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HPRA MEDICINAL PRODUCTS NEWSLETTER

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Human Medicines

Mock ups for labels and leaflets

The HPRA advises that mock-ups are no longer routinely reviewed or require submission when a product is not marketed.

Further information is in the HPRA guide to labels and leaflets.

Veterinary Medicines

Update on implementation of Regulation 2019/6 in relation to Good Laboratory Practice

On 30 January 2023 the European Commission published Delegated Regulation (EU) 2023/183 to amend Annex II to Regulation (EU) 2019/6. It gives clarification on how the provisions of Good Laboratory Practice (GLP) is applied to pre-clinical studies for veterinary medicines.

The Regulation clarifies that pre-clinical efficacy studies are not required to comply with GLP. Only pre-clinical safety studies must comply with GLP. The relevant sections in Annex II have been amended to refer to pre-clinical safety studies instead of pre-clinical studies.

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An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Future of joint labelling initiative with the UK

The HPRA and the UK's Veterinary Medicines Directorate (VMD) have a long-standing system for agreeing a common UK/Ireland label for veterinary medicines. This means that the relevant medicines can pass between both markets to facilitate trade and help mitigate shortages.

The effects of Brexit and the implementation of Regulation (EU) 2019/6 has challenged this system. Following discussions, both agencies have committed to work closely together to continue this initiative in the interests of animal health in Ireland and the UK.

The HPRA understands that current UK legislation is based largely on Directive 2001/82/EC. However, new legislation is being developed which is expected to be finalised later this year.

The HPRA is working to accommodate UK package requirements on joint UK/Ireland packages. This will help avoid a situation where separate UK and Irish packs would be necessary which could risk availability in one or both markets.

The HPRA will monitor developments to the UK legislation as well as the long-awaited national legislation, with a view to maximising the availability of veterinary medicines in Ireland.

Labelling requirements in relation to Regulation 2019/6

Regulation (EU) 2019/6 requires that all labelling on veterinary medicines in the EU must comply with new labelling requirements by 28 January 2027. The labelling requirements simplify and reduce the information required on product labels and outer packaging. Other details such as explanatory information, warnings, method of supply classification, marketing authorisation number and other details should be in the package leaflet.

Applications to implement the required changes fall under the category G.I. 18 variations and should follow the guidance of the EMA's QRD version 9. The HPRA has agreed to allow a period of 12 months to implement the labelling changes nationally.

Update on national legislation

The Veterinary Medicinal Products, Medicated Feeds and Fertilisers Regulation Bill is continuing through the stages in the national Parliament. A vote in the lower house, the Dáil, is expected to take place before the summer recess.

Following that, the Bill will be considered by the upper house (the Seanad). The Bill will then be considered and signed by the President of Ireland before it comes into effect.

The HPRA will continue to monitor developments and update stakeholders if there are any effects on the regulation of veterinary medicines once the legislation is finalised.

Pilot initiative to safeguard availability of veterinary medicines in Ireland

The HPRA is collaborating with the Spanish, Portuguese and French veterinary medicines agencies under the National Action Plan on Antimicrobial Resistance (PRAN) initiative to improve the availability of veterinary medicines within our countries.

PRAN is an initiative to address antibiotic resistance. One of its goals for veterinary medicines is to improve the effectiveness of existing antibiotics and to improve accessibility of existing medicines and vaccines among Member States.

The initiative is mainly directed towards improving availability of antibiotics and vaccines in the countries mentioned.

It aims to address any knowledge gaps or dossier data deficits by sharing real-world experiences from those countries where the medicine is already authorised. This will avoid the need to repeat animal studies to re-confirm safety and efficacy of the medicine.

Although the initiative is intended to address availability gaps it is open to all veterinary medicines. The HPRA is engaging in a pilot programme with volunteer applicants to investigate the potential of this initiative to meet national needs.

For further information contact Juliana.camargoteixeira@hpra.ie.

Updated guidance on presenting adverse event information

The EMA recently updated their guidance document on describing adverse events in the product information. The document has been updated to provide clarification and examples of how adverse events should be described in section 3.6 of the SPC and section 7 of the package leaflet.

Applicants should review the clarifications given before submitting G.I 18 variations to update the product information of their product(s). This will ensure the information on adverse events is presented as recommended in the guidance document.

It has been clarified that VeDDRA low level terms should be used. Additional information relating to the adverse event which is considered relevant for the prescriber or end user can also be included as a footnote under the adverse event table.

Applicants should write adverse events on their package leaflets clearly and in understandable terms for the public. Where an adverse event may not be understood by the public, applicants should use a more user-friendly term with the adverse low-level term. For example, the public may not understand the term 'ataxia', so it can be presented in the package leaflet as 'ataxia (incoordination)'.

Compliance

Quality defects and recalls

Updated guidance document

We have updated our guidance document on reporting and investigating quality defects in human and veterinary medicines. The guide merged two guidance documents listed below which are now obsolete.

- SUR-G0020 -2 - Quality Defect Investigation Reports
- SUR-G0023 -7 - Guide to Reporting and Initial Investigation of Quality Defects in Human and Veterinary Medicinal Products

The HPRA will host a webinar on 21 June 2023 to present the updated guidance document to relevant stakeholders.

Communications on Recalls

Since 1 April 2023, safety notices concerning pharmacy and patient-level recalls of human and veterinary medicines, are posted on the HPRA website. A safety alert is issued to subscribers with a link to the recall.

You can sign up for these alerts by registering for a MyHPRA account.

Requirements for GMP records for receipt of materials

Recurring deficiency

There has been a rise in deficiencies during inspection of records for receipt of deliveries. Checks were not performed to compare the details of labels on containers received against the details listed below.

Checks were not performed or recorded comparing the details of labels on containers received against the details of the approved supplier list and other delivery documentation.

GMP requirement for records of receipt of deliveries

Chapter 4, Chapter 5, Part II, and Annex 21 of the EU Guide to GMP outlines the requirements for records of receipt.

Chapter 4, paragraph 4.22, stipulates there should be written procedures and records for the receipt of each delivery of each starting material (including bulk, intermediate, and finished goods), primary, secondary and printed packaging materials.

Paragraph 4.23 details specific checks that should be included in receipt records.

Chapter 5, paragraph 5.30, also stipulates that there should be a record of receiving checks on each delivery. Similar to the requirements outlined in Chapter 4, this paragraph stipulates that *'for each delivery of starting material the containers should be checked for integrity of package, including tamper evident seal where relevant, and for correspondence between the delivery note, the purchase order, the supplier's labels and approved manufacturer and supplier information maintained by the medicinal product manufacturer.'*

Section 7.2, of Part II, also requires labels of containers be examined upon receipt.

Imported products

Section 5 of Annex 21 gives further clarity on the documentation needed for imported products. These documents include freight and customs documentation, listing both the site of origin and site of physical importation.

Review of records

Manufacturers and QP certification sites are required to ensure that there is a process in place for review of these records. They should also ensure that records are available for review during regulatory inspections.

Advertising human medicines in Ireland

Advertisements for human medicines in Ireland must comply with the Medicinal Products (Control of Advertising) Regulations of 2007 (S.I. No. 541/2007) and the conditions of the marketing authorisation for the product.

The table below answers the most asked questions about advertising human medicines in Ireland.

1. Who does the Medicinal Products (Control of Advertising) Regulations of 2007 (S.I. No. 541/2007) apply to?	The Regulations apply to anyone who advertises medicines within Ireland. This includes: • Marketing Authorisation Holders • Pharmacies • Non-pharmacy retailers • Online pharmacies • Non-pharmacy retailers who advertise medicines
2. What is 'advertising' in relation to a medicine?	'Advertising' in relation to a medicine is, *'any form of door-to-door information, canvassing activity or inducement designed to promote the prescription, supply, sale, or consumption of medicinal products.'* Any activity, where the purpose is to encourage the prescription, supply, sale, or consumption of a medicine, is advertising. These activities must comply with the provisions of these Regulations.
3. Are there any exemptions to these Regulations?	The exemptions to the Regulations are listed in Part 1 of the Regulations. It should be noted that trade catalogues and price lists are exempt if they don't inlcude medicinal claims about the product.
4. What human medicines cannot be advertised in Ireland?	Unauthorised/unregistered human medicines cannot legally be advertised in Ireland. It is illegal to advertise a human medicine in Ireland that does not have a: • Marketing authorisation • Certificate of traditional-use registration (for traditional herbal medicinal products) • Certificate of registration (for homeopathic medicines).
5. What medicines cannot be advertised to the public in Ireland?	It is illegal to advertise prescription-only medicines (e.g., any products containing Botulinum Toxins) and controlled drugs (e.g., codeine-containing medicines) to the public in Ireland. Additionally, the conditions of a products's marketing authorisation may restrict who the product is advertised to. (i.e., a product may only be advertised to Healthcare Professionals). There is an exemption to the above for vaccine advertisements, which are part of a vaccination campaign, provided that the campaign has been approved by the Minister for Health. This is outlined in regulation 13.

6. Where can I find information on whether a product is subject to medical prescription and on its advertising status in Ireland?

You can find information on whether a product is subject to prescription and its advertising status in the Find a medicine section of the HPRA website.

First, enter the product name. Then select the product of interest and review the information under the 'legal status' and 'advertising status' fields.

The 'advertising status' of a medicine indicates whether it can be legally advertised or promoted to the public or to healthcare professionals only.

7. What medicines can be advertised to those qualified to prescribe or supply medicines in Ireland?

All categories of authorised/registered medicines can be advertised to those qualified to prescribe or supply medicines in Ireland.

8. What information can be included in advertisements for registered homeopathic medicines in Ireland?

Only the information that is set out in the Schedule of the Regulations may be used in advertisements for registered homeopathic medicines in Ireland.

These advertisements must include the following:

- A clear mention of the words *'homeopathic medicinal product'*.
- The registration number allocated by the HPRA.
- The statement *'homeopathic medicinal product without approved therapeutic indications'*.
- A warning advising the user to consult a doctor if the symptoms persist.

9. What about advertising Exempt Medicinal Products (EMPs)?

Schedule 1 of the Medicinal Products (Control of Placing on the Market) Regulations 2007 (S.I. No. 540 of 200), as amended, states with respect to EMPs, that *'no advertisement or representation relating to the medicinal product is issued with a view to it being seen by the general public in the State and that no advertisement relating to the product, other than one that states only the trade name, pack size, price and dose, is issued at the request or with the consent of, the person selling the product by retail or by way of wholesale dealing or the person who manufactures it, and that the sale or supply is in response to a bona fide unsolicited order.'*

Schedule 2 of the Medicinal Products (Control of Wholesale Distribution) Regulation of 2007 (S.I. No. 538 of 2007), as amended, states that the holder of a wholesaler's authorisation, *'shall not issue any advertisement, other than one that states only the trade name, pack size, price and dose, relating to an exempt sourced medicinal product or make any representations in respect of such product'*.

10. What happens when non-compliant advertisements are identified by the HPRA?

Where non-compliant advertisements for medicines are identified, the HPRA takes the necessary follow-up action with the concerned party.

11. Where can I find further guidance on the regulation of the advertising of human medicines in Ireland?

You can find further information and guidance in the HPRA Guide to Advertising Compliance.

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