October 18, 2022
EMA/INS/GMP/837536/2022
Quality and Safety of Medicines Department

Revision 1

Annual report of the Good Manufacturing and Distribution Practice Inspectors Working Group 2022

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

Table of contents

1. Introduction

This document is the annual report of the GMP/GDP Inspectors Working Group (GMP/GDP IWG) for the year 2022. This group was established at EMA in 1996.

There was no annual report from 2018 to 2020 as a result of the EMA Business Continuity Plan (BCP) due to the effects of the UK withdrawal from the European Union. The BCP was extended in 2020 due to the COVID-19 public health emergency. The impact of the BCP on the work of the GMP/GDP IWG has resulted in a prioritisation of activities and shorter meetings, although the meeting frequency has been maintained. The GMP/GDP IWG has met through 2022 virtually via remote meeting platforms, with resumption of in person meetings in November 2022.

The GMP/GDP IWG provides input and recommendations on all matters relating directly or indirectly to Good Manufacturing Practice (GMP) and Good Distribution Practice (GDP).

The GMP/GDP IWG focuses on harmonisation and co-ordination of GMP and GDP related activities at EU level and maintains close co-operation with international partner authorities. The group's role and activities are described in more detail in its mandate, which was revised in 2013.

This annual report is set out in line with the format and objectives of the 2021 – 2023 3-year work plan.

2. Meetings

The plenary GMP/GDP IWG meetings took place on:

- 08 - 10 March 2022 (Meeting with Interested Parties on 10 March (WebEx meeting));
- 07 - 09 June 2022 (WebEx meeting);
- 20 - 22 September 2022 (Joint QWP-IWG on 21 September (Hybrid Meeting));
- 22 - 24 November 2022 (In person meeting).

Drafting group meetings were held by teleconference or through other virtual meeting technology.

The Compliance Group, managing the Joint Audit Programme (JAP) on behalf of HMA, also met on four occasions in 2022 in the margins of the above-mentioned plenary meetings.

3. GMP and GDP inspections in 2022

The current COVID-19 public health emergency continues to have a considerable impact on the work of GMP and GDP inspectors. Although on-site inspections have resumed where possible, travel restrictions and hygiene measures continue to impact on-site inspection as the primary means of verifying compliance with requirements.

In 2020, the IWG had adopted temporary measures to facilitate on-going compliance verification through use of "distant assessment" and agreed to the automatic extension of validity dates of EU GMP certificates entered into the EudraGMDP database. These measures were incorporated into questions

and answers on regulatory expectations for medicinal products for human and for veterinary use that were published by the European Commission[1].

These measures have been maintained since and during 2022, the GMP/GDP IWG agreed to extend these temporary measures until the end of 2023 and monitored the impact of the public health emergency on the conduct of inspections and on pharmaceutical supply chains.

4. Mutual recognition agreements (MRAs) and other agreements on GMP

4.1. MRA General

Despite the pandemic MRA related work was maintained in 2022.

4.2. MRA with US

Work continued on the inclusion of veterinary medicines, vaccines and plasma derived products in the operational scope of the EU – US Mutual Recognition Agreement. The implementation work also addressed aspects related to improving exchange of information between US and EU and steps towards recognition of FDA's third country inspections have been initiated. Work on the inclusion of pre-approval inspections remained on-hold.

The GMP/GDP IWG continued to provide the forum to discuss and clarify the technical and practical aspects for the implementation of the MRA.

A representative from US FDA attended GMP/GDP IWG meetings throughout 2022.

4.3. MRA with Japan

There were no changes to the existing MRA with Japan throughout 2022. Representatives from the Pharmaceuticals and Medical Devices Agency (PMDA) attended GMP/GDP IWG November 2022 meeting.

4.4. MRA with Canada

The Comprehensive Economic Trade Agreement (CETA) entered into provisional application in September 2017 pending ratification by all EU member states. The provisions of the existing MRA have been integrated into the CETA.

The EU assessment of Canada towards "API Listing" and inclusion of APIs in the operational scope MRA progressed during 2022.

Representatives from Health Canada attended GMP/GDP IWG meetings throughout 2022.

4.5. MRA with Switzerland

No changes were made to the MRA with Switzerland during 2022.

[1] Questions and Answers on Regulatory Expectations for Medicinal Products for Human Use during the Covid-19 Pandemic and ah_vet-med_covid-19_qandas.pdf (europa.eu).

Representatives from Switzerland attended GMP/GDP IWG meetings throughout 2022 and proactively shared the minutes of the Swiss Inspectorates Coordinating Committee (ICC).

4.6. MRA with Australia

There were no changes to the existing MRA with Australia throughout 2022.

A representative from the Australian Pesticides and Veterinary Medicines Authority (APVMA) and the Therapeutics Goods Administration (TGA) attended GMP/GDP IWG meeting throughout 2022.

4.7. MRA with New Zealand

There were no changes to the existing MRA with New Zealand throughout 2022.

Representatives of Medsafe or MPI did not attend any GMP/GDP IWG meetings in 2022.

4.8. ACAA with Israel

There were no changes to the existing ACAA co-operation with Israel in 2022.

A representative from the Ministry of Health attended June and November 2022 GMP/GDP IWG meetings.

4.9. Other international collaborations on GMP

The United Kingdom attended all four GMP/GDP IWG meetings in 2022 as an observer.

EDQM attended all four GMP/GDP IWG meetings in 2022 as an observer and informed the IWG during the year on a number of topics of common interest including the progress of sampling and testing programmes, the proceedings of the annual OMCL meeting, the EDQM reinspection programme and the CEP Steering Committee.

5. Harmonisation topics

5.1. Joint Audit Programme (JAP)

During 2022 the Compliance Group (CG), a Sub-group of the GMDP IWG, met on five occasions. Throughout the year the Compliance Group monitored the implementation of outstanding CAPAs, adopted 3 audit reports (GR, HU-h, CZ-v) and closed 2 audits (AT, GR). It implemented a new JAP report template and provided review of the update to the Union Procedure *EU/EEA Programme for Maintenance of Equivalence in Supervision of the Pharmaceutical Industry.*

The Compliance Group also collaborated with the EMA Secretariat, EC and PIC/S in organising a training event for JAP auditors which took place on 22 - 23 March 2022.

The CG together with GMDP IWG provided input to the application for *Joint action on quality of medicines* as part of the *EU4Health Programme* which amongst other will help strengthening the operation and resourcing of the JAP.

Due to the impact of the pandemic only three JAP audits essential for the implementation of the EU-US MRA for veterinary products were conducted on-site.

Two new CG members from FIMEA and AEMPS were nominated by the GMDP IWG for a renewable 3-year term to replace the departing CG members from ANSM and SUKL. The CG also confirmed a representative of AGES as the Vice-Chair.

5.2. Compilation of Union Procedures on Inspections and Exchange of Information

A new version (Version 18) of the Compilation of Union Procedures was published by on the Agency website: Good manufacturing practice | European Medicines Agency (europa.eu) and entered into force in July 2022.

In April 2022 a corrigendum of Revision 18 was published to correct 4 updated legal references.

Work continued through 2022 on updating legal references contained in the current text of the Compilation to take into account Regulation 2019/06 on veterinary medicinal products.

6. GMP and GDP guidance

GMP guidelines are developed in collaboration with PIC/S in accordance with the EMA-PIC/S co-operation agreement.

6.1. Annex 1: Manufacture of Sterile Medicinal Products

A revised Annex 1 Annex 1 was published by the European Commission in August 2022.

6.2. Annex 4: Manufacture of Veterinary Medicinal Products other than Immunological Veterinary Medicinal Products

Work has continued on the drafting of an updated Annex 4 during 2022.

6.3. Annex 5: Manufacture of Immunological Veterinary Medicinal Products

Work has continued on the drafting of an updated Annex 5 during 2022.

6.4. Annex 11: Computerised Systems

A concept paper for the update of Annex 11 has been adopted by the GMP/GDP IWG in October 2022 and published for stakeholder consultation in November 2022.

6.5. Annex 21: GMP for importers of medicinal products

Annex 21 was published by the European Commission in February 2022.

6.6. Chapter 4: Documentation

A drafting group has been formed to work on the update of Chapter 4.

6.7. Guideline on the responsibilities of the sponsor with regard to handling and shipping of investigational medicinal products for human use in accordance with Good Clinical Practice and Good Manufacturing Practice

The guideline was published by the European Commission in 2022.

6.8. Revised reflection paper on the use of interactive response technologies (interactive voice/web response systems) in clinical trials, with particular emphasis on the handling of expiry dates

The guideline, developed in collaboration with the GCP Inspectors Working Group, was published by the European medicines Agency in October 2022.

6.9. Questions & Answers (Q&As)

Work was carried out on a number of Q&As with a view to harmonising interpretation and expectations on various GMP topics. The following were published during 2022:

- Q&A on the requirements for active substances used as starting materials in veterinary medicinal products.
- Q&A for PMF Holders on PMF dossier requirements.

In addition, a stakeholder consultation was held during 2022 for a proposed Question and Answer on the physical attendance and the location of personal residency of the Qualified Person.

7. Inspections, Non-compliance, Quality Defects and Referrals

7.1. Nitrosamine contamination and Sartans Lessons Learnt Exercise (LLE)

General agreement was reached on the inclusion of risk-based selected Centrally Authorised Products (CAPs) in the sampling and testing programme as well as follow-up during routine inspections for non-compliant CAPs. The list of products will be extracted from the CAPs in scope of the call for review exercise recommended by CHMP Article 5 (3) Scientific Opinion on presence of nitrosamine impurities in human medicines.

A drafting group was formed to review all recommendations concerning GMP identified during the lessons learned exercise. The group has been working on some proposals which are currently under discussion within the network.

7.2 Inspection Reliance.

The GMP/GDP IWG discussed and agreed the launch of a one year pilot evaluating the reliance upon inspection reports issued by PIC/s participating authorities. The pilot was launched in October 2022.

8. EudraGMDP database

The following requirements arising from the new regulatory framework for veterinary medicines[2] have been implemented in the EudraGMDP database as of 28 January 2022:

- Integration of EudraGMDP with EMA's Organisation Management Service (OMS);
- Extension of the Wholesale Distribution Authorisation (WDA) and Active Pharmaceutical Ingredients Registration (API-Reg) to the veterinary domain.

In addition to the above, several changes have been implemented in all EudraGMDP modules in order to reflect the new legal references, adapt the related templates, provide additional details to the standard OMS addresses (i.e. (alternative trade names)..

The GMP/GDP IWG, as the Telematics Implementation Group (TIG) for EudraGMDP, was consulted on all proposed changes to the database and provided technical input and direction as needed, ensuring national systems were updated accordingly and that there was appropriate communication to stakeholders.

The GMP/GDP IWG agreed to a number of routine maintenance changes to the database during the year.

9. Collaboration with the European Commission

New legislative developments were monitored to assess and advise on the potential impact on GMP, GDP, inspections or inspection-related activities. In particular, attention was paid to developments related to the Joint Audit Programme and the revision of the pharmaceutical legislation for human and veterinary medicinal products. A drafting group has been formed to provide scientific advice on Implementing Acts on GMP for veterinary medicinal products and active substances for veterinary medicinal products.

10. Liaison with other groups

The GMP/GDP IWG maintained dialogue and monitored developments involving external groups in areas of common interest. The aim was to communicate the work of the Group and to assess the impact of other groups' activities on GMP/GDP guidance, the Compilation of Union Procedures and other inspection-related activities.

10.1. Pharmaceutical Inspection Co-operation Scheme (PIC/S)

The GMP/GDP IWG continued the close collaboration with PIC/S on the harmonisation of guidance and procedures, training events and the (re)-assessment of inspectorates as topics of strategic importance. The IWG and PIC/S liaisons have attended each other's meetings and working groups.

10.2. International Conference on Harmonisation for Registration of Pharmaceuticals for Human Use (ICH)

The GMP/GDP IWG continued to be consulted on a number of topics in connection with the revisions to specific chapters and annexes and developing specific training material for ICH guidelines including Q9

[2] Regulation (EU) 2019/6 and Commission Implementing Regulation (EU) 2021/16, Article 9(h)

(Quality Risk Management), ICH Q2 (Validation of Analytical Procedures), ICH Q13 (Continuous Manufacturing) and Q14 (Analytical Procedure Development).

10.3. International Conference on Harmonisation for Registration of Veterinary Products (VICH)

The GMP/GDP IWG was consulted on the development of GMP for veterinary active pharmaceutical ingredients.

10.4. Interested Parties

A formal interested parties meeting was held in March 2022.

The following organisations participated in 2022: AESGP (Association of the European Self-Medication Industry), APIC (Active Pharmaceutical Ingredients Committee), EFPIA (European Federation of Pharmaceutical Industries and Associations), Medicines for Europe, EIPG (European Industrial Pharmacists Group), EQPA (European QP Association), Animal Health Europe (formerly IFAH-Europe), ISPE (International Society for Pharmaceutical Engineering), PDA (Parenteral Drug Association), GIRP (European Healthcare Distribution Association), EAEPC (European Association of Euro-Pharmaceutical Companies representing Europe's licensed parallel distribution industry) and EBE (European Trade Association representing biopharmaceutical companies).

10.5. Quality Working Party

In addition to the annual joint meeting held in September 2022, the GMP/GDP IWG maintained regular exchanges on matters of joint interest.

The work of the Process Analytical Technology (PAT) Team was suspended in 2021 due to the BCP.

10.6. Innovation Task Force (ITF)

The GMP/GDP IWG agreed to take part in relevant ITF meetings in order to provide a platform for early interactions with companies in relation to new technologies. The IWG reviewed a small number of case studies on innovative manufacturing technologies during 2022.