EMA/INS/GMP/61300/2024
Human Medicines Division

Version 2

# The 3-year work plan for the Inspectors Working Group

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| Name of Working Party: | **GMDP Inspectors Working Group** |
| Chairperson: | Brendan Cuddy |
| Vice chair: | N/A |

Work plan period: January 2024 – December 2026

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# 1. Strategic goals:

This GMDP IWG 3-year workplan is developed with a focus on the Network Strategy and Regulatory Science Strategy (RSS) goals, with a particular emphasis on supply chain integrity and resilience, product quality and the impact of new manufacturing technologies on the supply chain. The workplan includes specific activities to achieve an objective as well as including routine activities that contribute to the overall strategic objective.

- **Enhance traceability, oversight and security in the human/veterinary medicine supply chain -** Network Strategy 3.5 Goal 1.
- **Enhance inspector capacity building at EU and international level -** Network Strategy 3.5 Goal 2.
- **Reinforce the responsibility for product quality by harmonising and reinforcing guidance -** Network Strategy 3.5 Goal 3.
- **Encourage supply chain resilience and review long-term risks resulting from dependency on limited number of manufacturers and sites. -** Network Strategy 3.5 Goal 4.
- **Analyse the possible implications of new manufacturing technologies in order to regulate the new supply chains needed. -** Network Strategy 3.5 Goal 5 & RSS Goal 1: Catalysing the integration of science and technology in medicines development.

## 2. Tactical goals: activities/projects to deliver the strategic goals

**Enhance traceability, oversight and security in the human/veterinary medicine supply chain -** Network Strategy 3.5 Goal 1.

- Improve EudraGMDP database records to facilitate the sharing of information regarding manufacturers, distributors, products and respective compliance.
- Liaise with the Expert Group on inspectional procedures for the inspection of the repositories systems.
- Implement the new Veterinary Regulation in the context of GDP for veterinary medicines and active substances (e.g. updates to CoUP, EudraGMDP templates).
- Explore the development of a GDP inspector training curriculum (may be in collaboration with PIC/S working through the EU4Health Joint Action 11 and associated Work Programme 6 "**Proposal to include GDP to JAP**´.

**Enhance inspector capacity building at EU and international level -** Network Strategy 3.5 Goal 2.

- Support the running of the International API programme and the restart of the sterile inspection pilot programme and foster the participation of all MS.
- Implement VMP and API GMP inspection provisions of the New Vet. Reg. on inspections and controls by other means, **linked to the future implementing acts to be published in 2025**..
- Harmonised update to Veterinary specific GMP guideline annexes 4 &5 in collaboration with PIC/S.
- Build on the recommendations of the Nitrosamines LLE report to increase MAHs responsibilities and supervision of API manufacturers.
- Seek to increase routine assessor-inspector joint inspections;
- Implement the New Vet. Reg. provisions on inspections and controls by other means into Community Procedures and EUDRAGMDP.
- Work with PIC/S to support ongoing initiatives concerning inspection **reliance** with a focus on identification of barriers preventing MSs from relying on other trusted authorities.
- Work with PIC/s and ICMRA on developing shared **definitions, best practices and harmonised approaches for distant assessments and hybrid inspections. Work with PIC/s to develop an inspector training course for the new Annex 1 and cooperate with professional and academic stakeholders on training for industry.**

**Reinforce the responsibility for product quality by harmonising and reinforcing guidance -** Network Strategy 3.5 Goal 3.

- Develop EU level data integrity guidance by adapting existing published Q&A's into Chapter 4 and Annex 11 of the GMP Guide in collaboration with WHO and PIC/S.

**Encourage supply chain resilience and review long-term risks resulting from dependency on limited number of manufacturers and sites. -** Network Strategy 3.5 Goal 4.

Identification of sites that produce medicinal products for a significant number of EEA markets or very significant numbers of products. Seek to organise a dedicated cooperative supervision between MS and strategic partners of these sites.

**Analyse the possible implications of new manufacturing technologies in order to regulate the new supply chains needed** - **Network Strategy 3.5 Goal 5 & RSS Goal 1: Catalysing the integration of science and technology in medicines development.**

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In collaboration with QIG, facilitate the continued integration of science and technology in medicines development and ensure that the network has sufficient competencies to support innovation and associated technology platforms / regulatory science at various stages of medicines development. This includes support to digitalisation and personalised medicines.

Evaluate the concept of decentralised manufacturing within the GMP Guide to medicinal products other than ATMP's.

## *2.1. Guideline activities:*

### 2.1.1. GMP Guide: Chapter 4 (Documentation)

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| **Target date** | Q1 2026 |
| **Comments** | To provide the European Commission with a final text for the amended chapter in order to assure data integrity in the context of GMP. This would be in parallel with similar consideration of Annex 11 (Computerised Systems).<br><br>To work with GCP IWG, GLP IWG and PhV IWG on this topic. |

### 2.1.2. GMP Guide: Annex 11 (Computerised Systems)

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| Target date | Q1 2026 |
| **Comments** | To provide the European Commission with a final text for the amended annex in order to assure data integrity in the context of GMP. This would be in parallel with similar consideration of Chapter 4 (Documentation).<br><br>To work with GCP IWG, GLP IWG and PhV IWG on this topic. |

### 2.1.3. Guidelines on Good Manufacturing Practice specific to Advanced Therapy Medicinal Products

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| **Target date** | Q4 2026 |
| **Comments** | Review the Guidelines in collaboration with CAT and the European Commission following the publication of a new regulation on standards of quality and safety for substances of human origin intended for human application and need to update legal references and definitions. |

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| | Review the Guidelines in the light of new Annex 1 Manufacture of Sterile Medicinal Products and consider whether any updates are necessary. |

### 2.1.4. GMP Guide: Annex 3 Manufacture of Radiopharmaceuticals

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| **Target date** | Q4 2026 |
| **Comments** | To provide the European Commission with a final text for an amended Annex 3 following a review and update of the Annex to reflect current state of the art. |

### 2.1.5. GMP Guide: Annex 4 (Manufacture Of Veterinary Medicinal Products Other Than Immunological Veterinary Medicinal Products)

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| **Target date** | Q1 2026 |
| **Comments** | To review comments received from concept paper stakeholder consultation and draft an updated text.<br>To provide the European Commission with a final text. |

### 2.1.6. GMP Guide: Annex 5 (Manufacture Of Immunological Veterinary Medicinal Products)

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| **Target date** | Q1 2026 |
| **Comments** | To review comments received from concept paper stakeholder consultation and draft an updated text.<br>To provide the European Commission with a final text. |

### 2.1.7. GMP Guide: Annex 6 Manufacture of Medicinal Gases

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| **Target date** | Q4 2026 |
| **Comments** | To provide the European Commission with a final text for an amended Annex 6 following a review and update of the Annex to reflect current state of the art.. |

### 2.1.8. GMP Guide: Annex 15 Qualification and Validation

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| **Target date** | Q4 2025 |
| **Comments** | To provide the European Commission with a final text for an amended Annex 15 in the context of new technology in facilities, products and processes and following up on LLE recommendations, and extend the scope to APIs. |

### 2.1.9. GMP Guide: Annex 16 Certification by a Qualified Person and Batch Release

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| **Target date** | Q4 2025 |
| **Comments** | To provide the European Commission with a final text for an amended Annex 16 following up on LLE recommendations. |

### 2.1.10. GMP Guide: GMP for Novel Veterinary Medicinal Products

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| **Target date** | Q4 2025 |
| **Comments** | To provide the European Commission with a final text. |

### 2.1.11. GMP Guide: GMP for Autogenous Veterinary Vaccines.

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| **Target date** | Q4 2025 |
| **Comments** | To provide the European Commission with a final text. |

### 2.1.12. GMP and Marketing Authorisation Holders

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| **Target date** | Q4 2025 |
| **Comments** | To revise the paper in line with recommendations from the Nitrosamines LLE, to strengthen guidance for MAHs in terms of having adequate quality agreement with manufactures |

### 2.1.13. ICH Q12: Lifecycle management

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| **Target date** | Q4 2025 |
| **Comments** | To support the EU members of the Expert Working Group (EWG) in developing the training materials on the guideline with particular emphasis on GMP inspection and Pharmaceutical Quality System aspects, in liaison with PIC/S initiative. |

### 2.1.14.

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| **Target date** | Q4 2023 |
| **Comments** | To support the EU members of the Expert Working Group (EWG) in developing the guideline and following up on LLE recommendations to make Annex 15 mandatory for API through inclusion in Q7. |

## *2.2. Communication and Stakeholder activities:*

### 2.2.1. Input into International activities (beyond (V)ICH guidelines)

To continue to promote and strengthen international collaboration and convergence through the existing MRA platforms and other programmes (ICMRA – International Coalition of Medicines Regulatory Authorities, PIC/S, WHO) with a view to supporting capacity building.

### 2.2.2. Mutual Recognition Agreements

To support the European Commission in the equivalency assessment of the supervision of pharmaceutical manufacturers by third country authorities at their request for any new agreements or changes to existing agreements.

To support the European Commission in re-assessments (audits) of MRA partners.

To promote alignment of MRA maintenance programmes between the different MRA partners.

To continue progress towards the use of the EudraGMDP database by MRA partners to replace the paper exchange of GMP certificates.

- **Australia**

  To continue to maintain the functioning of the MRA;

  To support the European Commission in assessment efforts should APVMA request recognition as equivalent inspectorate.

- **Canada**

  To support the implementation and ongoing maintenance of the Comprehensive Economic and Trade Agreement (CETA).

- **Israel**

  To continue to improve and maintain the functioning of the MRA (ACAA - Agreement on Conformity Assessment and Acceptance).

- **Japan**

  To continue to maintain the functioning of the MRA.

- **New Zealand**

  To continue to maintain the functioning of the MRA.

- **Switzerland**

  To continue to maintain the functioning of the MRA.

- **United States of America**

  To continue to support the implementation of the EU-US MRA.

- **United Kingdom**

  To continue to support the functioning of the GMP aspects of the EU – UK Trade Co-operation Agreement.

### 2.2.3. International Coalition of Medicines Regulatory Agencies (ICMRA).

Support the ICMRA goal of establishing a Pharmaceutical Quality Knowledge Management System (PQKMS) capability.

### 2.2.4. Other collaborations

- **EDQM (European Directorate for the Quality of Medicines and Healthcare)**

  To continue collaborative activities aimed at optimising the use of inspection and testing resources and capacity building.

- **India and China**

  To support collaborative initiatives with Indian and Chinese regulators (e.g. capacity building and training on EU GMP standards).

- **International collaboration on supervision of Heparin supply chain**

  To maintain an appropriate supervision for the heparin supply chain in consultation with international partners.

### 2.2.5. Contribution to dialogue and engagement with stakeholders and external parties

***Interested Parties Meeting***

Annual meeting with Industry Interested Parties from trade associations covering manufacture and distribution of human and veterinary medicines, as well as professional associations representing professionals working in the pharmaceutical industry on topics related to the IWG Workplan.

***Workshops***

To support training for inspectors on Annex 1.

Follow-up from workshop on support to quality development in early access approaches (PRIME/BD): toolbox guidance in collaboration with the Quality Working Party.

### Other activities with stakeholders and external parties

Improve collaboration with Industry associations and relevant professional associations (Interested Parties).

***In addition to the actions identified above, the working group can be involved in any other activities foreseen in its mandate:***

http://www.ema.europa.eu/docs/en_GB/document_library/Other/2009/10/WC500004873.pdf

## *2.3. Cross-domain activities:*

To maintain dialogue and monitor developments in areas of common interest in order to communicate the work of the group and to assess the impact of other groups' activities on GMP and GDP guidance, Compilation of Union Procedures and other inspection related activities:

- Joint CHMP/CVMP Quality Working Party

- Increase collaboration with Good Manufacturing Practise (GMP)/Good Distribution Practice (GDP) Inspectors Working Group (GMDP IWG) to support synergies between assessment and inspection activities
- Provide inspector input into the update of guidance related to the QP declaration and on co-processed excipients and is supported by annual joint meeting (also with BWP).
- Biologics Working Party.
- Increase collaboration with Good Manufacturing Practise (GMP)/Good Distribution Practice (GDP) Inspectors Working Group (GMDP IWG) to support synergies between assessment and inspection activities and is supported by an annual joint meeting.(also with QWP).
- Safety Working Party.
- Heads of Medicines Agencies' Working Group of Enforcement Officers.
- Innovation Task Force (ITF).
- Quality Innovation Group (QIG).
- In close collaboration with QIG, ensure learnings and knowledge gained from the QIG interaction on new manufacturing technologies and regulatory science developments is shared with GMDP IWG to equip EU GMP Inspectors with the skills required to assess these new technologies and ensure a hamonised approach.
- SPOC Working Party.
- Scientific Advice Working Party.
- Novel Therapy Working Party for veterinary medicines.

## *2.4. Any other relevant activities:*

### 2.4.1. Collaboration with European Commission

- EU enlargement: to develop contacts and collaboration in the field of GMP and GDP inspections with EU candidate and accession countries identified by the European Commission. These countries are invited to observe meetings of GMP/GDP IWG.
- Legislative developments: to monitor new legislation, to assess and advise on potential impact on GMP, GDP, inspections or inspection-related activities. Particular attention will be given to:
  - Assessment of the impact of the GMP Implementing Acts for veterinary medicines and active substances for veterinary medicines, on GMP inspection and related activities and agree on practical implementation steps;
  - Assessment of the impact of the regulation on veterinary medicinal products (regulation 2019/06/EC) on GMP inspection and related activities and agree on practical implementation steps;
  - Revision of the Pharmaceutical legislation for human medicines.
  - Revision of the legislation for Substances of Human Origin (SoHo).
- Article 111b(1) equivalency assessment: to support the European Commission in the equivalency assessment of the supervision of active substance manufacturers by third country authorities at their request.

### 2.4.2. Joint Audit Programme

- To contribute auditor resource to the audit programme;
- To collaborate with PIC/S (Pharmaceutical Inspection Convention/Co-operation Scheme) and MRA (Mutual Recognition Agreement) partners in joint audits.

Through the Compliance Group:

- To ensure that the agreed audit programme for the period covered by this workplan is carried out and to report to the Heads of Medicines Agencies on the audit programme;
- To implement risk-based audit procedures;
- To monitor the results of audits and follow up as necessary;
- To develop a formal process for the follow-up of significant issues raised in the programme.

### 2.4.3. Compilation of Union Procedures on Inspections and Exchange of Information

- To review the current structure of the Compilation of Union Procedures in order to facilitate the ongoing maintenance of the procedures.
- To gather during 2024-2026 GMP and GDP inspection related topics for development or revision of Union procedures, including necessary updates following the publication of implement acts for GMP for veterinary medicines and GMP for active substances for veterinary medicines.
- To identify and implement, as needed, updates following the publication of the PIC/ s procedures for Inspection Reliance and Assessment of PQS (support for ICH Q12 implementation), and following the evaluation of the results of the Reliance Pilot conducted by IWG.

### 2.4.4. EudraGMDP database

- To continue to oversee the operation and maintenance of the EudraGMDP database;
- To identify and implement associated changes needed to support the integration of the database with the Agency's Master Data Management project.
- To promote further use of the EudraGMDP as a tool for EU and international collaboration and reliance;

### 2.4.5. Training for the network and knowledge building

- To develop training for EU GMP inspectors in accordance with the GMDP IWG training strategy.
- To develop training for EU GMP inspectors, in collaboration with the European Commission, to support the implementation of Annex 1 during 2024.
- To develop training for EU Inspectors on the implementing acts on GMP for Veterinary Medicinal Products, in particular training on GMP for Autogenous Vaccines and GMP for Novel Therapies.

### *2.5. Other EU collaborations*

#### 2.5.1. Input into other European activities

The group will undertake any other relevant work referred to it by the European Commission, Heads of Medicines Agencies or the scientific committees of the European Medicines Agency. This will include contributing as needed in the EU regulatory network's response to crises resulting from serious quality/manufacturing problems and/or GMP non-compliance.

## 3. Operational goals: medicinal product-specific activities

### *3.1. Pre-Authorisation activities*

- Contribution to Innovation Task Force discussions as required.
- Contribution to scientific advice procedures as required.
- Contribution to marketing authorisation procedures as required;
- GMP expertise and support to scientific aspects related to accelerated access schemes;

### *3.2. Evaluation and supervision activities*

- Agreement on EMA's annual re-inspection programme;
- Development of procedures and co-ordination of inspections relating to centrally authorised products and plasma master files for third-country blood establishments;
- Review of GMP provisions in the context of 'disruptive innovation' and propose revisions to GMP guidance interlinking with EMA Quality Innovation Group (QIG) and Innovation Task Force (ITF) and similar initiatives, as appropriate.
- Contribute to European Medicines Regulatory Network Strategy to 2025 as appropriate.
- Making best use of EU inspection resources by leveraging information from international regulatory authority partners wherever possible and implementing other risk-based approaches agreed in Union procedures. Consideration will also be given to leveraging knowledge gained from the equivalency assessments involved in the listing of third countries by virtue of Article 111b of Directive 2001/83/EC when planning inspections of active substance manufacturers;
- Complete the two year pilot on Inspection reliance agreed in October 2022.
- Contribute as needed to the European Medicines Regulatory Network, the MSSG and SPOC Working Party on dealing with shortages and availability, with a focus on issues concerning product quality and manufacturing

## 4. Following up on Nitrosamines Lessons Learned recommendations.

This work includes considering the revision of several guidance documents as proposed in the sections above (i.e. Annex 15, 16, and also include cross-references and the reflection paper on GMP for MAHs) and to provide additional guidance on API manufacturers audits by MIAHs.

- Further collaboration with ICH and PIC/s on updates of guidance identified as a result of the Nitrosamine LLE.

- The work also envisages preparation of new tools, for example to:
  - Work with PIC/s to draft an aide memoire for inspectors in order to evaluate if API manufacturers are in control of activities at risk of presence of unexpected impurities.

  Develop a risk based model for triggering pre-approval inspections of API manufacturers.

# 5. Expertise required

The GMDP Inspectors Working group consists of senior GMP inspectors from all EEA human and veterinary inspectorates. It collaborates with GMP inspectors from international partner agencies in the development of guidelines where appropriate and with other working parties such as the QWP / BWP where appropriate.

# 6. Meetings scheduled for 2024-2026

Face-to-face/virtual meetings are planned for the following dates:

| 2024 | 2025 | 2026 |
|---|---|---|
| 5-7 March 2024 (remote) | 11-13 March 2025 (remote) | *10-12 March 2026.* |
| 11-13 June 2024 (F2F) | 17-19 June 2025 (F2F) | *16-18 June 2026.* |
| 17-19 September 2024 (remote) | 23-25 Sept 2025 (Joint QWP- IWG date TBC) (remote) | |
| 25th September 2024 (Remote) Joint QWP/BWP/GMDP IWG | | *22-24 Sept 2026.* |
| 25-27 November 2024 (F2F) | 25-27 Nov 2025 (F2F) | *25-26 Nov 2026* |

The above mentioned dates may be modified as needed. Additional virtual meetings may be organised ad-hoc to progress guidelines, as required.

Four meetings of the Compliance Group in the margins of the GMP/GDP IWG meetings.

Drafting group meetings will normally be held by teleconference but other virtual meeting technology may be used.