EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Standard operating procedure

Title Co-ordination of GCP inspections		
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1. Purpose

This SOP describes how GCP inspections are coordinated by the P-CI-CNC section in connection with human and veterinary medicinal products under the centralised procedure or in the context of a referral procedure. These inspections can be requested as a result of clinical data submitted as part of a MA dossier, clinical data provided as a result of specific obligations/follow-up measures, variations, line extensions, re-inspections, or other information received post-authorisation, e.g. in relation to safety updates, PSUR etc…

This SOP should be read in conjunction with the relevant documents mentioned in section 6.

2. Scope

This SOP applies to P-CI-CNC section only.

3. Responsibilities

It is the responsibility of the Section Head to ensure that this procedure is adhered to within his/her own section. The responsibility for the execution of a particular part of this procedure is identified in the right-hand column of section 9.

4. Changes since last revision

This is a new SOP. It replaces the GCP section of the SOP/INSP/2019:"Coordination of pre-approval GxP Inspections".

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5. Documents needed for this SOP

5.1. The following templates are available under the link Oracle Business Intelligence (OBI):

http://bi.eudra.org/dashboard/ Corporate GxP/GCP and PhV/templates/GCP templates

- Inspection Request (IREQ).
- Letter to the Applicant.
- Letter to the EEA Inspectors.
- Letter to the EEA Inspectors with contacts.
- Letter to third country inspector.

5.2. The following documents are saved under X:\Templates\Others\Compliance and Inspection\GCP:

(GCP-1 and GCP-2 are used in case of a joint inspection with FDA).

- GCP-1: announcement letter of joint EMA-FDA GCP inspection to Applicant.
- GCP-2: follow up Letter on GCP Inspection to Applicant_Joint EMA-FDA inspection.
- GCP-3: check¯¯ Checklist for validating GCP inspection reports-¯EMEA-INS-GCP-909-00.
- GCP-4: form¯¯Payment order generation form GCP inspections¯EMEA-INS-GCP-962-01
- GCP-5: form¯¯template Memo to gestionnaire with payment order generation form¯ EMEA-INS-GCP-964-01.

5.3. The following document is saved in DREAM under: Cabinets/04. Inspections/1. GCP/GCP Inspections

- EMA/426286/2012 Guidance on categorisation of GCP findings.

6. Related documents

1. SOP/EMA/0040 Evaluation of conflicts of interests of experts for involvement in EMA activities.
2. SOP/H/3004 Tasks of the product team on the handling of the initial Marketing Authorisation Application.
3. SOP/H/3206 Type II variations (30-day and 60-day procedures).
4. SOP/INSP/2005 Processing of financial transactions for inspections.
5. SOP/PDM/1004 Core master files of medicinal products for human and veterinary use following the centralised procedure.
6. WIN/INSP/2025 Announcement of Good Clinical Practice/Pharmacovigilance inspection to reporting inspectorate, applicant and 3rd country inspectorate prepared by P-CI-CNC.
7. WIN/INSP/2040 How to create reports from Scientific Memory Database.

8. GCP Inspection Policy for Centralised Procedures-resource and policy, EMEA/INS/GCP/45304/2004, which can be found in DREAM under Cabinets/Old EDMS Structure/Meetings/Regulatory Meetings/G C P/Inspection Policy.
9. User Manual for Corporate GxP: CorporateGxP GCP/PhV Inspections Full User Guide (http://corpgxp.eudra.org/corpgxp/us_ext_docs/gcpPhvHelp.pdf).
10. Procedure for coordinating GCP inspections requested by the EMEA, INS/GCP/1, which can be found on the EMA public website Home/Regulatory/Human medicines/Inspections/GCP compliance/Inspections procedure.
11. Procedure for reporting of GCP inspections requested by EMEA, INS/GCP/4, which can be found on the EMA public website Home/Regulatory/Human medicines/Inspections/GCP compliance/Inspections procedure.

7. Definitions

Abbreviations

- Applicant/MAH Applicant/Marketing Authorisation Holder.
- AR Assessment Report.
- Corporate GxP Corporate GxP
- CTs Clinical Trials.
- CxMP Committee for Medicinal Products for Human/Veterinary Use.
- GCP Good Clinical Practices.
- H-HM Human Medicines Special Areas sector.
- HoS Head of Sector.
- H-QM Quality of Medicines sector.
- H-SE Safety and Efficacy of Medicines sector.
- IIR Integrated Inspection Report.
- IR Inspection Report.
- IREQ Inspection Request.
- JAR Joint Assessment Report.
- OBI Oracle Business Intelligence
- MA Marketing Authorisation.
- P-CI-CNC Clinical and Non clinical Compliance section.
- PTL Product Team Leader.
- PTM Product Team Member.
- RI/LI Reporting Inspector/ Leading Inspector.
- SH Section Head.

- SMDB Scientific Memory Data Base.

GCP Inspection: The act by a competent authority of conducting an official review of documents, facilities, records, quality assurance arrangements, and any other resources that are deemed by the competent authority to be related to the clinical trial and that may be located at the site of the trial, at the sponsor's and/or contract research organisation's facilities, or at other establishments which the competent authority sees fit to inspect.

Reporting Inspector: The Inspector designated by the Reporting Inspectorate to co-ordinate the preparation of the inspection, the conduct of the inspection and the activities of the inspectors. The Reporting inspector has the following general duties:

- co-ordinating the
  - preparation of the inspection
  - practicalities of the inspection (with the inspectors and the MAH)
  - conduct of the inspection
- checking that the timelines for the inspection are kept
- writing and co-signing, together with the leading inspectors, the Integrated Inspection Report for multisite inspections with one inspection report per site inspected
- acting as the main communication point between the inspection team and the EMA Inspection Sector. The Reporting Inspector and the EMA Inspection Sector are responsible for the communication between the inspectorates and inspectors involved, the Rapporteur/Co-Rapporteur and the CXMP. The system of communication should however be flexible and there can be direct communication between the involved parties, including the assessors, where this is more practical
- management of the live central archive related to the GCP inspection
- the Reporting Inspector may also be the Lead Inspector (see below) for one or more sites.

Leading Inspector: The Inspector who has the following duties for the GCP inspections of at least one inspection site:

- evaluation of the feasibility of the inspection as requested and discussion with the Reporting Inspector
- organisation of the practicalities of the inspection with the inspectee
- leading the conduct of the inspection on site
- communication between the inspectee and the Reporting Inspector/EMA Inspection Sector. The system of communication should however be flexible and there can be direct communication between the involved parties where this is more practical
- writing and signing the Inspection Report
- reviewing and co-signing together with the Reporting inspector the Integrated Inspection Report

The Reporting Inspector and Lead Inspector will be the same person when only one site is concerned by the inspection.

Supporting Inspector: The Inspector who has the following duties for the GCP inspections of at least one inspection site:

- Support the Leading Inspector in the conduct of the inspection at the site
- Support the Leading inspector in the organisation of the inspection when required
- Review and co-sign the inspection report together with the leading inspector.

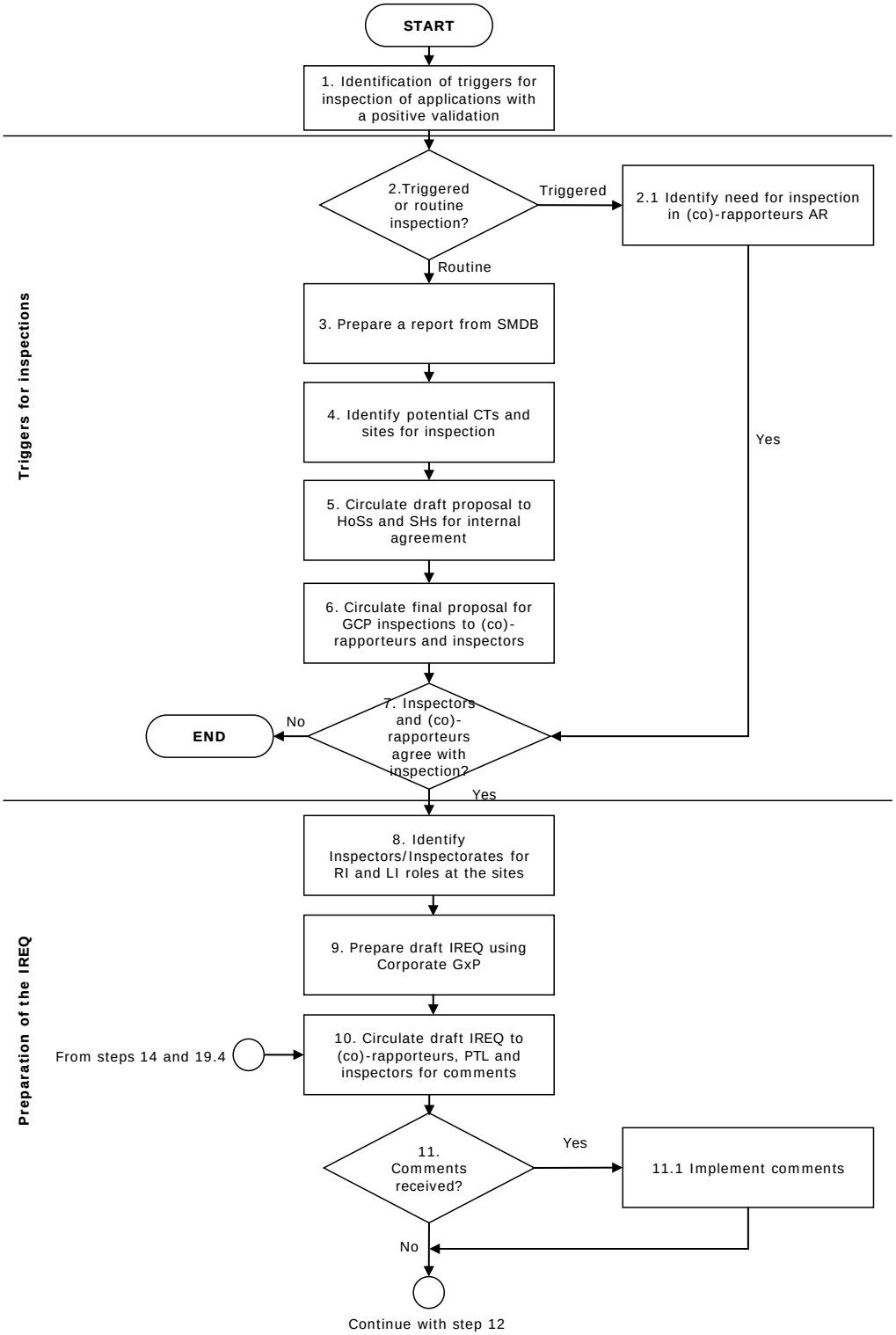
Inspection Report: An Inspection Report (IR) is prepared for each site inspected. It is written by the Lead Inspector and signed by the Lead Inspector and other inspectors as required by local legal requirements and SOPs. The Inspection Report will be written in English, unless required by local regulations to be in local language. In the latter case the Inspection Report will be translated / modified to English under the responsibility of the Lead Inspector prior to signature by all involved inspectors. The timelines for the finalisation of the IR will be extended as needed.

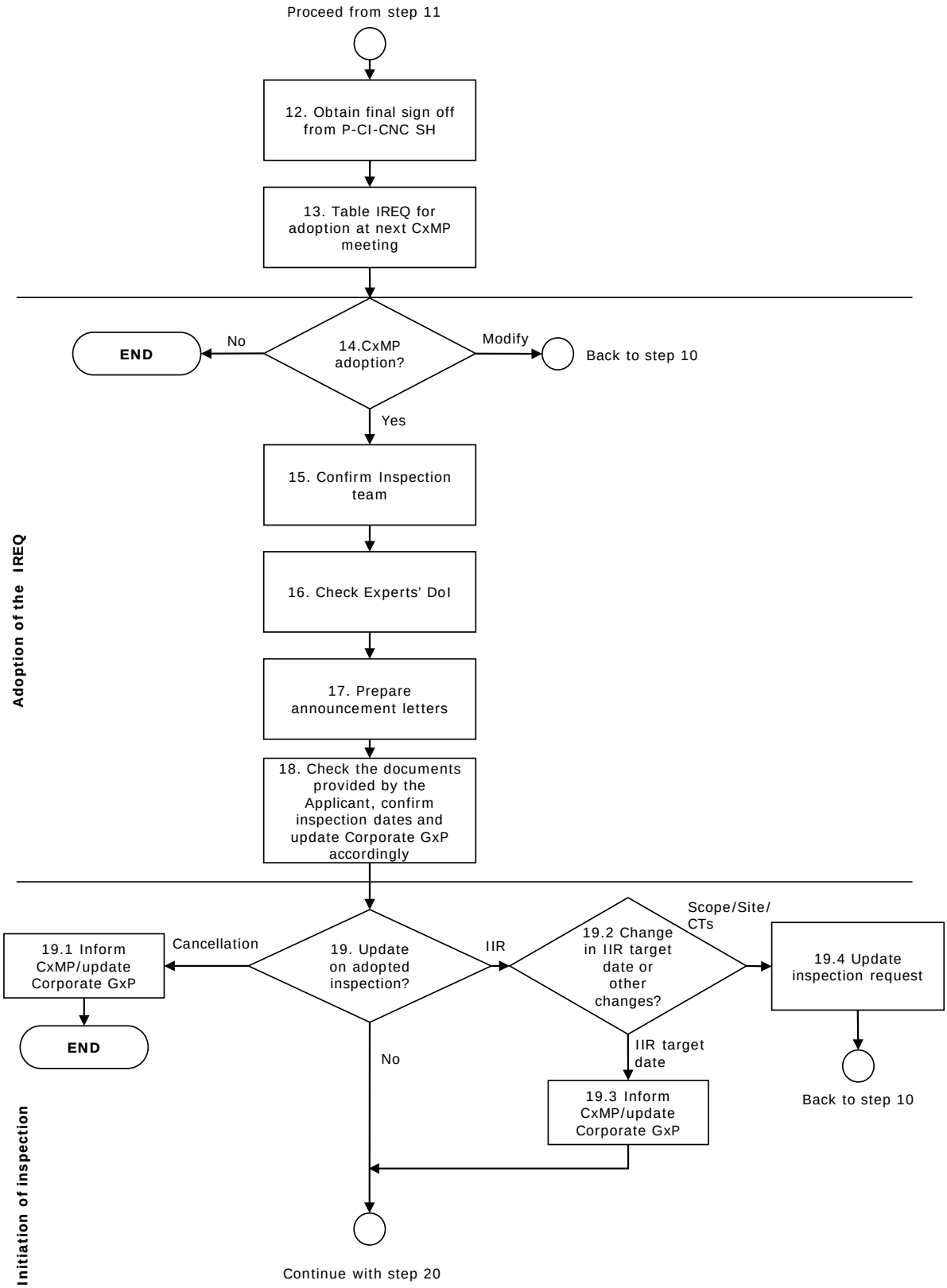
Integrated Inspection Report (IIR): For each GCP inspection request made by the CxMP one Integrated Inspection Report is prepared. This report is in English, and summarises the critical and major findings of the inspection of all sites involved.

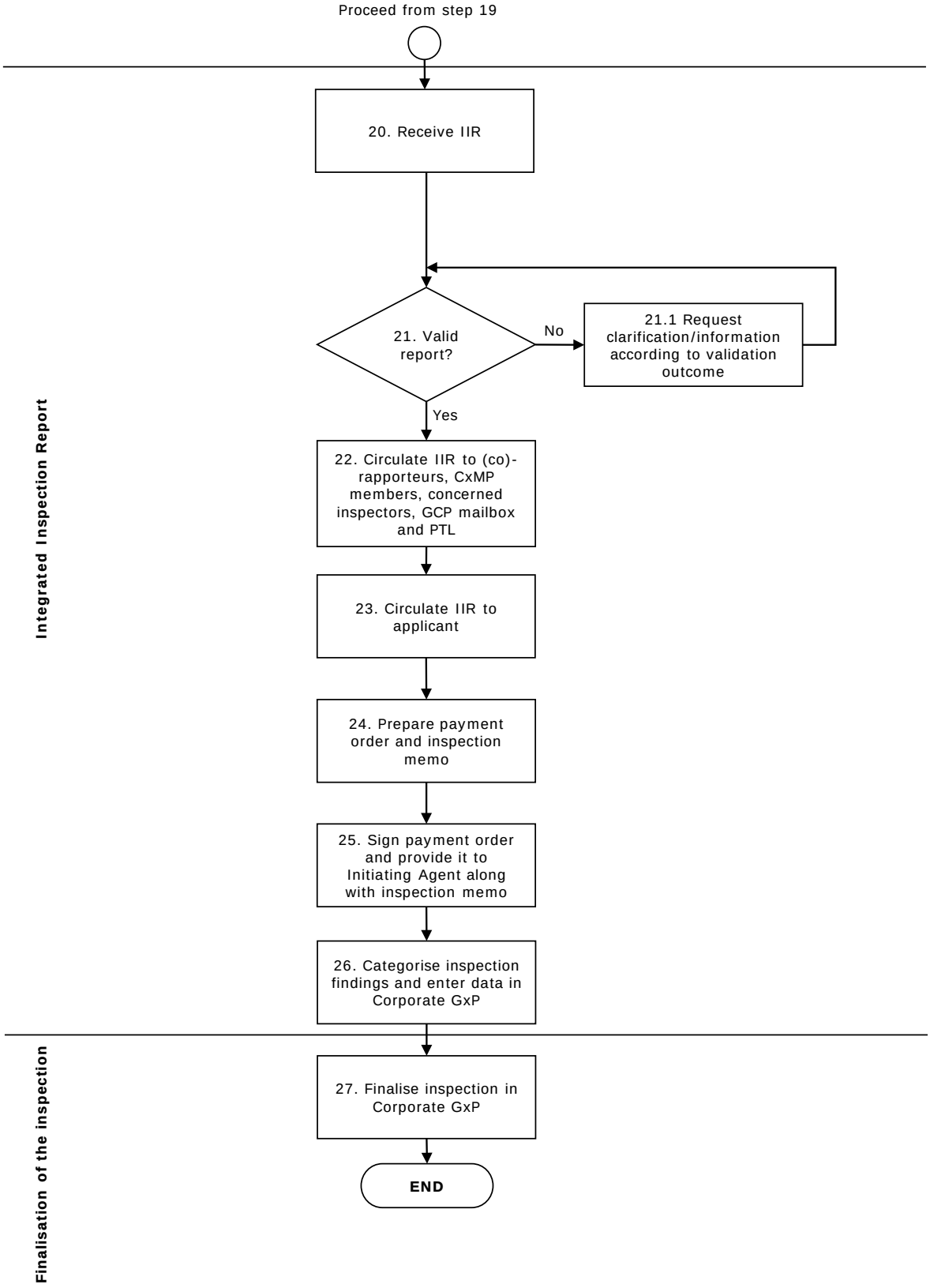
The report contains an evaluation of the quality of the data submitted and of the compliance with the principles of GCP based on the findings from all inspected sites. It is written and signed by the Reporting Inspector, and reviewed and signed by the Lead Inspectors. The IRs are attached to the IIR as appendices. Signature may be obtained by fax, and the originals mailed to the Reporting Inspector. Where there is only one site inspected the IIR and IR can be one document provided that they are in English and provided that a summary of the findings and conclusion is given – the report should fulfil the objectives of the IIR and IR.

Reporting Inspectorate: the Inspectorate from an EU/EEA country requested and accepting to designate the Reporting Inspector.

8. Process map(s) / flow chart(s)




Proceed from step 11
12. Obtain final sign off from P-CI-CNC SH
13. Table IREQ for adoption at next CxMP meeting
14.CxMP adoption?
No
END
Modify
Back to step 10
Yes
15. Confirm Inspection team
16. Check Experts' DoI
17. Prepare announcement letters
18. Check the documents provided by the Applicant, confirm inspection dates and update Corporate GxP accordingly
Adoption of the IREQ
19. Update on adopted inspection?
Cancellation
19.1 Inform CxMP/update Corporate GxP
END
IIR
19.2 Change in IIR target date or other changes?
Scope/Site/ CTs
19.4 Update inspection request
Back to step 10
IIR target date
19.3 Inform CxMP/update Corporate GxP
No
Initiation of inspection
Continue with step 20


Proceed from step 19
Integrated Inspection Report
20. Receive IIR
21. Valid report?
No
21.1 Request clarification/information according to validation outcome
Yes
22. Circulate IIR to (co)-rapporteurs, CxMP members, concerned inspectors, GCP mailbox and PTL
23. Circulate IIR to applicant
24. Prepare payment order and inspection memo
25. Sign payment order and provide it to Initiating Agent along with inspection memo
26. Categorise inspection findings and enter data in Corporate GxP
Finalisation of the inspection
27. Finalise inspection in Corporate GxP
END

9. Procedure

Step	Action	Responsibility
	Triggers for inspections	
1.	Two kinds of GCP inspections can be requested and coordinated by the P-CI-CNC Section. Routine inspections are proposed by P-CI-CNC while the triggered or "for cause" inspections are proposed by the (co)-rapporteurs. Identify trigger for routine inspection of an application with a positive validation.	P-CI-CNC PTM
2.	For triggered inspections, go to step **2.1.** In case of routine inspections, go to step **3.**	P-CI-CNC PTM
	Triggered GCP inspections	
2.1	• Pre authorisation applications : Identify the need for inspection in the (co)-rapporteurs Day 80 (D80) (human products)/D70 (veterinary products) AR. Exceptionally need for an inspection can be reflected in D150 (human products)/D160 (veterinary products) JAR. For human medicinal products, the AR is circulated by the PTL to all PTMs in accordance with step 21 of SOP/H/3004. • Post Authorisation applications (variations): Identify the need for an inspection in the (co)-rapporteurs AR. For human medicinal products, the AR is circulated by the PTL to all PTMs in accordance with step 22 of SOP/H/3206. In both cases, when the need for a triggered inspection is detected, go to step **7.**	P-CI-CNC PTM
	Routine GCP inspections	
3.	• Pre and post authorisation applications: After the GCP validation phase, prepare a report from the Scientific Memory Database (SMDB) in accordance with WIN/INSP/2040 to identify potential applications for routine inspections based on a set of predefined criteria, as described in GCP inspection Policy for the Centralised Procedure.	P-CI-CNC PTM
4.	Identify the potential clinical trials and sites for inspection.	P-CI-CNC PTM
5.	Circulate a draft proposal on the applications, clinical trials and sites for inspection to HoSs and SHs of H-SE, H-HM and H-QM for internal agreement.	P-CI-CNC PTM
6.	Circulate the final proposal agreed internally to the (co)-Rapporteurs and the inspectors to seek their agreement and identify inspection resources available, respectively.	P-CI-CNC PTM
7.	(Co)-rapporteurs agree with inspection and inspectors are available? If YES, go to step **8.** If (co)-rapporteurs do not agree and/or inspectors are not available, end of process.	P-CI-CNC PTM
	Preparation of the IREQ **Inspection Request State in Corporate GxP: Draft**	

Step	Action	Responsibility
8.	Identify the Inspectorates and Inspectors, in accordance with procedure GCP-1.	P-CI-CNC PTM
9.	Prepare the draft inspection request after entering information in Corporate GxP http://corpgxp.eudra.org/corpgxp/view/welcome and using the template available in Corporate DWH http://bi.eudra.org/dashboard/ Corporate GxP/GCP and PhV/templates/GCP template/Inspection Request.	P-CI-CNC PTM
10.	Circulate the draft IREQ to the(co)-rapporteurs, PTL and potential Inspectorates/Inspectors for comments within a given deadline.	P-CI-CNC PTM
11.	Are comments received? If YES, go back to step **11.1.** If NO, go to step **12.**	P-CI-CNC PTM
11.1	Implement the comments of the request and go to step 12.	P-CI-CNC PTM
	Inspection Request State in Corporate GxP: Requested	
12.	Once the draft Inspection Request is finalised, send the link of the IREQ to P-CI-CNC assistant and ask to obtain final sign off from the P-CI-CNC SH. Save in DREAM the final version of the IREQ and make sure it is marked as a core master file. Change the status in Corporate GxP from draft to requested.	P-CI-CNC PTM
13.	Table via MMD the final version of the IREQ for adoption at the next CxMP meeting.	P-CI-CNC Assistant
	Adoption of the IREQ **Inspection Request State in Corporate GxP: Adopted**	
14.	Has the IREQ been adopted by the CxMP? If YES, go to step **15.** If NO, end of process. If IREQ has been modified by CxMP, go to step **10**.	P-CI-CNC PTM
15.	Confirm Inspection team to be involved (RI, LI and supporting) and third countries contact point for those sites outside the EU. Enter information in Corporate GxP and change the status from requested to adopted. Inform assistant about adoption of the inspection request.	P-CI-CNC PTM
16.	Prepare binders for IREQ original hard copy as described in the WIN/INSP/2025. Check experts' Declaration of Interest in accordance with SOP/EMA/0040. If expert has risk level 2 or 3 proceed as described in section 3.4 of WIN/INSP/2025. ***Note: DoI of Experts with risk level 3 will be reviewed by Scientific Administrator in accordance with SOP/EMA/0040***	P-CI-CNC Assistant
17.	Prepare the announcement letters in accordance with WIN/INSP/2025 or using the templates listed under sections 5.1 and 5.2 of this SOP in case of joint inspections with FDA. Update Corporate accordingly and give the letters to the P-CI-CNC PTM for final sign off. Provide also a copy of letter to reporting inspectorate letter to the Initiating agent according to step 1 of SOP/INSP/2005. Save in DREAM the final version of the announcement letters and make sure it is marked as a core master file.	P-CI-CNC Assistant

Step	Action	Responsibility
	Go back to step **17** if there are changes in the inspection team, as applicable.	
	Initiation of the inspection **Inspection Request State in Corporate GxP: Initiated**	
18.	Check the documents provided by the Applicant as per announcement letter and confirm dates of inspection. Update Corporate GxP accordingly and change the status from adopted to initiated at the latest the day before the first inspection takes place. If there are changes in the inspection dates update the Corporate GxP accordingly and notify payments shared mailbox.	P-CI-CNC PTM
19.	Updates on adopted inspection request? - In case of cancellation of the inspection, go to step **19.1** - In case of changes in the IIR, go to step **19.2** - If NO updates on the Inspection Request, go to step **20.**	P-CI-CNC PTM
19.1	Inform the CxMP, update the Corporate GxP and inform Inspection_Payment@ema.europa.eu. End of process.	P-CI-CNC PTM
19.2	Changes in the IIR: - Target date (i.e.date postponed of 1 month), go to step **19.3** - Changes on Scope and/or Site and/or CTs, go to step **19.4**	P-CI-CNC PTM
19.3	Inform the CxMP, update the Corporate GxP and continue with step 20.	P-CI-CNC PTM
19.4	Update inspection request and go to step 10. Send the link of the new IREQ to Inspection_Payment@ema.europa.eu only in case of changes in the sites.	P-CI-CNC PTM
	Integrated Inspection Report **Finalise or amend without state change in Corporate GxP**	
20.	Ensure the IIR is sent to the EMA by the Reporting inspector according the agreed deadline. Any possible delay in providing the IIR should be notified to EMA by the RI.	P-CI-CNC PTM
21.	Validate the IIR received within 5 calendar days, as outlined in the document INS/GCP/1, against the currently used checklist (see GCP-3). Does validation fail? If YES, go to step **21.1.** In NO, go to step **22.**	P-CI-CNC PTM
21.1	Contact the Reporting Inspector in writing, ask for clarification on the failure detected and request amendment of the IIR if needed in which case go back to step 22.	P-CI-CNC PTM
22.	Circulate the IIR to (co)-Rapporteurs, CxMP members, concerned inspectors, GCP mailbox and the PTL. Ensure the topic is added to the next CxMP Agenda. Save in DREAM the final version of the IIR and make sure it is marked as a core master file.	P-CI-CNC PTM
23.	Circulate the IIR to the Applicant after agreement at the CxMP.	P-CI-CNC PTM
24.	Prepare payment order and the inspection memo in accordance with templates listed under point 5.2 and send an e-mail with links of these documents saved in DREAM to Inspection_Payment@ema.europa.eu	P-CI-CNC PTM

Step	Action	Responsibility
25.	Sign off the payment order and provide it to the Initiating Agent along with the inspection memo.	P-CI-CNC PTM
26.	Categorised all the findings detected in the IIR in accordance with Guidance EMA/426286/2012 Guidance on categorisation of GCP findings. Enter data in Corporate GxP accordingly.	P-CI-CNC PTM
	Finalisation of the inspection- Inspection Request State in Corporate GxP: Finalised	
27.	Change the Inspection Status from Initiated to Finalised once that the final opinion is given by the CXMP and the complete set of data for the product has been reviewed in Corporate GxP for data quality purposes.	P-CI-CNC PTM

10. Records

All completed forms and other records (i.e. correspondence and Inspection Reports) relating to the operation of this procedure will be collected by the P-CI-CNC GCP coordinators and will be stored in DREAM under:

Cabinet >01 Evaluation of Medicines> H-C (or V-C) > Product folder > GCP

The document “Table of contents Core Master File - Compliance and Inspection- SOP/PDM/1004, EMA/641169/2010” should be followed by P-CI-CNC PTMs and Assistants with regard to core master file documents to be saved in DREAM under the appropriate folder (product folder).

Hard copies will be saved under the appropriate product binder.

Note: Product mailboxes should always be copied for relevant correspondence.