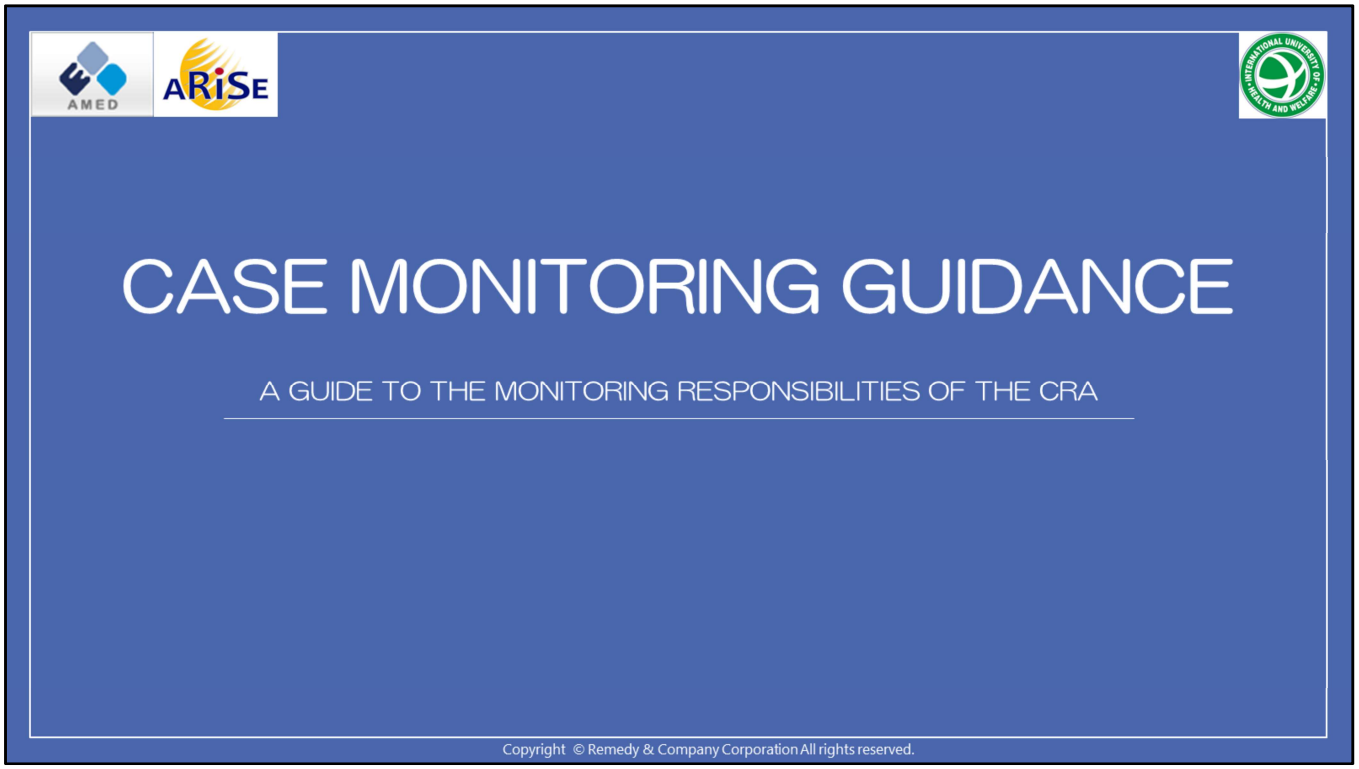
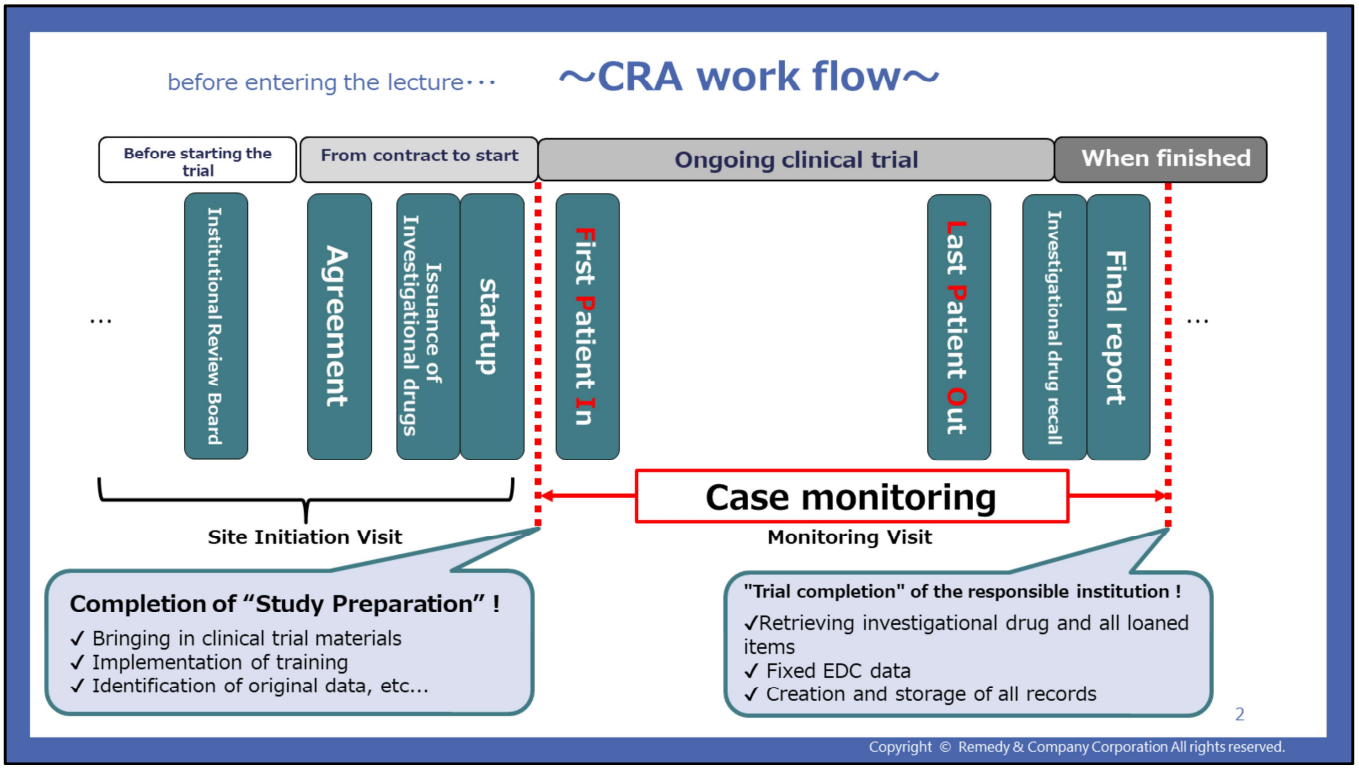


Hello there.

Today, we will be discussing Case Monitoring Guidance, with a focus on the key responsibilities of the Clinical Research Associate (CRA) during clinical trials.

As CRAs, it is critical to ensure that trials are conducted safely, ethically, and in accordance with protocol and regulatory standards. Let's dive into the core responsibilities that guide your work as a CRA.



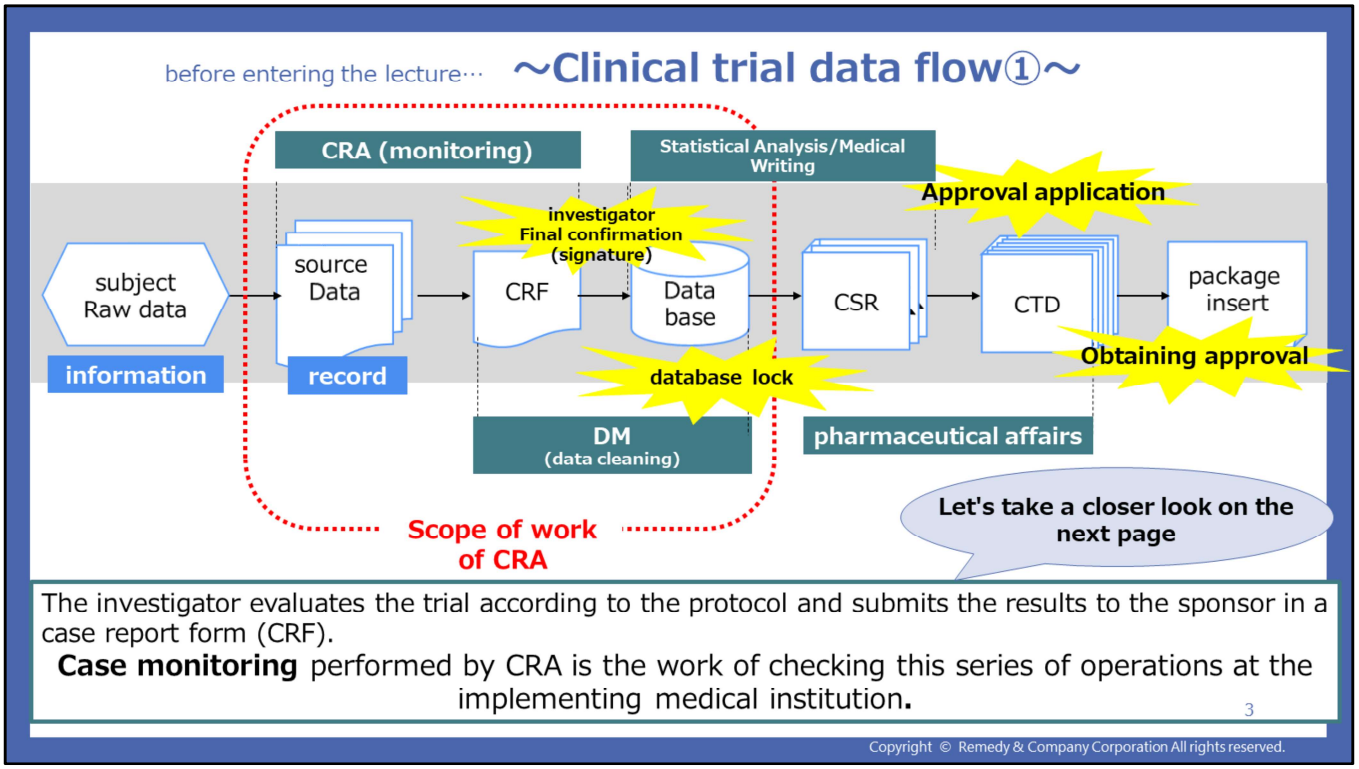
Before starting to discuss about how to perform the clinical trial monitoring I would like to introduce the workflow of a CRA to understand the regular activities performed by a CRA daily.

1.During the Site initiation process of the new clinical trial, the CRAs are involved in the discussion with the IRB negotiation for protocol review and RA approval along with the sponsor. They regularly visit the IRB, get IRB feedback, and help the sponsor understand the IRB requirements. After the regulatory approval, the CRAs are involved in the site contracts. The other activities of a CRA include IP procurement and management, site training, securing EDC access to all the users at the sites, and planning for the visit schedules.

2.During the study conduct phase, from the first patient in (FPI) to the Last patient Out (LPO), CRAs visit the clinical trial sites for various activities like data discrepancy management, Checking the study documentation in the site, IP management, patient visit schedule monitoring, source data verification, etc.,

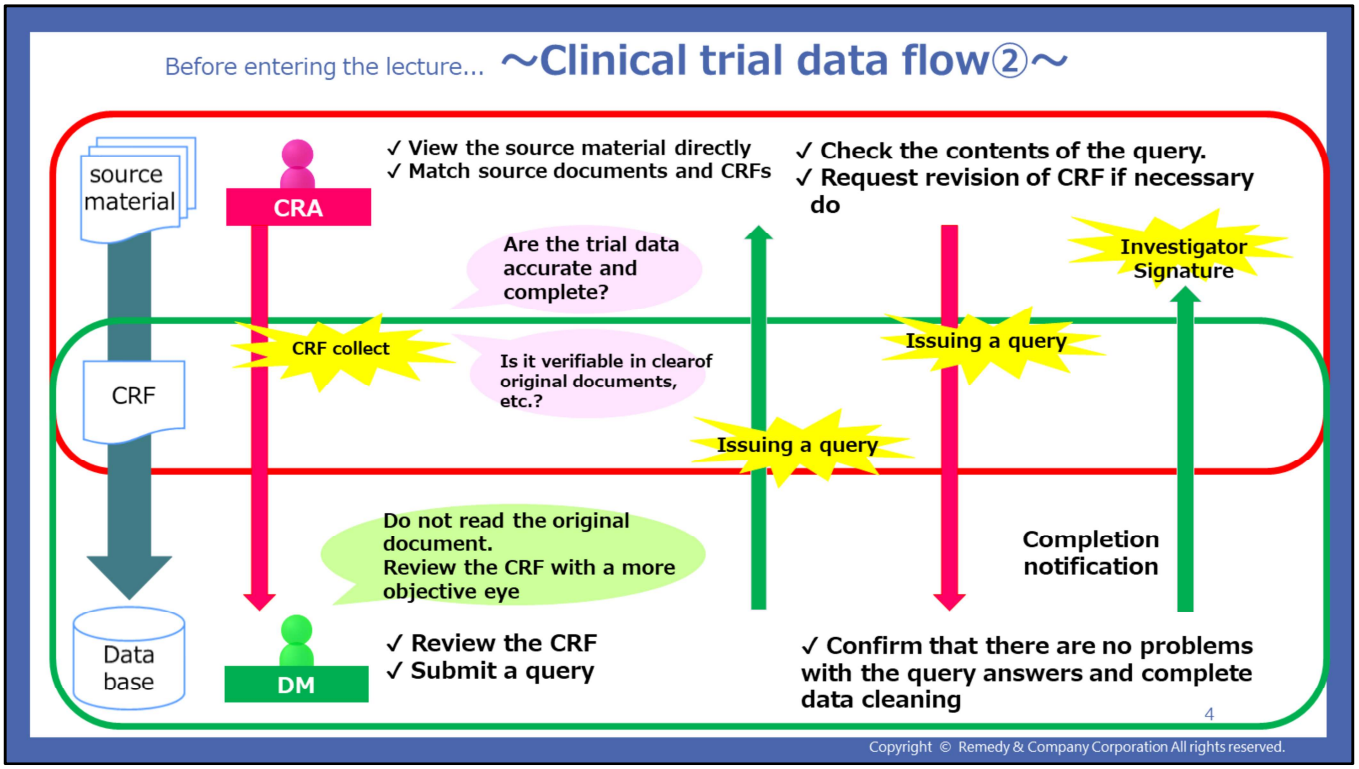
3.During the study closeout phase, CRAs check the archival process at each site, manage the IP unused and samples not required for the study, completion of all payments to all vendors, and close the site contracts.

Each phase of the study has different kinds of activities that the CRAs are responsible for.



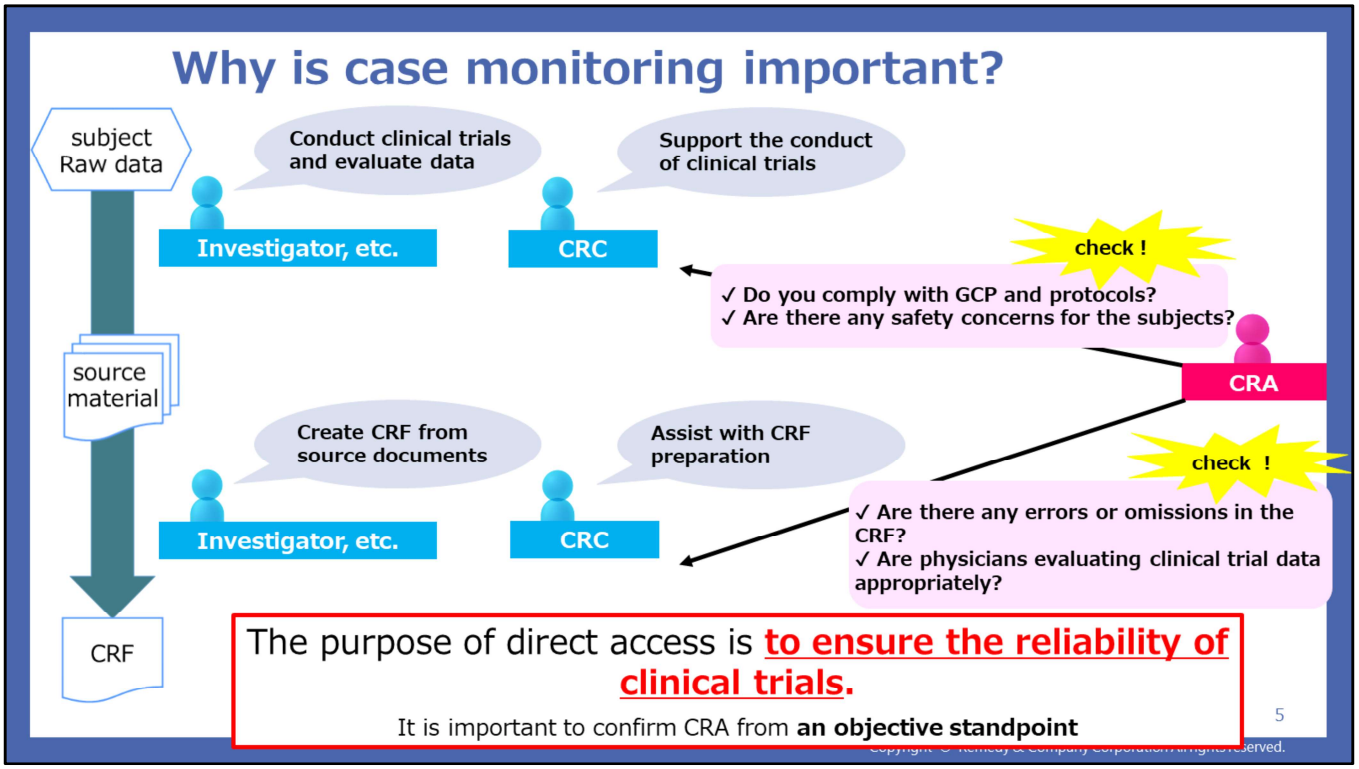
- The clinical trial data collection starts with the collection of the data from the patient/subject on a paper CRF worksheet also called raw data.
- The worksheets used for the data collection are the CRFs in a printable format.
- These documents are the source data records and the data from the source documents is entered into the eCRFs on the EDC system.
- Once all the data collected for the clinical trial is validated by data managers and clinical personnel, the investigator signs each eCRF and the data collected is locked into the EDC system so that no further changes can be made to this data by the data managers.
- This locking process is called Database Lock.

- After the database is locked the data is downloaded from the EDC system and the Clinical study report (CSR) is prepared with the combined efforts of statisticians and medical writers in a format acceptable to the local regulatory authority.
- Along with the other data related to the investigational product like the quality of the product, pharmacological and toxicological data, and the CSR made are compiled and the Common technical document CTD is made for submission to the Regulatory authority.
- In this flow of data in a clinical trial, the investigators are responsible for entering accurate data and providing judgment on the outcomes in the EDC system.
- The quality of the data entered in the EDC system is monitored by the CRAs by verifying it with the source documents and thus it gives a QC check for the data entered.
- Apart from data monitoring, other operations done by the clinical trial sites like laboratory tests conducted, adverse event management, IP management, etc also come under the CRA's responsibility.

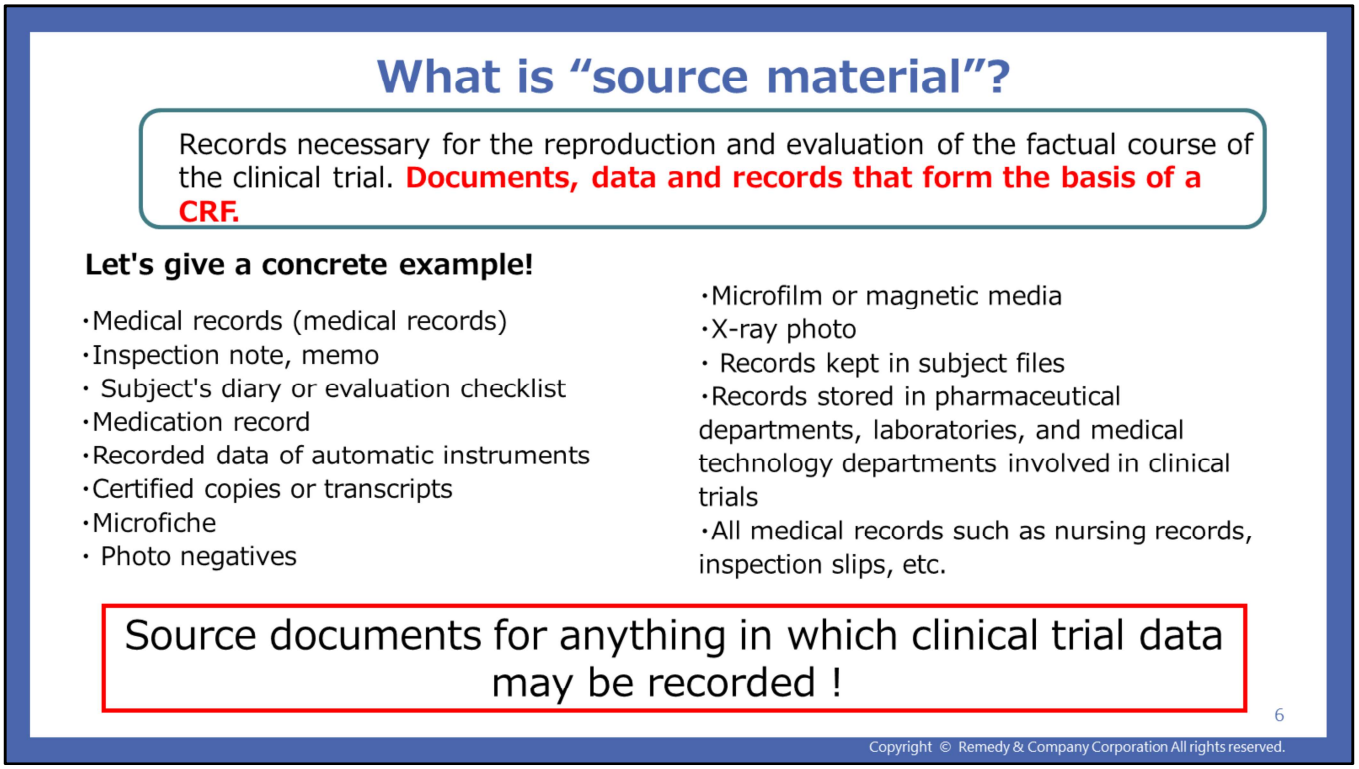


- The data collected in the EDC system is reviewed by the data managers regularly.
- If the data is not acceptable as per the protocol or if there is any issue with the data, the data managers post questions in the EDC system in the question where the discrepancy was observed.
- If a query is issued on any data question, the CRA and the site personnel like the CRC/PI are responsible for resolving the query.
- This is done by checking the source data in the sites by the CRA and ask the CRC to revise the CRF
- The Data manager reviews the corrected data and confirms the data accuracy and if not as expected the cycle repeats.

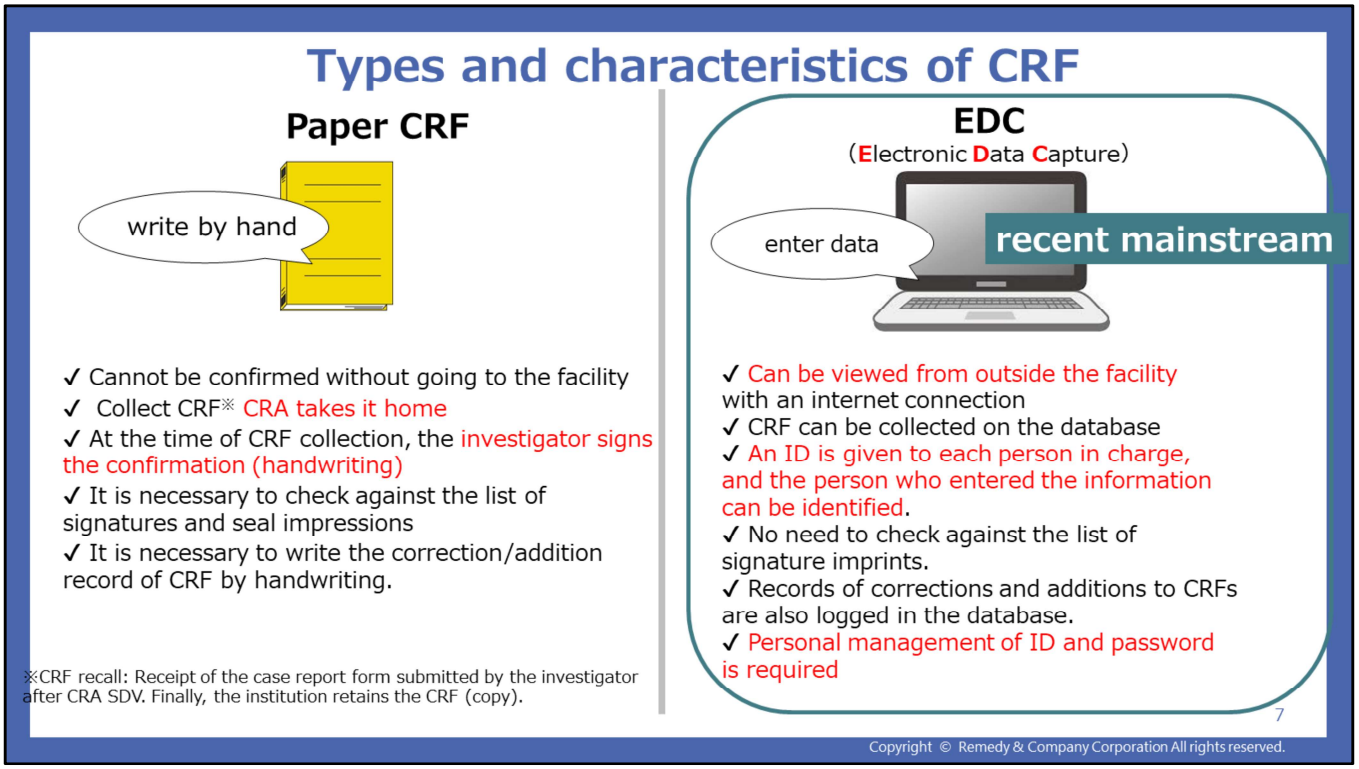
- Similarly, the CRA also has a responsibility to review the clinical trial data entered into the EDC system by checking the source data, in case there are any discrepancies.
- The CRAs check the source data and confirm the accurate date.
- All queries must be resolved, and the investigators must complete the signature on eCRFs before the Database lock.



- The medical institutions conducting clinical trials manage public health also and have heavy workloads daily.
- The investigators are medical doctors who are responsible for data collection and giving judgment on the events of the clinical trial.
- The CRCs are the supporting staff to the PI, and they perform many activities on the site.
- The procedures followed by PI and CRC from the general health maintenance perspective might be slightly different from those to be followed for clinical trials as per ICH-GCP.
- It is a CRAs responsibility to verify that the protocol guidelines are being followed and no data losses are happening at the site.
- In addition, the CRAs are also responsible for reviewing the investigator's evaluation in case of protocol deviations and adverse events.
- Thus, maintaining the quality of the data in the clinical trial is the responsibility of the CRA.



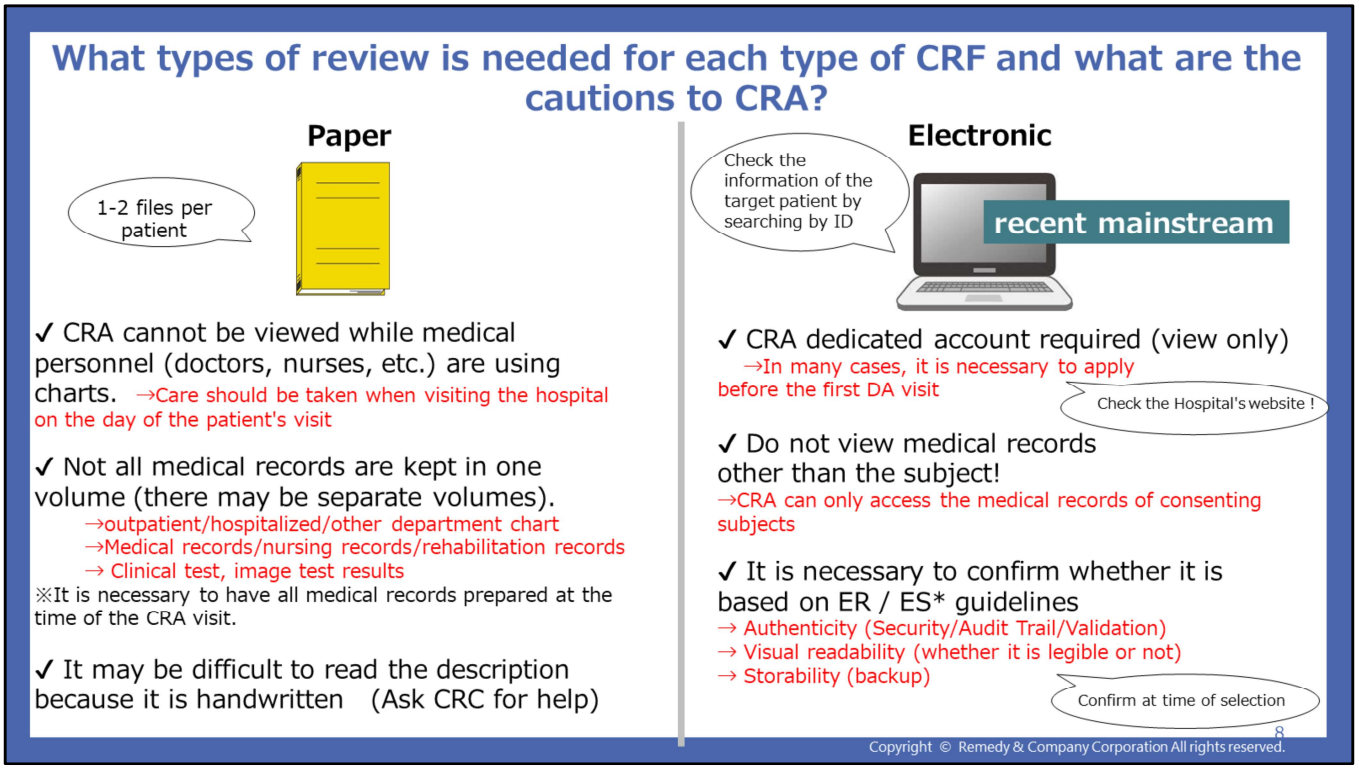
- Let us see what can be considered source documents in clinical trials.
- Source material refers to the original documents or data where the information regarding a patient’s health status or treatment is first recorded. This could include hospital records, lab results, or even participant diaries. These are crucial because they provide the raw data we rely on for analysis.
- Let’s see the examples!
- Examples include the medical records and reports, dairies etc., as listed out on the screen.
- These documents become the first documented data and act as the source data for further reports or documents built for the clinical trial reports.
- If any discrepancies are identified in the clinical trial data, these source documents act as the point of verification to help the clinical trial team to record the accurate data.



- The CRF can be a paper document or an electronic format of the paper document.

- In the case of paper CRFs, the physician enters the data into the paper CRF and the files are stored in the patient older at the site.
- Each time the CRA who needs to do the source data verification should visit that site collect the documents carried with them and verify and return to the site.
- Any corrections made to the data need to be manually documented and tracked
- The PI needs to sign the document page by page for approval.
- The documents are preserved in the site as bounded folders.

- In the case of eCRFs the data is entered into the computer or other electronic device by the site.
- It needs an internet connection, and the data collected is preserved in a repository called Database which can be cloud-based or any local server based in the hospital.
- Each user is given a user ID and password unique to the user and the account given per person is based on the role they have in the clinical study.
- Being electronic in format, a lot of manual effort is reduced in EDC systems.
- The corrections made are also recorded electronically as an Audit trial in the EDC system.



Let us see **What types of review is needed for each type of CRF and what are the cautions to CRA?**

In PAPER CRFs CRA cannot view charts while medical personnel (doctors, nurses, etc.) are using them.

- It is important to remember that the monitoring visit should be planned carefully, especially on days when patients have appointments. If not there might be delays.

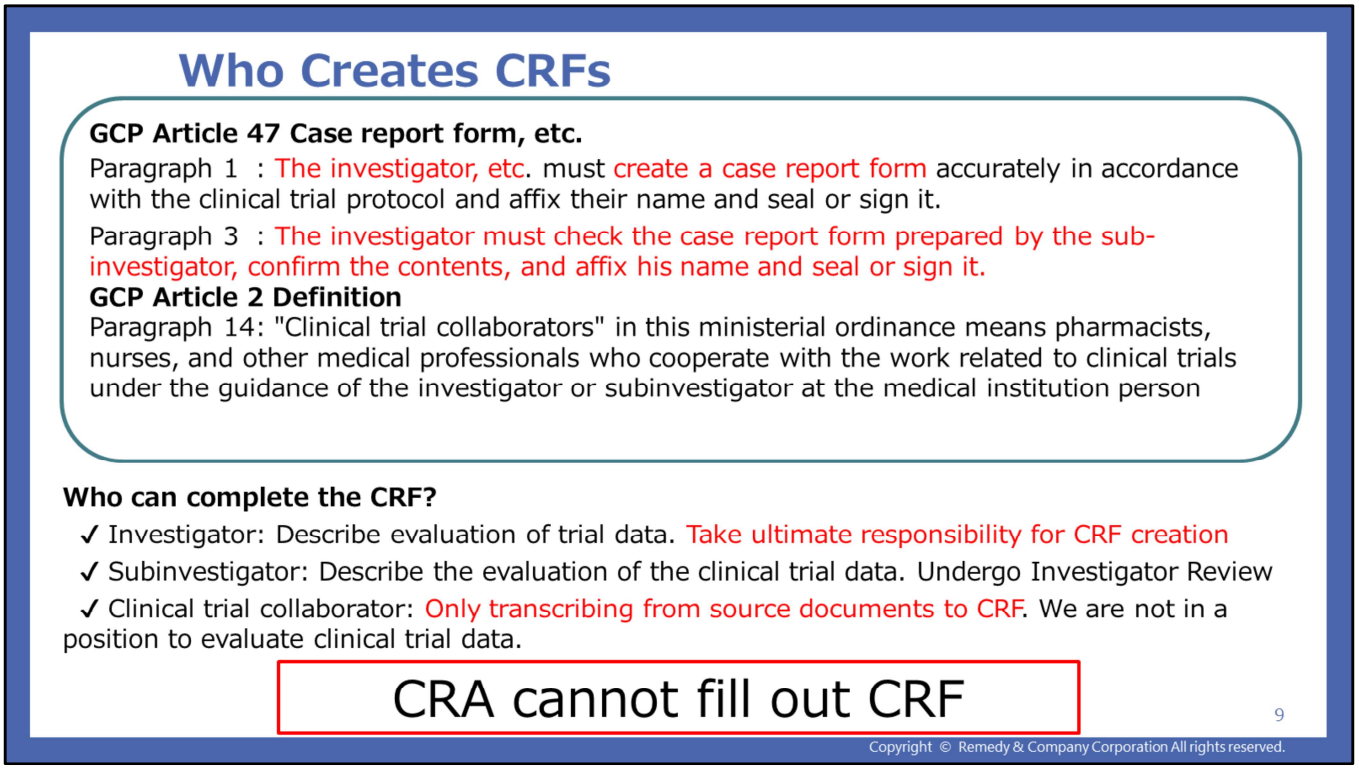
- Also, all the medical records are not kept in one place.
  - For example, there may be separate charts for outpatient visits, hospitalized records, or charts from different departments.
  - A CRA may also need to verify:
    - Medical records
    - Nursing records
    - Rehabilitation records
    - Clinical test results
  - So it is important to ensure that all relevant medical records are ready and accessible before the visit.
- Handwritten records can be difficult to read. So a CRA will need the CRC for assistance to avoid any mistakes.

In ELECTRONIC CRFs

- CRAs are provide a dedicated account on EDC system with view-only provision to access the electronic medical records. It is important to remember y need to apply for this account before your first Direct Access (DA) visit.

- Only the medical records of consented subjects should be accessed by CRAs !
  - Ensure that you're viewing only the records of subjects who have given informed consent.

- *Also the CRA should make sure if* the system complies with ER/ES standards by confirming 3 parameters namely: Authenticity, Visual readability and Storability.
  - Authenticity is checked by confirming if the security features, audit trails, and validations in place.
  - Visual readability is about the ease of reading and understanding the record.
  - Storability can be checked by looking if there a proper backup system for record preservation.



Clinical Report Forms (CRFs) are typically created by a variety of professionals involved in conducting clinical trials.

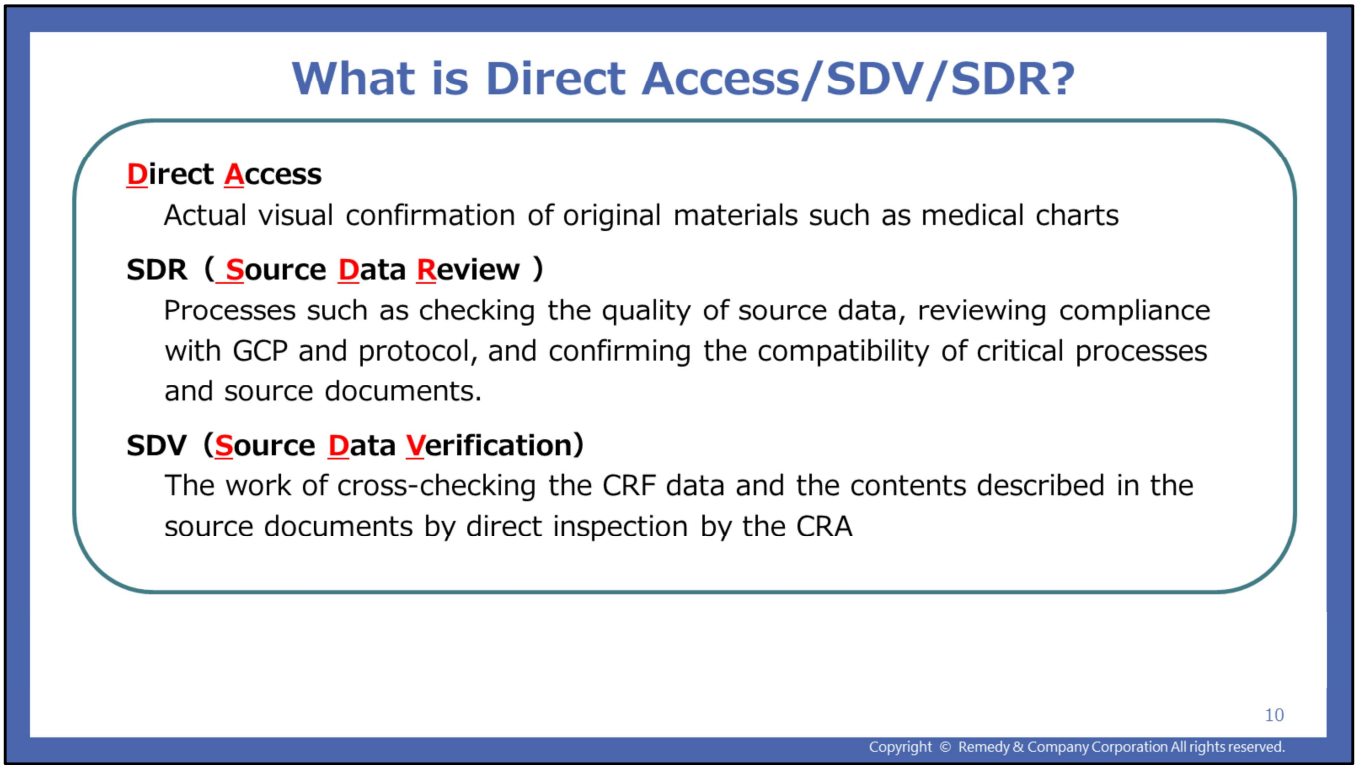
- **Clinical Research Coordinators (CRCs)** are the primary people responsible for creating and maintaining CRFs. They work directly with the investigators and are in charge of ensuring all data is collected and recorded accurately under the guidance of the investigator.

- **Principal Investigators** and Sub-Investigators who are the lead researchers on a clinical trial provide input on the types of data that need to be collected based on the trial's objectives and endpoints. PIs take ultimate responsibility for CRF creation.

- **Sponsors**: The organization funding the clinical trial (this could be a pharmaceutical company, a university, the NIH, etc.) will also have a say in what data needs to be collected. They may provide specific templates or guidelines that must be followed but cannot directly enter or change data in EDC.

- **Data Managers and CRAs** review the CRFs for completeness and accuracy. They may suggest changes to the forms to improve data quality but cannot directly enter or change data in EDC.

The process of creating a CRF often involves collaboration among this team to ensure the form captures all necessary data in a way that's clear, concise, and easy for site staff to complete.



Now that we've discussed who creates CRFs, let's talk about how that data is verified and reviewed.

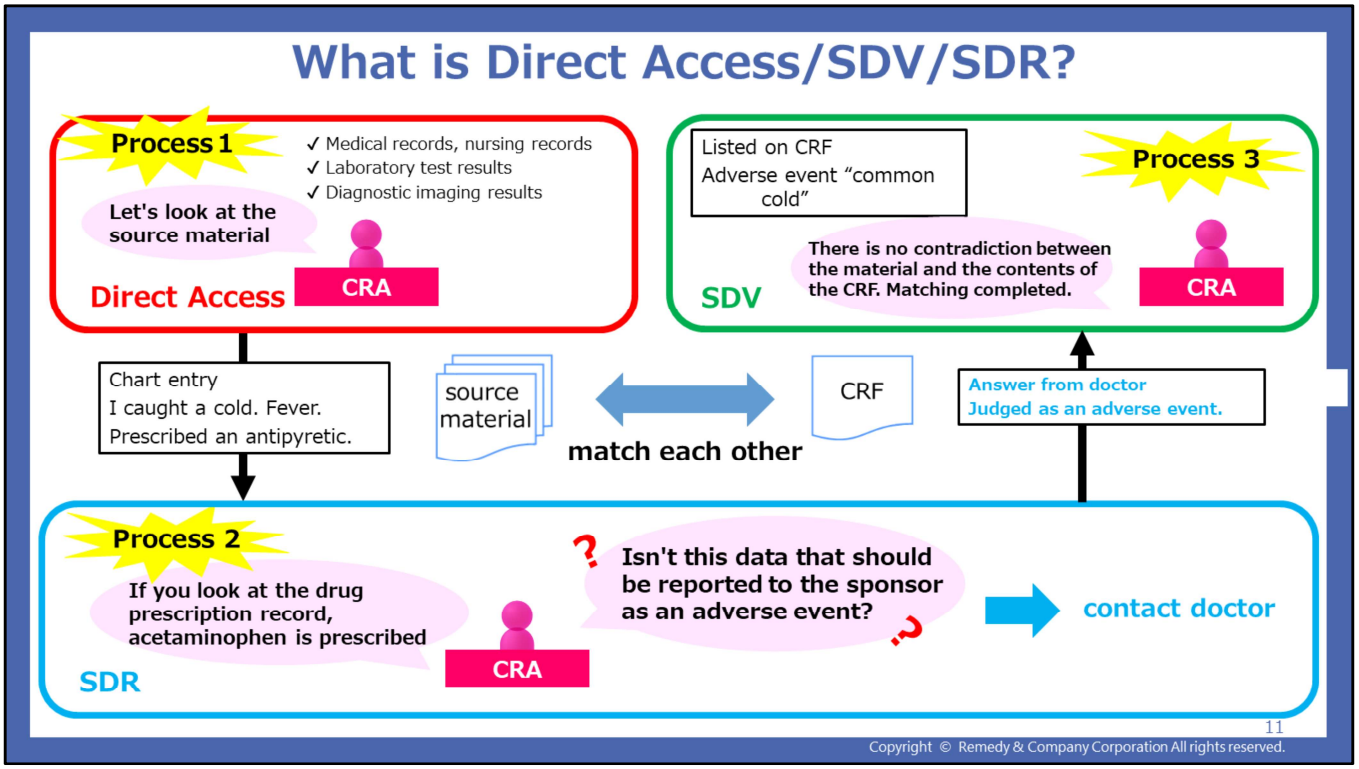
There are a few key terms you need to know: Direct Access, SDV, and SDR.

Direct Access refers to the actual visual confirmation of original materials like medical charts.
It's about going straight to the source to verify the information.

SDR, or Source Data Review, is a bit broader. It involves checking the quality of the source data, reviewing compliance with Good Clinical Practice (GCP) and the protocol, and confirming that critical processes and source documents align.

SDV, or Source Data Verification, is the process of cross-checking the data in the CRFs against the information in the source documents. This is done by directly inspecting the documents by the Clinical Research Associate (CRA).

To summarize: Direct Access is about confirming source data, SDR is about reviewing quality and compliance, and SDV is about verifying the data in the CRFs. All three are crucial steps in ensuring the accuracy and reliability of the data collected during a clinical trial.



Let us now learn about how the Direct Access/SDV/SDR processes are conducted.

1. In Direct Access the clinical research associate (CRA) visits the trial site and asks the site coordinator for direct access to the medical records and source documents of a participant enrolled in the trial.

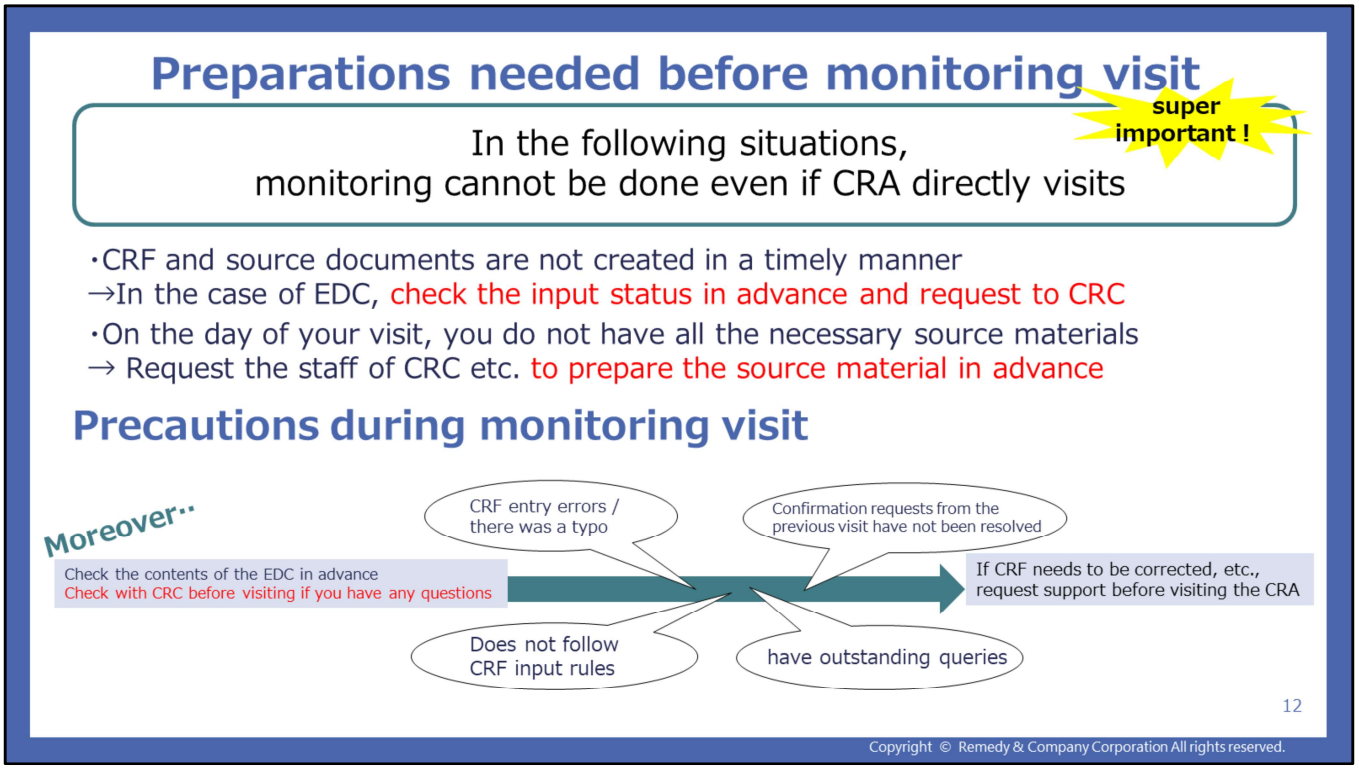
- The site coordinator logs into the hospital's electronic medical records (EMR) system and provides the CRA with the necessary credentials or access rights.
- The CRA views the participant's source documents (like., medical history, lab results, and treatment notes) directly from the EMR, ensuring they align with the data entered into the clinical trial database.

2. In addition to verifying specific data points, the CRA conducts a Source Data Review (SDR) to ensure the overall data quality and completeness.

- During SDR, the CRA checks the broader context of the participant's medical records—such as the consistency of medical history, any reported adverse events, and whether the site has followed the trial protocol (e.g., correct dosing, timing of visits).
- The CRA ensures that the trial data reflect the participant's treatment journey and that the site is adhering to good clinical practices (GCP).
- If any protocol deviations, incomplete records, or unreported adverse events are identified, the CRA communicates these findings with the site to make the necessary corrections or updates.

3. Once the CRA has direct access to the source documents, they start the Source Data Verification (SDV) process.

- Specific data points from the participant's source documents (like., blood pressure, lab results) are needed to be cross verified with the data entered in the Case Report Form (CRF) of the trial's electronic data capture (EDC) system.
- If discrepancies are found , the CRA flags the issue for correction and works with the site coordinator or investigator to resolve any discrepancies by reviewing the source documentation and ensuring the CRF reflects the correct data.



Before starting for a monitoring visit, it's crucial to ensure that all necessary preparations are in place to facilitate a smooth and effective process.
There are several situations that can hinder monitoring, even if the Clinical Research Associate (CRA) is physically present at the site. Let's discuss some key considerations.

- **<u>Timeliness of CRF and Source Documents:</u>**

  - One of the most common issues arises when Case Report Forms (CRFs) and source documents are not created in a timely manner.
  - For studies utilizing Electronic Data Capture (EDC) systems, it's important to check the input status in advance. Ensure that you communicate with the Clinical Research Coordinator (CRC) to address any delays.

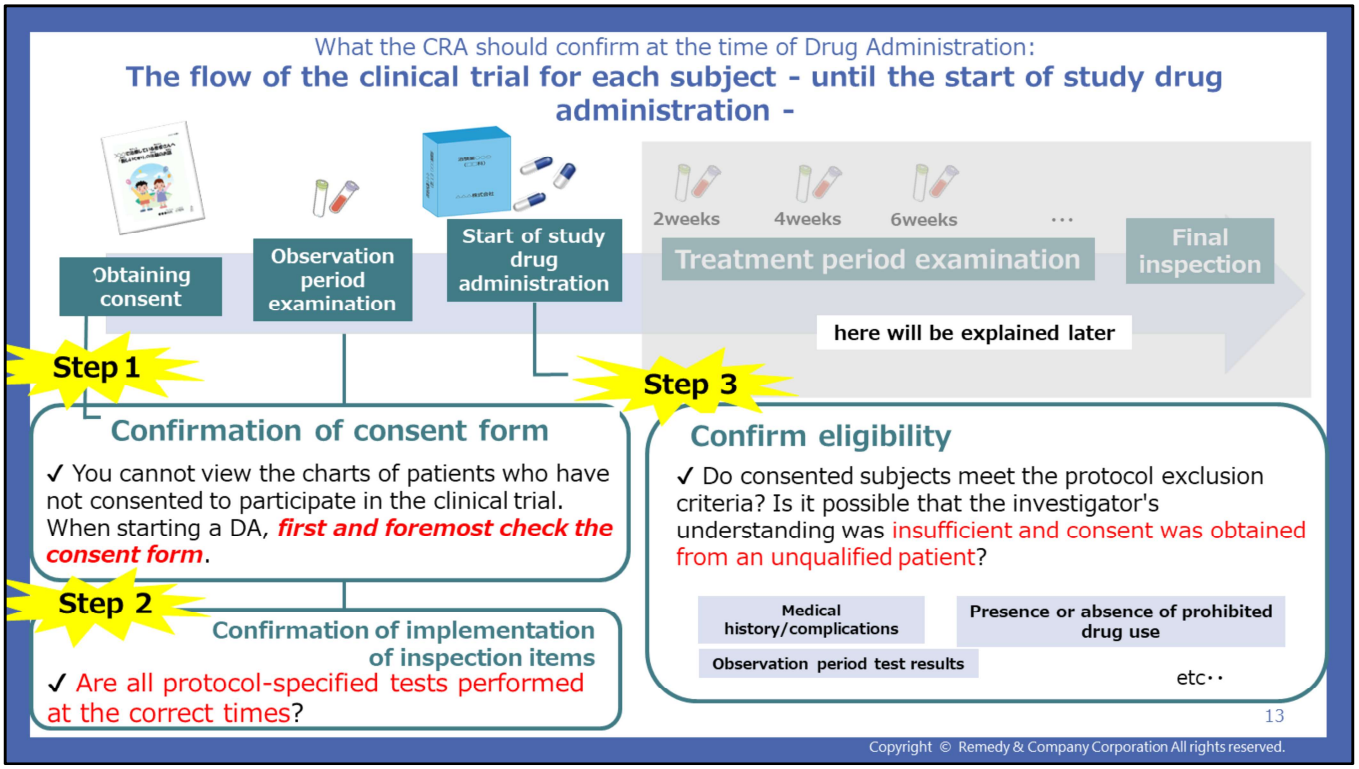
- Availability of Source Materials on Visit Day:

  - On the day of your visit, you must have all the necessary source materials ready for review.
  - To avoid any last-minute issues, request the CRC staff to prepare these materials ahead of time.

- **<u>Let us now see the Review EDC Content precautions:</u>**

  - It's essential to check the contents of the EDC in advance. If there are any questions or concerns, reach out to the CRC before the monitoring visit to clarify them.
  - Lookout for potential entry errors to the CRF or any typographical errors that may have occurred.
  - Confirm that any requests for clarification from your previous monitoring visit have been resolved. Check for any outstanding queries that need to be addressed during this visit.
  - If there are any necessary corrections to the CRF, request support from the CRC or relevant staff before your visit to ensure these issues are addressed in a timely manner.

By taking these preparatory steps, we can enhance the efficiency of our monitoring visits and ensure that all necessary materials and information are in place for a successful review.



As a Clinical Research Associate (CRA), it's essential to confirm specific details at the time of drug administration (DA) for each subject. This ensures the trial is progressing according to protocol and that subject safety is prioritized. Let's see the key steps in the clinical trial process and what needs to be confirmed after drug administration.

· **<u>For each subject, the flow of the clinical trial follows a structured process:</u>**

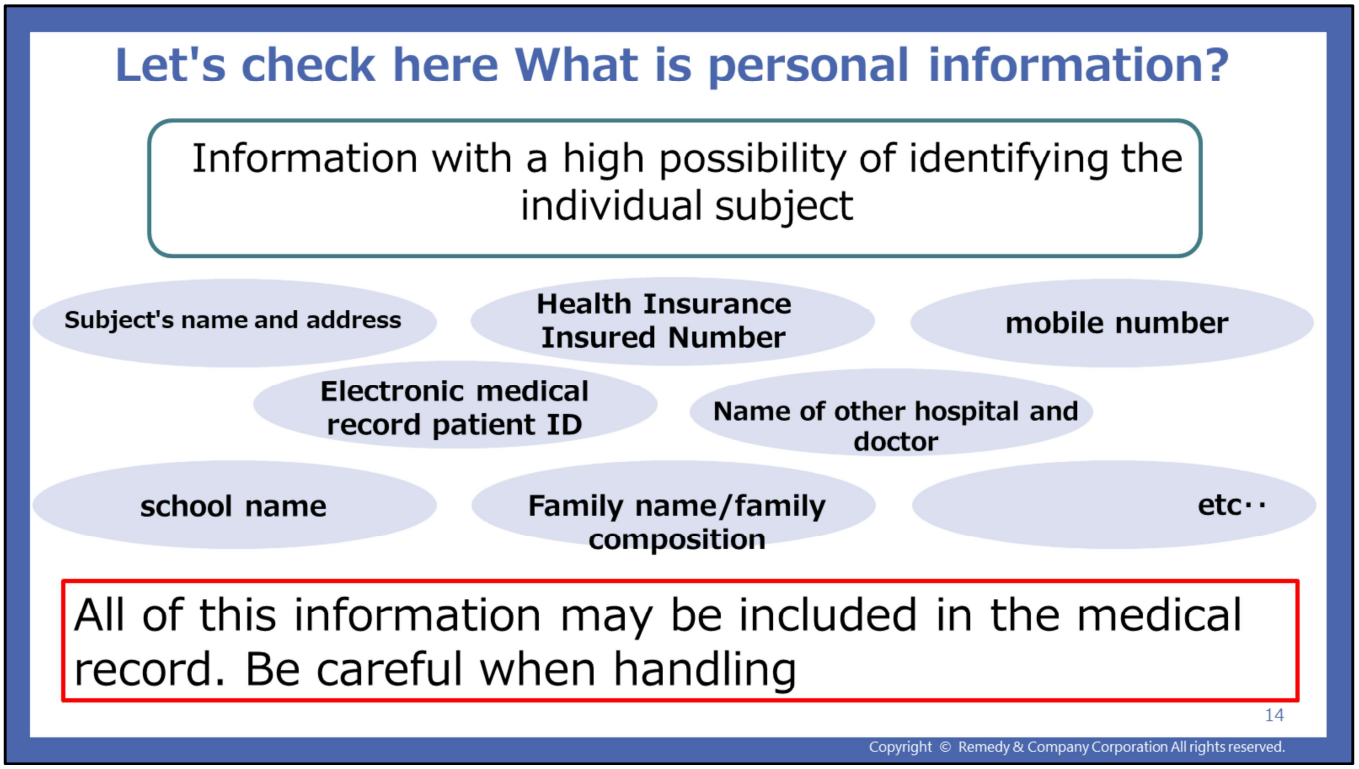
Let us see the flow until initiation of the study drug administration in this slide:

- The first thing to confirm is that informed consent was obtained during the screening period. This is a critical regulatory requirement, and the consent process must be thoroughly documented before any other trial activities begin. If the subject did not consent for the study, the subject related information which is considered as "Personal Information" should not be accessed by the CRA.

- Once consent is obtained and the screening period is complete, the next critical step is to check and confirm the implementation of all the screening tests needed as per the protocol.

- The next step is to confirm the subjects eligibility to the study has been confirmed and if the subject has passed all the examination criteria. In this stage it is required to resolve issues like,

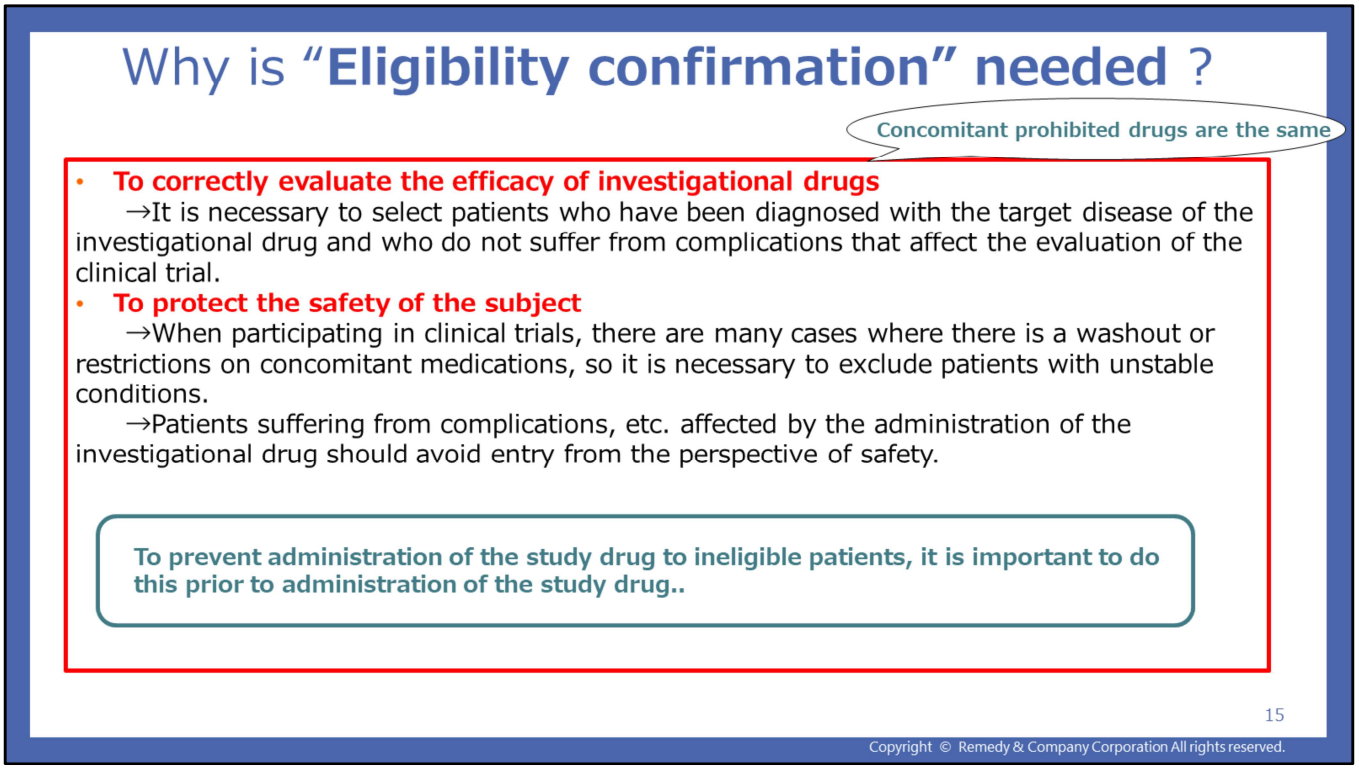
a. Wrong consent document being used,
b. Insufficient qualification of the subject for the eligibility by confirmation of the exclusion criteria like excluded medical history, Prohibited drugs usage, results of the screening tests.



As the word Personal Information is introduced in the previous slide, now, let's us see what we mean by 'Personal information.'

Personal information refers to any data that has a high potential to identify an individual subject. This can include a wide range of information that, when combined or used in context, can pinpoint a specific person.

- **Types of Personal Information:**
  - Examples of personal information include names, addresses, phone numbers, email addresses, social security numbers, and medical record numbers. Even seemingly innocuous details, such as a person's date of birth or specific demographic information, can contribute to identifying an individual.
  - Importantly, all of this personal information is often included in medical records. Medical records are comprehensive documents that can contain sensitive data about a patient's health history, treatments, and other personal identifiers.
  - Given the sensitivity and potential for misuse of personal information, it is crucial to handle it with care. This means adhering to strict confidentiality protocols and ensuring that only authorized personnel have access to this information.



Let us learn the crucial role of eligibility confirmation in clinical trials and its importance in ensuring both the efficacy of investigational drugs and the safety of participants.

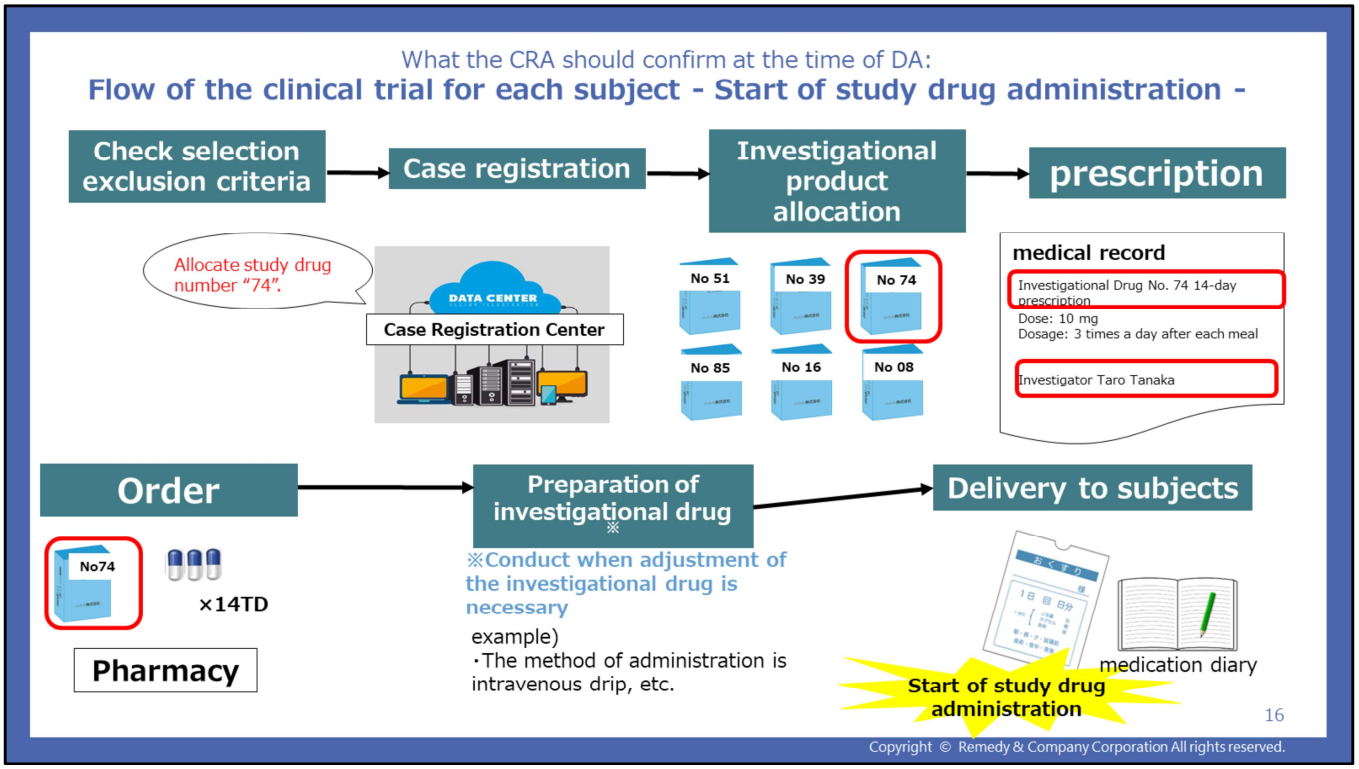
- Eligibility confirmation is essential to correctly evaluate the efficacy of investigational drugs. This means we must select patients who have been accurately diagnosed with the target disease for the investigational drug. Additionally, it is critical to exclude patients who suffer from complications that might influence the results of the clinical trial. This careful selection process helps us gather reliable data on how well the drug works in the intended patient population.

- In many clinical trials, participants may face restrictions on food or concomitant medications.

- When participating in clinical trials, there are many cases where there is a washout or restrictions on concomitant medications, so it is necessary to exclude patients with unstable conditions.

- Patients suffering from complications, etc. affected by the administration of the investigational drug should avoid entry from the perspective of safety.

- **To prevent administration of the study drug to ineligible patients, it is important to evaluate the subject thouroughly prior to administration of the study drug.**



In continuation to the CRA tasks in clinical trial process, let's walk through the key points that need to be verified during the study drug administration stage of the clinical trial process.

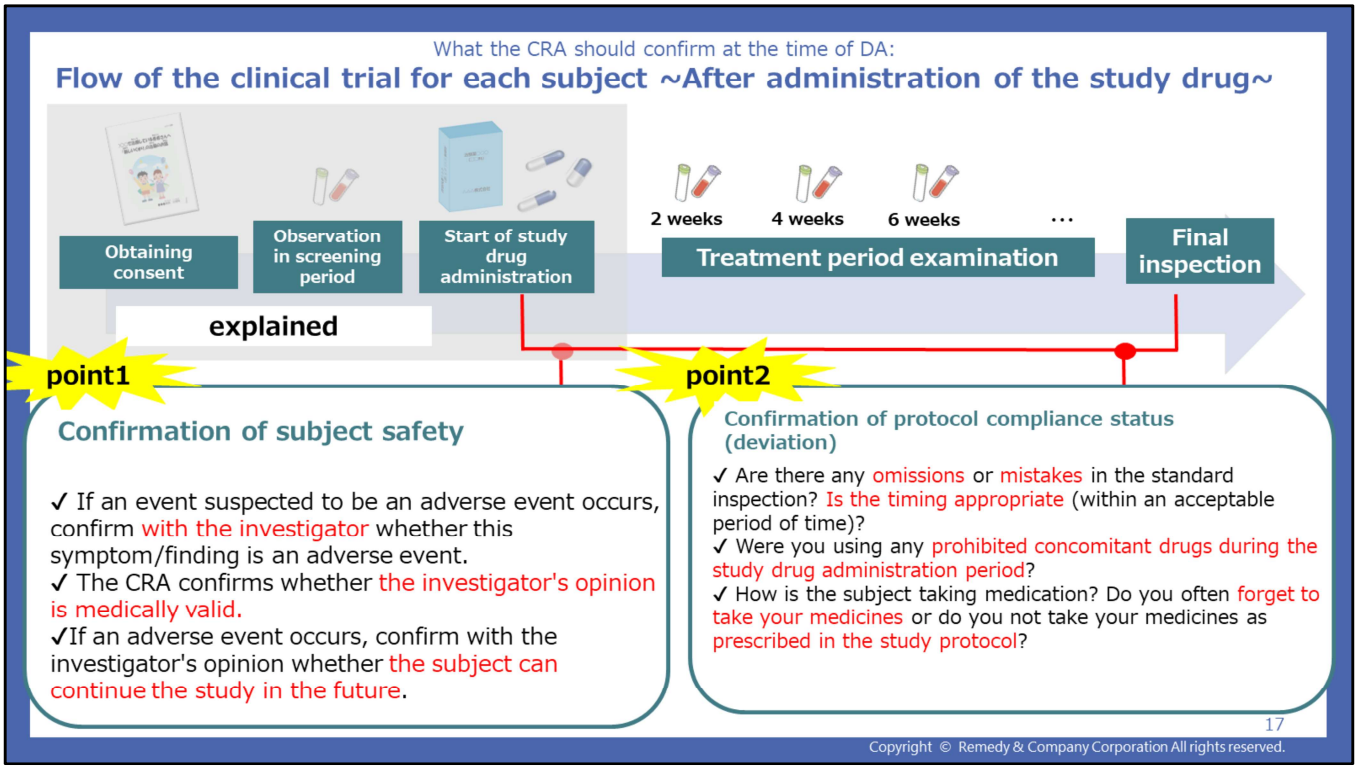
- Each subject in the clinical trial process follows a specific flow that ensures protocol adherence and subject safety. At the time of drug administration, it is crucial that you confirm **that the subject meets the selection criteria and does not fall under any exclusion criteria. This ensures that only eligible subjects receive the investigational drug.**

- Next, you need to verify that the subject has been properly registered in the trial. This includes ensuring that all documentation is in place and that the registration process complies with the trial protocol.

- The CRA must also confirm the correct allocation of the investigational product. Make sure the assigned study drug matches the subject's treatment group or randomization assignment as per the protocol.

- Following allocation, confirm that the prescription for the investigational product has been correctly issued and that the pharmacy has received the proper order. This is critical to ensure the right drug is prepared for the subject.

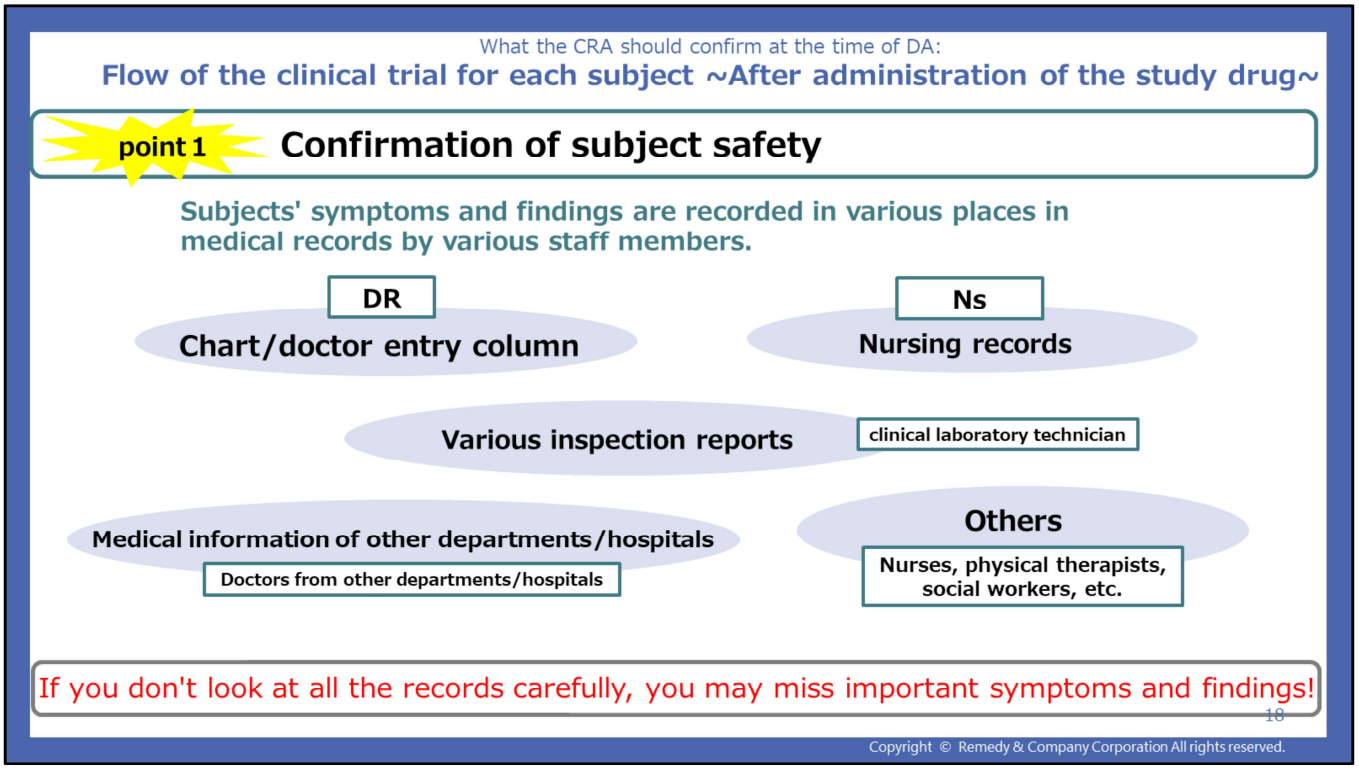
- The next step is to verify that the investigational drug is prepared according to the protocol and that the pharmacy follows the required preparation procedures. Once prepared, confirm that the drug is delivered to the subject in a timely manner.



- Let's walk through the key points that need to be verified after the study drug administration stage of the clinical trial process.

- **<u>During the treatment phase the first point is ensuring subject safety.</u>**
- A CRA needs to be vigilant in confirming that safety protocols are followed and that any potential adverse events are properly managed. Let's see the key points to confirm subject safety during monitoring.
- Confirming Suspected Adverse Events includes elements like observation of a symptom or finding that may be an adverse event, the first step is to confirm with the investigator whether it is indeed an adverse event. This determination is critical to the safety and well-being of the subject.
- Checking Investigator's Medical Opinion regarding the clinical significance of the adverse event. This involves reviewing the event within the context of the subject's medical history and the trial protocol.
- Future Participation After an Adverse Event includes tasks like consulting with the investigator to determine whether the subject can safely continue in the study when an adverse event is confirmed. This decision is based on the severity of the event and the investigator's medical judgment.

- **<u>The second point is confirmation of Protocol Compliance:</u>**
- In addition to monitoring subject safety, the CRA must ensure that the trial adheres to protocol requirements.
- Checking if there are any omissions or mistakes in the standard inspections is important. Also, ensuring that the timing of these inspections is appropriate and within the acceptable period as defined by the protocol.
- During the study drug administration period, verification that no prohibited concomitant medications were used by the subject is mandatory to avoid any interference with the study drug's efficacy or safety.
- Lastly, confirming how the subject is taking the study drug is needed. Are they adhering to the prescribed dosing schedule, or do they frequently forget to take their medications? Non-compliance with the medication regimen can affect the study's outcomes and needs to be addressed.
- A CRA role in confirming subject safety extends from monitoring potential adverse events to ensuring protocol compliance. By addressing these key areas, a CRA can help safeguard the subject and ensure the trial's integrity.

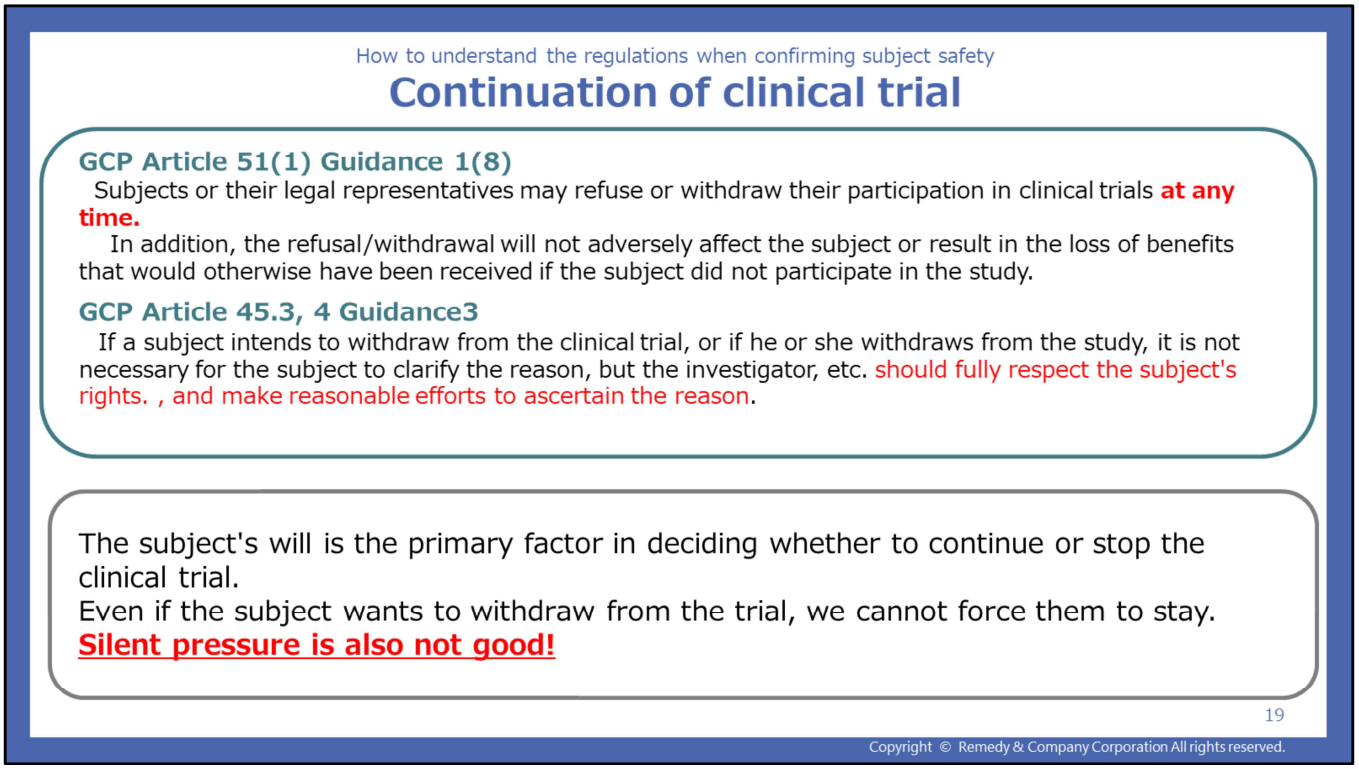


Let us see the 2 important elements of a CRA tasks at the time of Drug Administration in detail here starting with the first element "Confirmation of subject safety":

For ensuring the patient safety during the treatment phase a CRA should be carefully checking the Subjects' symptoms and findings are recorded in various places in medical records by various staff members.

The references include:

- Chart/doctor written script on the CRF worksheets or the observation note.
- Records of the nurses
- Medical history reports submitted to the hospital
- Patient records maintained in the hospital
- Any other related medical records
- Checking all the available data is needed to confirm the symptoms and findings.



- When confirming subject safety, it's important to understand the subject rights during the study progress and decisions to be made in the clinical trial. One key aspect of this is the continuation or withdrawal of a subject from the trial. Let's review the guidelines that govern this process.

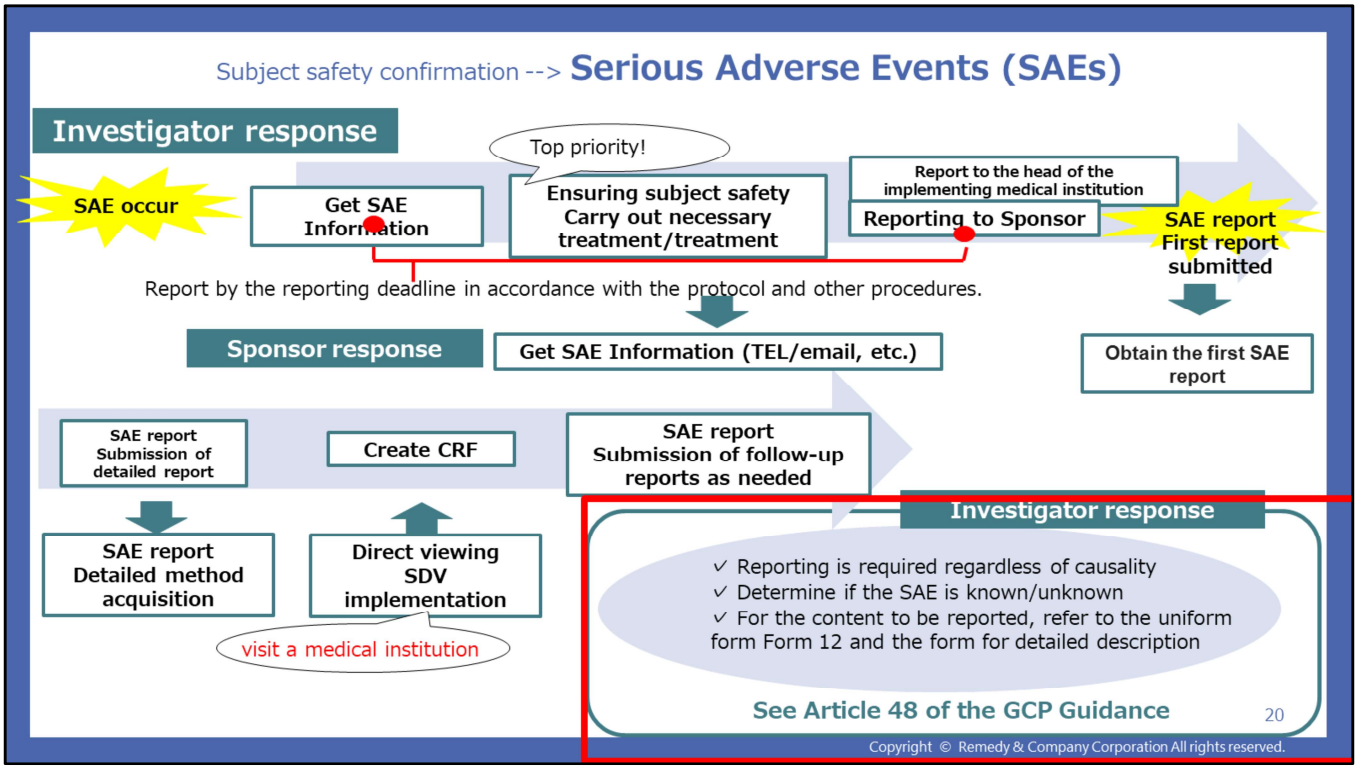
- According to GCP Article 51(1) and Guidance 1(8), subjects or their legal representatives have the right to refuse or withdraw their participation in a clinical trial at any time. This right is absolute and must be respected throughout the study.
- If a subject refuses or withdraws, it should not negatively affect them in any way. They will not lose any benefits or rights they would have had if they had chosen not to participate in the study.

- Under GCP Article 45.3 and 45.4 (Guidance 3), it is stated that if a subject intends to withdraw from the trial, or if they do withdraw, they are not obligated to provide a reason.

- However, it is important that the investigator respects the subject's rights and makes reasonable efforts to understand why the subject has decided to withdraw, while also making sure not to pressure them for an explanation.

****Respecting the subject's will is the key principle in clinical trials.**
- Ultimately, the subject's will is the primary factor in deciding whether to continue or stop participation in the clinical trial. If the subject expresses a desire to withdraw, it is essential that their decision is fully respected.

- Forcing or pressuring the subject to stay, even indirectly through silent pressure, is completely unacceptable. Respect and autonomy are key in ensuring ethical trial conduct.



- Now let us see the Serious adverse event reporting procedure for the confirmation of the safety of a subject.

- When a Serious Adverse Event (SAE) occurs during a clinical trial, the investigator role is crucial in ensuring that the event is managed appropriately, and that patient safety is prioritized. Let's walk through the key steps of the investigator's response to an SAE.

- The first step is for the investigator to immediately assess the SAE. This involves collecting the SAE information, evaluating the subject's current condition, identifying the severity of the event, and determining if any urgent medical intervention is needed to stabilize the subject.

- Ensuring the patient safety is of utmost importance. If immediate treatment is required, the investigator should ensure that the subject receives the necessary care and that the appropriate medical specialists are involved if needed.

- Once the subject is stabilized, the next critical step is to report the SAE. According to GCP guidelines, all SAEs must be promptly reported to the sponsor and the ethics committee via email or telephone and confirm the sponsors opinion about the SAE.

- The investigator must complete the SAE reporting forms and also prepare the detailed SAE report for submission, providing detailed information on the event, the subject's condition, and the investigator's initial assessment of causality. Timely reporting ensures that the sponsor can take any necessary actions, such as adjusting the study or notifying regulatory authorities.

- ECRF should be updated for all the SAE related data.

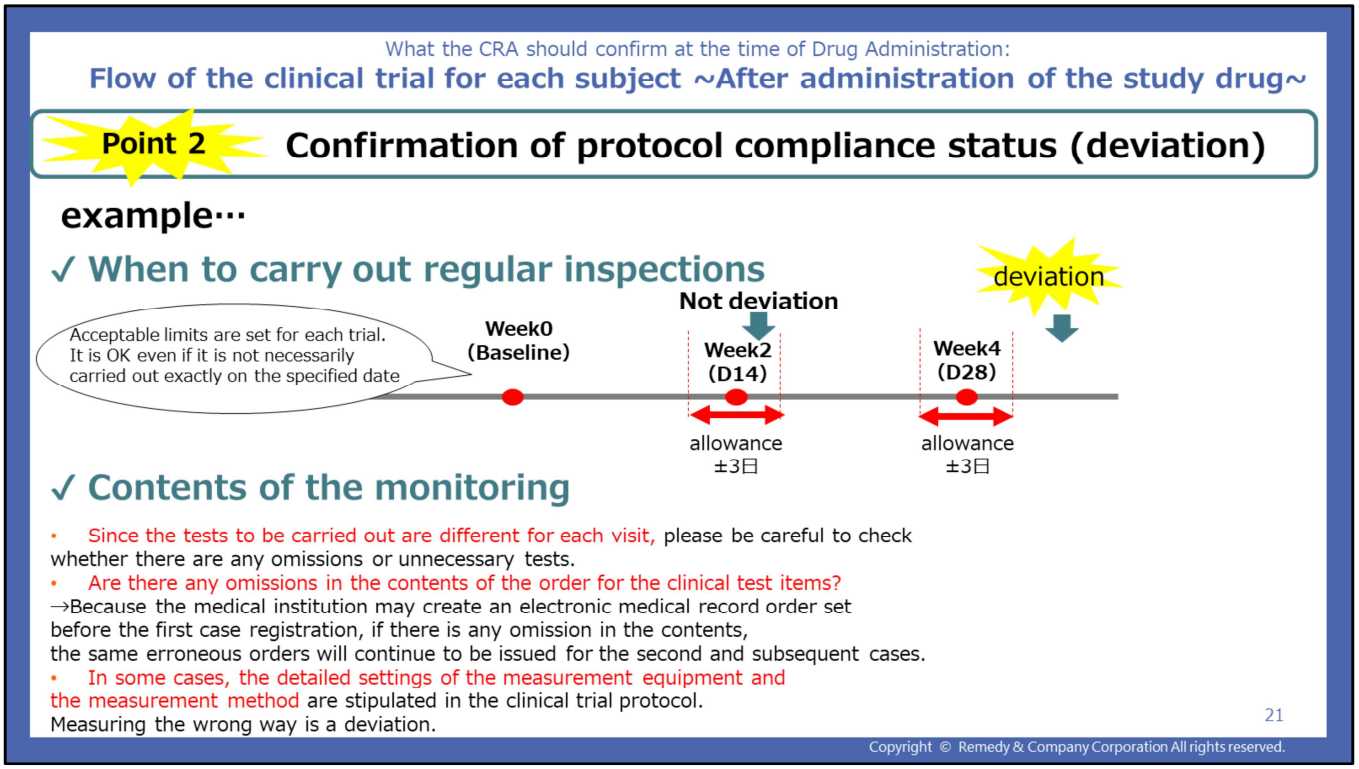
- Following the initial SAE report, the investigator should consult with the sponsor and the ethics committee to discuss the next steps.

- After the SAE, the investigator must closely monitor the subject's recovery and document any further developments. This includes recording follow-up information about the subject's condition, any additional treatments, and updates to the causality assessment.

- The documentation of this SAE followup is essential for the safety analysis of the trial

and may be required for future regulatory submissions.

• In this process CRAs role is to review the subject SAE report and the data reported on the CRF while conducting SDV in the medical facility.



Now let us see the second important element CRA tasks at the time of Drug Administration which is confirmation of protocol compliance status.

- After the administration of the study drug, CRAs must monitor each subject's progress to ensure the protocol is being followed.

- While regular inspections are necessary, the timing doesn't need to be exact. For protocol, clinical trials often have acceptable time windows for each visit, so confirm the timeline set for each trial and ensure compliance within those limits. If the visit is not conducted with in the given limit as per the recorded, then it is a deviation. It is a CRAs job to ensure that the deviation is properly recorded, and care is taken that the deviation does not happen again.

- **Key Areas for CRA Attention include checking**

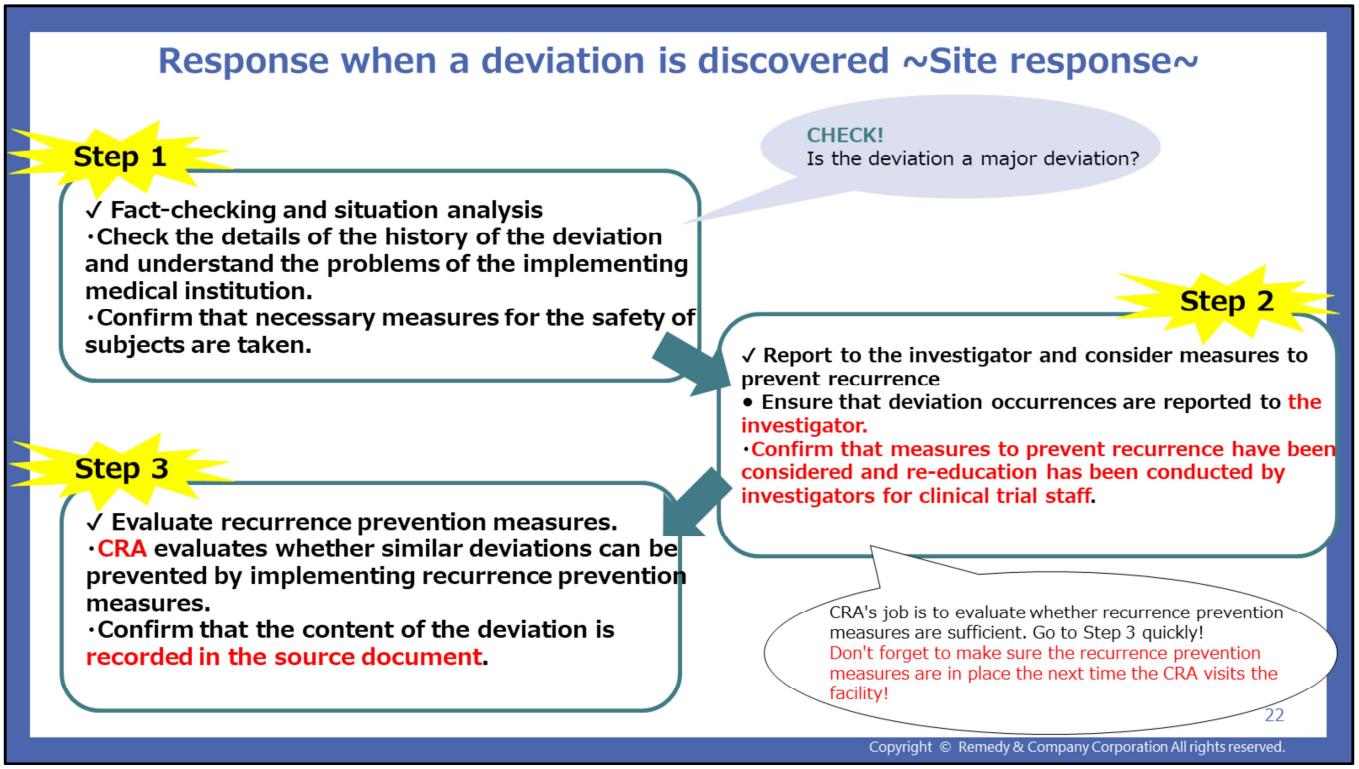
•The required tests are performed and that unnecessary tests are avoided. Missing tests or conducting extra ones can lead to deviations.

•Checking for Omissions in Clinical Test Orders.

•Verify that there are no missing orders for clinical test items. Medical institutions may create an electronic medical record order set before the trial starts, and if there's an omission in the first order, that same mistake may affect all future subjects. Catching these errors early is crucial to avoid ongoing issues.

•Confirming Measurement Methods and Settings.

•Some trials specify detailed requirements for how tests are conducted, including the settings of measurement equipment and the method of measurement. Ensure that the clinical site follows these exactly, as measuring incorrectly constitutes a protocol deviation.



When a protocol deviation occurred, let us see what are the steps to be taken at a site level:

Step 1 is

- Begin by checking the details of the deviation. Understand the nature of the problem at the medical institution. Is it a Major or a minor deviation?
- Confirm that all necessary measures for the safety of the subjects involved have been taken.

Step 2 is

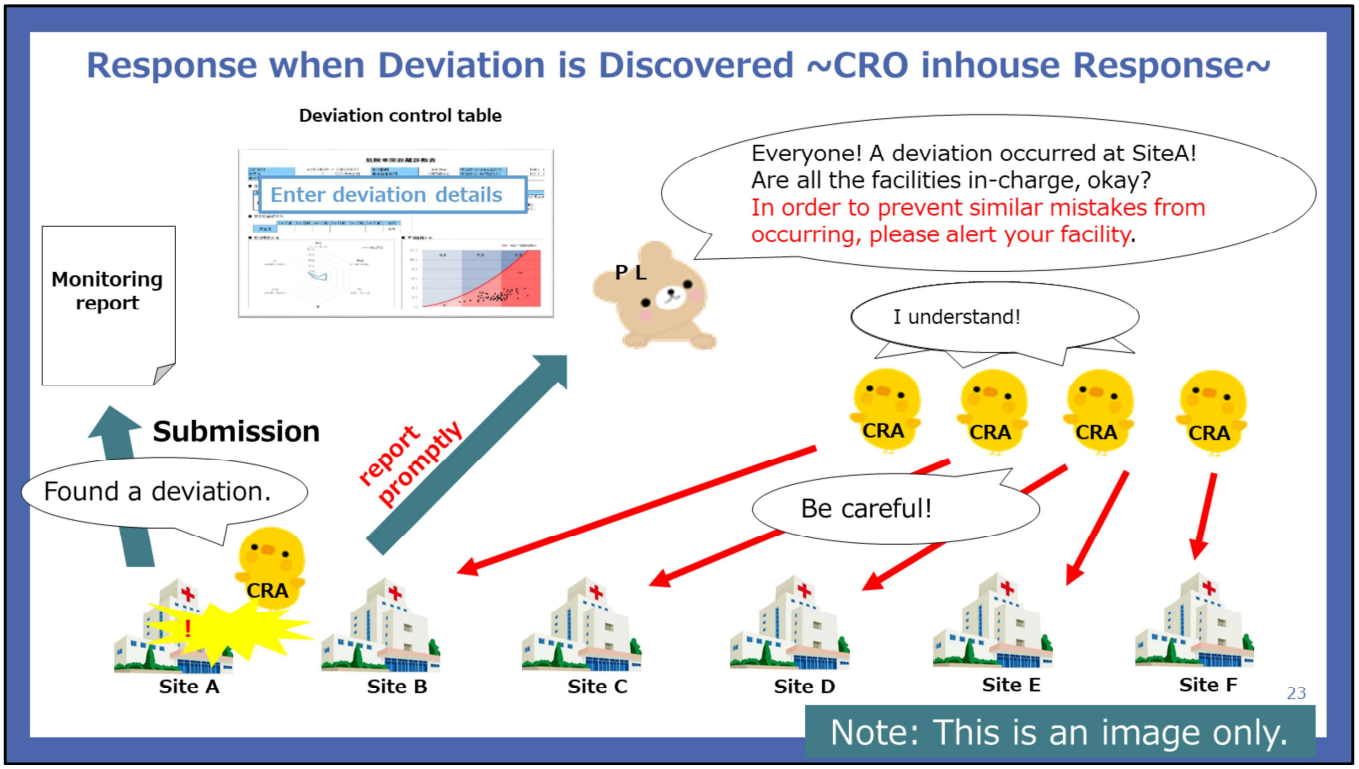
- Ensure that the deviation is promptly reported to the investigator.
- Investigate whether appropriate recurrence prevention measures have been put in place.
- The CRA must confirm that the clinical trial staff have been re-educated on these measures.
- The CRA's job is to evaluate the sufficiency of the proposed recurrence prevention measures.
- Don’t forget to confirm the measures are in place during your next visit to the facility!

Step 3 is

- Assess whether the recurrence prevention measures are effective in avoiding similar deviations in the future.
- Verify that the deviation has been accurately recorded in the source documents.

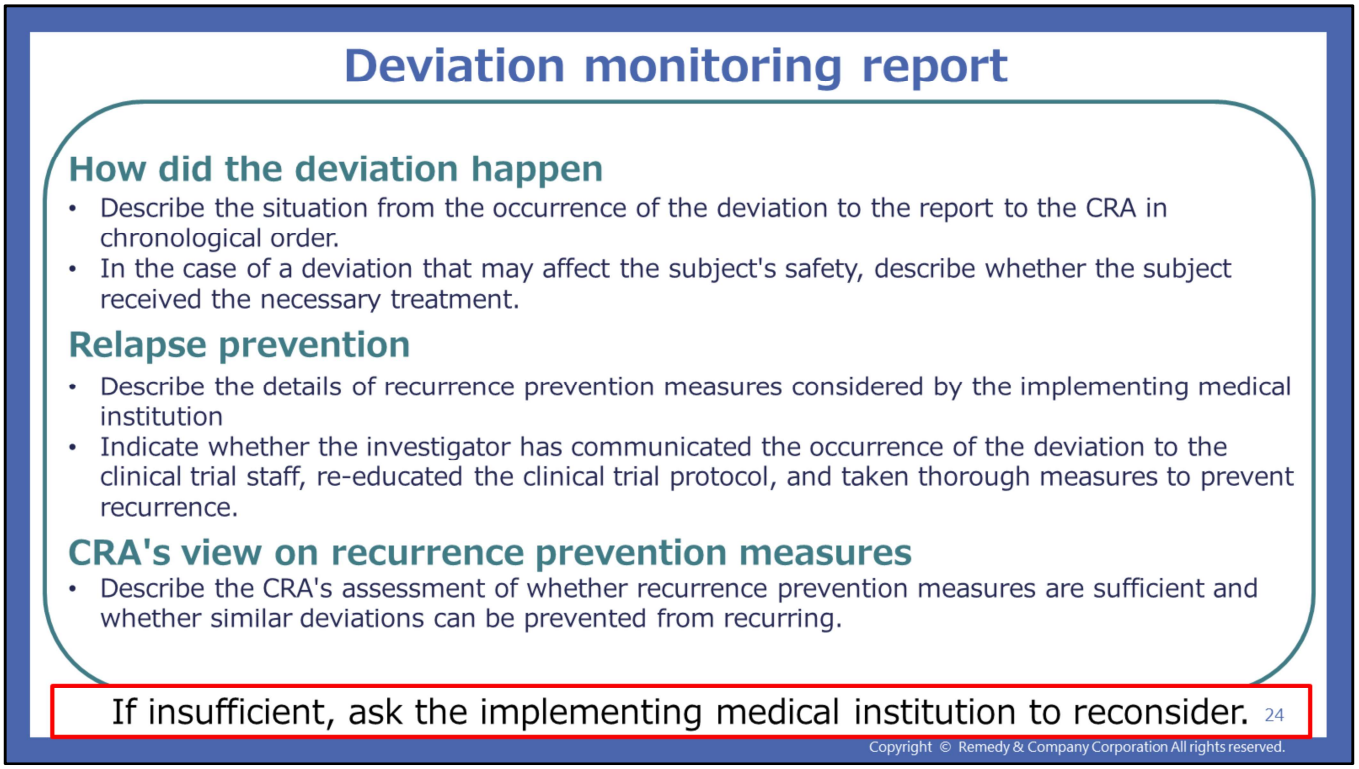
Closing:

The CRA plays a critical role in both the **evaluation and verification** of deviation handling at the facility, ensuring patient safety and trial integrity.



Now let us see what are the steps to be taken at the CRO level when a protocol deviation happens.

- The CRA must create a monitoring report detailing the nature and cause of the protocol deviation. This report should include specifics on the deviation, including its cause and any contributing factors.
- The report is shared with the project team for immediate awareness and action.
- The CRA must immediately inform the project lead about the deviation, either by phone or email. This ensures that prompt corrective actions are taken and that all team members are aware of the issue.
- The deviation should be logged in the Protocol Deviation Report, a shared document where all project members can view and track protocol deviations. This ensures transparency and helps the entire team understand the nature and status of the deviation.
- After reviewing the details, the project leader should inform the other CRAs involved in the same study at different sites. This step helps to ensure that similar deviations are prevented at other trial sites, promoting consistency and protocol adherence.
- Effective communication and documentation are critical when a protocol deviation occurs at the CRO level. Timely reporting ensures that all team members are informed and that preventive measures are taken across sites.



Let us see what should be covered in a Monitoring report in details:
The first-and-foremost step is to understand "how the deviation occurred or the cause of the deviation":

- Describe the situation chronologically
- Start by briefly summarizing cause or nature of the deviation occurred (e.g., incorrect dose administration, missed protocol step).
- Indicate the timeline of how this was discovered and by whom.
- Provide details on how and when the Clinical Research Associate (CRA) was notified of the deviation.
- If the deviation posed a risk to the subject's safety, describe what immediate actions were taken to mitigate risk, including any necessary treatment provided to the subject.

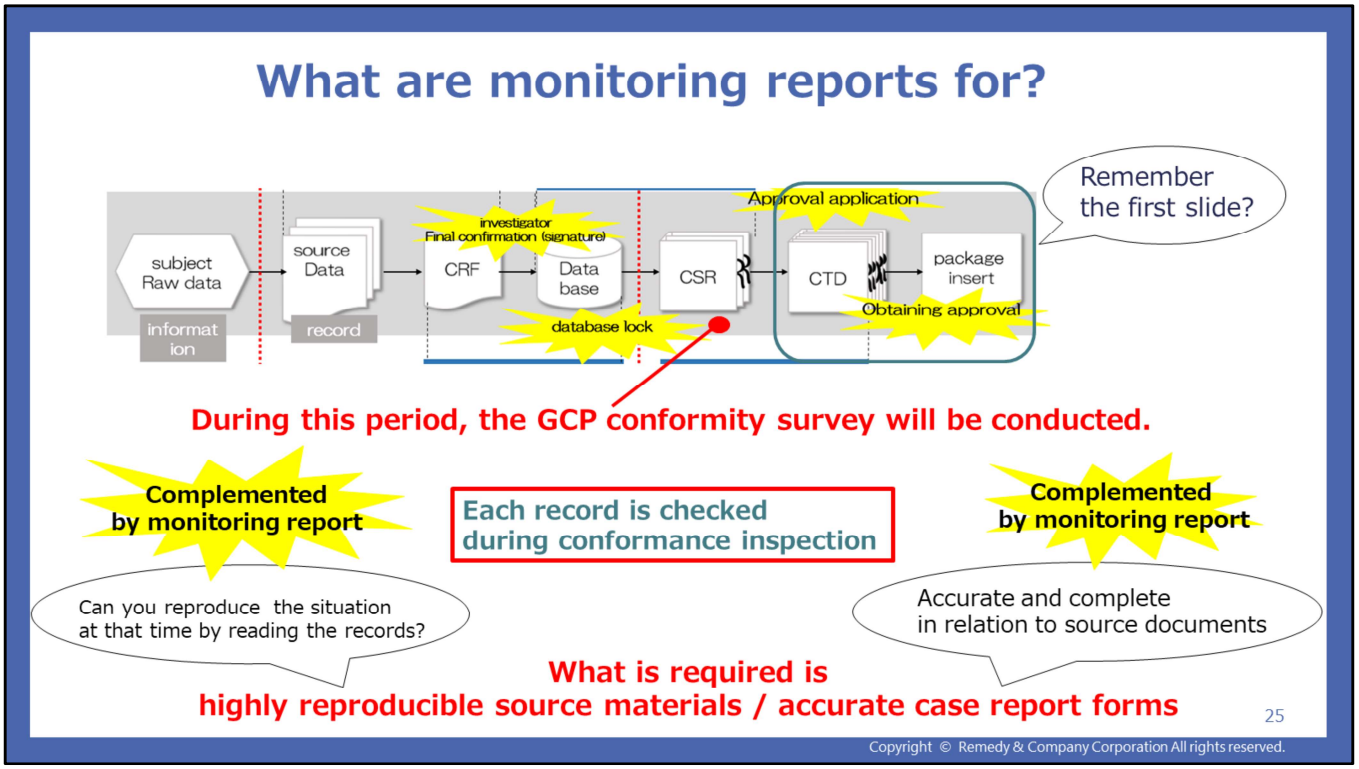
The next step is to record of the Relapse prevention measures. It includes recording:

- Details of recurrence prevention measures by medical Institution. Outline all the preventive measures implemented by the medical institution which Include details such as:
    1. Protocol review sessions
    2. Additional training provided to the clinical team
    3. New processes or checks implemented to avoid future deviations.
    4. State whether the investigator has communicated the deviation to the entire clinical trial team.
    5. Highlight any re-education efforts for the clinical trial protocol.
    6. Emphasize any specific actions taken to ensure recurrence prevention

The last part of the report includes the CRA's opinion on recurrence prevention measures:

- Present the CRA's assessment of the proposed prevention measures.
- Are the measures considered sufficient to prevent future deviations?
- If the measures are deemed insufficient, recommend additional steps or adjustments.
- If necessary, note that the implementing institution has been asked to reconsider and improve preventive measures to avoid similar deviations.

This structure ensures all key aspects of the deviation event, its handling, and the preventive steps are covered comprehensively, with a focus on corrective actions and CRA evaluations.

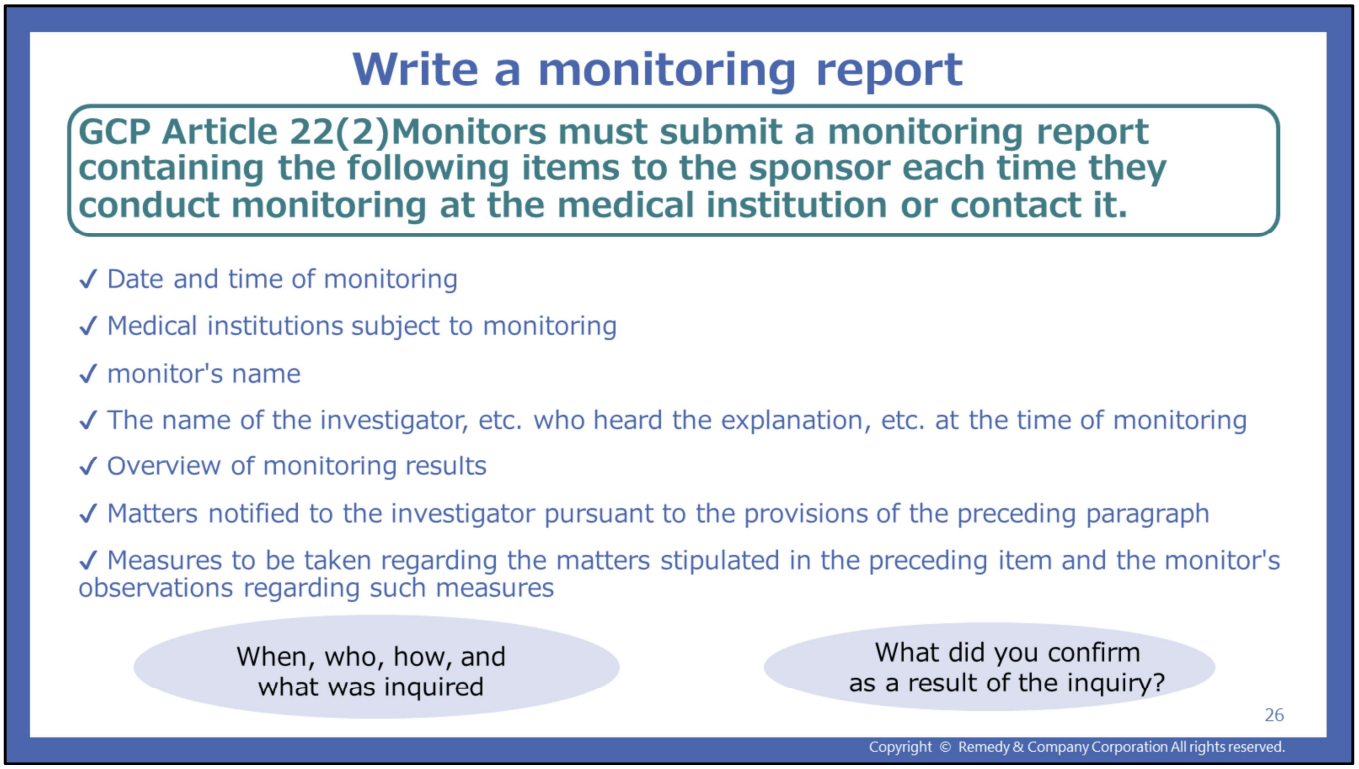


Let us look into the importance of the Monitoring reports. **What Are Monitoring Reports For?**

- Monitoring reports are essential documents created during clinical trials.
- They track trial progress, document any issues, and record protocol compliance.
- These reports serve as critical evidence in case of audits or GCP (Good Clinical Practice) inspections.
- Do you recall our earlier discussion from our first slide?
- During CSR (Clinical Study Report) creation, to ensure regulatory compliance, audits or GCP conformity checks are often conducted by regulatory authorities.
- Every record of the trial is examined during these inspections, and monitoring reports play a key role in this process.
- Regulatory inspectors may ask, “Can you explain the situation at that time by reading the records?”
- In this kind of situation monitoring reports provide the necessary clarification to regulatory agencies.
- These reports document trial events accurately, helping answer inspector queries effectively.
- Since clinical trials often span over many years, completed monitoring reports ensure that the information captured is:
    - Accurate
    - Complete
    - Timely
- If monitoring reports are not properly maintained, there’s a high risk of losing critical trial information over time, which can severely impact compliance and audit outcomes.

- To ensure audit readiness, it is crucial to have:
    - Highly reproducible source materials
    - Accurate case report forms (CRFs)
    - Well-maintained monitoring reports

In short, monitoring reports are the backbone of documentation during clinical trials. They provide clear, reproducible data, and ensure compliance during audits, making them a cornerstone of successful trial management.



Let us learn how to write an effective monitoring report, emphasizing the key elements outlined in GCP Article 22(2). This report is a crucial aspect of maintaining compliance and ensuring the integrity of clinical trials.

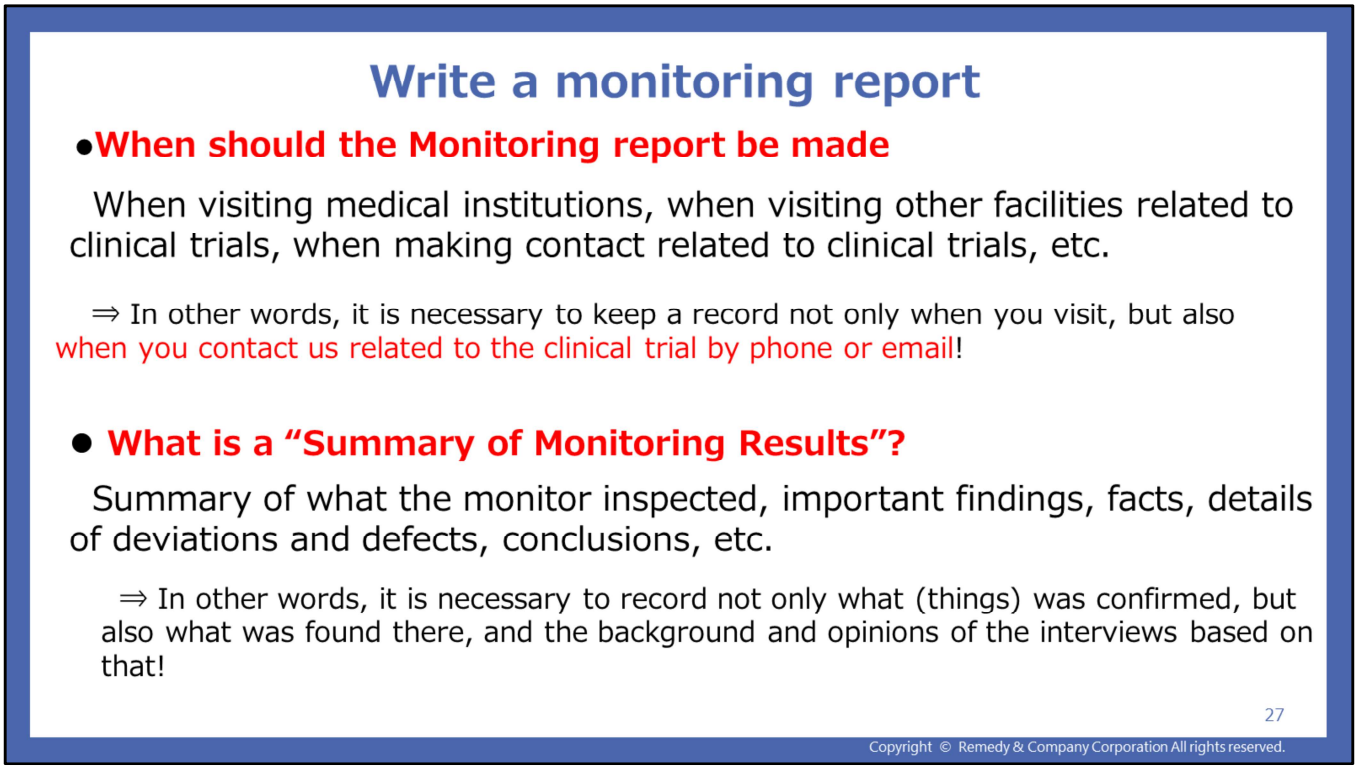
According to GCP Article 22(2), monitors are required to submit a monitoring report to the sponsor each time they conduct monitoring at a medical institution or have contact with it. This report must contain several essential items to ensure comprehensive documentation.

Key Components of the Report include

- Date and Time of Monitoring
- Medical Institutions Subject to Monitoring
- Monitor's Name
- Name of the Investigator
- Overview of Monitoring Results
- Matters Notified to the Investigator
- Measures to Be Taken
- Inquiry Details or description

- By including these key components in your monitoring report, you ensure that all relevant information is documented thoroughly and accurately.

- This practice not only supports regulatory compliance but also enhances the overall quality of the clinical trial process.



Writing a monitoring report is a crucial part of clinical trial oversight.
In this section, we will discuss when to write a monitoring report and what to include in the 'Summary of Monitoring Results.

The first question is {When Should the Monitoring Report Be Made?}

- A monitoring report should be created after each visit to a medical institution, but it's not just limited to visits. You should also write a report when visiting other facilities related to the clinical trial or after any contact related to the trial, whether by phone, email, or other means.

- It's essential to document not only when you physically visit the site but also when you have any communication related to the trial. This includes phone calls, emails, or any interaction that impacts the trial.

The next question is {What is a Summary of Monitoring Results?}

- The Summary of Monitoring Results is a comprehensive overview of what the monitor reviewed during their visit or contact. It includes important findings, key facts, any deviations or defects discovered, and conclusions drawn from the visit.

- In other words, one should record not just what was checked, but also what was found during the review. Any background details and summarize opinions or insights gathered from interviews or discussions with the medical team or investigators need to be included.

What to write in monitor special notes

Then, what should I write down during SDV?

- If you have an SDV checklist, be sure to fill it out
- Even if it is not on the SDV checklist, check all the source documents, check the doctor's opinion if there is any doubt, and take notes
- If you confirm a doubt, make a note so that you can know when, who, what, and why you confirmed it.
- Do not copy the entire medical record, only take notes of the necessary parts
- Do not write down information that can identify the subject (initials, etc.)

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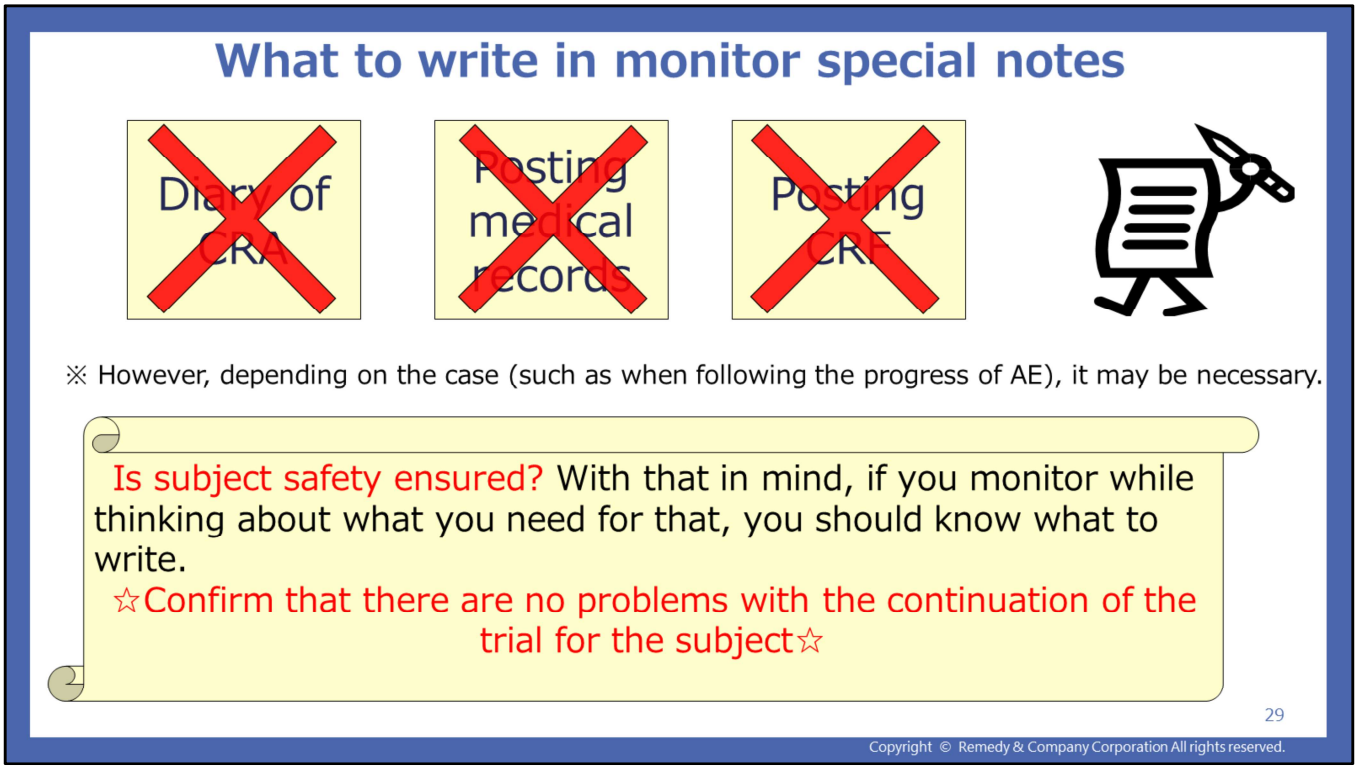
When conducting Source Data Verification (SDV), it's important to know exactly what to document in the monitor special notes. Clear, concise, and accurate notes will help ensure that all data is validated properly and any issues are addressed.

Even if something isn't on the SDV checklist, it's important to check all source documents thoroughly. If there are any doubts or discrepancies, consult with the doctor to clarify their opinion, and take detailed notes to record the process.

Avoid copying entire sections of the medical record. Instead, take notes of only the necessary parts that are relevant to the SDV process. This will keep your documentation focused and manageable.

Being mindful of the confidentiality is crucial. Do not write down any information that could identify the subject, such as names or initials. It's important to protect the subject's privacy throughout the verification process
With these approaches, the SDV documentation will be both complete and effective.



When monitoring a trial or subject's progress, special notes are not just optional but sometimes essential.
Depending on the case, particularly when following adverse events (AEs), these notes can be critical for ensuring subject safety.

Mentioning special notes, items like Dairy of the CRA, Posting medical records/ CRFs are not the special notes to be made.

One of the most important questions one should be asking oneself as and when writing in the monitor special notes is: 'Is the subject's safety ensured?' This thought should guide the documentation process.

If a CRA is tracking an adverse event, noting its progress and any changes in the subject's condition are critical. Be specific about the AE's timeline, any treatments administered, and how the subject has responded. These details help in evaluating if the AE has been appropriately managed.

If you consistently monitor with subject safety and trial integrity in mind, it will become clear what needs to be documented in the special notes. This proactive approach ensures you capture all relevant details to support safe trial continuation.

Special notes play a crucial role in trial safety. Focus on subject safety, monitor for any signs of adverse events, and ensure there are no barriers to the trial's continuation. By doing this, you'll always know what to write.

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