WHO GLOBAL BENCHMARKING TOOL (GBT) FOR EVALUATION OF NATIONAL REGULATORY SYSTEM OF MEDICAL PRODUCTS

CLINICAL TRIALS OVERSIGHT (CT): INDICATORS AND FACT SHEETS

Revision VI version 1

November 2018
Function: 08- CLINICAL TRIAL’S OVERSIGHT (CT)

Description: National Regulatory Authorities (NRAs) should have the legal mandate to authorize, regulate, and, if necessary, terminate clinical trials (CTs). The necessary requirements, guidelines, procedures, and forms should be developed to be in line with country and region-specific guidelines as well as major international CT guidance including guidelines from the Declaration of Helsinki, the Nuremberg Code, International Council on Harmonization, and World Health Organization Good Clinical Practices. CT oversight is aimed at protecting the safety and rights of humans participating in CTs, ensuring that trials are adequately designed to meet scientifically sound objectives, and preventing any potential fraud and falsification of data.

NRAs are responsible at two stages for the critical evaluation of the documentation supporting clinical studies: when CTs are being proposed for authorization and when the results are submitted in an application for marketing authorization. CT protocols should be reviewed and approved by Independent Ethics Committees before the trial commences. A CT review committee should review the protocols and should have the authority, when necessary, to require protocol revisions. The CT review committee should be composed of members who have the appropriate medical and scientific knowledge, experience, and skills and who are free of conflicts of interest.

In order to ensure the quality and safety of investigational products, the investigational products should be manufactured in compliance with Good Manufacturing Practices for investigational medical products, and the supporting preclinical studies should be in compliance with Good Laboratory Practices. Additionally, the importation, storage, use, and/or destruction of investigational products should follow national requirements. Qualified and experienced inspectors should carry out on-site inspections of the CT sites to verify compliance with Good Clinical Practices, ethical principles and regulatory requirements, and to provide assurance of the quality and reliability of the data obtained. The oversight activities should be conducted with due concern for confidentiality.

The legal provisions should allow the NRA to recognize and/or rely on relevant CT decisions, reports and...
information from other NRAs or from designated regional and international bodies. In special circumstances (e.g., for public health interest), the legal provisions should allow the NRA to elect not to follow the routine CT procedures. Transparency in the entire oversight process is fundamental to ensuring the safety of patients and to ensuring that no product with unacceptable benefit to risk balance will be made available to the public.

<table>
<thead>
<tr>
<th>Indicator:</th>
<th>CT01 Legal provisions, regulations and guidelines required to define regulatory framework of clinical trials oversight.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective:</td>
<td>The objective of this indicator is to ensure that the NRA has the legal mandate to both authorize and suspend the implementation of CTs. Among other benefits, the mandate will ensure that regulations and guidelines are in place to protect the safety and rights of the subjects participating in a trial and to ensure that trials are adequately designed to meet scientifically sound objectives.</td>
</tr>
<tr>
<td>Category:</td>
<td>Legal provisions, regulations and guidelines</td>
</tr>
<tr>
<td>Sub Indicator:</td>
<td>CT01.01: Legal provisions and regulations for clinical trials (CTs) oversight exist.</td>
</tr>
<tr>
<td>Maturity Level:</td>
<td>1</td>
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| Description: | The assessor should verify that the legal provisions and regulations for CTs oversight exist and are enacted and implemented. The legal provisions should clearly specify the entities with the mandate for CT oversight and the extent of the mandate for each entity. When more than one entity is involved, the provisions should specify the responsibilities shared among the entities. The assessor should verify that legal provisions and regulations that require National Regulatory Authority (NRA) authorization prior to initiation of clinical studies exist and are enacted and implemented. The assessor should check a representative sample of provided documentation to verify that acceptable procedures were followed. Examples include:
1. Review the mandate for on-site inspections that ensure the location is acceptable and that product quality is maintained during storage;
2. Review informed consent forms and investigator brochure to verify that information and documentation provided are following Good Clinical Practices (GCPs).
The assessor should be guided by the existing law and regulation before applying the scoring. |
<p>| Objective: | The objective of this sub-indicator is to ensure the existence of legal provisions and regulations that require that CTs be authorized by the NRA prior to initiation. The NRA should review the protocol and other relevant documentation to be sure safety of participants is considered and that all required aspects are conducted according to GCPs. |</p>
<table>
<thead>
<tr>
<th>Requirement:</th>
<th>Legislation on CT oversight</th>
</tr>
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</table>
| Evidence to review: | The assessor should ask for and review:  
1. Legal provisions and regulations that grant the NRA the legal mandate for CT oversight.  
2. The sections in the law that define the extent and scope of the CT oversight mandate allocated to the NRA and other entities involved in CT-related activities.  
3. Relevant sections of the law on CTs that stipulate that NRA authorization is required prior to initiating and conducting a clinical study.  
4. The guidelines that define the format and content of protocol, the procedure for submission, and the timeframe for review of application. |
2. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products (40) (http://apps.who.int/medicinedocs/en) |
| Framework: | Structure/Foundation/Input |
| Rating Scale: | NOT IMPLEMENTED (NI): There are no legal provisions or regulations for CTs oversight.  
ONGOING IMPLEMENTATION (OI): The NRA has recently drafted and adopted legal provisions for CTs oversight but they have not yet been followed.  
PARTIALLY IMPLEMENTED (PI): The NRA has legal provisions for conducting CTs oversight and has been applying it for less than two years.  
IMPLEMENTED (I): The NRA has legal provisions for conducting CTs oversight and has adequate documented evidence to support this. |
<p>| Limitations and remarks: | Scoring this sub-indicator as &quot;not applicable NA&quot; is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs). |
| Sub Indicator: | CT01.02: Legal provisions and regulations that stipulates that notification to the NRA and authorization from the NRA is required for any changes or variations (i.e., amendments) in the original protocol or in any relevant documents of the CT. |</p>
<table>
<thead>
<tr>
<th>Maturity Level:</th>
<th>2</th>
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<tbody>
<tr>
<td><strong>Description:</strong></td>
<td>The assessor should verify the existence, enactment, and implementation of legal provisions and regulations related to changes or variations to the original (approved) CT protocols. These provisions should state clearly that the NRA should be notified of any changes or variations to the original protocol, and that authorization from the NRA is required before the changes or variations (i.e., amendments) are implemented. The assessor should note that some protocol amendments may not require authorization from the NRA prior to implementation. Some changes may require a notification prior to or even after implementation, while others require NRA approval before implementation. The assessor should be guided by the existing laws and regulations before applying the scoring.</td>
</tr>
<tr>
<td><strong>Objective:</strong></td>
<td>The objective of this sub-indicator is to ensure that legal provisions and regulations require that the NRA should be notified of changes or variations (i.e., amendments) to the original protocol, and should authorize changes and variations to the original protocol before they are implemented.</td>
</tr>
<tr>
<td><strong>Requirement:</strong></td>
<td>Changes and variations to already approved (original) CT protocols</td>
</tr>
<tr>
<td><strong>Evidence to review:</strong></td>
<td>The assessor should ask for and review: &lt;br&gt; 1. Relevant sections of the legal provisions (laws, decrees, regulations or any legal binding documents) on CTs with emphasis on the requirement for notification and authorization prior to implementation of changes or variations to original protocol and related documents. &lt;br&gt; 2. The guidelines that specify the format and content of submissions related to changes or variations to original protocol, the procedure for submission, and the timeframe for review.</td>
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<tr>
<td><strong>Framework:</strong></td>
<td>Structure/Foundation/Input</td>
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**Rating Scale:**

- **NOT IMPLEMENTED (NI):** There are no legal provisions or regulations requiring notification to and authorization from the NRA when there are changes or variations (i.e., amendments) in the original protocol of the CT.
- **ONGOING IMPLEMENTATION (OI):** The NRA has recently drafted or adopted this legal provision but they have not yet been followed.
- **PARTIALLY IMPLEMENTED (PI):** The NRA has legal provision and has been applying it for less than two years.
- **IMPLEMENTED (I):** The NRA has legal provisions and regulations requiring notification to the NRA and authorization from NRA on changes or variations (i.e., amendments) in the original protocol of the CT; these amendments should be supported with documented evidence.

**Limitations and remarks:**

Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

**Sub Indicator:**

**CT01.03: Legal provisions and regulations requiring research centers, researchers, sponsors, clinical research organizations (CROs) and all relevant institutions in the CT to comply with GCP**

**Maturity Level:**

2

**Description:**

The assessor should verify the existence, enactment, and implementation of legal provisions and regulations that require stakeholders, including research centers, researchers, sponsors, CROs and everyone involved in CTs to comply with the principles of GCP. GCP is an international ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve the participation of human participants. Compliance with this standard provides assurance that the rights, safety and well-being of trial subjects are protected consistent with the principles established in the Declaration of Helsinki, and that CT data are credible. The legal provisions should be supported by detailed and published regulatory requirements for GCP. The published GCP principles should be current and up to date with information on inspections and on suspension or stoppage of trials. When GCP is referenced or adopted, documentation should be available to demonstrate compliance. The assessor should verify that Ethics Committees (ECs) and the NRA consider GCP principles when conducting evaluations.

**Objective:**

The objective of this sub-indicator is to ensure the existence of legal provisions and regulations that mandates stakeholders, including research centers, researchers, sponsors, CROs and everyone involved in CTs to comply with GCP. These provisions will ensure all stakeholders, including research centers, researchers, sponsors, CROs and everyone involved CTs operate within a set of globally-accepted standards for the conduct of biomedical research on human participants.

**Requirement:**

Stakeholder acting in compliance with GCP
### Evidence to review:
The assessor should ask for and review:
1. The legal provisions (laws, decrees, regulations or any legal binding document) that require stakeholders involved in CT to comply with GCP principles.
2. The current GCP requirements for all CTs. The GCP standards should be published and easily accessible.
3. Guidelines or similar documents (e.g., checklists and standard operating procedures (SOPs)) used to provide guidance in the application of the legal provisions and regulations.

### References:
1. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products (40) (http://apps.who.int/medicinedocs/en)

### Framework:
Structure/Foundation/Input

### Rating Scale:
- **NOT IMPLEMENTED (NI):** There are no legal provisions or regulations requiring research centers, researchers, sponsors, CROs and everyone involved in the CTs to comply with GCP
- **ONGOING IMPLEMENTATION (OI):** The NRA has recently drafted or adopted these legal provisions and regulations but they have not yet been followed.
- **PARTIALLY IMPLEMENTED (PI):** The NRA has developed this legal provision and has been applying it for less than two years, or not all involved organizations have fully followed this regulation.
- **IMPLEMENTED (I):** The NRA has legal provisions and regulations requiring research centers, researchers, sponsors, CROs and everyone involved in CTs to comply with GCP; compliance is supported with documented evidence.

### Limitations and remarks:
The assessor should consider that existing written documents are legally binding.

Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

### Sub Indicator:
**CT01.04: Legal provisions, regulations and guidelines requiring that investigational medical products (IMPs) comply with good manufacturing practices (GMP) for IMPs**
## Maturity Level: 3

### Description:
The assessor should verify the existence, enactment, and implementation of legal provisions, regulations and guidelines that require that IMPs comply with the GMPs for IMPs. The legal provisions should clearly state that only IMPs produced in compliance with current GMP standards for IMPs will be used in CTs, and that the applicant or sponsor of the CT is responsible for supplying IMPs produced in accordance with GMP principles. The legal provisions should be supported by regulations or guidelines that clearly present the applicable GMP requirements and the type of supporting evidence to present (e.g., certificates and summary product release documents). The assessor should note that some NRAs may not require a GMP certificate if the IMP is already licensed or registered in the country of origin. However, according to good regulatory practices, a current GMP certificate from the NRA of the country of origin should be required when the IMP has a marketing authorization in the country of origin or has a marketing authorization, but the original indication is modified for the purpose of the trial.

### Objective:
The objective of this sub-indicator is ensure the existence of legal provisions, regulations and guidelines that mandate that IMPs used in CTs comply with GMP requirements.

### Requirement:
IMPs GMP requirements

### Evidence to review:
The assessor should ask for and review:
1. The legal provisions (laws, decrees, regulations or any legal binding document) and guidelines requiring that IMPs used in CTs are produced in compliance with the principles of GMPs for IMPs.
2. The legal provisions, regulations and guidelines that state that it is the responsibility of the sponsors or applicants to supply IMPs produced in compliance with the principles of GMP for IMPs.
3. Documentation specifying the format for the IMP’s GMP certificate that is required prior to CT authorization. The GMP certificate should be issued by the national competent authority of the country of origin of the IMP.

### References:
1. WHO good manufacturing practices for pharmaceutical products: main principles (51) (http://digicollection.org/whoqapharm/p/about and http://apps.who.int/medicinedocs/en)
2. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products (40) (http://apps.who.int/medicinedocs/en)

### Framework:
Structure/Foundation/Input
### Rating Scale:

- **NOT IMPLEMENTED (NI):** There is no evidence of existence of legal provisions, regulations or guidelines requiring that IMPs comply with GMPs for IMPs.
- **ONGOING IMPLEMENTATION (OI):** The NRA has recently drafted or adopted these legal provisions, regulations and guidelines but they have not yet been implemented.
- **PARTIALLY IMPLEMENTED (PI):** The NRA has legal provisions, regulations and guidelines and has been applying them for less than two years.
- **IMPLEMENTED (I):** The NRA has legal provisions, regulations and guidelines requiring that IMPs comply with GMPs for IMPs.

### Limitations and remarks:

Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

### Sub Indicator:

**CT01.05:** There are legal provisions or regulations covering circumstances in which the routine CT evaluation procedures may not be followed (e.g. for public-health interests)

### Maturity Level:

2

### Description:

The assessor should verify the existence, enactment, and implementation of legal provisions or regulations that allow the NRA to apply non-routine CT procedures such as fast-track or expedited decision-making (e.g., receipt, screening, evaluation, review, and authorization) of a CT application under certain circumstances (e.g., public health emergencies). The legal provisions and regulations should provide clear directives on the circumstances under which the non-routine CT authorization should apply. The provisions should provide guidance on the relationship between the non-routine CT authorization and the mandate of the Independent Ethics Committee (IEC). The legal provisions should be supported with guidelines that describe the content (e.g., the critical requirements) and format of CT applications submitted for approval by the non-routine authorization procedure. This guidance should also describe the scope of the review and evaluation process (i.e., screening, verification, and other relevant activities). The supporting guidelines may provide clarity on whether a CT application rejected through the non-routine procedure could be re-submitted through the routine procedure. In addition, there should be a guidance document to provide direction to the NRA on how to justify application of the non-routine procedure to the CT.

The assessor should verify that the proposed procedures meet targeted timeframes for public health emergencies or any other unmet medical needs.

### Objective:

The objective of this sub-indicator is to ensure legal provisions and regulations are established to allow the NRA or responsible regulatory authority to apply non-routine CT procedures such as fast-track or expedited receipt, evaluation, and authorization of a CT application under certain circumstances (e.g. public health emergencies). This sub-indicator will establish whether there is an
<table>
<thead>
<tr>
<th>Requirement:</th>
<th>Exemptions from routine CT application evaluation procedures</th>
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<tr>
<td>Evidence to review:</td>
<td>The assessor should ask for and review: 1. Guidelines or similar document that provides the list of situations in which the routine CT procedures may not be required. 2. Legal provisions (laws, decrees, regulations or any legal binding document) that cover circumstances or instances under which the non-routine CT procedures such fast-track CT authorization may be applied. Assessor should review evidence that the legal provisions are published and implemented. 3. The supporting guidelines and regulations. 4. Guidelines describing the content and format of CT applications requesting application of non-routine CT procedures such as fast-track. 5. Guidelines specifying the scope of the evaluation process (i.e., screening, verification, or other relevant activities).</td>
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<tr>
<td>Framework:</td>
<td>Structure/Foundation/Input</td>
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<tr>
<td>Rating Scale:</td>
<td>NOT IMPLEMENTED (NI): There are no legal provisions or regulations to cover circumstances under which the NRA may elect to follow the non-routine CT application process. ONGOING IMPLEMENTATION (OI): The NRA has drafted or adopted these legal provisions or regulations, but they have not yet been followed. PARTIALLY IMPLEMENTED (PI): The NRA has legal provision or regulation and has been applying it for less than two years. IMPLEMENTED (I): The NRA has legal provisions or regulations to cover circumstances in which the NRA may elect to follow the non-routine CT application process (e.g., for public health interest).</td>
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<tr>
<td>Limitations and remarks:</td>
<td>The assessor should consider any kind of legal document that address this requirement.</td>
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<tr>
<td>Sub Indicator:</td>
<td>CT01.06: Legal provisions, regulations or guidelines exist for NRA to inspect, suspend or stop CTs</td>
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<tr>
<td>Maturity Level:</td>
<td>3</td>
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<tr>
<td><strong>Description:</strong></td>
<td>The assessor should verify the existence, enactment, and implementation of legal provisions or regulations that give the NRA enforcement powers to inspect, suspend or stop CTs. The legal provisions should be supported with clear regulations or guidance on when (i.e., routine, random or for specific reasons) and how to inspect, suspend or stop a CT. Clear guidance on what to inspect (e.g., evidence supporting quality and reliability of data and reported results or records for subjects, equipment, protocols, and environment) should also be considered.</td>
</tr>
<tr>
<td><strong>Objective:</strong></td>
<td>The objective of this sub-indicator is to ensure legal provisions or regulations are established to give the NRA enforcement powers to inspect, suspend or stop CTs.</td>
</tr>
<tr>
<td><strong>Requirement:</strong></td>
<td>Legal provisions, regulations or guidelines to inspect, suspend or stop CTs</td>
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</table>
| **Evidence to review:** | The assessor should ask for and review:  
1. The legal provisions (laws, decrees, regulations or any legal binding document) that give the NRA the enforcement power to inspect, suspend or stop CTs.  
2. Documents providing guidance on procedures to follow for inspecting, suspending or stopping CTs.  
3. List of CTs inspected, suspended or stopped. |
3. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products (40) (http://apps.who.int/medicinedocs/en)  
| **Framework:** | Structure/Foundation/Input |
| **Rating Scale:** | NOT IMPLEMENTED (NI): There are no legal provisions, regulations or guidelines for NRA to inspect, suspend or stop CT  
ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the regulations or guidelines, but these have not yet been followed.  
PARTIALLY IMPLEMENTED (PI): The NRA has legal provisions, regulations or guidelines and has been applying them for less than |
two years or the guidelines or regulations are not fully implemented for all CT applications.

IMPLEMENTED (I): The NRA has legal provisions, regulations or guidelines to inspect, suspend or stop CTs and these are implemented and followed for all approved CT applications.

Limitations and remarks:
If there is no CT ongoing, the assessor may score this sub-indicator as implemented by reviewing guidelines or other required documentation.

Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator: **CT01.07: There are legal provisions or regulations that require the establishment of an IEC**

Maturity Level: 2

Description:
The assessor should verify the existence, issuance, and implementation of regulations that require the establishment of an IEC. The regulations should be clear on the specific authority that should host the IEC and that should assist it to successfully discharge its duties and mandates. The legal provisions should provide guidance on what it means to be “independent”, and also provide supporting regulations and guidelines that ensure that the independence of the IEC is sustained. The objectives, functions and composition of the IEC should be clearly defined and documented, and a general policy on potential conflicts of interest for IEC members should be provided. The assessor should note that there may be more than one legally established IEC in a country. The assessor should therefore verify the legal mandate of the IEC in question and the scope of its activities.

Objective:
The objective of this sub-indicator is to ensure regulations are in place requiring the establishment of an IEC to review the CTs. For each CT, the IEC should verify that safety, integrity, and human rights of participating subjects are protected. The IEC should consider the general ethics of the trials, and thereby promote public reassurance.

Requirement: Establishment of IEC

Evidence to review:
The assessor should ask for and review:
1. Legal provisions (laws, decrees, regulations or any legal binding document) mandating the establishment of an IEC.
2. Documentation defining the identity of the designated authority that has the mandate to host the IEC and to assist the IEC in discharging its duties.
3. Documentation defining the selection criteria for the members of the IEC, the number of members on the IEC, and the term of office for each member.
4. Documentation defining the mechanisms and structures to ensure the independence of the IEC, and documentation providing
the code of conduct for ICE members.
5. The policy on potential conflicts of interest for members of the IEC.

References:
2. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products (40) (http://apps.who.int/medicinedocs/en)

Framework: Structure/Foundation/Input

Rating Scale:
- NOT IMPLEMENTED (NI): There are no legal provisions or regulations requiring the establishment of an IEC.
- ONGOING IMPLEMENTATION (OI): The legal provisions or regulations that require the establishment of an IEC have recently defined or drafted, but these have not yet been implemented.
- PARTIALLY IMPLEMENTED (PI): The legal provisions or regulations requiring the establishment of an IEC have been developed and the IEC has been established for less than two years.
- IMPLEMENTED (I): The NRA has legal provisions or regulations requiring the establishment of an IEC and the IEC is established.

Limitations and remarks: Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator: CT01.08: Legal provisions, regulations and guidelines that require authorization for the import or destruction of IMPs

Maturity Level: 2

Description:
The assessor should verify the existence, enactment, and implementation of legal provisions, regulations and guidelines requiring that the NRA authorize the import, export or destruction of IMPs. The legal provisions should be supported with regulations and guidelines that provide guidance on the permitted quantities to export or import. The assessor should note that the quantities to import, export or destroy should be justified in relation to the timelines for the CT and the use of the IMPs as specified in the CT protocol. The provisions should provide guidance on the import, export or destruction process, and define the roles and responsibilities of the various stakeholders, including the sponsor, principal investigator, and other participants. The guidelines should include:
1. Guidelines on the acceptable or allowable quantities of IMPs to import or export;
2. Guidelines on the appropriate destruction methods (i.e., by the NRA or supervised by the NRA);
3. Procedures for a feedback mechanism to inform the NRA on quantities left over after the CT.

The guideline and application forms should be developed and easily available to the sponsor and other stakeholders. The
<table>
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<tr>
<th><strong>Objective:</strong></th>
<th>The objective of this sub-indicator is to ensure the existence of legal provisions, regulations and guidelines that require the NRAs (or responsible regulatory authority) to authorize import, export or destruction of IMPs.</th>
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<tbody>
<tr>
<td><strong>Requirement:</strong></td>
<td>Legal provisions, regulations and guidelines to import, export and destroy IMPs</td>
</tr>
</tbody>
</table>
| **Evidence to review:** | The assessor should ask for and review:  
1. Legal provisions (laws, decrees, regulations or any legal binding document) and guidelines on the import, export and destruction of IMPs. The assessor should verify that IMPs imported or exported for the purposes of CT application submissions require authorization.  
2. The guidance documents and application forms for requesting assistance from the NRA to import, export or destroy IMPs, as well as guidance on the processes to be executed upon receipt of an application.  
3. Records of IMPs imported, exported or destroyed since the last NRA inspection.  
4. Guidelines or similar documents providing guidance on the justifiable quantities of IMPs that should be imported or exported relative to the timelines in the CT protocol.  
5. Guidance defining the stage in the CT application process at which IMPs may be imported or exported. |
| **References:** | 1. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products (40) (http://apps.who.int/medicinedocs/en)  
| **Framework:** | Structure/Foundation/Input |
| **Rating Scale:** | NOT IMPLEMENTED (NI): There are no legal provisions, regulations or guidelines that require authorization for the import, export and destruction of IMPs.  
ONGOING IMPLEMENTATION (OI): The legal provisions, regulations or guidelines that require authorization for the import, export and destruction of IMPs exist, but these have not yet been implemented.  
PARTIALLY IMPLEMENTED (PI): The legal provisions, regulations or guidelines that require authorization for the import, export and
destruction of IMPs have been established for less than two years.

IMPLEMENTED (I): The NRA has legal provisions, regulations or guidelines that require authorization for the import, export and destruction of IMPs, and there is documented evidence that it is applied to all IMPs

Limitations and remarks: Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator: CT01.09: There are requirements for monitoring and reporting of adverse events and reactions during conduct of CT.

Maturity Level: 2

Description: The assessor should verify the existence and implementation of requirements for monitoring and reporting of adverse events and reactions. Such requirements should clearly provide guidance on monitoring of adverse reactions and on following up when they are observed. The guidance should provide clarity on the roles, responsibilities, and duties of all stakeholders, including the NRA. The guidance should also specify the exact requirements for monitoring during the period of the CT, including, for example, collection and evaluation of data and reporting of adverse reactions and events. The guidance should define the type, nature, and form of adverse reactions or events to report. In the event that reporting to more than one NRA, authority, or stakeholder (e.g., sponsor) is required, the sequence for reporting should be indicated. The guideline should be supported by a form for monitoring and reporting adverse reactions and events.

Objective: The objective of this sub-indicator is to ensure the existence of requirements that mandate that investigators and sponsors monitor all subjects involved in CTs. The requirements should include an obligation to report, to the NRA or responsible regulatory authority, all adverse or serious adverse reactions and events within the approved time frame for reporting.

Requirement: Monitoring and reporting adverse reactions and events

Evidence to review: The assessor should ask for and review:
1. The guidelines and regulations on monitoring and reporting of adverse events and reactions, as well as the guidance on required follow up. The assessor should verify that the guidelines have been implemented.
2. Documentation that specifies the exact roles, responsibilities, and duties of each stakeholder. These should be compared to World Health Organization (WHO) recommendations or other international standards.
3. The NRA recommendations to the sponsors and investigators on the procedures for monitoring and reporting of adverse events and reactions. The assessor should verify that the recommendations are in line with WHO or other international standards.
4. Documentation establishing the committee responsible for reviewing reports of adverse reactions and events, and
Guidelines defining the timelines allocated for reporting adverse reactions and events on the part of the investigator or sponsor and timelines for generating and submitting a report on the adverse reaction or event to the NRA.

6. Examples of records of completed forms sent to the NRA. The assessor should verify that the format and content is in compliance with applicable guidelines.

References:
2. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products (40) (http://apps.who.int/medicinedocs/en)

Framework: Structure/Foundation/Input

Rating Scale:
- NOT IMPLEMENTED (NI): There are no requirements or guidelines on monitoring and reporting of adverse events and reactions.
- ONGOING IMPLEMENTATION (OI): The requirements on monitoring and reporting of adverse events and reactions are drafted or defined, but these have not yet been followed.
- PARTIALLY IMPLEMENTED (PI): The requirements and guidance on monitoring and reporting of adverse events and reactions have been developed for less than two years or there are no reports from any CTs.
- IMPLEMENTED (I): The requirements and guidance on monitoring and reporting adverse events and reactions exist and all sponsors are following them.

Limitations and remarks:
The assessor may score this sub-indicator as implemented if there are no records because there are no ongoing CT studies.

The review of the reported adverse events and reactions can be conducted by internal staff if the NRA has access to adequate number of competent reviewers and experts.

Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator: CT01.10: There are guidelines on the format and content of CT applications

Maturity Level: 2

Description: The assessor should verify that guidelines on the format and content of CT applications exist and are issued and implemented. The guidelines should provide clear guidance on the format and content (i.e., a list of required information and documents) of the CT application dossier to be submitted to the NRA. The content may include but is not limited to;
1. CT registration with a registry that is approved and recognized by the NRA;
| 2. covering letter addressed to head of the NRA;  
3. completed CT application forms that should be signed and dated by authorized persons;  
4. CT Protocol;  
5. investigator’s brochure;  
6. investigational product dossier;  
7. GMP certificate;  
8. evidence of approvals from EC and institutional review board;  
9. evidence of insurance coverage (from a recognized insurance company);  
10. statement or evidence of financial support and declaration of support;  
11. data safety monitoring board membership and signed charter;  
12. evidence of contractual agreement between sponsor and principal investigator;  
13. sample of informed consent form;  
14. assent forms (if applicable);  
15. statistical analysis plan, if applicable;  
16. professional profile (i.e., qualifications, experience, expertise, evidence of excellent knowledge of local CT regulatory requirements, and list of previous CTs managed) for potential principal investigator, study pharmacist, local monitor, and other relevant participants. |

The guidelines should also provide guidance on the sequence of events to be followed before the actual submission (e.g., meetings, workshops, seminars, IEC meetings, and other relevant activities). The guidelines may provide guidance on choosing a CT site and selection of subjects.

**Objective:**

The objective of this sub-indicator is to ensure the existence of a clear guidance document that guides the applicant and sponsor on the information (i.e., content and format) to be included in the application package. The guidance should include the procedure for submitting the application to the NRA for evaluation. The content of the guidance document should be sufficient to facilitate CT activities.

**Requirement:**

Format and content of CT applications

**Evidence to review:**

The assessor should ask for and review:

1. Evidence that the guidelines on the format and content of the CT application are available, implemented and published on the NRA’s website.
2. Evidence that accessory documents such as CT application forms and other CT related forms exist and are issued and used.
3. Documentation specifying the format and nature of CT application submission package (i.e. electronic or face-to-face communications, hard or soft copies, and number of copies to be submitted).
4. List of critical documents that should be included in the application package.

References:
2. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products (40) (http://apps.who.int/medicinedocs/en)

Framework:
Structure/Foundation/Input

Rating Scale:
NOT IMPLEMENTED (NI): There are no guidelines on the format and content of CT applications.
ONGOING IMPLEMENTATION (OI): The guidelines on the format and content of CT applications have been drafted or adopted, but they have not yet been implemented.
PARTIALLY IMPLEMENTED (PI): The format and content of CT applications has been established and they have been applied for less than two years.
IMPLEMENTED (I): The NRA has guidelines on the format and content of CT applications and they are being followed for all received CT applications.

Limitations and remarks:
Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

Sub Indicator:
CT01.11: Legal provisions or regulations allow the NRA to recognize and use relevant CT decisions, reports or information from other NRAs or from regional and international bodies.

Maturity Level:
1

Description:
The assessor should verify the existence, enactment, and implementation of legal provisions or regulations that allow the NRAs to recognize and use relevant CT decisions, reports or information from other NRAs or from regional and international bodies. The legal provision and regulations should provide guidance on the modalities, processes and procedures to employ when recognizing
and using relevant CT decisions, reports or information from other NRAs or from regional and international bodies. The legal provisions should also provide guidance on the conditions (i.e., when and how) to recognize and use relevant CT decisions, reports or information from other NRAs or from regional and international bodies. The legal provisions and regulations should also provide clear directives on the scope or extent of recognition and use of the CT decisions, reports or information from other NRAs or from regional and international bodies.

**Objective:**
The objective of this sub-indicator is to ensure the existence of legal provisions or regulations that allow the NRA to recognize and use relevant CT decisions, reports or information from other NRAs or from regional and international bodies.

**Requirement:**
Recognition of and reliance on CT application decisions and information

**Evidence to review:**
The assessor should ask for and review:
1. The legal provisions (laws, decrees, regulations or any legal binding document) that permits the NRA to recognize and use relevant CT decisions, reports or information from other NRAs or from regional and international bodies.
2. Guidelines that define the scope and extent of recognition and use of relevant CT decisions, reports or information from other NRAs or from regional and international bodies.
3. Examples of instances or situations in which the NRA permitted recognition and use relevant CT decisions, reports or information from other NRAs or from regional and international bodies.
4. List of NRAs or regional and international bodies whose relevant decisions, reports or information may be used to influence a CT application decision. Documentation that indicate whether those NRAs or regional and international bodies are aware that their relevant CT decisions, reports or information on certain CTs may be used (i.e., aware of the legal provision).

**References:**

**Framework:**
Structure/Foundation/Input

**Rating Scale:**
- **NOT IMPLEMENTED (NI):** There are no legal provisions or regulations that allow the NRA to recognize and use relevant CT decisions, reports or information from other NRAs or from regional and international bodies.
- **ONGOING IMPLEMENTATION (OI):** The legal provisions or regulations that allow the NRA to recognize and use relevant CT decisions, reports or information from other NRAs or from regional and international bodies are drafted or pending for adoption.
- **PARTIALLY IMPLEMENTED (PI):** Legal provisions or regulations allowing the NRA to recognize and use relevant CT decisions, reports or information from other NRAs or from regional and international bodies have been established and the NRA has been applying...
them for less than two years.

**IMPLEMENTED (I):** There are legal provisions or regulations allowing the NRA to recognize and use relevant CT decisions, reports or information from other NRAs or from regional and international bodies; this is supported with adequate documentation (e.g., criteria for selection or list of NRAs recognized or used)

**Limitations and remarks:** Reliance or recognition should be considered optional if the NRA has the expertise, capacity, and resources to conduct reviews of all CT applications received.

**Indicator:** CT02 Arrangement for effective organization and good governance

**Objective:** The objective of this indicator is to ensure that there is a legal basis for the organizational structure and governance that allows for the smooth exchange of information within and outside the entity responsible for CTs (e.g., NRA, ethical committee, or clinical research organization). The arrangement should define the roles and responsibilities of those persons within the entities which are in charge of the various component activities within the CT. The arrangement should also clarify how the roles of these individuals relate to the governance structure of the organization responsible for CTs, as well as how they relate to outside organizations such as the other CT-related NRAs or other competent regulatory authorities. Effective implementation of these arrangements will ensure that the NRA responsible for CTs has complete control of all the information related to CTs, including information about ongoing CTs, new directives, authorizations, suspensions and rejections, and other relevant activities.

The objective of this indicator is to establish that structures are in place at the organizational and governance levels to promote effective intra- and inter-NRA relationships so that information traffic is efficiently managed.

**Category:** Organization and governance

**Sub Indicator:** CT02.01: There is a defined structure with clear responsibilities to conduct CT oversight activities

**Maturity Level:** 2

**Description:** The assessor should verify that the existence and implementation of a defined structure with clear responsibilities to conduct CT oversight activities. The organizational structure should be supported by legal provisions, regulations and guidelines. These legal provisions should clearly delineate the roles, responsibilities and duties of all stakeholders inside and outside the NRA. The guidelines should define the scope and extent of the roles and responsibilities of those within the NRA with respect to CT oversight activities. Additionally, lines of reporting should be clearly established. The structure of the entity or authority, with respect to
relationships and ranks, should be established and implemented. Similarly, the mechanisms for information exchange within and outside (e.g., the IEC) the entity or authority should be established and implemented. Assessor should verify the existence and implementation of guidelines for the establishment of advisory committees (e.g., technical expert committees or external expert committees) with clearly-defined objectives, functions, composition, and terms of reference (ToRs).

| Objective: | The objective of this sub-indicator is to ensure there are structures in place, with clearly defined roles and responsibilities for each structural and governance level, for CT oversight activities. |
| Requirement: | Structure and Responsibilities |
| Evidence to review: | The assessor should ask for and review:  
1. Guidelines that define the roles, responsibilities, and duties of the entity responsible for CT oversight within the NRA, and guidelines that define their placement on the organizational chart in relation to other entities involved in CTs.  
2. The regulations or guidelines that provide the mandate to this entity or authority to conduct CT oversight activities within the NRA.  
3. Documentation of a clearly defined policy on conflicts of interest.  
4. The operational manual (or similar document) of the entity responsible for this activity. The manual should contain all the authorized and approved guidelines (published or not), application forms (published or not), and SOPs (or similar documents).  
5. Published CT application processing flow diagrams and corresponding timelines.  
6. Published schedule of any applicable fees and charges. |

References:

Framework: Structure/Foundation/Input

Rating Scale:

NOT IMPLEMENTED (NI): There is no defined structure with clear responsibilities to conduct CT oversight activities.  
ONGOING IMPLEMENTATION (OI): The NRA has recently drafted a defined structure with clear responsibilities to conduct CT oversight activities.  
PARTIALLY IMPLEMENTED (PI): The NRA has established a defined structure with clear responsibilities to conduct CT oversight activities; however there is the need to improve this function by providing required support for effective implementation and coordination.  
IMPLEMENTED (I): The NRA has established a defined structure with clear responsibilities to conduct CT oversight activities that is fully supported with required resources.
<table>
<thead>
<tr>
<th>Limitations and remarks:</th>
<th>Scoring this sub-indicator as &quot;not applicable NA&quot; is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sub Indicator:</strong></td>
<td><strong>CT02.02: Documented procedures are implemented to ensure the involvement and communication among all stakeholders relevant to CTs</strong></td>
</tr>
<tr>
<td><strong>Maturity Level:</strong></td>
<td>3</td>
</tr>
<tr>
<td><strong>Description:</strong></td>
<td>The assessor should verify the existence and implementation of documented procedures that promote involvement and communication among all stakeholders. The procedures should provide clear directives on the regulatory divisions and guidance on how to implement the operational procedures to ensure the involvement and communication among all stakeholders within and outside the NRA (e.g., the entity responsible for CT oversight, IEC, GCP inspectorate, sponsors, principal investigator, and other relevant entities). Procedures should be clear on the scope and extent of the roles and responsibilities of each stakeholder. In addition, the procedure should be supported by an information and documentation transfer policy to ensure that directives, information, and documentation reach the intended recipients and that feedback is received. SOPs or similar documents and guidelines should be approved, authorized and implemented.</td>
</tr>
<tr>
<td><strong>Objective:</strong></td>
<td>The objective of this sub-indicator is to ensure there are documented procedures, structures, and mechanisms in place to ensure proper relationships within and among the entities involved in CTs in order to ensure effective and efficient exchange of information among stakeholders.</td>
</tr>
<tr>
<td><strong>Requirement:</strong></td>
<td>CT stakeholders interactions</td>
</tr>
</tbody>
</table>
| **Evidence to review:**  | The assessor should ask for and review:  
1. Evidence that procedures are documented and implemented, and that the impact of the implementation is periodically assessed.  
2. SOPs or similar documents that guide and inform effective communication and collaboration among stakeholders.  
3. The CT application guidelines that capture the duties, roles and responsibilities of the various stakeholders involved in CT activities. The assessor should request evidence that the document is known to the relevant organizations, institutions, and departments.  
4. Documentation for the CT application processing flow that captures the roles, duties and responsibilities of the various stakeholders and that defines the timelines allocated to the various stages  
5. Documentation for the feedback mechanisms in the information and documentation transfer policy among the various stakeholders. |
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<table>
<thead>
<tr>
<th>References:</th>
<th></th>
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<tr>
<th>Framework:</th>
<th>Process</th>
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<tr>
<th>Rating Scale:</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>NOT IMPLEMENTED (NI): There are no procedures to ensure involvement and communication with all stakeholders relevant to CTs.</td>
<td></td>
</tr>
<tr>
<td>ONGOING IMPLEMENTATION (OI): The NRA has recently drafted procedures to ensure involvement and communication among all stakeholders relevant to CTs.</td>
<td></td>
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<tr>
<td>PARTIALLY IMPLEMENTED (PI): The NRA established the procedures to ensure involvement and communication among all stakeholders relevant to CTs but these have not been fully incorporated and are not consistent with relevant guidance.</td>
<td></td>
</tr>
<tr>
<td>IMPLEMENTED (I): The NRA has implemented procedures to ensure involvement and communication with all relevant stakeholders including required documentation and records of communications and of feedback for these communications.</td>
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<table>
<thead>
<tr>
<th>Limitations and remarks:</th>
<th>Scoring this sub-indicator as &quot;not applicable NA&quot; is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).</th>
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<table>
<thead>
<tr>
<th>Indicator:</th>
<th>CT03 Human resources to perform clinical trials oversight activities.</th>
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</table>

<table>
<thead>
<tr>
<th>Objective:</th>
<th>The objective of this indicator is to ensure that all entities within an NRA are adequately resourced with a trained, experienced and skilled workforce that is empowered to fully perform CT oversight activities. This will ensure that CT oversight activities are performed in accordance with international best practices.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>The objective of this indicator is to evaluate the human resource capacity of the entities with respect to the number of personnel, the skills and experience of the personnel, and the overall composition of the workforce, with the goal of evaluating whether the workforce possesses the specific expertise required to perform CT oversight activities. The assessor should consider that some NRAs may outsource CT activities.</td>
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<table>
<thead>
<tr>
<th>Category:</th>
<th>Resources (HR, FR, infrastructure and equipment)</th>
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</table>

<table>
<thead>
<tr>
<th>Sub Indicator:</th>
<th>CT03.01: Sufficient competent staff (i.e., education, training, skills and experience) are assigned to perform CT oversight activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maturity Level:</td>
<td>3</td>
</tr>
<tr>
<td>----------------</td>
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</tr>
<tr>
<td><strong>Description:</strong></td>
<td>The assessor should verify that the human resources assigned to perform CT oversight activities should be sufficient with respect to numbers and competent with respect to the requisite skills, education, experience and training. There should be technical documents and SOPs that provide guidance on the required background for CT oversight activities and that consider the requirements for educational background, competencies, skills, experience, and training. The assessor should verify that the NRA estimated the number of staff required to effectively and efficiently perform CT oversight function and that the NRA actually recruited that number. In addition, the assessor should verify that these competency requirements are well-established and maintained by the NRA. Metrics and statistics on the different activities performed as well as performance indicators can be used for estimating the adequacy of the number of the assigned staff. The assessor should also verify that the competency of the assigned staff is built, maintained and improved through recruitment as well as continuous on-the-job training.</td>
</tr>
<tr>
<td><strong>Objective:</strong></td>
<td>The objective of this sub-indicator is to ensure the existing human resources for CT oversight is sufficient, in terms of numbers, experience, and specific competencies, to perform all the activities along the entire CT oversight chain.</td>
</tr>
<tr>
<td><strong>Requirement:</strong></td>
<td>Sufficient number of competent human resources in charge of CT oversight activities</td>
</tr>
<tr>
<td><strong>Evidence to review:</strong></td>
<td>The assessor should ask for and review: 1. Evidence that the number of staff members involved in each of the documented activities along the entire CT oversight process flow is adequate. 2. Evidence that the systems and structures are in place to ensure appropriate placement of staff with respect to competence and skills. 3. Evidence that the system and structures have been implemented. The documentation should include the records to verify that the staff competence is appropriate for the job requirements. 4. Evidence that the professional profiles of the human resources engaged in CT oversight activities are appropriate with respect to education, skills, and expertise, to perform a particular function along the CT oversight chain. Documentation should include a list of the requisite skills and training for each position. 5. Recruitment plan.</td>
</tr>
<tr>
<td>Framework:</td>
<td>Structure/Foundation/Input</td>
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</tbody>
</table>
| Rating Scale: | **NOT IMPLEMENTED (NI):** The NRA does not have enough competent staff (i.e., education, training, skills and experience) to perform CT oversight activities  
**ONGOING IMPLEMENTATION (OI):** The NRA has recently developed a plan to recruit adequate competent staff; however, the plan has not been implemented.  
**PARTIALLY IMPLEMENTED (PI):** The NRA has initiated the implementation of the human resources development plan; however, there is need to complete the competency profile.  
**IMPLEMENTED (I):** The NRA has a sustained number of competent staff (i.e., education, training, skills and experience) assigned to perform CT oversight activities. |
| Limitations and remarks: | Assessment of the adequacy and appropriateness of the number of staff members is quite subjective and should be linked to some process or output indicators. When estimating staff adequacy, the assessor should consider the workload, backlog, and delays in delivery based on established timeframes.  
Assessor should recognize the existence of personnel from other departments who are often engaged in CT oversight functions such as assessments of protocols and GCP inspections. All of these, together with in-house staff, should be included when number and competency of CT oversight staff are evaluated. Other government officials from outside the NRA should also be included in this assessment.  
Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs). |
| Sub Indicator: | **CT03.02: Duties, functions, and responsibilities of the staff in charge of CT oversight activities are established and updated in the respective job descriptions** |
| Maturity Level: | 3 |
| Description: | The assessor should verify that procedures are in place to maintain a current and updated structure for managing job descriptions for personnel participating in CT oversight activities. In addition, job descriptions should address current staff duties, responsibilities and the requisite competencies. A job description with this format and content should be established and implemented for all staff. The management of job descriptions should be supported by a guidance document that provides direction on when and how to update the information, and where the information should be kept for easy access. The guidance
Document should present the appropriate duties and responsibilities that are assigned to each member of the organization involved in CT oversight activities. Thus, the professional profiles of staff are reflected in their respective roles and responsibilities within the NRA. There should be procedures to guide responsible persons to document that duties, functions and responsibilities are revised and kept up to date. In addition, procedures should be available to guide the keeping and documenting of up to date work schedules and enforcing the implementation of the documented guidelines and procedures.

**Objective:**

The objective of this sub-indicator is to ensure that duties and responsibilities of the staff are clear and well defined, that job descriptions are kept up to date with current duties, functions and responsibilities, and that these activities are adequately documented.

**Requirement:**

Duties, roles and responsibilities of the staff relevant to CT oversight activities.

**Evidence to review:**

The assessor should ask for and review:

1. Procedure and guidelines that guide placement of staff members within the NRA;
2. The professional profiles of staff (i.e., job descriptions) and documentation that they are related to their current roles and duties;
3. The professional profiles of the external experts and documentation that the profiles provide a composition that is complete and consistent with that prescribed in the legal provisions;
4. Procedures to guide the documentation of up to date duties and work schedules and to enforce the implementation of the documented guidelines and procedures;
5. Job descriptions for designated staff.

**References:**

<table>
<thead>
<tr>
<th>Framework:</th>
<th>Structure/Foundation/Input</th>
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</thead>
<tbody>
<tr>
<td>Rating Scale:</td>
<td>NOT IMPLEMENTED (NI): There is no evidence of defined or established duties, functions, responsibilities, respective job descriptions and necessary required competencies. ONGOING IMPLEMENTATION (OI): The NRA has recently drafted or developed the role and responsibilities document but it has not yet been implemented. PARTIALLY IMPLEMENTED (PI): The NRA has initiated implementation of this requirement but it has not been defined or followed for all staff or the roles and responsibilities documents, including staff job descriptions, are not up to date. IMPLEMENTED (I): The NRA has defined and established all required duties, functions, and responsibilities, and respective job descriptions are up-to-date.</td>
</tr>
<tr>
<td>Limitations and remarks:</td>
<td>Scoring this sub-indicator as &quot;not applicable NA&quot; is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).</td>
</tr>
<tr>
<td>Sub Indicator:</td>
<td>CT03.03: Training plan developed, implemented and updated at least once a year for staff in charge of CT oversight activities.</td>
</tr>
<tr>
<td>Maturity Level:</td>
<td>3</td>
</tr>
<tr>
<td>Description:</td>
<td>The assessor should verify that training plans are developed, implemented and updated at least once every year to reflect the current situation by considering education and experience of the staff. The training plan should be complemented with guidelines or similar documents that guide the development and implementation of training plans. The assessor should ensure that induction training for new staff as well as continued on-the-job for staff is planned and implemented. There should be procedures to approve the training plan and the budget allocated for implementing and updating the training plan. The plans should present clearly defined training goals and should include training in certain topics and skills to address identified deficiencies. Learning objectives, training methods and activities, evidence of learning, and evaluation and assessment of training should be documented. This documentation should confirm that the learning objectives were achieved and were designed to address weaknesses within the entities. Procedures should be in place to ensure that a training plan is developed, implemented and updated at least once every year. The assessor should verify that there is a system in place for monitoring the implementation and effectiveness of the training plan and for documenting the skills acquired in training activities for internal and external experts.</td>
</tr>
<tr>
<td>Objective:</td>
<td>The objective of this sub-indicator is to ensure that a training plan for staff exists, and that it is implemented and updated annually. Through the training plan, NRA can be sure that competency of staff in charge of CT oversight activities is maintained and</td>
</tr>
<tr>
<td>Requirement:</td>
<td>Implementation of training plan</td>
</tr>
<tr>
<td>--------------</td>
<td>---------------------------------</td>
</tr>
</tbody>
</table>
| Evidence to review: | The assessor should ask for and review:  
1. Guidelines for development, implementation and annual update (i.e., at least once per year) of the training plan. Guidelines should also provide for a mechanism to measure effectiveness of training.  
2. Documentation for the system or structures used to approve the training plan and to evaluate the adequacy of the budget allocated to the training activities.  
3. The current or existing staff training plan (or matrix) for staff. The assessor should assess this in relation to the respective individual job descriptions.  
4. SOP for developing and maintaining the training plan.  
5. Evidence that the NRA has investigated and identified training needs.  
6. List of trainings performed.  
7. Example records for training activities. |


<p>| Framework: |  |
| Rating Scale: | NOT IMPLEMENTED (NI): There is no systematic training program including training plan (or matrix). |</p>
<table>
<thead>
<tr>
<th>ONGOING IMPLEMENTATION (OI):</th>
<th>The NRA has recently drafted or developed the training plan but there is no evidence of implementation.</th>
</tr>
</thead>
<tbody>
<tr>
<td>PARTIALLY IMPLEMENTED (PI):</td>
<td>The NRA has developed and initiated the training plan implementation. However, the NRA has not fulfilled all required planned training or has been applying the plan for less than two years.</td>
</tr>
<tr>
<td>IMPLEMENTED (I):</td>
<td>The NRA has an updated training plan developed that is supported by adequate records to demonstrate effective plan implementation, including induction training for new staff and routine on-the-job training for recruited staff.</td>
</tr>
</tbody>
</table>

**Limitations and remarks:**

- Training plans must be updated regularly; ideally on an annual basis, but not less frequently that once every two years.
- Some regulatory functions may include many training activities that are not incorporated in the institutional training programme. Such training normally is offered by invitation. In this case, the assessor should recognize reports from non-routine CT oversight-relevant training not included in the NRA training plan.
- Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

**Sub Indicator:**

CT03.04: The NRA generates and maintains records of staff training activities and training effectiveness verification.

**Maturity Level:**

3

**Description:**

The assessor should verify that records of staff training that is performed or organized by the NRA are generated, maintained, regularly updated. This activity should be supported by guidelines that direct the NRA to generate and maintain records of staff training activities. Procedures should be in place to document and propose staff training needs and to allocate a budget for continuous staff capacity building and development. The assessor should check that there is an evaluation or assessment mechanism to verify the quality of learning, and to confirm that learning objectives are achieved. Documentation should include an inventory (i.e., soft and/or hard) system that records all impactful and non-impactful trainings and identifies all staff members who participated. A system to measure or estimate impact of trainings should be established.

**Objective:**

The objective of this sub-indicator is to ensure that training organized by the NRA or responsible regulatory authority is adequately documented and that the training records are adequately maintained and kept. Staff training records are considered an integral part of staff file and are a tool for measuring and tracking staff competency, development and adequacy.

**Requirement:**

Training records
<table>
<thead>
<tr>
<th>Evidence to review:</th>
<th>The assessor should ask for and review:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1. Guidelines or similar documents that guide the NRA to generate and maintain records of staff training activities;</td>
</tr>
<tr>
<td></td>
<td>2. Evaluations of training effectiveness;</td>
</tr>
<tr>
<td></td>
<td>3. The training inventory, and procedures for completing the inventory;</td>
</tr>
<tr>
<td></td>
<td>4. Examples of archived records of staff training, and procedures for the archiving system</td>
</tr>
</tbody>
</table>


| Framework: | Output |

| Rating Scale: | NOT IMPLEMENTED (NI): There is no evidence that the NRA generates and maintains records of staff training activities. |
|              | ONGOING IMPLEMENTATION (OI): The NRA has recently initiated plans to generate, document and keep records of staff training activities, however they are not yet followed. |
|              | PARTIALLY IMPLEMENTED (PI): The NRA has recently initiated plans to generate, document and keep records of staff training activities but they are not fully followed for all training activities or they have been established for less than two years. |
|              | IMPLEMENTED (I): The NRA generates and maintains records of staff training activities. |

<p>| Limitations and remarks: | The assessor should note that some NRAs out-source training including staff capacity development activities. In this case the assessor should request the identity of the provider, as well as evaluations of the provider. The assessor may request the professional profiles of tutors or resource persons used to offer training. The assessor may also request records covering the archiving systems in place. |
|                         | Scoring this sub-indicator as &quot;not applicable NA&quot; is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs). |</p>
<table>
<thead>
<tr>
<th>Indicator:</th>
<th>CT04 Procedures established and implemented to perform clinical trials oversight.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective:</td>
<td>The objective of this indicator is to ensure that the NRA (or responsible regulatory authority) has documented procedures establishing how CTs should be implemented. The documented procedures should be efficiently designed to assist in the preparation of the CT application and in the receipt and evaluation of the enclosed information. The procedures should present an overview of the activities to be carried out, the steps to be followed, the resources required, the processes to be followed in evaluation of the submitted documents, and the interrelationships among the various documents. The responsible authority should verify that all procedures follow and address all legal principles. The established procedures will give guidance on how CT applications are handled to ensure efficient CTs. The objective of this indicator is to establish whether procedures have been established and implemented to effectively perform CT oversight activities.</td>
</tr>
<tr>
<td>Category:</td>
<td>Regulatory process</td>
</tr>
<tr>
<td>Sub Indicator:</td>
<td>CT04.01: NRA has access to an advisory committee for review of CT applications and post-approval safety and compliance issues.</td>
</tr>
<tr>
<td>Maturity Level:</td>
<td>4</td>
</tr>
<tr>
<td>Description:</td>
<td>The assessor should verify that the involvement of an advisory committee, which is external to the NRA and which participates in the review of CT applications, is documented and supported by legal provisions and regulations. The assessor should also verify that the legal provisions and regulations that guide the establishment and use of an advisory committee in the review of CT applications are established and implemented. There should be clear guidance on when and how to use the committee, as well as guidance on the scope and extent of the use of committee expertise in the review of CT applications and in the evaluation of post approval safety and compliance issues. The ToRs of the members of the committee should be available and documented. There should be documented objectives and functions for the committee and for each member of the committee. Professional profile of the committee members should be available, and the composition of the committee should be guided by a legal provisions or regulations. In addition, supporting guidelines should clearly define, for each member of the committee, their roles and responsibilities in the review of CT applications. The code of conduct for the committee members, as well as a general policy on conflicts of interest, should also be documented and available. The assessor should note that some NRAs (or responsible regulatory authorities) may not involve the advisory committee in the review of the submitted CT applications. In such cases, the...</td>
</tr>
</tbody>
</table>
NRAs may consult the advisory committee for direction in response to adverse events or reactions including serious ones.

**Objective:**  
The objective of this sub-indicator is to ensure that the NRA has the option, when needed, of using an advisory committee in the review of CT applications and in the evaluation of post approval safety and compliance issues. This option is particularly important in the event of new or emerging technology.

**Requirement:**  
Advisory committee for CT

**Evidence to review:**  
The assessor should ask for and review:  
1. Legal provisions (laws, decrees, regulations or any legal binding document) for the establishment and use of an advisory committee in the review of CT applications  
2. The ToRs of the committee and members of the committee, including their signed updated conflicts of interest forms.  
3. Documentation of the composition of the advisory committee, and evidence that it is in line with the directives prescribed in the legal provision and regulations  
4. Guidelines that define the scope and extent of the advisory committee contributions in the review of CT applications.  
5. SOPs for the advisory committee activities.  
6. Records of advisory committee reports

**References:**

**Framework:**  
Process

**Rating Scale:**  
NOT IMPLEMENTED (NI): The NRA does not have access to an advisory committee involved in the review of CT applications or post-approval safety and compliance issues.  
ONGOING IMPLEMENTATION (OI): The NRA has drafted a proposal to establish the advisory committee that is involved in the review of CT activities.  
PARTIALLY IMPLEMENTED (PI): The advisory committee has been established for less than two years or is not involved in all required CT activities.  
IMPLEMENTED (I): The expert advisory committee is established, officially endorsed and involved in all required CT activities, as needed, to ensure quality of CT reviews.

**Limitations and remarks:**  
In the case the NRA has all required internal resources for CT oversight activities, this sub-indicator can be scored as not applicable.
The assessor should consider this sub-indicator as implemented, if the NRA can provide adequate evidence of access to advisory committees when needed.

<table>
<thead>
<tr>
<th><strong>Sub Indicator:</strong></th>
<th><strong>CT04.02: The existence of the ECs with clearly defined composition.</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Maturity Level:</strong></td>
<td>3</td>
</tr>
<tr>
<td><strong>Description:</strong></td>
<td>The assessor should verify the existence, enactment, and implementation of legal provisions and regulations that define the composition of the ECs. The legal provisions and regulations should stipulate that the composition of the ECs should be multidisciplinary and multi-sectorial and should have a balanced age and gender distribution. Additionally, the EC should include members with relevant scientific expertise and laypersons who represent the interests and the concerns of the community. The legal provisions should be supported with guidelines or SOPs that provide guidance on selection of members, on selection of the committee chair, and on the ToRs for members. The legal provisions and regulations should also provide direction on how the activities of the ECs should be regulated.</td>
</tr>
<tr>
<td><strong>Objective:</strong></td>
<td>The objective of this sub-indicator is to ensure there is a defined and documented composition of the ECs for CT activities.</td>
</tr>
<tr>
<td><strong>Requirement:</strong></td>
<td>Existence, performance and composition of ECs</td>
</tr>
</tbody>
</table>
| **Evidence to review:** | The assessor should ask for and review:  
1. Legal provisions (laws, decrees, regulations or any legal binding document) that provide guidance on the composition of the ECs  
2. The ToRs for each member along with guidelines on the selection process. The assessor should review the ToRs and SOPs that provide guidance.  
3. Professional profiles for members of the ECs. Assessor should assess these for balance in terms of relevant expertise, gender, age and representation.  
4. Current list of the EC members. |
3. WHO guidelines on the nonclinical evaluation of vaccines adjuvants and adjuvanted vaccines (119) |
<table>
<thead>
<tr>
<th>Framework:</th>
<th>Structure/Foundation/Input</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rating Scale:</td>
<td>NOT IMPLEMENTED (NI): ECs are not established for CT activities. ONGOING IMPLEMENTATION (OI): The composition of the ECs has been recently drafted but the committees have not been implemented. PARTIALLY IMPLEMENTED (PI): The ECs are established but are not officially approved or are not routinely involved in CT activities. IMPLEMENTED (I): The ECs are established, officially endorsed and routinely involved in CT activities.</td>
</tr>
<tr>
<td>Limitations and remarks:</td>
<td>The assessor should note that in most cases, the NRA will not be the agency that hosts the EC, and as a result may not be able to provide sufficient information to address this sub-indicator. The assessor may have to consult the Ministry of Health or the relevant Ministry or institution for more information. Failure to secure information should justify the scoring of this sub-indicator as &quot;not or partially implemented&quot;. Scoring this sub-indicator as &quot;not applicable NA&quot; is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).</td>
</tr>
<tr>
<td>Sub Indicator:</td>
<td><strong>CT04.03: Nonclinical data is considered within CT application review.</strong></td>
</tr>
<tr>
<td>Maturity Level:</td>
<td>3</td>
</tr>
<tr>
<td>Description:</td>
<td>The assessor should verify the existence and implementation of the regulations and guidelines on the preclinical data requirements for CT applications. The guidelines should clearly state that the CT application requirements include submission of preclinical data which is generated in accordance with the principles of Good Laboratory Practices. The guidelines should provide guidance on the type and scope of data to submit to support the CT application.</td>
</tr>
<tr>
<td>Objective:</td>
<td>The objective of this sub-indicator is to ensure the availability of data from preclinical studies that will provide sufficient insight into potential safety issues which may influence eventual clinical application of the IMP. The objective of the sub-indicator is to ensure that preclinical data are part of the application package, and that the data submitted are reviewed according to a documented procedure.</td>
</tr>
<tr>
<td>Requirement:</td>
<td>Preclinical data as part of CT application</td>
</tr>
</tbody>
</table>
### Evidence to review:

The assessor should ask for and review:
1. The regulations and guidelines that states that nonclinical data may be required in a CT application.
2. SOPs that provide guidance during the review of the nonclinical data submitted as part of the CT application.
3. Sample records of CT application forms.

### References:

1. Guidelines for good clinical practice (GCP) for trials on pharmaceutical products (40) (http://apps.who.int/medicinedocs/en)

### Framework:

<table>
<thead>
<tr>
<th>Rating Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOT IMPLEMENTED (NI): The NRA does not require submission and review of nonclinical data within CT application.</td>
</tr>
<tr>
<td>ONGOING IMPLEMENTATION (OI): The NRA has recently drafted guideline or similar documents to consider nonclinical data as part of CT application.</td>
</tr>
<tr>
<td>PARTIALLY IMPLEMENTED (PI): The NRA considers nonclinical data as part of CT application however there is no systematic review, records or capacity to review these data.</td>
</tr>
<tr>
<td>IMPLEMENTED (I): The NRA requires submission of nonclinical data within CT applications, and these data are reviewed.</td>
</tr>
</tbody>
</table>

### Limitations and remarks:

Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

### Sub Indicator:

**CT04.04: There are defined roles for ECs at all levels (e.g., national, sub-national, or institutional).**

### Maturity Level:

3

### Description:

The assessor should verify that the legal provisions, regulations and guidelines which establish the EC, also provide guidance on the composition of the EC, and on the roles and responsibilities at each level. These legal provisions should be up to date. The regulations and guidelines should define the objectives, functions, mandates, missions, roles and responsibilities of the ECs as a whole, as well as for each member of the EC. In addition, the scope and extent of their mandate should be well-described. The interactions among the different levels of ECs should be defined and documented.

### Objective:

The objective of this sub-indicator is to ensure that there are defined roles for the ECs at all levels.
## Requirement: Defined roles for ECs

**Evidence to review:**

The assessor should ask for and review:
1. The legal provisions (laws, decrees, regulations or any legal binding document) and guidelines that provide defined roles for the EC at each level of CT activity including guidance on information sharing and interactions with relevant stakeholders.
2. Guidelines detailing the objectives, functions, roles and responsibilities of the EC at each level of CT activity.
3. Evidence that the legally mandated scope of work is acceptable according to WHO guidelines.
4. Records of interaction among different EC levels.

**References:**


**Framework:**

Process

**Rating Scale:**

- **NI:** The role and responsibilities of all levels of ECs have not been defined.
- **OI:** The role and responsibilities of ECs have been drafted at all levels however they are not yet followed.
- **PI:** The role and responsibilities of ECs have been assigned at all levels however they have been used for less than two years or they are not fully documented.
- **I:** The role and responsibilities of ECs have been established and documented for CTs, and there is evidence of consistent implementation.

**Limitations and remarks:**

Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

**Sub Indicator:**

CT04.05: Documented and implemented procedures exist to review CT applications

**Maturity Level:**

3
### Description:
The assessor should verify the existence and implementation of guidelines or SOPs that provide the guidance needed for review of CT applications. The guidelines or SOPs should provide guidance on how to review the various components of the CT application. The guidance should be supported by a checklist or CT application review form that should be completed during the review process. Such a form or checklist should be used to generate a review report that captures the recommendations and comments that are used to justify authorization, rejection or deferral of the CT application.

### Objective:
The objective of this sub-indicator is to ensure a uniform evaluation of CT applications that is devoid of bias. There should be regulations and guidelines instituting a defined set of criteria for the NRA (or responsible regulatory authority) to follow and use in the discharge of their duties. Employment of this approach will avoid bias.

### Requirement:
Document procedures to review CT applications

### Evidence to review:
The assessor should ask for and review:
1. The guidelines and SOPs that establish the criteria for reviewing CT applications.
2. Evidence that the guidelines and SOPs are implemented during the review process.
3. Examples of completed review reports. The assessor should review completed review reports and compare for compliance with the applicable guidance.

### References:

### Framework:
- Process

### Rating Scale:
- **NOT IMPLEMENTED (NI):** There are no documented procedures for review of CT applications.
- **ONGOING IMPLEMENTATION (OI):** The NRA has drafted or adopted the documented procedures for review of CT applications.
- **PARTIALLY IMPLEMENTED (PI):** The NRA developed and officially approved the documented procedures for review of CT applications less than two years ago or there is no evidence to demonstrate the implementation of this procedure for all applications.
- **IMPLEMENTED (I):** The NRA has developed and implemented the documented procedures for review of CT applications and has adequate evidence to demonstrate that they have been followed for all CT applications.

### Limitations and remarks:
Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).
**Sub Indicator:** CT04.06: There are procedures for EC responsibility for clearance and follow up until completion of the CT  

<table>
<thead>
<tr>
<th>Maturity Level:</th>
<th>3</th>
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<tbody>
<tr>
<td><strong>Description:</strong></td>
<td>The assessor should verify the existence, documentation, implementation of procedures that provide guidance on the ECs responsibility for clearance and follow-up until completion of the CT. The documentation of procedures should be in the form of guidelines or SOPs, and should provide detailed guidance on the roles and responsibilities of the EC in the clearance and follow-up processes through the completion of the CT. The guidelines should specify the scope and extent of the EC’s activity in the CT activities, the corresponding timelines for each activity, the expected outcomes of their activities, and the impact of each activity on the entire CT. Importantly, EC retains these responsibilities until CT is completed.</td>
</tr>
<tr>
<td><strong>Objective:</strong></td>
<td>The objective of this sub-indicator is to ensure the NRA (or responsible regulatory authority) has established procedures on the responsibilities of the EC from CT clearance until the completion of the CT.</td>
</tr>
<tr>
<td><strong>Requirement:</strong></td>
<td>Documented procedures for the EC along the entire CT authorization chain</td>
</tr>
</tbody>
</table>
| **Evidence to review:** | The assessor should ask for and review:
1. The regulations, guidelines and SOPs detailing the roles and responsibilities of the EC in the clearance and follow-up process of CTs until completion of the trial. The assessor should verify that the procedures have been appropriately documented and implemented.
2. Documentation that defines the scope and extent of EC responsibility at each stage of the CT.
3. The processes and procedures guiding the EC operations and activities at each stage of the CT. |
| **References:** | |
| **Framework:** | Process |
| **Rating Scale:** | NOT IMPLEMENTED (NI): There are no procedures that define EC responsibility for clearance and follow up until completion of the CT. ONGOING IMPLEMENTATION (OI): There are drafted or adopted procedures to define EC responsibility for clearance and follow up until completion of the CT. PARTIALLY IMPLEMENTED (PI): There are procedures to define EC responsibility for clearance and follow up until completion of the CT, however they have not been implemented. |
### IMPLEMENTED (I): The defined procedures regarding EC responsibility for clearance and follow up until completion of the CT are implemented and supported with documented evidence.

### Limitations and remarks:
The assessor should note that some ECs may have a limited mandate along the entire CT chain in accordance to the existing regulations. In such cases, the assessor should be guided by the existing laws or regulations. The scoring may be partial or not applicable depending on the country regulation.

Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

### Sub Indicator:
**CT04.07**: The same policies are used for the evaluation of CT applications regardless of the applicant (e.g., domestic, foreign, public sector, or private sector)

### Maturity Level:
3

### Description:
The assessor should verify the existence, enactment, and implementation of regulations and guidelines that dictate that the criteria applied to evaluate CT applications should be the same regardless of the applicant. A single set of criteria for the evaluation process should be employed during evaluation of all CT applications. The criteria should be supported with a checklist or evaluation form that should be completed during the evaluation process. The assessor should note that in some instance, such as emergencies, this defined set of criteria for evaluating CT applications may not apply. The assessor should request for and review the documented and implemented procedures and processes that are used to provide guidance for the review of CT applications in the event of emergencies.

### Objective:
The objective of this sub-indicator is to ensure that the same criteria are applied to evaluate CT applications from various sources. Use of consistent procedures will avoid bias.

### Requirement:
Uniform criteria and policy for evaluating CT application regardless of applicant

### Evidence to review:
The assessor should ask for and review:
1. The regulations and guidelines that require that all CT applications are evaluated with the same single set of criteria regardless of the applicant.
2. The guidelines and SOPs that specify the detailed criteria to be used for evaluating CT applications.
3. Evidence that the reviewers of CT applications are aware of the criteria and understand how to apply the criteria in their assessment activities. Assessor should review evidence that the criteria are documented, published and implemented.
### Framework:
Process

### Rating Scale:
- **NOT IMPLEMENTED (NI):** There are no defined policies and criteria, or different policies are used for the evaluation of CT applications from different sources (e.g. domestic, foreign, public sector, or private sector).
- **ONGOING IMPLEMENTATION (OI):** There is a drafted policy or documentation that requires that the same criteria should be followed for the evaluation of CT applications regardless of the applicant (e.g. domestic, foreign, public sector, or private sector).
- **PARTIALLY IMPLEMENTED (PI):** There are regulations or guidelines that require that the same criteria are used for the evaluation of CT applications regardless of the applicant (e.g. domestic, foreign, public sector, or private sector); however, these have been available for less than two years or there is no evidence to demonstrate full implementation for all received CT applications.
- **IMPLEMENTED (I):** The same criteria and policy are used for the evaluation of CT applications regardless of the applicant (e.g. domestic, foreign, public sector, or private sector) for all received and approved CT applications.

### Limitations and remarks:
The assessor should note that in some countries only one source may exist. The assessor can score this sub-indicator as implemented if all regulation and requirements are the same.
The assessor should consider there are different requirements based on the nature of each product.
Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

### Indicator:
CT05 Mechanism exists to promote transparency, accountability and communication.

### Objective:
The objective of this indicator is to ensure mechanisms are in place to ensure that information on CT applications, including authorized, suspended, rejected and completed CTs, are published to promote transparency and information sharing among stakeholders and potential stakeholders such as trial subjects.

### Category:
Transparency, accountability and communication

### Sub Indicator:
CT05.01: There is clarity about the funding of the EC and its members

### Maturity Level:
3

### Description:
The assessor should verify that the source of funding for the EC activities is known, documented, perceived as appropriate, and
devoid of any conflicts of interest. The source of funding for EC activities should be documented and supported by regulations that provide clarity on the funding mechanisms and on the management and disbursement of funds. All fees and charges should be legally approved and implemented. The regulation should provide clarity on the source of funding and provide assurance about the absence of any conflicts of interest.

**Objective:**

The objective of this sub-indicator is to ensure that there is a dedicated source of funding for the operations of the EC and that the source of funding is known, transparent and devoid of any conflicts of interest.

**Requirement:**

Clarity on the source of funding

**Evidence to review:**

The assessor should ask for and review:

1. The regulation detailing the source of funding that is made available to the EC to fund its activities.
2. Evidence that the identity of the source is in compliance with the general policy on conflicts of interest.
3. Evidence that the level of transparency regarding the source of funding and the management of the funds is sufficient to eliminate doubts on conflicts of interest.
4. Evidence that the fees and charges are legally approved.
5. Records and reports of EC funding.

**References:**


**Framework:**

Structure/Foundation/Input

**Rating Scale:**

- **NOT IMPLEMENTED (NI):** NRA does not have information or clarity about the funding of the EC and its members.
- **ONGOING IMPLEMENTATION (OI):** There are drafted procedures and policies to provide information about the funding process of the EC and its members.
- **PARTIALLY IMPLEMENTED (PI):** There are procedures to provide information about the funding process of the EC and its members, however there is no evidence to demonstrate availability of this information regarding all ECs.
- **IMPLEMENTED (I):** The NRA has clear information about the funding of the EC and its members. Information is supported with
Limitations and remarks: Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

**Sub Indicator:** CT05.02: The list of the CTs (approved and rejected applications), including summarized evaluation reports by the NRA, are publicly available or recorded in a domestic or international database

**Maturity Level:** 4

**Description:** The assessor should verify the existence of regulations, guidelines or similar documents that dictate that all CT applications, either approved or rejected, should be listed in a domestic or international database. This database should also include summaries of the evaluation for each CT application. The regulations should be supported with guidelines that provide guidance on the information to be listed, as well as the content, format and information that should be included in the summary evaluation reports that are made available to the public. The guidelines should provide guidance on the database to the used (i.e., local, international, hosting organization, and other relevant details) and on the mechanism to be used for updating the database.

**Objective:** The objective of this sub-indicator is to ensure that approved and rejected CT applications, as well as summarized CT evaluation reports, are listed and published in a local or international database.

**Requirement:** Publication of approved and rejected CT applications as well as CT evaluation reports

**Evidence to review:** The assessor should ask for and review:
1. Regulations and guidelines that require that all approved and rejected CT applications, as well as summary evaluation reports, should be listed and available in an easily-accessible local or international database.
2. Regulations and guidelines that require that the list of all approved and rejected CT applications, as well as summary evaluation reports, should be updated periodically.
3. Documentation for the rate (i.e., when and how) at which the list is updated.
4. The list of approved and rejected CT applications, as well as summary evaluation reports, on the local or international database.
5. Guidelines and SOPs that provide guidance on the content, format and information that should be uploaded to the database.
6. Evidence that stakeholders are aware of the availability of the list, and that they have a clear understanding of how and where to access the list and its contents.

**References:**

<table>
<thead>
<tr>
<th>Framework:</th>
<th>Output</th>
</tr>
</thead>
</table>
| Rating Scale: | NOT IMPLEMENTED (NI): There is no list of CTs (approved and rejected applications), including summarized NRA evaluation reports, that is publicly available or recorded in a domestic or international database.  
ONGOING IMPLEMENTATION (OI): There is a draft procedure to publish the list of CTs (approved and rejected applications), including summarized NRA evaluation reports, however it is not yet published.  
PARTIALLY IMPLEMENTED (PI): There is a list of CTs (approved and rejected applications), including summarized NRA evaluation reports, and list is publicly available or recorded in a domestic or international database; however, it is not updated or it was published less than two years ago.  
IMPLEMENTED (I): There is an updated list of CTs (approved and rejected applications), including summarized NRA evaluation reports, that is publicly available or recorded in a domestic or international database. |
| Limitations and remarks: | Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs). |
| Indicator: | CT06 Mechanism in place to monitor regulatory performance and output. |
| Objective: | The objective of this indicator is to ensure that CT oversight mechanisms are in place to verify that all CT activities are subjected to quality controls and other checks to reduce errors, increase objectivity and ensure that the processes are consistent. These activities will generate an assured output and enhance the reliability of results at the various stages of the CT application processing flow.  
Oversight activities should cover the various stages of the CT application processing flow, including receipt of CT applications, acknowledgement of applications, processing, evaluation, and assessment of the various parts of the applications, generation of recommendations (i.e., approval, deferral, or rejection) following the evaluation and assessment process, issuance of certificates, implementation of regulatory actions when necessary (e.g. stoppage or termination of CTs) and publication of the decision made for each application (i.e., approval or rejection) along with summary evaluation reports.  
This would lead to consistency in the regulatory performance of the CT oversight function as well as reliable outputs. |
<table>
<thead>
<tr>
<th>Category:</th>
<th>Monitoring progress and assessing outcomes and impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sub Indicator:</td>
<td>CT06.01: There is an internal list or database of all approved and rejected CTs, and the NRA maintains a record of each approved and rejected CT</td>
</tr>
<tr>
<td>Maturity Level:</td>
<td>3</td>
</tr>
<tr>
<td>Description:</td>
<td>The assessor should verify the establishment of a register, list, or database into which all approved or rejected CT applications are entered. The register, list or database should be continually updated and maintained to reflect the current situation. The establishment and maintenance of the register, list, or database should be supported by guidelines and SOPs. These procedures should also provide guidance on the content, format and type of information to enter and maintain in the database and guidance on procedures (i.e., when and how) to update the register, list or database. In addition, guidance on who should be given access to the stored information should be clearly documented.</td>
</tr>
<tr>
<td>Objective:</td>
<td>The objective of this sub-indicator is to ensure that an internal list or database is kept for all approved and rejected CT applications and that the NRA (or responsible regulatory authority) maintains a record of all approved and rejected CTs.</td>
</tr>
<tr>
<td>Requirement:</td>
<td>Internal list or database for all CT applications</td>
</tr>
<tr>
<td>Evidence to review:</td>
<td>The assessor should ask for and review:</td>
</tr>
<tr>
<td></td>
<td>1. The guidelines requiring the establishment and maintenance of a register, list or database of approved or rejected CT applications.</td>
</tr>
<tr>
<td></td>
<td>2. The register, list or database of all CT applications that have been approved or rejected, including details of the type of information that was entered and kept.</td>
</tr>
<tr>
<td></td>
<td>3. List of persons with the authority to access stored information, as well as information on the documentation that must be completed before access is granted.</td>
</tr>
<tr>
<td></td>
<td>3. WHO guidelines on the nonclinical evaluation of vaccines adjuvants and adjuvanted vaccines (119)</td>
</tr>
</tbody>
</table>
### Framework:
Output

### Rating Scale:
- **NOT IMPLEMENTED (NI):** There is not an internal list or database of all approved and rejected CTs.
- **ONGOING IMPLEMENTATION (OI):** There is a drafted procedure to create an internal list or database; however the list or database does not yet exist.
- **PARTIALLY IMPLEMENTED (PI):** There is an internal list or database of all approved and rejected CTs, and the NRA maintains a record of each approved and rejected CT; however, the list or database is not up to date or all applications are not included.
- **IMPLEMENTED (I):** There is an updated internal list or database of all approved and rejected CTs, and the NRA has maintained records of each approved and rejected CT for more than two years.

### Limitations and remarks:
Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

### Sub Indicator:
**CT06.02: Performance indicators for CT oversight activities are established and implemented**

### Maturity Level:
4

### Description:
The assessor should verify the existence and implementation of performance indicators for different activities included under the CT oversight functions. Specifically, the system should define key performance indicators (KPIs) along the entire CT oversight activity chain and all indicators should be adequately justified. For the purpose of clarity and consistency, established KPIs should be supported with guidelines for monitoring and maintenance of the KPIs. The guidelines in turn should be supported by SOPs and tools that define the procedures to be used for monitoring and evaluating the performance indicators and that define procedures and timelines for reviewing and revising the indicators.

Examples of performance indicators for CT oversight function include: CT applications received, granted or rejected, timelines for CT application processing, and regulatory actions taken with respect to CTs.

Established KPIs might be qualitative, quantitative or combination of both. In general, quantitative indicators are preferred to avoid bias or misinterpretation. However, qualitative indicators are also accepted. Qualitative indicators may or may not include scoring or scaling to render them semi-quantitative and thus more informative. The assessor should ensure that indicators are measured on a regular basis to monitor progress and advancement.

In addition, the assessor should verify measured indicators are analyzed to identify trends or abnormalities. Justifications for any
identified abnormalities should be provided; when necessary, process optimizations should be introduced to avoid recurrence.

**Objective:**
The objective of this sub-indicator is to ensure that a system, mechanism, or procedure exists to require the NRA to establish performance indicators along the entire CT oversight chain. Additionally, the objective is to ensure that KPIs are actually contributing to monitoring of regulatory performance, to measuring effectiveness of CT oversight regulatory activities, and to making any necessary adjustments or optimizations.

**Requirement:**
KPIs for CT oversight activities

**Evidence to review:**
The assessor should ask for and review:
1. Documents supporting the system, mechanism, or procedure compelling the NRA to establish and implement performance indicators along the entire CT oversight activity chain.
2. Evidence that the performance indicators have been established and implemented, and that the members of staff involved in the CT oversight function are aware of the indicators and the guidelines and SOPs used for monitoring and evaluating their performance.
3. The current performance indicators for CT oversight activities
4. Analyses of the measured indicators along with the investigations done to identify trends or abnormalities.
5. Documentation for follow-up of any observed abnormalities, including justifications for any identified abnormalities as well as any process optimizations introduced to avoid recurrence.

**References:**

**Framework:**
Structure/Foundation/Input

**Rating Scale:**
NOT IMPLEMENTED (NI): There are no KPIs for CT oversight activities.
ONGOING IMPLEMENTATION (OI): The NRA has recently drafted KPIs for CT oversight activities but they have not yet been reported.
PARTIALLY IMPLEMENTED (PI): The NRA has developed KPIs for CT oversight activities and has been applying them for less than
two year or they have not covered all critical steps. 

IMPLEMENTED (I): The NRA has established and implemented KPIs for CT oversight activities. The indicators are reviewed regularly, and appropriate actions are taken and decisions made.

Limitations and remarks: When they refer to outcomes, indicators may be ambiguous and difficult to interpret, as outcomes are the result of many factors that are difficult to disentangle. When they refer to processes, indicators are often too specific, as they may focus on a particular intervention or condition or they may quickly become outdated as business models develop.

Different methodologies are used to measure the NRAs performance on CT oversight activities. In this case, the assessor should verify that adequate supporting documents are available. The assessor should consider that developed performance indicators should be Specific, Measurable, Achievable, Realistic, and Time-bound (i.e., “SMART”).

Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

<table>
<thead>
<tr>
<th>Sub Indicator:</th>
<th>CT06.03: Progress reports from sponsors or CROs during and after CTs sent to and shared among NRAs and ECs.</th>
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</thead>
<tbody>
<tr>
<td>Maturity Level:</td>
<td>3</td>
</tr>
<tr>
<td>Description:</td>
<td>The assessor should verify the establishment and implementation of mechanisms to receive, store and disseminate information received from stakeholders during and after CTs. The mechanism should be supported with guidelines that state that feedback reports along the entire CT chain should be sent periodically by the sponsor (or CRO) to the NRAs and ECs. Receipt of the reports should be documented by the NRAs and ECs. The guidelines should provide guidance on the content and format for preparing the reports, as well as guidance on the procedures for submitting the reports. In addition, SOPs should provide guidance on how to review, summarize and store the reports received. The database where reports are kept should be documented.</td>
</tr>
<tr>
<td>Objective:</td>
<td>The objective of this sub-indicator is to ensure a progress reporting and documentation system is in place to receive, store and disseminate reports from sponsors or CROs.</td>
</tr>
<tr>
<td>Requirement:</td>
<td>Accessibility and availability of feedback from stakeholders</td>
</tr>
</tbody>
</table>
| Evidence to review: | The assessor should ask for and review:  
1. The guidelines that stipulate that feedback reports along the entire CT chain should be sent periodically by the sponsor (or CRO) to the NRAs and ECs and that the NRAs and ECs should document receipt of the reports. The content of these reports may differ between NRA and ECs. |
2. Guidelines on the content and format for preparing the reports, as well as on the procedure for submitting the reports.
3. Documented list of reports received from sponsors or CROs. Content and format should be reviewed for compliance with guidelines.
4. Examples of reports from sponsors and CROs.
5. Documentation for the database or data storage facility where the reports are stored.

### References:

### Framework:
- Process

### Rating Scale:
- **NOT IMPLEMENTED (NI):** There is no mechanism for feedback and progress reporting between sponsors or CROs and NRAs and ECs during and after CTs.
- **ONGOING IMPLEMENTATION (OI):** There are draft guidelines to define feedback mechanisms and to send progress reports from sponsors or CROs to NRAs and ECs during and after CTs; however, it is not followed.
- **PARTIALLY IMPLEMENTED (PI):** There are mechanisms for feedback and progress reporting from sponsors or CROs to NRAs and ECs during and after CTs, however all reports are not available.
- **IMPLEMENTED (I):** There are mechanisms for feedback and progress reporting from sponsors or CROs to NRAs and ECs during and after CTs. The mechanisms have been established for more than two years and are supported with adequate documentation, guidelines and records.

### Limitations and remarks:
Scoring this sub-indicator as "not applicable NA" is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).

### Sub Indicator:
- **CT06.04:** There are timelines for the assessment of CT applications and an internal tracking system to follow the targeted time frames

### Maturity Level:
- 3

### Description:
The assessor should verify the establishment and implementation of documented timelines and internal timeline tracking systems.
that guide the CT application processing. These timelines should be supported by guidelines requiring that CT applications should be processed and assessed according to published timelines. The timelines should be monitored internally for compliance. The guidelines should be supported with SOPs that provide guidance on how to establish the timelines and how to monitor the established timelines. The guidance should be designed to be adaptable for routine and non-routine CT applications (e.g., public health emergencies). In addition, the guidance should be designed to address each stage of the CT application process flow. The timelines should be known by all stakeholders for the purposes of transparency and trust.

**Objective:**
The objective of this sub-indicator is to ensure that timelines exist for processing CT applications and that internal systems or mechanisms are in place to monitor the CT application processing for compliance with the timelines.

**Requirement:**
Availability of timelines and a system to monitor processing of CT applications

**Evidence to review:**
The assessor should ask for and review:
1. The guidelines that stipulate that CT applications should be processed and assessed according to prescribed timelines.
2. Regulations establishing that timelines for CT application assessment should be internally monitored for compliance with published timelines.
3. Documentation for the prescribed timelines for CT application assessment, and guidelines for the internal tracking system used to monitor the timelines for effectiveness;
4. Sample report from the internal tracking system for CT application assessment. Assessor should review for content as well as for compliance with CT application assessment guidelines.
5. The work schedules and work plans for staff responsible for monitoring timelines.

**References:**

**Framework:**
Process

**Rating Scale:**
NOT IMPLEMENTED (NI): There are no defined timelines for the assessment of CT applications and no internal tracking system to follow the targeted time frames.
<table>
<thead>
<tr>
<th><strong>Limitations and remarks:</strong></th>
<th>Scoring this sub-indicator as &quot;not applicable NA&quot; is excluded (i.e. this sub-indicator will always apply for all benchmarked NRAs).</th>
</tr>
</thead>
</table>

| **ONGOING IMPLEMENTATION (OI):** | There are drafted timelines and an internal tracking system to follow the targeted time frames for the assessment of CT; however, they are not followed. |
| **PARTIALLY IMPLEMENTED (PI):** | The timelines for the assessment of CT applications are defined; however, the internal tracking system to follow the targeted time frames has not been fully documented. |
| **IMPLEMENTED (I):** | The timelines for the assessment of CT applications and an internal tracking system to follow the targeted time frames have been implemented for more than two years. |