ICH GCP Free Study Guide

An **adverse drug reaction (ADR)** should be considered as potential side effects of any medication, even if they seem minor compared to other possible outcomes. You must meet **applicable regulatory requirements** to conduct a clinical trial. These include any law or regulation that addresses the conduct of such trials and anything else in your country's system for regulating pharmaceuticals as well. Institutional review boards are important for **Approval** in making sure that people in research studies are treated fairly and that their rights, health and safety are protected. An **audit** is an examination of trial related activities to see if they were done accurately and followed the protocol, SOPs, and GCP regulations. **Audit certificates** are a statement by the auditor that an audit has happened. The **Audit Trail** allows documentation to be re-examined on occasions.

Blindings/masking mean single-blinding or double-blind assignments for parties involved in this trial respectively - usually meaning one party doesn't know what they're doing while others do!

The **Case Report Form (CRF)** is a document used to record all the data required by the sponsor for each clinical trial. A **clinical trial** is any investigation of an investigational product (a new drug or treatment) conducted in human subjects, with the goal of determining its safety and/or effectiveness. The **Clinical Trial/Study Report** is a written summary of the trial. A **comparator** is a product that is used as a benchmark in a clinical investigation. This can be an investigational or marketed product, or placebo. **Compliance** means following all the rules for a trial, including the requirements for Good Clinical Practice and any relevant regulations.

A **deal** is an agreement between two or more people. It sets out any arrangements on delegation and distribution of tasks and duties, if appropriate, on financial issues. The protocol could serve as the foundation of a contract.

A **coordinating committee** is a group that a sponsor may organize to work together on a multicentre trial. The **Coordinating Investigator** is responsible for coordinating the investigators at several centers participating in a multicentre trial. A **Contract Research Organization (CRO)** is an individual or a business that is hired by a sponsor to do some of the work related to a clinical trial.

Documentation is any kind of record (written, digital, etc.) that describes how a trial was conducted, the behavior or effects of the trial, and the factors that affected the trial. **Critical documents** are those that allow us to understand a study and the quality of data generated from it. These documents are essential in helping us evaluate a study and its results.

Immediate Access means that we can look at, study, and copy any records and reports that are important to evaluating a medical trial. Any person or organization (like national and international regulatory authorities, sponsor's monitors and auditors) that has direct access should take all reasonable measures to keep subjects' identities and sponsor's proprietary information confidential.

Good Clinical Practice is a set of guidelines for clinical trials. It helps to make sure that the data from the trial is accurate and can be trusted, and that the people taking part in the trial are treated fairly and their rights are protected.

An **Independent Data-Monitoring Committee** (IDMC/Data and Safety Monitoring Board, Monitoring Committee, Data Monitoring Committee) is a separate group of people who are not associated with the clinical trial. This group is responsible for assessing the progress of the trial, safety information, and critical efficacy endpoints. They will then recommend to the sponsor whether to continue, change, or discontinue the trial.

An **impartial witness** is someone who is not involved in the trial and cannot be influenced by anyone associated with the trial. If the subject or the subject's legally acceptable representative cannot read, the impartial witness will attend the informed consent process and read the informed consent form and any other written information provided to the subject.

The **Independent Ethics Committee (IEC)** is a body made up of caregivers and non-medical associates. Its job is to make sure that the rights, safety and wellbeing of human subjects involved in a study are protected. This includes reviewing and approving the trial procedures, the arrangements for the investigators, the facilities and the processes and materials to be used in obtaining informed consent from trial subjects. **Informed consent** is a way for people to agree, in writing, to take part in a study. People taking part in a study must be told about the details of the study before they decide whether or not they want to be in it.

The **inspection** is when the people in charge check to see if everything is being done right in the trial. They look at the records and other things related to the trial, like on the website or at the place where the trial is happening. An **institution** is a private or public entity, agency, medical facility, or dental facility where clinical trials have been conducted. The **Institutional Review Board (IRB)** is a group of people with different expertise who work together to make sure that human subjects involved in a trial are treated fairly and safely. The IRB reviews, approves, and provides continuing review of the trial protocol and amendments, as well as the methods used to obtain informed consent from trial subjects.

Investigational Merchandise is a product with an active ingredient or placebo being tested in a clinical trial, such as a product that is being used in a different way than what is approved, or for an unapproved reason, in order to get more information about an approved use. The **partner** is the person responsible for the clinical trial at a trial site. The investigator is the leader of the group and might be known as the researcher.

The phrase "**investigator or institution**" means the investigator and/or institution as required by the applicable regulatory requirements. The **Investigator's Brochure** is a document that contains all of the information about the investigational product(s) that is relevant to the study of those

products in human subjects. The **Legally Acceptable Representative** is a person or organization that is allowed by law to agree, on behalf of someone who might take part in a clinical trial, that the person can participate in the trial.

Monitoring is the act of making sure a clinical trial is done correctly, according to the protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP), and the applicable regulatory requirement(s). The **monitoring report** is a written report from the monitor to the sponsor after each site visit or other communication related to the trial, according to the sponsor's standard operating procedures. A **multicentre trial** is a clinical trial that is conducted according to a single protocol but at more than one site. This means that it is carried out by more than one investigator.

A **nonclinical study** is a biomedical study that is not performed on human subjects. The **opinion** of an Independent Ethics Committee (IEC) is the judgement and/or advice provided by the committee.

A **protocol** is a document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents. Throughout the ICH GCP Guideline the term protocol refers to protocol and protocol amendments. A **protocol amendment** is a description of a change or clarification to a protocol.

Quality Assurance is a system that helps to make sure that clinical trials are done correctly and that the data generated is reliable. **Quality Control** is a way to make sure that the things we do to get ready for a trial meet the standards we need.

Randomization is the process of assigning trial subjects to treatment or control groups using an element of chance to determine the assignments in order to reduce bias. **Regulatory Authorities** have the power to control or oversee something. In the ICH GCP guideline, Regulatory Authorities refers to the authorities that review submitted clinical data and those that conduct inspections (see 1.29). These bodies are sometimes called competent authorities.

A **serious adverse event (SAE) or serious adverse drug reaction (Serious ADR)** is any negative medical occurrence that, at any dose: - results in death, - is life-threatening, - requires a hospital stay or makes a current hospital stay longer, - causes significant disability or incapacity, or - is a congenital anomaly/birth defect. **Source data** is all the information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial that is necessary for the reconstruction and evaluation of the trial. Source data is contained in source documents (original records or certified copies).

Source Documents are the **original records** and data from a clinical trial, like hospital records, office charts, laboratory notes, subjects' diaries, data from automated instruments, microfiches, photographic negatives, microfilm or magnetic media, x-rays, and records kept at the pharmacy, laboratories and medico-technical departments involved in the clinical trial.

A **sponsor** is a person or group who pays for and helps plan a clinical trial. A **sponsor-investigator** is a person who starts and does a clinical trial. This person is in charge of the trial

and is responsible for giving the investigational product to subjects, or overseeing its use. A sponsor-investigator has both the obligations of a sponsor and an investigator.

Standard Operating Procedures (SOPs) are detailed, written instructions that ensure the uniform performance of a specific function. **Subinvestigators** are any members of the clinical trial team designated and supervised by the investigator at a trial site to perform critical trial-related procedures and/or make important trial-related decisions. **Subjects/Trial Subjects** are individuals who participate in a clinical trial, either as recipients of the investigational product(s) or as controls

The **Subject Identification Code** is a number that is given to each person in a study. This code is used instead of the person's name when the researcher reports any problems that happened during the study. The **Trial Site** is where the study activities happen. An **Unexpected Adverse Drug Reaction** is a problem that happens during the study that is not normal.

Vulnerable Subjects are individuals whose willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or of a retaliatory response from senior members of a hierarchy in case of refusal to participate. The **well-being** of trial subjects refers to their physical and mental integrity.

THE PRINCIPLES OF ICH GCP

1. Clinical trials should follow ethical principles from the Declaration of Helsinki, and be consistent with good clinical practices and applicable regulatory requirements.

2. Before starting a trial, we should weigh the foreseeable risks and inconveniences against the anticipated benefit for the individual trial subject and society. We should only start and continue a trial if the anticipated benefits justify the risks.

3. The rights, safety, and well-being of the trial subjects are more important than anything else, and should always come first over interests of science or society.

4. We should have enough nonclinical and clinical information on an investigational product before starting a clinical trial for that product

5. Clinical trials need to be done carefully and have a plan that is easy to understand.

6. A trial should be conducted following the protocol that has received approval from an institutional review board (IRB) or independent ethics committee (IEC).

7. The medical care given to subjects and the medical decisions made on their behalf should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist.

8. Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective task(s).

9. Informed consent should be obtained from every subject prior to clinical trial participation.

10. All information related to clinical trials should be recorded, stored, and handled in a way that allows for accurate reporting, interpretation, and verification.

11. The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with applicable regulatory requirements.

12. Investigational products should be manufactured, handled, and stored in accordance with applicable good manufacturing practice (GMP) guidelines. They should be used in accordance with the approved protocol.

13. Systems with procedures that assure the quality of every aspect of the trial should be implemented.

INSTITUTIONAL REVIEW BOARD/INDEPENDENT ETHICS COMMITTEE (IRB/IEC)

3.1 Responsibilities

The IRB/IEC should make sure that all trial subjects are safe and treated fairly. They should pay special attention to trials that involve vulnerable subjects.

The IRB/IEC should get the following documents from the investigator: trial protocol(s)/ amendment(s), written informed consent form(s) and consent form updates that the investigator proposes for use in the trial, subject recruitment procedures (e.g. advertisements), written information to be provided to subjects, Investigator's Brochure (IB), available safety information, information about payments and compensation available to subjects, the investigator’s current curriculum vitae and/or other documentation evidencing qualifications, and any other documents that the IRB/IEC may need to fulfil its responsibilities.

The IRB/IEC should review a proposed clinical trial and write down their thoughts within a reasonable amount of time. This way, we can keep track of the trials, the documents that were reviewed, and the dates of the following: - approval/favourable opinion; - modifications required prior to its approval/favourable opinion; - disapproval / negative opinion; and - termination/ suspension of any prior approval/favourable opinion.

The IRB/IEC should review the investigator's qualifications for the proposed trial, as documented by a current curriculum vitae and/or by any other relevant documentation the IRB/ IEC requests. The IRB/IEC should conduct continuing review of each ongoing trial at least once per year, or more often if needed. The IRB/IEC may request more information to be given to subjects than is outlined in paragraph 4.8.10 when the additional information would help protect the subjects' rights, safety and/or well-being.

The IRB/IEC should make sure that the proposed protocol and/or other document(s) adequately address relevant ethical concerns and meet applicable regulatory requirements for non-therapeutic trials that are carried out with the consent of the subject's legally acceptable representative.

If the protocol says that we can't get consent from the person in the trial or their legal guardian, the IRB/IEC should check that the proposed protocol and/or other document(s) address ethical concerns and meet regulatory requirements for such trials (for example, in emergency situations).

The IRB/IEC should review both the amount and method of payment to subjects to assure that neither presents problems of coercion or undue influence on the trial subjects. Payments to a subject should be prorated and not wholly contingent on completion of the trial by the subject.

The IRB/IEC should make sure that the written informed consent form and any other written information given to subjects includes details about how much subjects will be paid for participating in the trial, including how the payment will be divided up.

3.2 Composition, Functions and Operations

The IRB/IEC should have a reasonable number of members who collectively have the qualifications and experience to review and evaluate the science, medical aspects, and ethics of the proposed trial. It is recommended that the IRB/IEC should include: (a) At least five members. (b) At least one member whose primary area of interest is in a nonscientific area. (c) At least one member who is independent of the institution/trial site. Only those IRB/IEC members who are independent of the investigator and the sponsor of the trial should vote/provide opinion on a trial-related matter. A list of IRB/IEC members and their qualifications should be maintained.

The IRB/IEC should do its job according to written operating procedures. This means that it should keep records of its activities and minutes of its meetings. It should also follow good clinical practices and the applicable regulatory requirement(s).

The IRB/IEC should make decisions at announced meetings when at least a quorum of people are present, as stipulated in its written operating procedures. Only members who join the IRB/IEC discussion and review should vote/provide their opinion and/or advise.

The investigator can answer any questions the IRB/IEC has about the trial, but should not join in their discussions or vote. The IRB/IEC may invite experts from outside the group to help with special areas.

3.3 Procedures

The IRB/IEC should establish, document in writing, and follow its procedures, which should include: Determining the names and qualifications of its members and the authority under which it is established. Scheduling, notifying its members of, and conducting its meetings. Conducting initial and continuing review of trials. Determining the frequency of continuing review, as appropriate

The IRB/IEC should be able to review and approve changes to ongoing trials quickly. No subjects should be admitted to a trial until the IRB/IEC has approved it in writing. Any changes to the protocol need written approval from the IRB/IEC, except when it is necessary to protect the subjects or when the change is only logistical (like changing monitors or telephone numbers).

The investigator should report to the IRB/IEC if there are any changes to the protocol that could eliminate immediate hazards to the trial subjects, if there are any changes that would increase the risk to subjects or affect the conduct of the trial, all adverse drug reactions that are both serious and unexpected, or any new information that may adversely affect the safety of subjects or the conduct of the trial.

The IRB/IEC must write to the investigator/institution to let them know about: (a) Any decisions or opinions relating to the trial. (b) The reasons for these decisions or opinions. (c) How to appeal these decisions or opinions.

3.4 Records

The IRB/IEC should keep all important records (for example: written procedures, membership lists, lists of occupations/affiliations of members, submitted documents, minutes of meetings, and correspondence) for at least 3 years after the trial is over. The IRB/IEC may be asked by investigators, sponsors or regulatory authorities to provide its written procedures and membership lists.

4. INVESTIGATOR

4.1 Investigator's Qualifications and Agreements

The person or people investigating should be qualified for the job by their education, training, and experience. They should also meet all other qualifications that are required by the rules. The investigator should provide evidence of their qualifications with a resume or other documentation if requested. The investigator should also be familiar with the product that is being investigated and how to use it according to the protocol.

The investigator should know about and obey the rules in the Good Clinical Practice guidelines. The sponsor of the research project, or a government agency, should be allowed to check up on the investigator and make sure they are doing everything correctly. The investigator should have a list of people who have been delegated important duties for the trial.

4.2 Adequate Resources

The investigator should demonstrate that they can find enough subjects who are good for the study within the time period that was agreed upon. The investigator should have enough time to do the study and finish it within the time that was agreed upon. The investigator should have enough people to help with the study who know what they are doing and have access to good facilities throughout the duration of the study.

4.3 Medical Care of Trial Subjects

A doctor or dentist who is part of the trial should be responsible for all medical or dental decisions related to the trial. During and after a subject's participation in a trial, the investigator/ institution should make sure that the subject has access to adequate medical care for any adverse

events, laboratory values, or intercurrent illnesses related to the trial. The investigator/institution should inform subjects when they need to seek medical care for any reason.

The investigator should tell the subject's primary physician about the subject's participation in the trial if the subject has a primary physician and if the subject agrees to the primary physician being informed. If a subject withdraws prematurely from a trial, the investigator should try to find out why, while respecting the subject's rights.

4.4 Communication with IRB/IEC

Before starting a trial, the investigator or institution should have written approval from the IRB/IEC for the trial protocol, informed consent form, updates to the consent form, subject recruitment procedures (for example, advertisements), and any other written information that will be given to subjects. As part of the investigator's or institution's written application to the IRB/IEC, the investigator or institution should also provide a current copy of the Investigator's Brochure. If the Investigator's Brochure is updated during the trial, the investigator or institution should supply a copy of the updated Investigator's Brochure to the IRB/IEC.

The investigator/institution should provide the IRB/IEC with all relevant documents during the trial.

4.5 Compliance with Protocol

The investigator and institution should do the trial in a way that agrees with the protocol. The protocol is a plan that was approved by the sponsor and regulatory authority, if required. The IRB/IEC also gave their approval. The investigator and sponsor must sign the protocol, or another contract, to agree on the arrangements.

The investigator shouldn't do anything different from what is in the protocol without agreement from the sponsor. An amendment is a change to the protocol. The investigator needs approval/a favourable opinion from the IRB/IEC before making an amendment, unless it is necessary to eliminate a hazard or when the change only affects logistical or administrative aspects of the trial (e.g., change in time, change of phone number).

The investigator may make changes to the protocol to eliminate an immediate hazard(s) to trial subjects without previous IRB/IEC approval/favourable opinion. When possible, the implemented deviation or change, the causes of this, also, if appropriate, the proposed protocol amendment(s) ought to be filed: (a) into the IRB/IEC for inspection and approval/favourable view, (b) to the sponsor for agreement and, when necessary, (c) into the regulatory authority(ies).

The investigator or institution may assign some or all of their duties for investigational product accountability at the trial site to a pharmacist or other suitable person, if allowed or required.

The person in charge of the investigation or the pharmacist should keep records of when the product is delivered to the trial site, how much is left, who uses it, and what happens to the product that is not used. These records must include dates, numbers, batch/serial numbers,

expiration dates (if applicable), and the code numbers assigned to the investigational product(s) and trial subjects. The researcher should keep records that show that subjects were given the doses specified by the protocol and reconcile all investigational product(s) obtained from the host.

The investigational product(s) should be kept as defined by the host and in compliance with applicable regulatory requirements. The investigator should ensure that the investigational product(s) are used only in compliance with the accepted protocol. The investigator or a person designated by the investigator/institution must describe to each subject how to use the investigational product(s) properly and check at times appropriate for the trial that each subject is following directions correctly. If the trial is blinded, the investigator should promptly document and explain to sponsor any early unblinding of investigational product(s).

4.8 Informed Consent of Trial Subjects

The investigator must follow the rules for getting and documenting informed consent. This means getting approval from the IRB/IEC before the trial starts. The investigator must also follow the principles in the Declaration of Helsinki.

The written informed consent form and any other written information given to subjects must be revised whenever important new information becomes available that may affect the subject's approval. Any revised written informed consent form, and written advice, must get the IRB/IEC's approval before it can be used. The subject or the subject's legally acceptable representative should be informed as soon as possible if new information becomes available that may affect the subject's willingness to continue participating in the trial. The communication of this information should be documented.

The investigator or a person working with the investigator should tell the subject or the subject's legally allowed representative about everything important about the trial, including what is written in the advice and also the approval/favourable opinion by the IRB/IEC.

The language used in the trial, including the written informed consent form, must be non-technical and clear to the subject or the subject's legally acceptable representative and the impartial witness (if applicable).

Before obtaining informed consent, the investigator should offer the subject or the subject's legally acceptable representative ample time to ask questions about details of the trial and to choose whether or not to take part in the trial. All queries concerning the trial ought to be answered to the satisfaction of the topic or the subject's legally acceptable representative.

The person being studied must sign a form that says they know what the study is and what will happen. The form must be dated. The person conducting the study must also sign the form.

If a person cannot read or if their legal representative cannot read, an impartial witness must be present for the entire discussion about informed consent. This way, the person will understand what they are agreeing to. After the discussion, if the person agrees to be in the trial, they will sign the form. The witness will also sign and date the form. The trial should have a purpose that

will help the person being tested. If there is no benefit to the person, they should be told about other treatments that might help them and what the risks and rewards of each treatment are. The person should also be told about what will happen if they get hurt during the trial and how much it will cost them to participate. The monitor, auditor, IRB/IEC, and regulatory authority will be allowed to look at the subject's medical records to make sure the clinical trial is being done correctly, without violating the subject's confidentiality. The subject or the subject's legally acceptable representative must sign a form authorizing this access. The records identifying the subject will be kept confidential and won't be made publicly accessible, as long as it is allowed by regulations or laws. If the outcomes of the trial have been published, the subject's identity will stay confidential. The person doing the study will tell the person being studied right away if there is any new information that might affect whether or not they want to keep being in the study. They will also tell them who to talk to if they have any questions or problems, and how long the study will last.

Before participating in the trial, the person or their legal guardian should be given a copy of the signed and dated informed consent form. This form has information about what will happen during the trial. During a subject's involvement in the trial, they or their legal guardian should get a copy of any updates to the consent form and any amendments to the written information given to subjects.

When a clinical trial (therapeutic or non-therapeutic) includes subjects who can only be registered in the trial with the permission of the subject's legally acceptable representative (e.g., minors, or individuals with severe dementia), the subject ought to be informed about the trial to the extent that they can understand it. If they are capable, the subject should sign and personally date the written informed consent form.

When a clinical trial (therapeutic or non-therapeutic) includes subjects who can only be registered in the trial with the permission of the subject's legally acceptable representative (e.g., minors, or individuals with severe dementia), the subject ought to be informed about the trial to the extent that they can understand it. If they are capable, the subject should sign and personally date the written informed consent form.

In emergency situations, when it is not possible to get permission from the person beforehand, we should try to get permission from their legally acceptable representative. If we can't get permission from the person or their representative, we should follow the procedures described in the protocol, with approval from the IRB/IEC. The person or their representative should be told about the trial as soon as possible and agree to continue with additional approval if needed.

4.9 Records and Reports

The investigator should make sure that the information they report to the host is accurate, complete, legible, and timely. Data reported on the CRF should match the source documents, or any discrepancies should be clarified.

Any changes made to a CRF should be dated, initialed, and explained. This includes both written and electronic changes. The original entry should not be obscured. Sponsors should provide advice to investigators or the researchers' designated representatives on making such corrections.

The investigator/institution must keep the trial documents as stated in Essential Documents for the Conduct of a Clinical Trial (see 8.) The investigator/institution must take steps to avoid accidental or premature destruction of those records.

Essential documents should be retained until at least two years following the final approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least two years have elapsed since the formal discontinuation of clinical development of the investigational item. These records should be kept for a longer period however if required by the relevant regulatory requirements or by having an arrangement with the host. It's the obligation of4.9.6 The financial details of the trial ought to be recorded in an agreement between the host and the investigator/institution.

The investigator or institution must have available all requested documents related to the trial, when asked for them by the monitor, auditor, IRB/IEC, or regulatory authority.

4.10 Progress Reports

The investigator must submit written reports about the status of the trial to the IRB/IEC every year, or more often if asked. The investigator should also provide written reports promptly about any changes that could affect the subjects' safety or that raise the risk to subjects. These reports must identify subjects by code numbers instead of using subjects' names, personal identification numbers, or addresses. The investigator must also follow the applicable regulatory requirements for reporting unexpected serious adverse drug reactions to the regulatory authorities along with the IRB/IEC.

If there are any laboratory abnormalities or events that could affect safety, they should be reported to the host according to the coverage requirements and within the time intervals specified by the host in the protocol.

4.12 Premature Termination or Suspension of a Trial

If the trial is stopped early or suspended for any reason, the investigator/institution should immediately notify the trial sponsor, the host institution, and the IRB/IEC. The investigator/ institution should also provide a detailed written explanation of why the trial was stopped or suspended.

If the sponsor terminates or suspends a trial, the investigator must immediately notify the institution. The investigator/institution should also immediately inform the IRB/IEC and supply the IRB/IEC with a detailed written explanation of the termination or suspension. If the IRB/IEC terminates or suspends its approval/favorable view of a trial, the investigator must inform the institution. The investigator/institution should also immediately notify the host and supply the sponsor with a detailed written explanation of the termination or suspension.

4.13 Final Report(s) by Investigator

Upon completion of the trial, the investigator should notify the institution. The investigator/ institution must offer the IRB/IEC a review of the trial's result. The regulatory authority(ies) must be notified of any required reports.

5. SPONSOR

5.1 Quality Assurance and Quality Control

The host is responsible for making sure that trials are conducted and data are generated, documented (recorded), and documented according to the protocol, GCP, and the applicable regulatory requirement(s), by implementing and maintaining quality assurance and quality management systems with written SOPs. The host is also responsible for securing agreement from all involved parties to ensure immediate access (see 1.21) to each of trial related websites, origin data/documents, and reports for the purpose of monitoring and auditing by the sponsor, as well as review by domestic and international regulatory authorities. Quality control ought to be applied to every point of data handling to make sure that all data are reliable and have been processed properly.

The host must have agreements in writing with all the investigators/institutions and other parties involved in the clinical trial. These agreements can be in this protocol or in another arrangement.

5.2 Contract Research Organization (CRO)

A sponsor may transfer any or all of the host's trial-related responsibilities and functions to a CRO, but the ultimate responsibility for its integrity and quality of the trial data always resides with the host. The CRO should apply quality assurance and quality management. Any trial-related responsibility and function that's transferred to and assumed by a CRO ought to be given in writing. Any trial-related responsibilities and functions not specifically transferred to and assumed by a CRO are retained by the host. All references to a host within this guideline apply to a CRO to the extent that a CRO has assumed the trial related duties and functions of a host.

5.3 Medical Experience

The sponsor must designate qualified medical staff that are available to counsel trial related health questions or issues. If needed, external advisors can be used for this function.

5.4 Trial Design

The host of the clinical trial must use qualified people, such as biostatisticians, clinical pharmacologists, and physicians, during all phases of the trial process. This includes designing the protocol and CRFs and preparing investigations into assessing and preparing interim and final clinical trial reports.

5.5 Trial Management, Data Handling, and Record Keeping i.e. ICH GCP guidelines for clinical data management

The host of this trial must use people who are qualified to do the job to supervise the trial. This includes confirming information, conducting statistical analyses, and preparing reports. The IDMC should have written operating procedures and keep records of its meetings.

When using electronic trial data management and/or remote electronic trial information programs, the host needs to: (a) Ensure and document that the electronic data processing procedure(s) adheres to the sponsor's established requirements for completeness, accuracy and reliability, and consistent intended performance (i.e. identification). (b) Maintains SOPs for utilizing such systems. (c) Make sure that these systems are intended to allow data changes in such a manner in which the data changes are documented and that there isn't any deletion of input data (i.e. keep an audit trail, information path, edit path). (d) Keep a safety system which prevents unauthorized access into this information. (e) Keep a list of people who are allowed to change information (see 4.1.5 and 4.9.3). (f) Protect the blinding, if some (for example, keep the data during data entry and processing system).

When data is transformed during processing, it must still be possible to evaluate the original observations and data with the processed data.The host must use an unambiguous subject identification code (visit 1.58) which enables identification of all of the information reported for every topic. The host, along with other owners of this information, should keep each sponsor-specific necessary documents of interest to the trial. The sponsor must maintain all sponsor-specific necessary files in conformance with all applicable regulatory requirement(s) of this country(ies) in which the item is accepted, or at which the sponsor intends to submit an application for approval(s).

If the sponsor stops developing the investigational solution, they must tell all of the trial investigators/institutions and most of the regulatory authorities. Any time this information is transferred to someone else, it must be reported to the proper authority. The sponsor must tell the investigator(s)/association(s) in writing when they need to keep documents and when they can get rid of them.

5.6 Investigator Choice

The host is responsible for choosing the investigator(s) or association(s). The investigators should be experienced and have enough money to do the trial properly. If a coordinating committee or investigator will be used in multicentre trials, the sponsor is responsible for their company and/or choice.

Before agreeing with an investigator or institution to do a trial, the sponsor must give them the routine and an up-to-date Investigator's Brochure. They should also have enough time to read the protocol and other information provided.

The sponsor must make sure the investigator/institution agrees to the following things: (a) conducting the trial according to GCP and all applicable regulatory requirements; (b) complying with processes for information recording/reporting; (c) allowing tracking, auditing, and review; and (d) keeping the trial associated essential files until told by the host that they are no longer needed. The host and investigator/institution need to sign the protocol or another file to verify this agreement.

5.7 Allocation of Duties

The sponsor should set up the trial and assign most responsibilities before it starts.

5.8 Compensation to Subjects and Investigators

If required by the law, the company must offer insurance or a way to pay for medical bills if something bad happens during the trial, except for cases when it is not their fault. The company's policies and procedures must include a plan for how to pay for medical treatment if something bad happens to a person in the trial, in agreement with the law. When people in the trial receive money back for participating, the procedure and way of giving them this money must follow the law.

5.9 Funding

The financial details of the trial should be recorded in an agreement between the host and the investigator/institution.

5.10 Notification/Submission into Regulatory Authority(ies)

Before starting any clinical investigations, the host (or the host and the investigator, if required by applicable regulations) must submit any necessary programs to the proper authorities for approval and/or consent to start the trial. This submission should be dated and include enough information to identify the study. Additionally, there should be a statement from the IRB/IEC that it is functioning in accordance with GCP and applicable regulations. There should also be documentation of IRB/IEC approval as well as, when requested by the host, a recent copy of protocol, written informed consent form(s), and any other written information that will be given to participants.

The sponsor must get written approval from the IRB/IEC for any changes to the trial, including the protocol, informed consent form, or other written information given to subjects. The sponsor must also get documentation from the investigator/institution of any reapprovals, withdrawals, or suspensions of approval from the IRB/IEC.

The sponsor must make sure that there is enough information from studies on the product to know if it is safe and works well before doing trials with people. The sponsor must also update the Investigator's Brochure with new information as it becomes available.

5.13 Manufacturing, Packaging, Labeling, and Coding Investigational Product(s)

The host should ensure that the investigational product(s) (such as active comparator(s) and placebo(if appropriate) is distinguished as appropriate for the stage of growth of the item (s), is fabricated according to any relevant GMP, and can be coded and tagged in a way that safeguards the blinding, if appropriate. Additionally, the labelling must comply with all applicable regulatory requirement(s).

The sponsor must determine, for the investigational product(s), decent storage temperatures, storage requirements (e.g. protection against mild), storage times, reconstitution fluids and

processes, and apparatus for product extract, if any. The host should notify all parties that are involved (e.g. tracks, researchers, pharmacistsand storage managers) of those determinations

The product being investigated should be packed to avoid contamination and deterioration during storage and transport. In clinical trials, the programming system for the investigational product must have a mechanism which allows rapid identification of the product if there is a health crisis, but doesn't allow for imperceptible breaks in the blinding.

If the investigational or comparator product(s) are significantly changed during clinical improvement, the results of some additional studies (e.g. stability, dissolution rate, bioavailability) of the new formula should be available before using the new formula in clinical trials.

5.14 Supplying and Handling Investigational Product(s)

The person hosting the event is responsible for providing the investigator(s)/association (s) with all the investigational product(s)). The host shouldn't provide an investigator/institution with the investigational product(s) before the host obtains all necessary documentation (e.g. approval/ favorable view from IRB/IEC and regulatory authority(ies)).

The host must have written procedures that contain directions for the investigator/institution to follow for storing and handling investigational product(s) for your trial and documentation. The processes should address receipt, handling, storage, unloading, recovery of fresh product in issues, and yield of unused investigational product(s) to the host (or other disposition if approved by the host and in accordance with all the applicable regulatory requirement(s)).

The host needs to: (a) make sure that the investigational product(s) are delivered on time to this investigator(s). (b) Keep records of when the product is sent, received, used, and destroyed (see 8). (c) Maintain a method for getting investigational products back and recording that this recovery happens (e.g. for deficient product remember, recover after trial completion(expired merchandise recover).

The host needs to make sure that the investigational product(s) are stable over the length of usage. They also need to maintain adequate quantities of the investigational product(s) used in trials, so they can confirm specifications if necessary. Samples should be kept until all trial data has been investigated or as needed by applicable regulatory requirements, whichever time period is longer.

5.15 Record Access

The host must make sure that the investigators and associations have access to source data and documents, like trial observations, tests, IRB/IEC inspections, and regulatory reviews. The host must also check that every subject has agreed, in writing, to let the trial observers, auditors, IRB/ IEC inspectors, and regulatory authorities see their medical records from the trial. If the sponsor finds something that could negatively affect the safety of subjects or change how the trial is done, they must tell all of the concerned investigators and associations immediately, as well as the regulatory authority.

The sponsor must submit security upgrades and periodic reports to the regulatory authority. This is according to applicable regulatory requirements.

5.18 Tracking

The main things that monitors do are: (a) Make sure that subjects' rights and wellbeing are protected. (b) Check that the trial is being done according to the approved plan, following Good Clinical Practices, and meeting all other relevant regulations. (c) Ensure that monitors have the training and knowledge needed to carry out their duties satisfactorily. The qualifications of each monitor should be documented.

The host should make sure that the trials have been monitored. The sponsor must decide how much observation is needed. The factors that should be considered include the purpose, function, style, complexity, blinding, size, and endpoints of this trial. Generally speaking there's a demand for onsite observation before, during, and after the trial however in some cases the host may decide that central observation with processes such as researchers' meetings and training can make sure the trial is done according to GCP standards. Statistically controlled sampling could be an acceptable way of selecting which information to check.

5.18.4 Monitor's Responsibilities

The tracks need to make sure that the trial will be done right by doing the following things: (a) Checking that the investigator has enough qualifications and tools to do the job. (b) Making sure that there are enough facilities and employees to safely and properly conduct the trial. (c) Providing the investigational product(s) only to subjects who are qualified for it and in the protocol given dose(s). The people in charge of the study need to make sure that everyone understands how to use the products being tested and that they are stored and used correctly. They also need to keep track of how much product is used at each site and make sure that there is enough product for everyone who needs it. They also need to make sure that any unused product is disposed of properly according to all applicable laws and regulations. Finally, they need to make sure that each person involved in the study has given their informed consent prior to participating and that the investigator has all of the materials and information they need to conduct the study properly. The host will check to see if the investigator and their staff are still working on the trial, in accordance with the protocol and other agreements. They will also check to see if the investigator is only enrolling qualified subjects. The host will also report on the recruitment rate. Additionally, they will check to see if all source files and other documents are accurate and up to date, and that they have been preserved. Finally, they will assess the accuracy and completeness of all essential documents, notifications, applications, and admissions. The monitor should check that the right information has been reported on the CRFs. This includes any changes in dose or treatment, as well as any adverse events, medications, or disorders. The monitor should also make sure that visits, tests, and other activities are properly documented. If there are any mistakes on the CRFs, the monitor should ensure that they are corrected and initialed by the investigator. This permission should be written down. Checking if adverse events happen during the study are being reported at the times that are required by GCP, the protocol, the IRB/IEC, the host, and the regulatory requirement(s). (Checking if the investigator is keeping track of important events.)

5.18.5 Monitoring Procedures

The host's written SOPs must be followed in addition to the processes given by the host for tracking a particular trial.

5.18.6 Monitoring Report

After every trial-site visit or communication related to a trial, the screen must submit an official report to the host. The report must include the date, website, title of the track, and title of the investigator or other person(s) contacted. The report must also include a summary of the track reviewed along with the track's statements regarding any substantial findings/facts, deviations and deficiencies, decisions and actions taken or to be taken, and/or activities recommended to procure compliance. The host's designated agent should follow up and review this observation report with the host.

5.19 Audit

When people do audits as part of quality assurance, they should think about the purpose of the audit. The purpose is to assess whether people are following the protocol and SOPs and whether they are compliant with GCP and applicable regulatory requirements. The sponsor must appoint qualified individuals who are independent of their clinical trials/systems to run research. The sponsor must appoint independent individuals to run research. The sponsor should make sure that the auditors are qualified by experience and training to conduct audits properly. An auditor's qualifications must be recorded. The sponsor should make sure that the clinical trials/systems are audited according to the written procedures. This includes deciding what to audit, how to study it, how often to do it, and what the reports will look like. The host's audit program and processes for a trial should be based on how important the trial is, how many subjects are in the trial, how complex the trial is, and any identified issues. The auditor(s) should document their findings and observations. To maintain the freedom and importance of the audit function, the regulatory authority(ies) shouldn't routinely ask for the audit accounts. Regulatory authority(ies) could find entry to an audit report if there are signs of critical GCP non-compliance, or even during legal proceedings. If required by law or regulation, the host must offer an audit certification.

5.20 Noncompliance

If an investigator or institution does not follow the protocol, SOPs, GCP, or relevant regulatory requirements, or if a member of their host's staff does not follow these requirements, the host should take immediate action to ensure compliance. If an observation or audit reveals that an investigator or institution has been noncompliant for a long period of time, the host must terminate their involvement in the trial. Once an investigator's or institution's participation is terminated due to noncompliance, the host must notify the regulatory authority immediately.

5.21 Premature Termination or Suspension of a Trial

When a trial is prematurely terminated or suspended, then the host should immediately inform the investigators/institutions, along with the regulatory authority(ies) of their conclusion or suspension and the reason(s) for the termination or suspension. The IRB/IEC also needs to be

advised promptly and given the rationale (s) for the termination or suspension from the host or from the investigator/institution, according to the applicable regulatory requirement(s).

5.22 Clinical Trial/Study Reports

When a clinical trial is completed or stopped, the sponsor needs to make sure that the clinical trial results are given to the regulatory agency. The host must also make sure that the clinical trial reports in advertising programs meet the criteria of this ICH Guideline for Structure and Content of Clinical Study Reports. (NOTE: The ICH Guideline for Structure and Content of Clinical Study Reports reveal that abbreviated study reports may be appropriate in certain instances.)

5.23 Multicentre Trials

For multicentre trials, the sponsor must make sure that:

All researchers conduct this trial from strict compliance with the protocol agreed to by the host and, if necessary, from the regulatory authority(ies), also awarded approval/favorable remark by the IRB/IEC.

The CRFs are made to capture the essential information at all multicentre trial websites. For those researchers that are collecting further information, supplemental CRFs must also be supplied that are intended to capture the extra data.

The duties of the coordinating investigator(s) and other participating investigators are recorded before the trial begins. All researchers are given directions on how to follow the protocol, how to comply with a uniform set of criteria for evaluating clinical and laboratory findings, and on finishing the CRFs.

6. But some site-specific advice might be given on separate protocol pages, or in another agreement. And some of the info listed below can be included in other protocol documents, like an Investigator's Brochure. Any changes must also have the amendment number(s) and date(s).

The name and signature of the individual (s) authorized to sign the protocol and any changes to the protocol for your host company.

The name, address, and phone number(s) of their host company's medical practitioner (or dentist when appropriate) for the study.

The name and signature of the investigator(s)) who is/are responsible for conducting the trial, along with the address and phone number(s) of the trial site(s).

The name, address, and phone number of the doctor who is responsible for making medical decisions related to the trial site (if different from the investigator).

The title and address of the clinical laboratory or other technical or medical department involved with the trial.

6.2 Background Information

In this section, you will need to provide the following information:

- The title and description of the investigational product(s)- A list of findings in nonclinical studies that potentially have clinical significance and from clinical trials which are linked to this trial- Summary of the known and possible risks and advantages, if any, to human subjects- An announcement that the trial will be run in accordance with the protocol, GCP and the applicable regulatory requirement(s)- Description of the population to be researched- References to literature and information which are related to the trial, which provide background for your trial

6.3 Trial Objectives and Purpose

The goals and objectives of the trial are listed here.

6.4 Trial Design

The scientific integrity of this trial and the trustworthiness of the information from the trial depend considerably on the trial layout. A description of the trial design, must contain:

A particular statement of the principal endpoints and the secondary endpoints, if any, to be measured throughout the trial. An outline of this type/design of trial must be performed (e.g. double sided, placebo-controlled(parallel design) and a schematic diagram of trial design, processes and phases. A description of the measures required to minimize/avoid prejudice, such as: (a) Randomization. An outline of the trial treatment(s) and the dose and dose regimen of the investigational product(s).

The expected duration of subject participation, and a description of this order and duration of all trial periods, such as followup, if any. A description of the "stopping rules" or "discontinuation criteria" for different topics, elements of trial and complete trial. The identification of any data to be recorded directly on the CRFs (i.e. no previous written or electronic record of data), also to be regarded as source data. (b) The type and timing of this information to be collected for withdrawn subjects. (d) The followup to subjects withdrawn from investigational product treatment/trial therapy.

6.6 Treatment of Topics

The medication(s) being tested must be described in detail, including the name(s) of the medication(s), the dose(s), how often it is taken, and how long the treatment will last. Other medications that are allowed or not allowed during the course of the study must also be listed. Methods and timing for assessing, recording, and assessing of efficiency parameters must be described. The timing and methods for assessing, recording, and assessing safety parameters must also be described. The kind and length of follow-up after adverse events must be described.

6.9 Statistics

There are a few things to consider when planning a statistical analysis for a clinical trial, including:

Timing of any interim analyses. Number of subjects enrolled in the trial. Degree of importance placed on the results. Criteria for ending the trial early. Procedures for reporting any deviations from the original plan. Choice of population being studied (e.g. all enrolled subjects, all subjects who received the study drug, all eligible subjects, evaluable subjects)

The host must ensure that the investigator(s)/association(s) will allow trial-related tracking, audits, IRB/IEC inspection, and regulatory review(s), providing immediate access to supply data/ documents.

Data handling and record keeping must be done according to the protocol. Financing and insurance must be addressed in a separate agreement if not already handled. The publication policy, if not handled in another agreement, must be followed. Supplements (additional relevant information) can be found in the ICH Guideline for Structure and Content of Clinical Study Reports.

INVESTIGATOR'S BROCHURE

7.1 Introduction

The Investigator's Brochure (IB) is a set of data on the investigational product(s) which relate to the analysis of the merchandise (s) in human subjects. Its objective is to deliver the researchers and others involved with the trial using all the data to facilitate their comprehension of the rationale behind, and their compliance with, several important features of this protocol, like the dosage, dosage frequency/interval, techniques of management: and security monitoring processes. The IB also gives insight to help the clinical direction of their research subjects throughout the course of this clinical trial. The info ought to be displayed in a concise, simple, objective, balanced, and also non-promotional type that allows an individual clinician, or possible

The amount and type of information available about a product will change over time as the product grows. If the product is promoted and its pharmacology is widely known by medical professionals, a comprehensive IB might not be necessary. Where permitted by law enforcement, a basic product information booklet, package leaflet, or data sheet could be a suitable choice, as long as it includes comprehensive, current, and accurate information on all aspects of the investigational product that may be of significance to the investigator. If a promoted product has been studied for a new use (i.e., a new indication), an IB specific to this new use should be prepared. The IB must be reviewed at least annually and revised as needed in accordance with changes in the investigational product.

According to Good Clinical Nutrition, important new information might be so significant that it needs to be conveyed to the researchers, and maybe into the Institutional Review Boards (IRBs)/ Independent Ethics Committees (IECs) or regulatory governments before it's contained in a revised IB. Usually, the host is responsible for ensuring an up-to-date IB is made accessible for the investigator(s) and the researchers are responsible for supplying the up-to-date IB into the accountable IRBs/IECs. In the instance of a worker sponsored trial, then the sponsor-investigator must find out if a booklet is available in the industrial maker. If the investigational product is supplied by this sponsor-investigator, then they must offer the essential info to the trial staff.

When it's not practical to have a proper IB, the sponsor-investigator must supply an enlarged background information element instead. This includes the minimal present data described in this principle.

7.2 General Considerations the IB should comprise:

The title page should include the name of the person hosting the study, as well as the identification of every investigational product. This includes the study number, compound or accepted generic title, and transaction name(s). The sponsor may also want to include a statement asking the investigator/recipients to keep the information in the IB private.

7.3 Contents of the Investigator's Brochure

The IB should include these segments, each with literature references where appropriate: Table of Contents An illustration of the Table of Contents is provided.

A short summary (preferably not exceeding two pages) ought to be granted, highlighting the substantial physical, chemical and pharmaceutical, pharmacological, toxicological, pharmacokinetic, metabolic, and clinical data available that's pertinent to this point of clinical development of the investigational item.

The statement should include the name of the product being studied, all of the active ingredients, what the product is expected to do, and why the study is being done. The statement should also explain how the product will be tested.7.3.4 Physical, Chemical, and Pharmaceutical Properties and Formulation

This passage is discussing the need for a description of the investigational product material, including physical, chemical, and pharmaceutical properties. It also states that storage and management directions for the dose form should be provided. Any similarities with other substances should be noted.

ICH GCP E6 R2

On Mar 8, 2018, the FDA updated ICH E6(R1) with **E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1).** Here are some noticeable changes and how they will impact the industry.

One of the key improvements is the new definition of a licensed copy of a situation report form (1.11). This improved definition states that a newspaper or digital copy of the first document is confirmed as valid if it has a dated signature or was generated through a validated procedure that makes an exact copy with all the same features and data as the original. This improvement helps explain how to better ascertain the validity of trial-related documents duplicates, such as source files.

Additionally, the definition of tracking (1.38) has been broadened to incorporate the observation program, which can be described as an outline of methods, duties, and requirements for tracking the trial.

The Investigator department (part 4) has been suggested for improvements. For one, part 4.2.6 has been updated to say that researchers should make sure that anyone they hire to help with research is qualified and able to do the job correctly, and that they have procedures in place to make sure data produced is reliable. These qualifications and responsibilities were not mentioned explicitly in the previous edition, but it was assumed that researchers would follow these guidelines anyway. The updated statements today represent FDA's well-established advice on the researcher's supervisory responsibilities.

There is a new definition for "identification of automatic systems" under the definition for sudden adverse drug response (1.60). However, it is not clear how this new definition relates to adverse medication reactions. It might make more sense to create a new definition for computer validation (1.61) and renumber the definitions for vulnerable themes and well-being into 1.62 and 1.63, respectively. This can be done when the final record is published.

Tracking Report has a new section that says the people who are responsible for the trial and website should get the [tracking] results in a timely manner. They need to review it and take follow up action as needed. The outcomes of monitoring activities must be recorded so we can confirm that people followed the observation program.

The draft for the new sponsor guidelines includes a new segment on quality management (5.0). This segment focuses on risk management procedures for clinical trials, which are not yet widely used in the healthcare sector. The new guidelines will require sponsors to get training and tools to establish risk management principles. Two helpful resources are ICH Q9 (a summary of risk management fundamentals) and ISO 14971 (a worldwide safety standard for medical devices).

The draft does not suggest any changes to Department 3, Institutional Overview Board/ Independent Ethics Committee. In section 4.9, Records and Reports, a new introductory statement (4.9.0) was added which says "[the] investigator must keep accurate and adequate source records and trial documents which have all applicable observations on each of the website's trial topics. Source data should be conducive, legible, contemporaneous, first, authentic, and complete. Changes to supply data should be traceable, shouldn't obscure the original entrance, and should be clarified if required (e.g., through an audit trail)."

Regularly review submitted data. Identify any lost information, conflicting data, outliers, or sudden lack of variability which could indicate mistakes in data collection and reporting on a website, or possible data manipulation or integrity issues. Use statistical analysis to identify trends in the data, like the consistency and range of information within and across websites. Evaluate website features and performance metrics. Select websites and/or procedures for targeted onsite monitoring.

The previous modification increases section 8.1 (Introduction) the following improvements:"[the] host and investigator/institution need to keep a listing of the place(s) of the individual key documents.' The storage method (no matter the media used) need to supply for record identification, research, and recovery. Based upon the actions being completed, individual trials will call for additional files not particularly mentioned in the vital document listing. The host or investigator/institution should incorporate these within this trial master document. The host should make sure that the investigator has command of continuous access to the CRF

information reported to the host. The host shouldn't have management of these data. When a backup is utilized to replace a first record,

The new draft for clinical trials includes several changes. These changes are to the scale, sophistication, and expense of clinical trials. The reason for the changes is because the former version was not well received. Clinical research workers have access to innovative technologies and risk management procedures that might raise efficacy and concentrate on important clinical research actions. E6 has been amended to promote the implementation of advanced and more effective methods to clinical trial design, conduct, supervision, documenting, and reporting. The upgrade also includes changes to describe criteria on electronic documents and documents that are essential. In the end, the new record is intended to assist clinical research protect human subjects and keep information integrity.

The part of the segment on tracking that talks about risk-based observation has been changed to include the components in the FDA's recent advice on risk-based observation. These changes have been made in section 5.18.3 (Extent and Nature of Monitoring) and include the following improvements: "The host must create a systematic, guaranteed, risk-based method of tracking clinical trials. The flexibility at the scope and character of monitoring described in this section is meant to enable diverse approaches that enhance the efficacy and efficiency of observation. A combo of onsite and concentrated monitoring actions could be proper. The sponsor must file the rationale behind the selected observation approach (e.g., from the monitoring program)."

If someone does not follow the rules, they will be punished. This is because people expect others to follow the rules and if they don't, it causes problems. The new rule says that if someone breaks the rules in a big way, they will be investigated and punished.

The draft for the new segment 5.18.7 says that the person hosting the trial must make a plan to deal with any risks. This plan must say what will be done, who is responsible for doing it, how it will be done, and why this is the best way to do it. The plan should also talk about observing things that are not part of regular clinical practice and might need extra training.

Section 5.2 of the Contract Research Organization (CRO) states that sponsors need to be more active in overseeing their CROs. This is especially important for small and startup manufacturers who rely heavily on CROs for all or most trial-related activities. The modifications state that patrons cannot abdicate this duty and have to be more involved in the supervision of the CROs.

ICH is upgrading its procedures to include centralized tracking of data systems as a way to reduce the need for onsite observation. This upgrade will modify Section 5.5.3 (b) to include expectations for normal operating procedures (SOPs) for digital data systems and handling. The new language will require that SOPs cover topics such as system installation, setup, and usage; system identification and performance testing; information collection and handling; shift management; information backup and recovery; contingency planning; and decommissioning.

The people who are responsible for the unmanned systems, the employees, and other people connected to it must make sure that everyone understands what they are responsible for. The consumers must be given instructions on how to use the system. This is important because it

makes sure that the software upgrades or changes to the system are done correctly and that everyone knows what they are supposed to do.