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Quality and Safety of Medicines Department

Annual report of the Good Manufacturing and Distribution Practice Inspectors Working Group 2023

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Introduction

This document is the annual report of the GMP/GDP Inspectors Working Group (GMP/GDP IWG) for the year 2023. 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 public health emergency due to COVID-19. The EMA BCP has ceased during 2022 and the GMDP IWG has gradually resumed some of the suspended activities as well as regular in person meetings, alternating with remote meetings.

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.

Meetings

The plenary GMP/GDP IWG meetings took place on:

- 07 – 09 March 2023 (Meeting with Interested Parties on 09 March (WebEx meeting)
- 13 – 15 June 2023 June 2022 (In Person Meeting);
- 26-28 September 2023 (Joint QWP- IWG on 27 September (Hybrid Meeting);
- 21 - 23 November 2023 (In Person Meeting).
- An ad hoc meeting of the GMDP IWG was held on 30 October 2023 (WebEx 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 2023 in the margins of the above-mentioned plenary meetings.

GMP and GDP inspections in 2023

Although the end of the COVID-19 public health emergency was declared by WHO in May 2023, the restrictions applied during the pandemic continue to have a considerable impact on the work of GMP and GDP inspectors. On site inspections have also resumed, and despite progress from the EU inspectorates, it is acknowledged that there was still a backlog of sites awaiting to be inspected.

During 2023, the GMDP IWG agreed to extend based on risk the validity dates of EU GMP Certificates entered into EudraGMDP database until end of 2024 and will continue to monitor the impact of the public health emergency on the conduct of inspections and on pharmaceutical supply chains.

Mutual recognition agreements (MRAs) and other agreements on GMP

MRA General

MRA related work was maintained in 2023.

MRA with USA

Work continued on the inclusion of veterinary medicines in the operational scope of the EU – US Mutual Recognition Agreement and on 30 May 2023 the expansion to veterinary products was officially confirmed. At that stage the EU recognised the US FDA as equivalent for GMP inspections of manufacturers of veterinary products, while the US FDA recognised the national competent authorities responsible for veterinary products in the EU it had assessed. Until the end of 2023, the US FDA had assessed 18 EU national competent authorities. The assessment of the remaining veterinary authorities is ongoing and is expected to conclude in 2024.

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 all GMDP IWG meetings throughout 2023.

MRA with Japan

There were no changes to the existing MRA with Japan throughout 2023.

A representative from PMDA attended all GMDP IWG meetings throughout 2023.

MRA with Canada (CETA)

No changes were made to the agreement with Canada during 2023. The parties concluded mutual technical assessments for the inclusion of active substances in the scope of the agreement.

A representative from Health Canada attended all GMDP IWG meetings in 2023.

MRA with Switzerland

No changes were made to the MRA with Switzerland during 2023.

A representative from Swissmedic attended all GMDP IWG meetings throughout 2023.

MRA with Australia

Representatives from Australia attended all GMDP IWG meetings throughout 2023.

Australia completed a number of equivalency assessments of EU GMP Inspectorates.

MRA with New Zealand

There were no changes to the existing MRA with New Zealand throughout 2023.

A representative from Medsafe attended the March 2023 GMDP IWG meeting.

New Zealand completed a number of equivalency assessments of EU GMP Inspectorates.

ACAA with Israel

There were no changes to the existing ACAA co-operation with Israel in 2023.

A representative from the Ministry of Health attended the March 2023 GMP/GDP IWG meeting.

Other international collaborations on GMP

EDQM attended all four GMP/GDP IWG meetings in 2023 as an observer and informed the GMDP 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.

WHO and PIC/S observers also attended the GMDP IWG meetings throughout 2023.

The United Kingdom attended all four GMP/GDP IWG meetings in 2023 as an observer.

Harmonisation topics

Joint Audit Programme (JAP)

During 2023 the Compliance Group (CG), a Sub-group of the GMDP IWG responsible for coordination of the JAP, met on four occasions. The GMDP IWG confirmed the reappointment of the Chair of the Compliance Group and confirmed the renewal of the membership of several members. Throughout 2023 the Compliance Group monitored the implementation of open corrective and preventive actions (CAPAs), adopted 5 JAP audit reports and closed 5 audits.

The Compliance Group worked also closely with the EU4Health Joint Action 11 in the review of JAP procedures and supported the organisation of a JAP/JRP auditor training webinar in October 2023. During 2023 11 JAP on-site audits were conducted.

Compilation of Union Procedures on Inspections and Exchange of Information

The latest version (Version 19.1) was published by the Agency during 2023 with updates including:

- Modifications as a result of the entry into application of Regulation (EU) 2019/6 on veterinary medicinal products and repealing Directive 2001/82/EC and Regulation (EU) 2019/5 amending Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency.
- A new procedure on EU/EEA Programme for Maintenance of Equivalence in Supervision of Good Manufacturing Practice (GMP) Compliance of Pharmaceutical Companies.
- GMP and GDP guidance

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

Manufacture of Veterinary Medicinal Products Other Than Immunological Veterinary Medicinal Products (Annex 4).

Work has continued on the drafting of an updated Annex 4 during 2023.

Manufacture Of Immunological Veterinary Medicinal Products (Annex 5)

Work has continued on the drafting of an updated Annex 5 during 2023.

Chapter 4 of the guidelines on good manufacturing practice – documentation

A drafting group has been formed to work on the update of Chapter 4. The group are working in partnership with the drafting group on Annex 11.

Annex 11 – validation of computerised systems

Work has continued on the drafting of an updated Annex 11 during 2023.

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 2023.

- Question and Answer on the physical attendance and the location of personal residency of the Qualified Person.
- Question and Answer on Chapter 7: Outsourced activities and the use of indirect agreements between MAHs and manufacturers
- use of X-ray sterilization for single use systems (QIG).
- In addition, work had been done on an update to the Questions and Answers on Annex 1.

Inspections, Non-compliance, Quality Defects and Referrals

Nitrosamine contamination and Sartans Lessons Learnt

Work continued on the implementation of the GMP related recommendations arising from the Sartans Lessons Learned exercise. The IWG continued to be informed of the latest developments concerning nitrosamines as discussed by the Nitrosamines Implementation Oversight Group (NIOG).

1. EudraGMDP database

Several minor changes have been implemented in EudraGMDP modules in order to reflect network needs. The GMP/GDP IWG was consulted / informed 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.

2. 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 Revision of the Pharmaceutical Legislation for human and veterinary medicinal products.

The GMDP IWG adopted the scientific advice for the European Commission on the principles of GMP to be considered for inclusion on the implementing acts on GMP for medicinal products, active substances, autogenous vaccines and novel therapy veterinary medicinal products.

(https://www.ema.europa.eu/en/veterinary-regulatory-overview/veterinary-medicinal-products-regulation/scientific-and-technical-recommendations-veterinary-medicines-regulation#ema-inpage-item-7274)

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.

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 participated attended each other's meetings and working groups.

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 Q9R1 (Quality Risk Management), ICH Q2(R2) (Validation of analytical procedures), ICH Q13 (Continuous Manufacturing), Q14 (Analytical Procedure Development).

International Conference on Harmonisation For Registration Of Veterinary Products (VICH)

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

Interested Parties

A Formal interested parties meeting was held in March 2023.

The following organisations participated in the meeting with Interested Parties in 2023: 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).

Quality Working Party

The annual joint meeting was held in September 2023 and there were regular exchanges on matters of joint interest during the year.

Innovation Task Force (ITF)

The GMDP 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 and they reviewed a small number of case studies on innovative manufacturing technologies during 2022.

Quality Innovation Group

The GMDP IWG has been closely informed and consulted where necessary on the work of the Quality Innovation Group. The QIG representatives reported on the work of the group in 2023, including the 2 Listen and Learn Focus Group meetings, as well as the requests for scientific advice received from applicants as well as 1:1 meetings between the QIG and applicants. The IWG was also consulted by QIG in specific topics concerning inspections and GMP expectations.