



Standard operating procedure

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| Title: Co-ordination of GLP inspections | | |
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1. Purpose

This SOP describes how GLP inspections of the non-clinical safety, toxicological and pharmacological studies proposed in the human and veterinary applications for marketing authorisations submitted to the Agency are coordinated by the P-CI-CNC section.

This SOP applies to all GLP inspections that may be requested by the CxMP throughout the lifetime of a marketing application: pre-authorisation and post-authorisation GLP inspections under the centralised system.

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

New SOP superseding the GLP section of SOP/INSP/2019 Coordination of pre-approval GxP Inspections.



5. Documents needed for this SOP

The templates needed for this SOP are located on the X drive under: X:\Templates\Others\Compliance and Inspection\GLP:

- Template 1: GLP Inspection Request template.
- Template 2: Announcement letter to applicant/MAH.
- Template 3: Announcement letter to Inspecting Authorities.
- Template 4: Example of Contract in English.
- Template 5: Checklist for Inspections Sector for Validating GLP Inspection Reports.
- Template 6: Inspection report quality review and instruction for payment order generation.
- Template 7: Inspection outcome letter.

6. Related documents

- Directive 2004/10/EC on the Principles of GLP.
- Directive 2004/9/EC on the inspection and verification of GLP.
- SOP/EMA/0040 Evaluation of conflicts of interests of experts for involvement in EMA activities.
- SOP/H/3004 Tasks of the product team on the handling of the initial Marketing Authorisation Application.
- SOP/H/3206 Type II variations (30-day and 60-day procedures).
- SOP/INSP/2005 Processing of financial transactions for inspections.
- SOP/PDM/1004 Core master files of medicinal products for human and veterinary use following the centralised procedure.
- Core Master File – Compliance and Inspection. Doc. Ref.: EMA/641169/2010.

7. Definitions

- **Inspection:** On-site assessment of the compliance with the OECD GLP principles as adopted by the Community, performed by officials of Community Competent Authorities or authorities found equivalent under a Mutual Recognition Agreement.

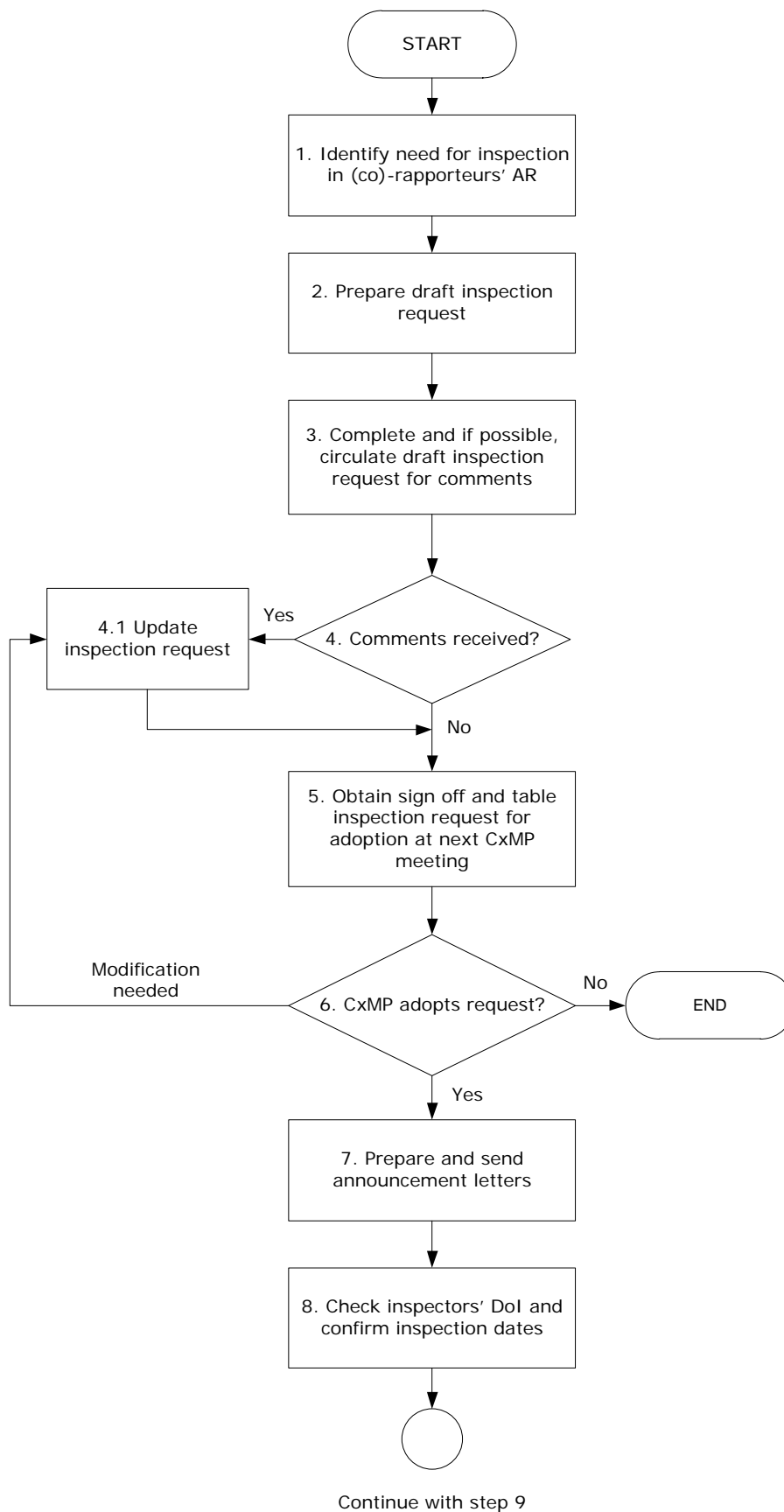
The inspection referred to in this SOP is typically a **study related** audit which is performed when it is requested to assess in retrospect specific issues related to the assessment of Module II and IV of an application (focused on the adherence of the study to the requirements of GLP and on the data and documentation related to the marketing authorisation application or studies performed post-authorisation) or other aspect of the study.

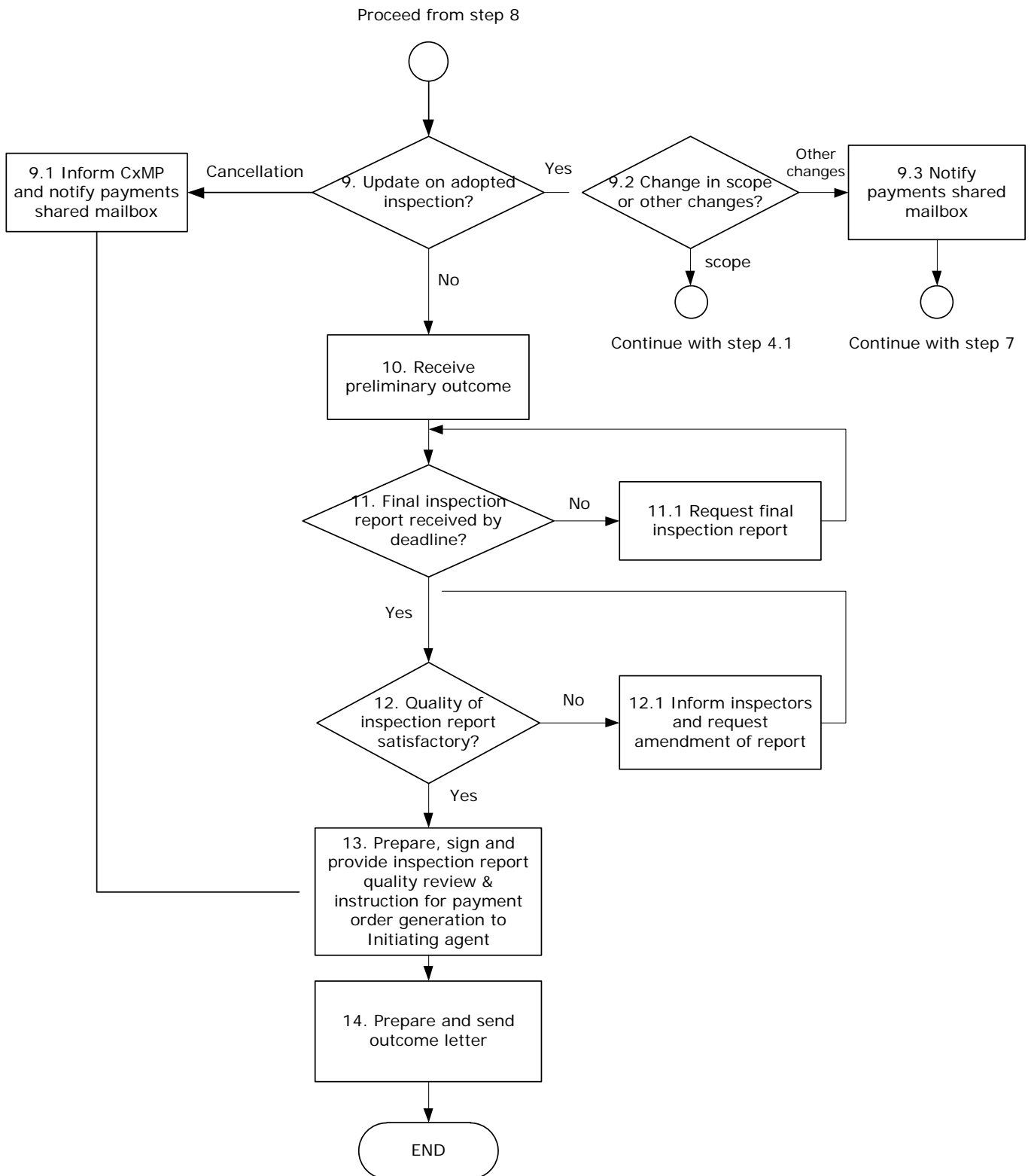
Exceptionally a **general GLP Inspection** covering general GLP compliance of a test facility could be carried out in accordance with Directive 2004/10/EC and Directive 2004/9/EC.

- **Inspection Report:** Report prepared by the official representing the Competent Authority stating whether the test facility inspected in general complies with the Community GLP principles and/or satisfactorily covers the study related issues arising from the assessment of the application.
- **GLP monitoring authority:** Competent authority of the Member State in which the test facility is located. For test facilities in 3rd countries or OECD countries outside the EU the CxMP will nominate authorities in its inspection request if necessary.

- AR Assessment report
- CHMP Committee for Medicinal Products for Human use
- CMF Core Master File
- CVMP Committee for Medicinal Products for Veterinary use
- CxMP Committee for Medicinal Products for Human/Veterinary use
- GLP Good Laboratory Practice
- JAR Joint Assessment report
- MAH Marketing Authorisation Holder
- MoU Memorandum of Understanding
- NCA National Competent Authority
- P-CI-CNC Clinical and non-clinical Compliance section in the Inspection and Compliance sector in the Patient Health Protection unit
- PM Project Manager
- PTL Product Team Leader
- ToD Table of decisions

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





9. Procedure

| Step | Action | Responsibility |
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| Assessment of GLP compliance | | |
| 1. | <ul style="list-style-type: none"> Pre-authorisation (initial marketing authorisation applications and line extensions): 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 (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. | GLP co-ordinator |
| Preparation of inspection request | | |
| 2. | Prepare draft inspection request using template 1, save it in DREAM, print out a copy and provide it to P-CI-CNC PTM. | P-CI-CNC Assistant |
| 3. | Complete draft inspection request. If time permits, circulate draft inspection request to the (co)-rapporteurs, PTL and potential Inspectorates/Inspectors for comments with a proposed timetable for reporting on the inspection. | GLP co-ordinator |
| 4. | Are comments received? If yes, go to step 4.1. If no, go to step 5. | GLP co-ordinator |
| 4.1 | Update inspection request. | GLP co-ordinator |
| 5. | Obtain sign off from Section Head. Scan signed copy of the request, save it in DREAM, print and file it in the appropriate binder. Table scanned copy of the inspection request for adoption at the next CxMP meeting. | P-CI-CNC Assistant |
| 6. | Is the inspection request adopted by CxMP? If yes, inform P-CI-CNC and go to step 7. If no, the procedure ends. If a modification is needed, go to step 4.1. | GLP co-ordinator |
| Preparation of announcement letters | | |
| 7. | Prepare inspection announcement letters to applicant/MAH and GLP Monitory Authority using templates 2 and 3. Print letters and obtain signature from appointed GLP co-ordinator. Scan, save in DREAM and send out signed announcement letters using Eudralink within 10 working days after adoption of inspection by CxMP. | P-CI-CNC Assistant |

| Step | Action | Responsibility |
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| | <p>Provide original letter to GLP Monitoring Authority to Initiating agent according to step 1 of SOP/INSP/2005.</p> <p>If not covered by MoU, prepare two copies of contract with GLP Monitoring Authority using template 4. Save them in DREAM, print and provide them to the Head of Sector for signature. Send these contracts along with the paper copy of the letter to the relevant GLP Monitoring Authority by post. One of the two copies needs to be signed by the relevant Authority and sent back to the Agency.</p> <p><i>Note: When saving signed announcement letters in DREAM, make sure they are marked as CMF. Also, mark adopted inspection request as CMF in accordance with SOP/PDM/1004.</i></p> | Administrator |
| | <p>After CxMP meeting, check CHMP's ToD (for human medicinal products) or CVMP's minutes (for veterinary medicinal products) for adopted inspections against paper copies of requests. In case there are any mistakes in the ToD or minutes, inform CHMP or CVMP secretariat by the specified deadline.</p> | |
| 8. | <p>Check inspectors' declaration of interests in accordance with SOP/EMA/0040.</p> <p>Confirm dates of inspection with GLP Monitoring Authority.</p> | GLP co-ordinator |
| 9. | <p>Are updates received after adoption of inspection?</p> <p>If no, go to step 10.</p> <p>If the inspection is cancelled (e.g. due to withdrawal of the application), go to step 9.1.</p> <p>If there are any other changes, go to step 9.2.</p> | GLP co-ordinator |
| 9.1 | <p>Inform CxMP and notify payments shared mailbox (Inspection_Payment@ema.europa.eu).</p> <p>Continue with step 13 if necessary (i.e if fees apply after cancellation, the relevant instruction for payment order generation needs to be prepared).</p> | GLP co-ordinator |
| 9.2 | <p>Does the change relate to the scope of the inspection request (e.g. addition or deletion of studies)?</p> <p>If yes, notify payments shared mailbox (Inspection_Payment@ema.europa.eu) and continue with step 4.1.</p> <p>If no (change relates to the GLP Monitoring Authority involved or to the date of inspection), go to step 9.3.</p> | GLP co-ordinator |
| 9.3 | <p>If the update involves a change in the GLP Monitoring Authority:</p> <ul style="list-style-type: none"> - notify payments shared mailbox (Inspection_Payment@ema.europa.eu); - inform previous GLP Monitoring Authority and - continue with step 7 (i.e. update and send out amended inspection announcement letters to applicant/MAH and GLP Monitoring Authority). <p>If the date of inspection changes before its proposed first day, no</p> | GLP co-ordinator |

| Step | Action | Responsibility |
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| | further action is required. However, if the date changes after the proposed first day of inspection, inform payments shared mailbox. | |
| Validation of inspection report | | |
| 10. | Receive preliminary outcome and prepare for appropriate actions if necessary. | GLP co-ordinator |
| 11. | Is final inspection report received by deadline? | GLP co-ordinator |
| | If yes, go to step 12. If no, go to step 11.1 | |
| 11.1 | Contact inspectors to request final inspection report and continue with step 11. | GLP co-ordinator |
| 12. | Is the quality of the inspection report satisfactory (i.e. in accordance with template 5)? The validation of the report should be performed within 15 working days from the day of receipt. | GLP co-ordinator |
| | If yes, go to step 13. If no, go to step 12.1. | |
| 12.1 | Inform inspectors, request amendment of the report and continue with step 12. | GLP co-ordinator |
| | <i>Note: In case the quality of the report does not satisfy the validation after having requested amendment to the concerned inspectors, P-CI-CNC may consider withholding the payment after consultation with the Section Head/Head of Sector.</i> | |
| Preparation of outcome letters | | |
| 13. | Prepare inspection report quality review and instruction for payment order generation by using template 6, print it out, sign and provide it to Initiating agent according to step 13 of SOP/INSP/2005. | GLP co-ordinator |
| 14. | Prepare inspection outcome letter using template 7. Print letter and obtain signature from appointed GLP co-ordinator. | P-CI-CNC Assistant |
| | Scan, save in DREAM and send out signed outcome letter by Eudralink within 10 working days after validation of the inspection report. Also, save inspection report validation checklist, instruction for payment order generation and inspection report in DREAM. | |
| | <i>Note: When saving signed outcome letter and the inspection report in DREAM, make sure they are marked as CMF, in accordance with SOP/PDM/1004.</i> | |

10. Records

Electronic copies of all records generated using the templates referred to in this SOP are saved in DREAM under Cabinets/01. Evaluation of Medicine/H-C/A-Z/Product folder/07 Inspection (for human medicinal products) or Cabinets/01. Evaluation of Medicine/V - C/Active applications/A-Z/Product Folder/07 Inspection (for veterinary medicinal products).