures during clinical trials 】

- Amendments to Clinical Trial Documents -

This section explains how to handle any changes or updates to clinical trial documents during the trial.



Overview of Clinical Trial Process and Document Amendments

The clinical trial process is divided into four main parts:

Part 1: Before the trial begins (yellow section)

Part 2: From contract signing to trial start (green section)

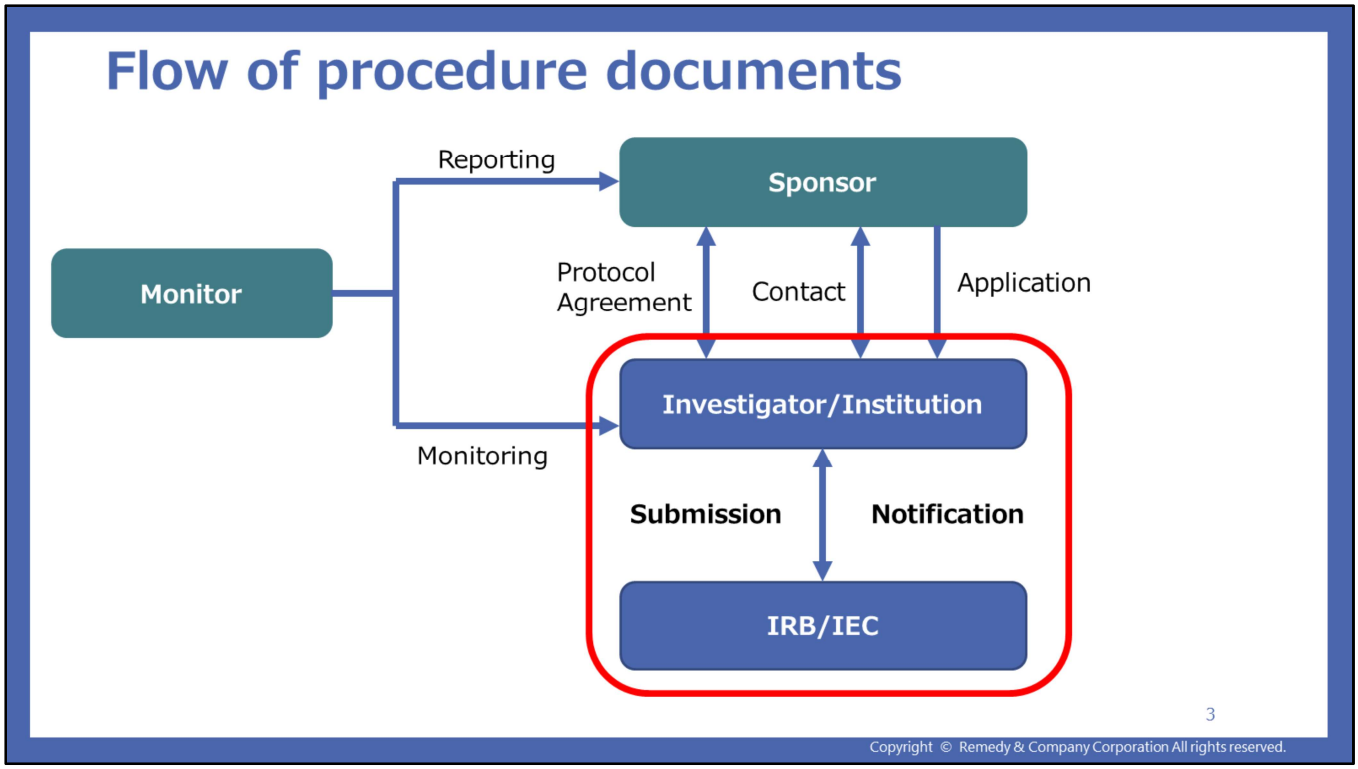
Part 3: During the trial (pink section)

Part 4: After the trial is completed (dark green section)

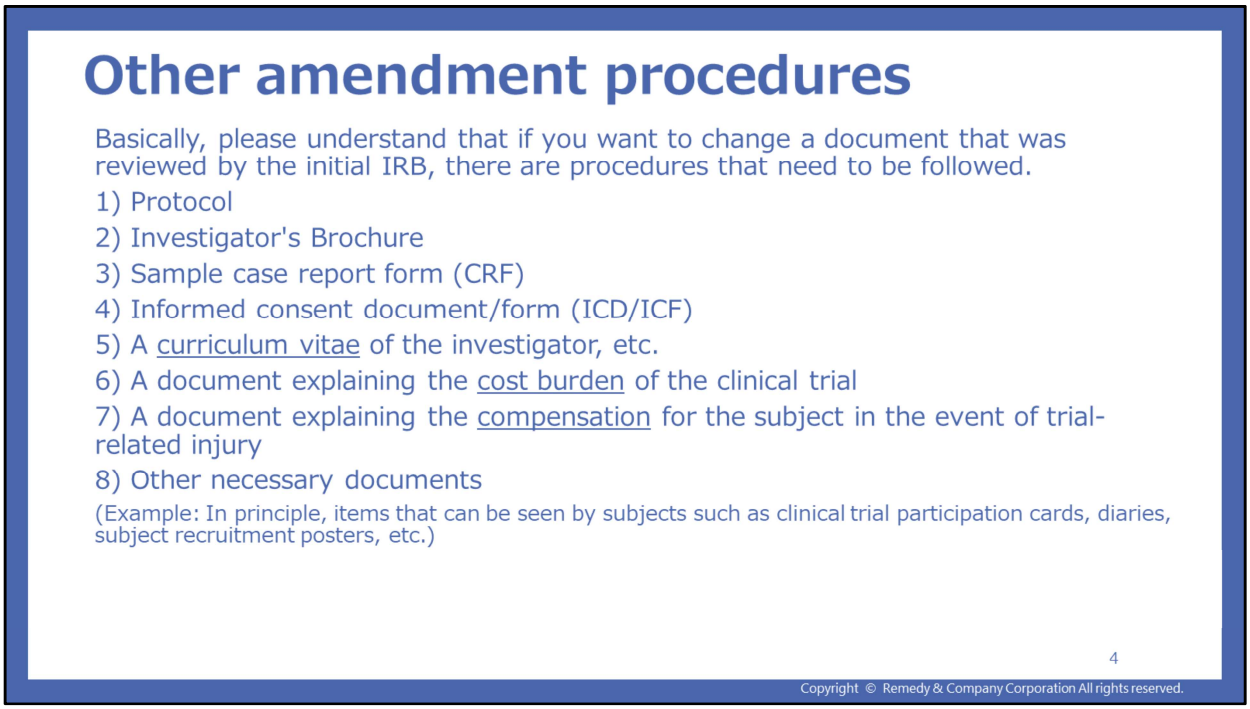
Document Amendments:

Any changes to clinical trial documents (such as protocol, informed consent forms (ICF), or patient-facing materials) may be required from **Part 2 to Part 4**.

- If a change impacts participant safety, clinical sites and participants must be informed as soon as possible with all necessary documentation.
- All amendments must be properly tracked and documented.
- Each change should be reviewed to assess its impact on the clinical site and participants, including whether the trial can continue as planned.



This flow is presenting the person involved when there is an amendment to clinical trial documents.
Once changes are confirmed and documented using the required site-specific form, the clinical site (investigator/institution) must submit the updated documents to its Institutional Review Board (IRB) or Independent Ethics Committee (IEC) for review and approval.
It is crucial to remember that **only IRB/IEC-approved documents** can be implemented at the clinical site.



Document Amendments Requiring IRB Review

If you need to make changes to documents that were initially reviewed by the IRB, specific procedures must be followed. The documents that may require updates include:

1. Protocol
2. Investigator's Brochure
3. Sample Case Report Form (CRF)
4. Informed Consent Document/Form (ICD/ICF)
5. Investigator’s Curriculum Vitae
6. Document outlining the cost burden of the clinical trial
7. Document explaining compensation in case of trial-related injury
8. Other necessary documents (e.g., materials visible to participants like trial participation cards, diaries, or recruitment posters)

There maybe some additional documents/forms required as per local specific requirement, so please make sure to confirm with local guideline and submit necessary documents .

This slide is presenting about sponsor role as per ICH-GCP.

Key Points are below.

1. Sponsor Responsibilities:

   a. Obtain the name and address of the investigator's/institution's IRB/IEC.

   b. Get a statement from the IRB/IEC confirming compliance with Good Clinical Practice (GCP) and relevant laws.

2. Approval Documentation:

Secure documented IRB/IEC approval or favorable opinion for the trial.

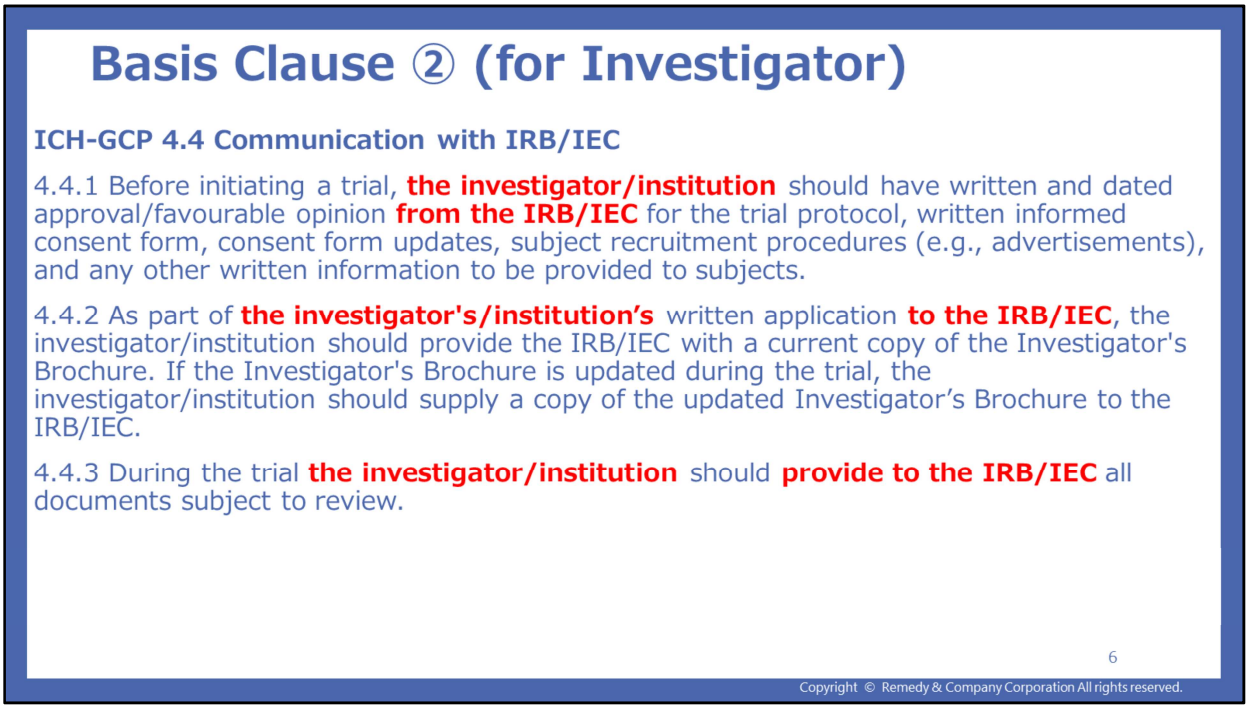
If requested, the sponsor should also receive a copy of key documents such as the protocol, informed consent forms, subject recruitment procedures, and any other materials provided to subjects or requested by the IRB/IEC.

3. Handling Conditional Approvals:

If the IRB/IEC requires modifications to the protocol, informed consent, or other materials, the sponsor must obtain copies of the modified documents along with the date of final approval.

4. Reapprovals/Re-evaluations:

The sponsor must also collect records of any reapprovals or re-evaluations by the IRB/IEC, including the dates these approvals were issued.



This slide presents the investigator role as per ICH-GCP.

Key Points regarding **Communication with IRB/IEC** are below.

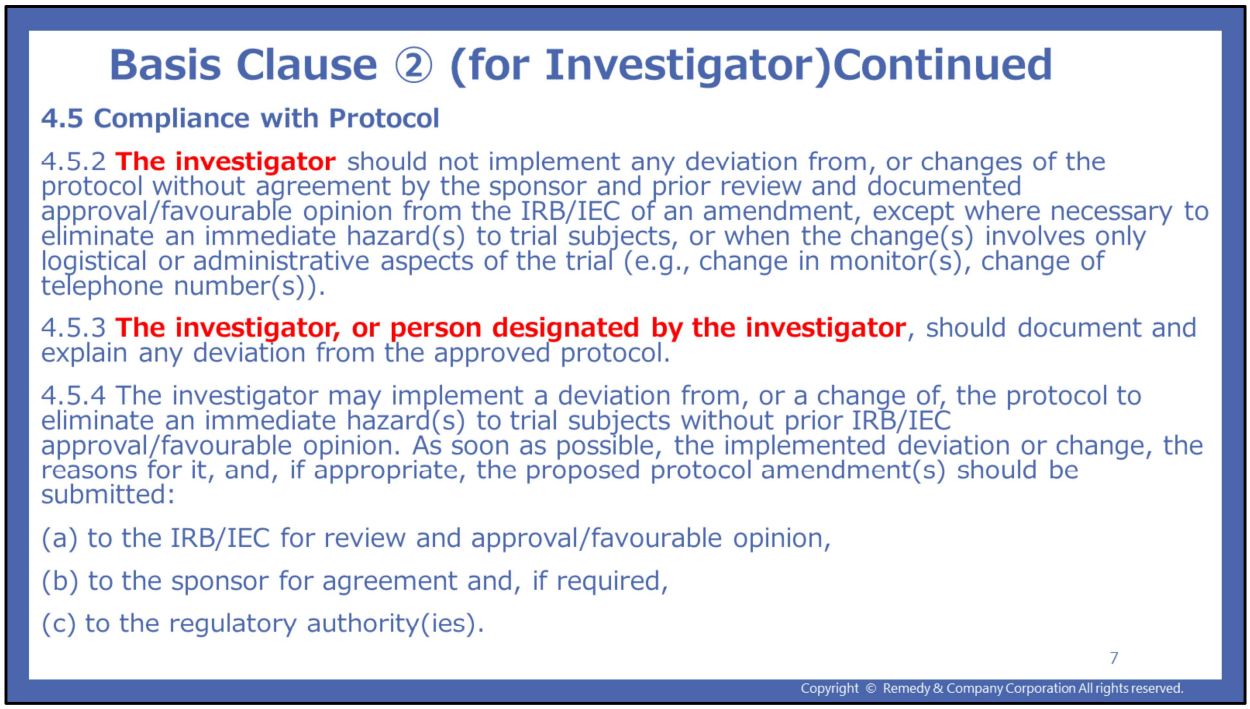
Pre-Trial Approvals (4.4.1): Before starting the trial, the investigator/institution must obtain written and dated IRB/IEC approval or a favorable opinion for:

- The trial protocol
- Written informed consent forms (and updates)
- Subject recruitment materials (e.g., advertisements)
- Any other written information provided to subjects

Submission of Investigator's Brochure (4.4.2):

- The investigator/institution must provide the IRB/IEC with a current Investigator's Brochure as part of their application.
- If the Investigator's Brochure is updated during the trial, a copy of the updated version must be submitted to the IRB/IEC.

Ongoing Communication During the Trial (4.4.3):During the trial, the investigator/institution must continue to submit all documents that require IRB/IEC review.



Key Points regarding **Compliance with Protocol** are below.

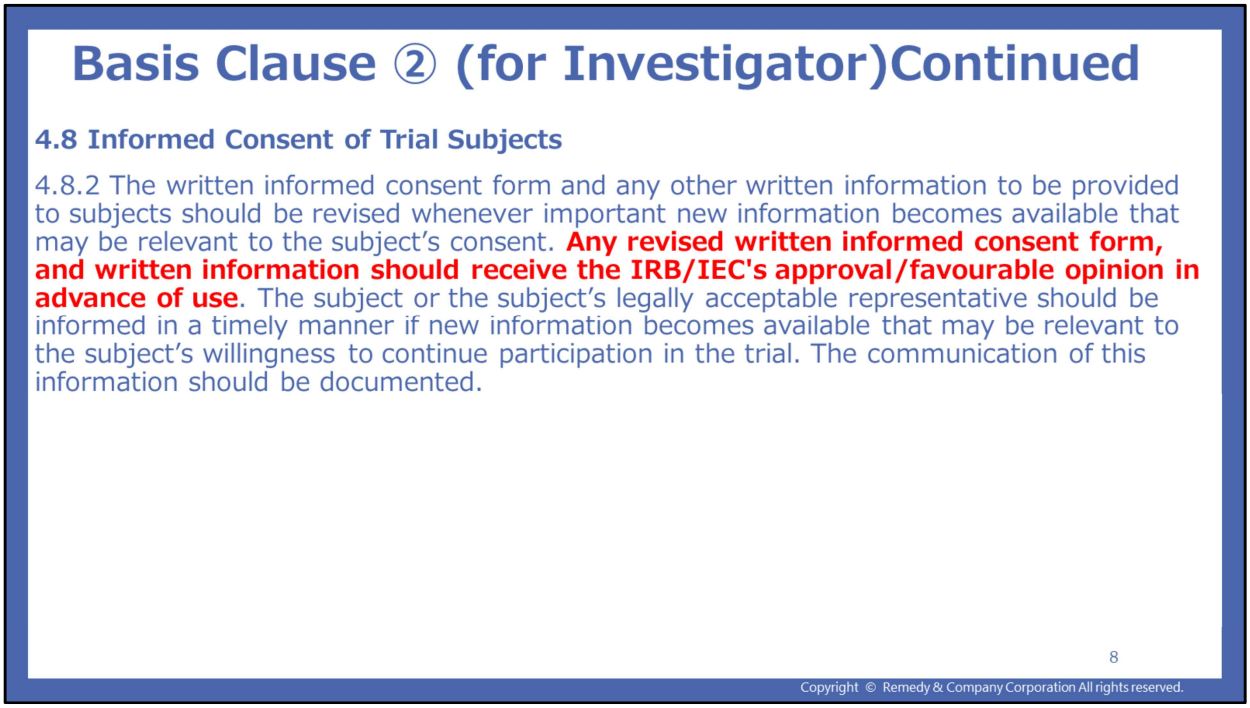
Protocol Changes Require Approval (4.5.2):The investigator must not make any changes to the protocol without:

- Approval from the sponsor
- Prior review and approval from the IRB/IEC, unless:
- The changes are necessary to protect trial subjects from immediate danger, or
- The changes are purely logistical or administrative (e.g., changing monitors or contact information).

Document Deviations (4.5.3):Any protocol deviations must be documented and explained by the investigator or a designated team member.

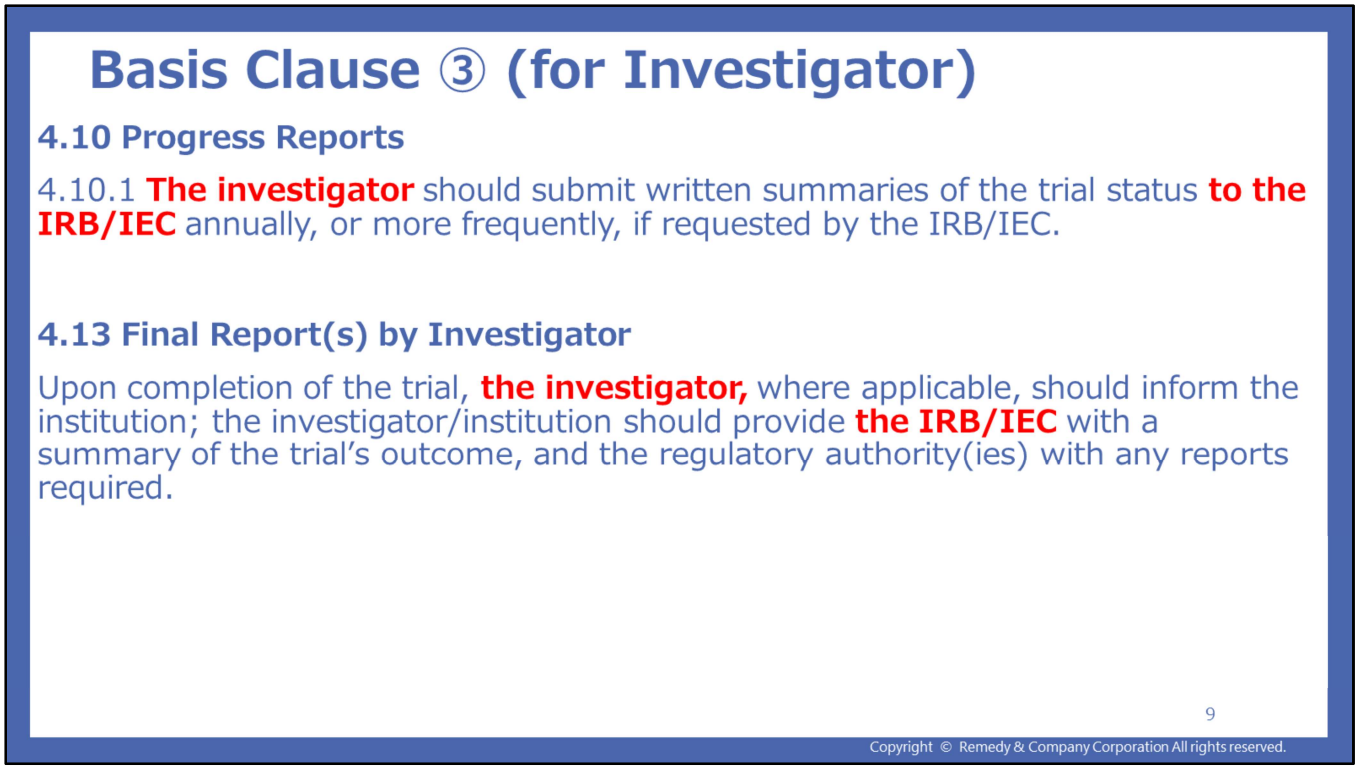
Emergency Changes to Protect Subjects (4.5.4):The investigator can make urgent protocol changes without IRB/IEC approval if required to remove an immediate hazard to participants. Afterward:

- The changes must be submitted to the IRB/IEC for review as soon as possible.
- The sponsor must be informed and agree to the changes.
- Regulatory authorities must also be informed if required.



Key points regarding **Informed Consent** are below.

- Revisions and Approval: Written informed consent forms must be updated whenever new relevant information arises, and any revisions must receive prior approval from the Institutional Review Board (IRB) or Independent Ethics Committee (IEC).
- Timely Communication: Subjects or their representatives must be promptly informed of significant new information that could affect their willingness to continue participation, with all communications documented for clarity.



Lastly, regarding **Submission of Progress Reports:**

Investigators must submit written summaries of the trial status to the Institutional Review Board (IRB) or Independent Ethics Committee (IEC) at least annually, or more frequently if requested by the IRB/IEC. It is important to also check with local site requirements and make sure to report within the required timeline.

Final Reporting after the trial's completion, the investigator must inform the institution and provide the IRB/IEC with a summary of the trial's outcomes, along with any required reports to regulatory authorities.

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