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HPRA MEDICINAL PRODUCTS NEWSLETTER

ISSUE 72

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Human Medicines

Clinical trials – deadlines, supports and upcoming training

Deadlines

Applicants should make themselves aware of the following deadlines in relation to the Clinical Trials Regulation (CTR).

- **New applications** must be made under the CTR after **31 January 2023**. This deadline applies to all clinical trials including academic/non-commercial trials, and mono-national trials.
- **Substantial amendments** can be made to trials authorised under the Clinical Trials Directive (CTD) up to **31 January 2025**.
- All clinical trials will be regulated under the CTR from **31 January 2025**, and therefore ongoing CTD trials **must transition** to the CTR before this date.

End of trial processes

- **End of trial declarations** should be notified to the HPRA using the Declaration of the end of trial form.
- The HPRA must be notified within 90 days of the end of trial, or within 15 days if the trial has ended earlier than planned.
- **Clinical trial summary (end of trial) reports** should be submitted to EudraCT.

Training and supports

- Applicants can avail of training and supports from the HPRA and the EMA. Supports from the HPRA can be found on the CTR section of the HPRA website. EMA supports are available on the CTR and CTIS section of the EMA clinical trials webpage.
- It is mandatory to submit CTR clinical trials using the CTIS. Non-commercial sponsors can use the EMA Introductory guide CTIS for SMEs and Academia for guidance.
- Upcoming CTIS training and information events are listed on the information and events section of the EMA CTIS webpage.

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An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Veterinary Medicines

Change of HPRA representation at the CVMP

Dr Paul McNeill has been appointed as the Irish member of the Committee for Veterinary Medicinal Products (CVMP) and took up this role on 23 July 2022. Dr McNeill previously served as an alternate member, and before that as a member of the Coordination Group for Mutual Recognition and Decentralised Procedures for Veterinary Medicinal Products (CMDv). Dr J.G. Beechinor has been appointed as an alternate member of the CVMP.

Update on new national legislation

A new draft bill, known as the Veterinary Medicinal Products, Medicated Feed and Fertilisers Regulation Bill 2022, was published by the Department of Agriculture, Food and the Marine on 14 July 2022. Amongst other items, the bill provides for:

- a new legislative framework for the elaboration of national regulations on veterinary medicines;
- a new national electronic prescription system for veterinary medicines;
- the reinstatement of the national supply categories for non-prescription categories of supply that were abolished by the repeal of SI No. 786 of 2007.

The HPRA understands that the bill is scheduled for debate and adoption by the national parliament, the Oireachtas, before the end of this year. We will continue to monitor developments and update our work processes and amend associated forms and guidelines as the legislation is elaborated.

Union Product Database on veterinary medicines

The Union Product Database (UPD) was developed by the EMA in response to the legislative requirement in Regulation 2019/6 for a single source of information on all veterinary medicines authorised in the European Union. It contains information on the availability and Summaries of Product Characteristics (SPCs) of all products which can be accessed by the public. For marketing authorisation holders, it also provides additional functionalities that allow the submission of certain categories of variations that do not require assessment.

Although there were initial performance issues with the UPD when it went live on 28 January 2022, the EMA has been working to improve the UPD and to ensure that legacy product uploads from EU Member States are completed. More than 90% of all legacy products have already been uploaded and further version improvements are expected in the months ahead.

More information is available on the UPD webpage on the EMA website.

Regulation 2019/6: Update on the implementation of new labelling standards for veterinary medicinal products

The HPRA welcomes the publication of Regulation 2022/839 on 30 May 2022. The regulation provides legal certainty regarding transitional arrangements in Article 152 provisions of Regulation 2019/6 as they affect veterinary medicines that were already authorised prior to the date of application on 28 January 2022.

The new interpretation from the European Commission allows for the packaging and labelling of veterinary medicinal products that were on the market in Ireland prior to 28 January 2022 to continue to be supplied in existing packaging until 29 January 2027. Exceptions to this regulation are antibiotics affected by ongoing regulatory initiatives for antimicrobial resistance and for which new warnings or modifications of indications are expected. This new regulation addresses the potential negative effect on availability and administrative burden that may have resulted otherwise.

Marketing authorisation holders who wish to update their product labelling in line with the provisions of Regulation 2019/6 may do so by submitting an application to vary the authorisation.

The relevant variation category is VRA G.I.18:

One-off alignment of the product information with version 9.0 of the QRD templates i.e. major update of the QRD templates in accordance with Regulation (EU) 2019/6, for veterinary medicinal products authorised in accordance with Directive 2001/82/EC or Regulation (EC) No 726/2004.*

The variation should be submitted so that it is finalised and implemented on the printed labelling and package leaflet before 29 January 2027. Grouping with other variations in chapter G affecting the product information texts for the same product is recommended.

Compliance

Quality function responsibilities in Environmental Monitoring (EM) sampling

As per paragraph 2.9 of Chapter 2 of the EU GMP Guide, quality and production have joint responsibilities for the monitoring and control of manufacturing environments. The HPRA has identified deficiencies in EM sampling programmes through inspections and in some of these cases there was inadequate oversight of the sampling programme by the quality function.

The level of quality supervision of EM sampling should provide assurance that the correct sampling techniques, location of sampling and duration of sampling meets requirements.

The following EM deficiencies have been cited through GMP inspection:

- sampling device (settle plates, air samplers) not located in the correct location as per the EM sampling procedure.
- start and finish time of sampling (e.g., settle plates opening and closing) was not recorded, as such it was not clear how it was confirmed that sampling was performed for the correct duration.
- settle plates only partially opened during sampling exercise.
- active air-sampling equipment not connected to air supply.
- no reconciliation of samples prior to incubation resulting in missed or invalid tests identified during reading of results.
- quality function had never observed EM sampling performed by production.

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Updates to the EU Compilation of Union Procedures on Inspections and Exchange of Information

Updates to the EU Compilation of Union Procedures on Inspections and Exchange of Information were adopted in September 2021 with a period of 9 months before coming into force at the end of June 2022. The changes are relevant for holders of GMP and GDP authorisations.

The Compilation consists of a series of documents that provide the basis for cooperation between GMP and GDP inspectorates of the Members States and as a means of achieving harmonisation. It also includes a procedure that provides the foundation for national GMP/GDP inspectorates quality systems. The Compilation has been restructured into Part I and Part II.

- **Part I:** Compilation procedures
- **Part II:** Interpretation documents together with templates.

Updates to Part II are regulatory, apply directly to the work of inspectorates and may not be of immediate relevance to stakeholders. The documents in Part I provide information on the operation of the GMP and GDP network in the event of product quality defects or chronic non-compliance. Familiarity with these updates may assist applicants' understanding of regulatory procedures and processes.

Part I

The following documents have been **revised** in Part I:

- Management of Reports of Suspected Quality Defects in Medicinal Products – the procedure has been revised to provide more comprehensive guidance following quality risk management principles.
- Management of Rapid Alerts Arising from Quality Defects Risk Assessment – the procedure has been revised to provide more comprehensive guidance following quality risk management principles.
- Procedure for dealing with serious GMP non-compliance requiring co-ordinated measures to protect public or animal health – the procedure has been revised because of experience with the superseded procedure.
- Appendix 6: Supervisory Risk Assessment has been updated.
- Outline of a Procedure for Co-ordinating the Verification of the GMP Status of Manufacturers in Third Countries has been updated.
- A Model for Risk Based Planning for Inspections of Pharmaceutical Manufacturers has been updated.

New in Part I:

- Procedure for compliance management – new procedure

Part II

The following documents have been **revised** in Part II:

- Interpretation of the Union format for a wholesale distribution authorisation (medicinal products for human use) – new procedure.
- Interpretation of the Union format for GMP certificate has been updated.
- Union Format for a GMP Certificate has been updated.
- The issue and update of GMP certificates – a minor update has been made, primarily to align the procedure with experience.
- Serious GMP Non-Compliance Information - from Third Countries or International Organisations has been updated.
- Statement of non-compliance with GMP Interpretation of the Union Format for Manufacturer/Importer Authorisation has been updated.

New in Part II:

- Interpretation of the Union format for a wholesale distribution authorisation (medicinal products for human use).