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SCIENCE MEDICINES HEALTH

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Human Medicines Division

Developing the 3-year work plan for the Quality domain Input from GMDP IWG

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

Work plan period: January 2021 – December 2023 (following a first review point after one year in March 2022)

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1. Strategic goals:

The 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 finalise the sterile inspection pilot programme and foster the participation of all MS.
- Implement API inspection provisions of the New Vet. Reg. on inspections and controls by other means.
- 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.

Consider whether a GMP annex should be developed to address the adoption of new and innovative technologies in the manufacture of 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: Annex 1 (Manufacture of Sterile Medicinal Products)

Target date	Q1 2022
Comments	To provide the European Commission with a final text.

2.1.2. GMP Guide: Chapter 4 (Documentation)

Target date	Q4 2023
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). To work with GCP IWG, GLP IWG and PhV IWG on this topic.

2.1.3. GMP Guide: Annex 11 (Computerised Systems)

Target date	Q4 2022
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). To work with GCP IWG, GLP IWG and PhV IWG on this topic.

2.1.4. GMP Guide: Annex 15 Qualification and Validation

Target date	Q2 2023
Comments	Review the annex in the light of new technology in facilities, products and processes and consider whether any updates are necessary. Following up on LLE recommendations, consider whether the scope can be extended to APIs.

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

Target date	Q2 2023
Comments	Following up on LLE recommendations, consider revision of annex in order to provide additional guidance on batch traceability.

2.1.6. GMP Guide: Chapter 1 (Pharmaceutical Quality System)

Target date	Q4 2023
Comments	To provide the European Commission with a final text for the amended chapter in order to encourage industry adoption of risk-based approaches to prevention of shortages, taking account initiatives such as HMA-EMA Taskforce and the industry inter-association guidelines.

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

Target date	Q4 2023
Comments	To review comments received from concept paper stakeholder consultation and draft an updated text. To provide the European Commission with a final text.

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

Target date	Q4 2023
Comments	To review comments received from concept paper stakeholder consultation and draft an updated text. To provide the European Commission with a final text.

2.1.9. GMP Guide: GMP for Novel Veterinary Medicinal Products

Target date	Q4 2023
Comments	To provide the European Commission with a final text.

2.1.10. GMP Guide: GMP for Autogenous Veterinary Vaccines.

Target date	Q4 2023
Comments	To provide the European Commission with a final text.

2.1.11. ICH Q9: Quality Risk management

Target date	Q4 2023
Comments	To support the EU members of the Expert Working Group (EWG) in developing the training materials on ICH Q9 with particular emphasis on risk identification and risk management, in liaison with the dedicated PIC/S expert circle.

2.1.12. GMP and Marketing Authorisation Holders

Target date	Q4 2023
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

Target date	Q4 2021
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. ICH Q7: GMP for Active Substances

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.

2.1.15. ICH Q13: Continuous Manufacturing

Target date	Q4 2023
Comments	To support the EU members of the Expert Working Group (EWG) in developing the guideline .

2.1.16. VICH: GMP for API's for Veterinary Medicines

Target date	Q4 2023
Comments	To support the EU members of the Expert Working Group (EWG) in developing the guideline.

2.1.17. VICH: Other Q Guidelines for Veterinary Medicines

Target date	Q4 2023
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Comments

To support the EU members of the Expert Working Group (EWG) in any future adaptations of existing ICH Q Guidelines such as Q9/Q10 to veterinary medicines.

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 finished product manufacturers by third country authorities at their request for any new agreements or changes to existing agreements.

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

2.2.5.1. 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.

2.2.5.2. 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.

2.2.6. 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;
- EU Process Analytical Technology team;
- Biologics Working Party;
- Safety Working Party;
- Heads of Medicines Agencies' Working Group of Enforcement Officers.
- Innovation Task Force (ITF)
- Quality Innovation Group

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 Clinical Trials Regulation (Regulation (EU) No 536/2014) 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 the human medicines.
- 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 2020 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 procedure on quality systems framework for GMP inspectorates;
- To review the guideline on training and qualifications of GMP inspectors;
- To finalise the procedure for dealing with serious GDP non-compliance;
- To continue to identify GMP and GDP inspection related topics for development as Union procedures;
- To identify and implement, as needed, editorial updates following the entry into force of the new regulation for veterinary medicinal products,;
- To identify and implement, as needed, updates following the publication of the GMP guideline for ATMPs.
- 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).

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 support the European Commission with organising the JAP – JRP auditor training organised in collaboration with PIC/s in Q1 2022.

2.5. Other EU collaborations

2.5.1. Other input into 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 Innovation Task Force 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;

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, but also include cross-references in chapter 1, 7 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. Work modalities/Architecture

7. Meetings scheduled for 2021-2023

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

2021	2022	2023
2-4 March 2021	1-3 March 2022 (meeting with Interested Parties)	7-9 March 2023
22-24 June 2021	7-9 June 2022	6-8 June 2023
20-23 September 2021 (Joint with QWP on 22 September)	20-22 September 2022 (Joint with QWP on 21 September)	26-28 September 2023 (Joint QWP- IWG on 28 September TBC)
23-25 November 2021	22-24 November 2022	21-23 November 2023 (meeting with Interested Parties TBC)

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.

8. Any other feedback

The work programme and resources of the GMDP IWG will be affected by business continuity plans at Agency, Network and international level as a result of the ongoing COVID-19 pandemic.