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**Human Medicines**

**Approval Dates for Package Leaflets**

The approval date for a Package Leaflet (PL) is the date that the case implementing or amending the PL was closed by the HPRA. Replacement of a PL on the HPRA website only occurs where the PL text is materially changed during a case. Where only the revision date has been updated, the PL text is not replaced.

**Nitrosamine Impurities**

‘Call for review’ on nitrosamine impurities – deadline for submission of responses

In line with the CHMP Article 5(3) Scientific Opinion ‘call for review’ process, marketing authorisation holders of human medicinal products which contain chemically synthesised or biologically derived active substances are required to review their medicinal products to determine the risk for the presence of nitrosamines, and to complete the required risk evaluation. Where any risk for the presence of nitrosamines is identified, confirmatory testing must be performed, and a suitable control strategy implemented as required. The steps required by the ‘call for review’ process and relevant deadlines are summarised as follows:

<table>
<thead>
<tr>
<th>Step Number</th>
<th>Chemical Medicinal Products Deadline</th>
<th>Biological Medicinal Products Deadline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step 1 – Risk Evaluation</td>
<td>31 March 2021</td>
<td>01 July 2021</td>
</tr>
<tr>
<td>Step 2 – Confirmatory Testing</td>
<td>26 September 2022</td>
<td>01 July 2023</td>
</tr>
<tr>
<td>Step 3 – Submission of relevant variations</td>
<td>26 September 2022</td>
<td>01 July 2023</td>
</tr>
</tbody>
</table>

Note that the deadlines differ between chemical and biological medicinal products.
The HPRA reminds marketing authorisation holders (MAHs) that the deadline has now passed for submission of step 1 risk evaluations for medicinal products containing chemically synthesised active substance. MAHs that have not submitted the step 1 risk evaluations for these medicines must comply with the conclusions of the CHMP Scientific Opinion and provide a response to step 1 as a matter of priority. MAHs are reminded of their responsibility to ensure the quality and safety of their medicines.

MAHs are also reminded of the approaching timeline for submitting step 1 risk evaluations for biological medicinal products, which is 1 July 2021.

Further practical and scientific guidance on the preparation and submission of these responses is available on the CMDh website under Advice from CMDh -> Nitrosamine impurities.

**Article 31 Referral for Sartan Medicines – Reminder**

The CHMP initially concluded a review of a class of medicines called sartans (angiotensin II receptor antagonists) in January 2019. This review examined the potential presence of certain nitrosamine impurities in sartan-containing medicinal products. In October 2020, the CHMP concluded that the outcome of the Article 31 referral on angiotensin II receptor antagonists (sartans) containing a tetrazole group (EMEA/H/A-31/1471) should be aligned with the outcome of the Article 5(3) assessment on nitrosamines (EMEA/H/A-5(3)/1490) – see Decision (2021) 1309 of 19 February 2021. The main change concerns the limits for nitrosamines, which previously applied to the active ingredients but now apply instead to the finished products. Marketing authorisation holders (MAHs) of sartan medicines (candesartan, irbesartan, losartan, olmesartan, valsartan) are advised to refer to the relevant European Commission implementing decision for the revised list of conditions to the marketing authorisations that must be complied with.

Further guidance on the practicalities of submitting responses is available on the CMDh website under Advice from CMDh -> Q&A on the implementation of the outcome of the Art. 31 referral on angiotensin-II-receptor antagonists (sartans) containing a tetrazole group’. In particular, Question 4 highlights the condition categories, implications and due dates of the new Commission Decision. The MAH must ensure that the manufacturing processes of the active substances used for their finished products are reviewed for the potential risk of formation of n-nitrosamines and changed as necessary to minimise nitrosamine contamination as much as possible, in line with the recommendations adopted by CHMP on 25 June 2020 (article 5(3) procedure). The due date for this action was 17 April 2021. By 30 June 2021, the MAH must introduce specifications for NDMA and NDEA into the finished product specification, as appropriate. Question 7 outlines which variations must be submitted to lift the conditions on the risk assessment and control strategy for the active substance and finished product. MAHs for medicinal products are required to familiarise themselves with the requirements, ensure compliance and submit the appropriate variations by the required timelines.

When submitting these variations, please clearly indicate in the cover letter and ‘scope and background’ section of the variation application form that the variation is being submitted to lift the conditions on the MA of tetrazole sartans and state which condition it relates to (A,B,C,D).

**Preparation of Labelling for Joint IE/UK (NI) Packs**

The HPRA has received a number of queries on the approach that marketing authorisation holders (MAHs) should take when preparing joint IE/UK (NI) packs for medicinal products. We would like to highlight the flexibility already available in the HPRA Guide to Labels and Leaflets. Section 10.3 of the guide details some minor amendments to the labelling and packaging leaflet that do not require prior notification to the HPRA, as long as there are no changes to the livery layout, design or font size result. These include:

- Addition, deletion or change in foreign MA numbers and/or foreign MA holder details, which does not affect any other aspects of the livery layout and font size.
- Addition, deletion or change in the administrative information for an EU MS or the UK placed within the ‘blue box’, which does not affect any other aspects of the livery layout and font size.
- Change to the details for reporting of side effects in other Member States not affecting the details for reporting of side effects in Ireland (joint country package leaflets).
- Change/deletion of a product name in another Member State in section 6 of the patient information leaflet (MRP products only).
- Change in the details of a distributor/wholesaler/local representative.

A designated blue box is not required for the inclusion of such information for national or MR/DCP authorisations.

Applicants should carefully evaluate whether this flexibility could apply to their proposed changes. In such instances, the revised labels or patient leaflet should be submitted to the HPRA at the next regulatory activity involving a change in the product information. However, where changes to livery layout design or font size result, an Article 61.3 notification should be submitted in advance as usual.

For MR/DCP procedures, no divergences of the PL, SmPC or of the labelling requirements from those in the EU common template would be envisaged, and the name must be the same for IE and UK (NI) to avoid any confusion.

Applicants who wish to discuss this possibility further may submit their query to brexit@hpra.ie.

The HPRA would also like to highlight the guidance included in the HPRA Guide to Labels and Leaflets on the development of multilingual packaging (section 5.3 of the guide).
Audits of Type IA Notifications: 2019/2020 Review

The HPRA performs regular audits of Type IA notifications in order to verify that submissions have been appropriately categorised; the relevant conditions fulfilled and necessary documents submitted; and to ensure a consistent approach in the processing of these variations both by marketing authorisation holders and the HPRA. Recent audits of Type IA notifications have identified a number of deficiencies, some of which required corrective actions from the applicants. The most common deficiencies identified were:

- ‘EC Classification Guideline’ page not submitted;
- Missing or incomplete documentation;
- Conditions relevant to the chosen Type IA category not fulfilled;
- Type IAIN notifications not submitted immediately after the implementation of the change in the quality system of the marketing authorisation holder;
- Incorrect classification of Type IA notifications where the wrong Type IA notification subcategory was selected or where a change was incorrectly classified as a Type IA notification when a Type IB variation was required.

As a result, and in order to reduce the number of incorrect Type IA submissions, the HPRA would like to remind applicants of the following:

- All changes which fall under the Type IA classification are outlined in the ‘EC Classification Guideline’, accompanied by a list of conditions and documentation requirements for each category. In order for the variation to be classified as a Type IA, all of the conditions outlined in the guideline for the relevant category must be fulfilled and all of the required documentation should be provided. Otherwise, the variation should be submitted as a Type IB (default category) or a Type II variation (if the proposed change may have a significant effect on the overall quality, safety or efficacy of the finished product). Applicants should carefully consider the list of conditions of the relevant category to make certain the variation is appropriately classified as Type IA. The audits for 2019/2020 (Q4 and Q1) and 2020 (Q2 and Q3) found that a number of submissions did not meet the conditions of a Type IA classification and therefore, these applicants were requested to resubmit the applications as Type IB variations, for example, ‘unchanged additional specifications for impurities’, ‘minor change in the manufacturing process of the active substance’.

- The relevant page(s) of the ‘EC Classification Guideline’ including confirmation of compliance with all relevant conditions and documentation requirements must be submitted for each change applied for under a grouped variation. Conditions will only be considered to be fulfilled if they have been ticked on the submitted guideline page.
- Type IAIN notifications must be submitted immediately after the implementation of the change in the quality system of the marketing authorisation holder and Type IA notifications must be submitted within 12 months of implementation. The date of implementation of each change should be stated in the application form.
- All of the documentation requirements should be adhered to, for example, the details of changes should be outlined in the present and proposed sections of the application form and amended relevant section(s) of the dossier, GMP certificates, QP declarations, etc., as applicable, to each variation category should be provided. Updated labelling and/or leaflet text must be submitted with the variation where the change results in changes to the label and/or leaflet text.
- Minor issues, for example, submission of an incorrect or incomplete application form, are also communicated to applicants via an email outlining the deficiency. Although no corrective action may be required for these deficiencies at the time, if applicants do not address these issues and such deficiencies continue to arise, the HPRA will consider requesting that applications are resubmitted.

Finally, the HPRA would like to remind applicants that the EMA has published a ‘Pre-notification checklist for Type IA variations’ intended to support the submission of complete and accurate Type IA notifications. Applicants are advised to review this checklist prior to submission of Type IA notifications.

Reference Medicinal Products – Updated CMDh Brexit Guidance

A generic or hybrid application, in accordance with Article 10 of Directive 2001/83/EC, refers to information that is contained in the dossier of a reference medicinal product (RefMP) that is or has been authorised in the Union. As the Brexit transition period has now ended, the CMDh has published updated guidance on RefMPs in the latest version of the Practical guidance for procedures related to Brexit for medicinal products for human use approved via MRP/DCP (Feb 2021). Specifically, for MAHs of generic products the HPRA wishes to draw your attention to the responses to Question 34 and 39 of the guidance document.

For generic, hybrid and biosimilar new applications, applicants are advised to carefully consider the advice in Q34 for the use of the UK RefMP, which varies depending on which subsection of the application form (1.4.2 or 1.4.3) is under consideration. The suitability for use depends on when the UK reference authorisation was granted, when the authorisation for the generic/hybrid will be granted, and the timing of completion of the final study report for pivotal studies.

Guidance on dealing with new DCPs, and variations that are cross-referring to UK marketing authorisations for product information alignment, is addressed in the response to Q39 and also included in Section 4.1 of the CMDh minutes, January 2021.

For new marketing authorisation applications (MAAs) a European reference product (ERP) should now be used unless the exceptional case outlined in Q34 of the CMDh Brexit guidance arises. However, for ongoing generic new applications, while the UK ERP may be kept as being the RefMP of the original application, the applicant should align the product information to a suitable RefMP within the global marketing authorisation (GMA). For variations, while it is not possible to change the RefMP of the original application, another EEA RefMP product from the same GMA should be used for the purposes of product information alignment, is addressed in the response to Q39 and also included in Section 4.1 of the CMDh minutes, January 2021.
information, or adaptation to a different EEA product could be considered. The CMDh minutes provide details of variation classifications and highlight the need to keep product information up to date.

Please note that if the new reference product (from the same GMA) is not harmonised with the UK reference product, a variation needs to be submitted as a type II variation under C.I.2.b to align the product information with this new reference product. In case no other product from the same GMA is available, adaptation to a different product, not being the reference product might be possible by a type II variation C.I.4. In the absence of another reference product from the same GMA, or where the MAH does not wish to adapt to a different product, MAHs are reminded of their legal obligation to keep their product information up to date. Often safety updates of the product information are linked to recommendations by PRAC or CMDh and can be implemented via type IA/IB variations. Bibliographic reviews should also be performed, where relevant, to support an update.

Finally, MAHs of generic medicinal products in such situations are requested to clearly highlight in the cover letter for variations the reference medicinal product used, and further substantiate their choice e.g. in ‘notes for reviewers’.

The choice of RefMP is the responsibility of the applicant/MAH, and HPRA cannot provide specific advice. General reference medicinal product related queries can be submitted to: submissions@hpра.ie.

**Clinical Trial Regulation Progress**

On 24 April 2021, the EMA’s Management Board confirmed that the introduction of the Clinical Trial Regulation (Regulation (EU) No 536/2014) was on track to be introduced on 31 January 2022.

The introduction of the new regulation will see a significant change in how trials are processed across Europe, with a more streamlined approach being adopted. Under the regulation, sponsors of clinical trials will be able to submit one application to numerous Member States across the EU using an online portal and database called the Clinical Trial Information System (CTIS). In Ireland, the implementation of the regulation will result in clinical trial applications being reviewed in tandem by both the HPRA and the National Research Ethics Committee for Clinical Trials (NREC-CT), with a single national decision being issued. The introduction of a more harmonised submission and assessment process under the regulation will also result in increased transparency in the area of trials across Europe while also increasing efficiency in the approval process, which will benefit Irish patients.

To ensure national preparedness in advance of the regulation being introduced, the HPRA is working closely with both the Department of Health and the National Office for Research Ethics Committees (nrecoffice.ie) as well as contributing to a number of working groups at EMA level. Furthermore, the HPRA has created a dedicated page on its clinical trial section of the website to keep stakeholders informed of all the latest developments regarding the launch of the regulation: hpra.ie/CTR. The website not only informs stakeholders of the latest guidance in relation to the regulation but also provides a number of links to key presentations delivered by both the EMA and other European organisations that deal with a wide range of topics from the introduction of CTIS to the submission and assessment of trials under the regulation.

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**Clinical Trial Regulation: Timeline**

- **April 2014**: CT Regulation adopted
- **April 2021**: Expected date for application of the CT Regulation and for go-live of CTIS
- **31 January 2022**: New CT applications to be submitted under CT Regulation only
- **6 months before go-live**: New CT applications can be submitted under the Directive or CT Regulation
- **Year 1 after go-live**: Year 2 & Year 3 after go-live
- **End of year 3 after go-live**: All ongoing CTs required to have transitioned to CT Regulation

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CT Clinical Trial | CTIS Clinical Trial Information System | EC European Commission | EMA European Medicines Agency

* Valid as of April 2021 and may be subject to change. Stakeholders are encouraged to monitor the Clinical Trial Regulation page on the EMA website for the most up-to-date information regarding the go-live date.
** Ongoing CTs previously authorised under the Directive can remain or transition to the Regulation.

hpra.ie/ClinicalTrials

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Veterinary Medicines

HPRA Appearance before Oireachtas Committee on Agriculture and the Marine

The HPRA appeared before the Oireachtas Committee on Agriculture and the Marine on 27 April 2021 to discuss the regulation of veterinary medicines, including the implementation of Regulation 2019/6. A recording of the event and the HPRA’s opening statement to the committee are available.

HPRA Veterinary Medicines Information Day 2021

The HPRA expects to host an Information Day for marketing authorisation holders and manufacturers of veterinary medicines on the implementation of the new requirements during Q4 2021.

The focus of this event will be to assist stakeholders in understanding the new requirements and their implications. For more details on this event going forward, please consult the HPRA website for up-to-date news. It is the preference of the HPRA to host a physical meeting, rather than a virtual event, if possible.

Submission of Variations to Change MAH’s Local Representative for MR Products

Applicants are reminded that a variation to change a MAH’s local representative, as listed in the product labelling, need only be submitted to the RMS and to the CMS(s) where the change is being applied. The change should be classified as a Type 1A C.II.6.a variation.

This information is taken from the January 2018 meeting minutes of the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Veterinary and Interested Parties.

Clinical Trial Regulation-National Collaboration Project

The HPRA, in tandem with the National Research Ethics Committee for Clinical Trials of Investigational Medicinal Products (NREC-CT), are pleased to announce the creation of the Clinical Trial Regulation-National Collaboration Project (CTR-NCP). The CTR-NCP represents just one of the ways in which Ireland is actively preparing nationally for the introduction of the Clinical Trial Regulation. The CTR-NCP will mimic the joint assessment and approval model set out under the regulation in that applications submitted will receive, in effect, a single national decision. The CTR-NCP will run until December 2021 and Sponsors are encouraged to contact either clinicaltrials@hpra.ie or clinicaltrials@nrec.ie for further information regarding submitting under this joint project.

Clinical Trial Regulation Information Sessions 2021

The HPRA is planning to host a number of information sessions on the upcoming Clinical Trial Regulation in November 2021. The information sessions will be delivered remotely by the HPRA and will provide attendees with an insight into the practical application of the regulation, and the accompanying Clinical Trial Information System (CTIS), including requirements for sponsors ahead of its introduction. The meeting will be of interest to those involved in the submission and management of clinical trials in Ireland. Colleagues from the National Office for Research Ethics Committee and the Department of Health will also attend. Should you have suggested areas you would like to see discussed, please feel free to email these to clinicaltrials@hpra.ie, quoting Clinical Trial Regulation Info Day 2021 in the subject heading. Interested parties are encouraged to monitor the News and Events section of the HPRA website for additional information and instructions regarding confirmed agenda topics and registration closer to the planned date.
Veterinary Medicinal Products and Labelling-related Revisions

Whilst the review of mock-ups during the various regulatory procedures remains a valuable activity, the HPRA continually strives to reduce the administrative burden associated with this task for both applicants and regulators. To this end, a number of HPRA labelling-related guidance documents and requirements have been revised to ensure a clear and efficient process for all involved.

1. Joint Labelling document

Following the withdrawal of the UK from the EU, the HPRA remain committed to supporting the joint labelling procedure. The procedure involves the coordination of approval of final colour mock-ups between Ireland and the UK for veterinary medicines and enables marketing authorisation holders (MAHs) to create one set of mock-ups for whichever markets the MAH wishes to combine; IE and GB, IE and UK (NI) or IE and UK (which includes both GB and NI). To address these Brexit-related procedural changes, applicants are advised that the previous guidance document “HPRA/VMD Joint-labelling of product literature between UK and Ireland” has now been replaced with the HPRA Guide to Joint Labelling for Veterinary Medicinal Products for use in Ireland and the UK. This revised guidance document sets out the steps to both achieve and maintain joint labelling between IE and the UK.

2. Product literature standard

The HPRA Guide to Product Literature Standard (PLS) for Veterinary Medicinal Products (previously a joint document with the VMD) has been transformed into a more compact, user-friendly document, which aims to assist applicants in the creation of mock-ups for assessment. The re-vamped document focusses on both general labelling requirements, which will assist applicants with the layout and design of their mock-ups and national HPRA requirements related to method of sale etc. Appendix I of this Guide includes a practical checklist for consultation prior to mock-up submission. For joint labels, applicants are advised to also consult the UK’s Product Literature Standard as published by the VMD.

3. Submission of mock-ups for variations

Recent updates have been made to the HPRA Guide to Submission of Mock-ups for Variations. The updates result in the list of variation categories no longer requiring routine mock-up submission being expanded. Applicants should note, however, that the submission of mock-ups may be requested by the HPRA for any variation category on a case-by-case basis where a review is deemed necessary.

4. Labelling notification requirements

Historically, changes to mock-ups that did not affect the font size, layout or legibility required notification by way of email to the HPRA. In an effort to reduce administration burden for both MAHs and the competent authority, the HPRA no longer requires notification of such minor changes and it will be assumed that the labelling remains essentially as previously approved. A non-exhaustive list of what constitutes a minor change can be found on the HPRA website. If the criteria of a minor change is not met and formal approval of the labelling is requested, please submit a Type IB (C.II.6.b) variation with a cover letter and revised mock-ups. If you are in doubt about whether a variation is needed, please contact vetinfo@hpra.ie.

Update on Implementation of HPRA Report on the Method of Supply of Antiparasitic Veterinary Medicinal Products Intended for use in Food-producing Animals

The HPRA is actively engaged in implementing the change of labelling process for changing products from Licensed Merchant (LM) to Prescription Only Medicines (POM) currently. All new antiparasitic veterinary medicinal products for food-producing species that have been authorised since 30 April 2021 bear a prescription medicine supply category, while variation applications to change existing products are being processed currently. The HPRA hopes to approve all products concerned by 28 July 2021. The HPRA will follow the policy outlined in the HPRA Guide to Implementation of Packaging Changes to Authorised Veterinary Medicinal Products in implementing the changes to the labelling (specified as ‘other safety restrictions’ – item 3.2 of that policy). This means that Marketing Authorisation Holders should:

- Coordinate the supply/importation of stock to ensure the introduction of the amended product labelling and literature as soon as possible and in any case, within six months of the approval of the variation. Products in old livery containing the LM supply designation should not be released after six months from the date of approval of the variation (i.e. the labelling of all products released for the Irish market must be compliant with the prescription requirement at the latest by 28 January 2022).
- Plan to avoid having large quantities of product in old livery in the marketplace in the second half of 2021. Where they exist, MAHs should place notices in the farming press and/or professional journals as appropriate, alerting users to the changes.
- Inform retailers of the changes. The HPRA is working with the Department of Agriculture, Food and the Marine to raise awareness of this change with stakeholders.
Update on Implementation of Regulation 2019/6 and New National Legislation to Replace SI No 786 of 2007

The HPRA is mid-way through a project to implement the requirements of Regulation 2019/6 on the authorisation and monitoring of veterinary medicinal products. This project, which is being led by Ms Elaine Hynes, HPRA Planning and Authorisation Manager, has a number of different objectives:

- the HPRA’s authorisation and monitoring processes operate in compliance with the new legislation;
- the HPRA authorisation and monitoring processes provide maximum efficiency;
- the HPRA authorisation and monitoring systems interface correctly with the external environment (e.g. the EMA’s Union Product Database and pharmacovigilance systems);
- the HPRA can positively influence the new national legislation that is being elaborated by the Department of Agriculture, Food and the Marine;
- the HPRA’s suite of guidelines, application forms, internal procedures and other documents are updated;
- stakeholders are provided with regular and appropriate communications on developments;
- the HPRA’s personnel are trained on developments;
- any implications for the HPRA’s business planning and model is fully understood.

The HPRA provides a monthly update on progress on our website. We would encourage marketing authorisation holders to review their own operational processes too, to ensure that they are in line with any new requirements. If you have queries relating to the implementation of the new legislation, please email newvetreg@hpra.ie.

Pharmacovigilance Changes Arising from the New Veterinary Regulation (EU) 2019/6

The HPRA wishes to highlight the fact that Periodic Safety Update Reports (PSURs) will no longer be required under the new veterinary regulation. Instead, MAHs will be required to carry out a signal management process for their veterinary medicinal products, the outcome of which must be recorded on the European Medicines Agency’s (EMA) Union Pharmacovigilance database (currently being developed).

In accordance with Article 76.2 of the regulation, from 28 January 2022 MAHs will need to upload all suspected adverse event reports that are reported to them to the Union Pharmacovigilance database within 30 days of receipt of the reports.

As submission and assessment of PSURs after 28 January 2022 is not foreseen in the regulation, only PSURs submitted to the HPRA prior to 28 January 2022 will be assessed, i.e. those submitted after 28 January 2022 will not be assessed.

Consequently, holders of marketing authorisations with a PSUR data lock point (DLP) of 27 November 2021 or earlier will need to submit those PSURs for assessment prior to 28 January 2022. Marketing authorisations with a PSUR DLP falling between 28 November 2021 and 27 January 2022 may also be submitted prior to 28 January 2022 for assessment.

The HPRA is aware that for a number of marketing authorisations currently on a 3-year PSUR submission cycle, and for which the DLP for the next PSUR submission falls on or after 28 January 2022, those non-serious adverse event reports that would normally be reported in a PSUR will not be available for review by the HPRA within the context of a PSUR assessment. However, it is expected that those adverse event reports will be included within the first signal management process to be conducted by marketing authorisation holders in accordance with Article 81 of the regulation.

QPPV Data Requirement for the Union Product Database

Article 55(1) of the New Veterinary Regulation (EU) 2019/6 requires the Agency to establish and, in collaboration with the Member States, maintain a Union database on veterinary medicinal products, also referred to as the “product database”, “Union Product Database”, or “UPD”. The Commission Implementing Act (EU) 2021/16 of 8 January 2021 lays down the necessary measures and practical arrangements for the UPD and details the specifications to implement in order to fulfil the requirements of the Regulation.

Information on the qualified person for pharmacovigilance (the QPPV) is required for upload to the UPD in respect of ‘legacy’ product data. ‘Legacy’ data is defined as any data on a veterinary medicinal product authorised in a Member State with a marketing authorisation or registration valid on or before 28 January 2022. In order to meet this requirement, the HPRA will write to marketing authorisation holders shortly to request specific QPPV information. We will specify what is required and the deadline for providing this information. It is important we receive this data and have time to update our systems. We will be unable to complete the submission of our product data to the UPD without these details.

If you have any queries, please do not hesitate to contact us at newvetreg@hpra.ie.

Guidance on signal management is currently being drafted by the EMA and will be published on their website in due course.

In the meantime, further information on the new veterinary regulation is available from the dedicated section on the HPRA’s website: hpra.ie/NewVetReg.
### Uploading of Product Data to the EMA’s Union Product Database

The Union Product Database (UPD) will contain information on all veterinary medicinal products that are authorised in the EU, when it goes live to the public on 28 January 2022. This will be a significant step in improving transparency in respect of veterinary medicines in the EU, as it is expected to provide information on more than 30,000 individual medicines, once uploaded by Member States, in due course. The database will include extensive and searchable information on products, including Summaries of Product Characteristics and package leaflets. In accordance with the EMA’s implementation guide, the HPRA will commence uploading information on veterinary products authorised nationally using the decentralised or mutual recognition procedures in the period up to 30 September 2021. Data in respect of the other nationally authorised veterinary products will be uploaded in a second phase, with the upload of all data to be completed by 28 January 2022.

The HPRA intends to maintain its own national listing of authorised veterinary medicinal products on the HPRA website at least until the end of 2022, but will reconsider the position at that point in the light of experience gained with the UPD.

### Change to VPO and VPO-1 Category of Supply

In accordance with Article 34 of Regulation 2019/6, the Union Product Database (UPD) will record veterinary medicinal products as either being ‘subject to veterinary prescription’ or ‘not subject to veterinary prescription’.

All nationally authorised veterinary medicinal products that are currently authorised with a VPO or VPO-1 category of supply will be mapped in the UPD as subject to veterinary prescription. The HPRA is in discussion with the Department of Agriculture, Food and the Marine and expects that the use of VPO and VPO-1 categories of supply will be discontinued in Ireland, and will instead be replaced by prescription supply. However, any warnings and restrictions for use by veterinary practitioners will be stated in the Summary of Product Characteristics (SPC) and product literature, in accordance with the requirements of Article 35 (1)(xi) of Regulation 2019/6. The net effect will be that the words ‘for use by veterinary surgeons only’ will be stated in the SPC and product literature, while the VPO and VPO-1 symbols will no longer appear on the product labelling. The HPRA expects that the QRD template, which is currently being updated, will provide additional explanation of this point.

The HPRA understands that the DAFM plans to continue current national supply categories in respect of products that are not subject to veterinary prescription (i.e. POM(E), PS, LM and CAM), in accordance with Article 103 of the Regulation.

### Revision of National Legislation on Veterinary Clinical Field Trials

Veterinary clinical field trials will be subject to new controls under Regulation 2019/6 from 28 January 2022. The existing national controls specified by Sl. No. 786 of 2007, as amended, will be revised by the Department of Agriculture, Food and the Marine to ensure that they complement Regulation 2019/6 and are not in conflict with it. The HPRA understands that the overall process for submitting and processing applications for clinical field trials will remain largely similar to that in operation currently. Applicants are requested to keep in touch with developments, which will be reported on the HPRA website (hpra.ie/NewVetReg). The new national legislation is not expected to be available until the end of 2021.

### Update on Irish Language Case

In respect of proceedings relating to the provision of bilingual packaging of veterinary medicines in the Irish and English languages brought against the Department of Agriculture, Food and the Marine (DAFM) in 2016, the European Court of Justice (ECJ) gave its ruling on 17 March 2021. The EU Court said that the Directive 2001/82/EC language requirement for the labelling of veterinary medicines had been incorrectly transposed into Irish national law. It also found that the fact that Regulation 2019/6, which applies from 28 January 2022 and provides that Member States can choose the language of the text to be used in the package leaflet and labelling, cannot justify disregarding the obligation in the directive. It stated that the High Court is required to uphold the application for a declaration that Ireland is under an obligation to remedy the incorrect transposition of the directive.

The judgment is expected to be returned to the High Court in Dublin to decide on what to do next. The HPRA will continue to monitor developments in this case.
Compliance

Authenticity Verification of Authorisations and Certificates issued by the HPRA

Since 1 September 2020, the HPRA has issued electronic authorisations with e-signatures and no longer routinely issues hard copies of Manufacturing Authorisations/Licences, Wholesale Distribution Authorisations and Active Substance Registrations. Authenticity of electronic authorisations issued by the HPRA may be verified on the EudraGMDP database or, alternatively, enquiries can be submitted to the compliance mailbox (compliance@hpra.ie).

GMP and GDP certificates will be uploaded to the EudraGMDP database upon receipt of responses to the deficiencies and points for clarification outlined in the inspection report, which have been deemed acceptable. The HPRA will not routinely issue hard copies of GMP/GDP certificates and their authenticity may be verified on the EudraGMDP database. Hard copies of GMP/GDP certificates may be requested via the export certification process, details of which can be accessed on the Export Certification webpage of the HPRA website.

Certificates of Free Sale for Devices Approved under the New Medical Devices Regulation 2017/745

As of 26 May 2021, the HPRA accepts applications for certificates of free sale under the new Medical Devices Regulation 2017/745, which became fully applicable on that date. A new application form and a revised guidance document have been published on our website. Completed applications should be submitted to exportcerts@hpra.ie. All queries in relation to certificates of free sale can also be emailed to exportcerts@hpra.ie.

EU and UK Trade and Cooperation Agreement Summary of Annex on Technical Barriers to Trade (TBT) 2 – Medicinal Products

The EU and UK Trade and Cooperation Agreement (TCA) was published on 24 December 2020. The TCA includes an Annex for human and veterinary medicinal products, which sets out the conditions for the recognition of Good Manufacturing Practice (GMP) inspections between regulatory authorities in EU Member States and the United Kingdom.

Below are some key summary points from Annex TBT – 2 on medicinal products:

- The UK and the EU will recognise GMP inspections at manufacturing sites carried out by either party in their jurisdictions and in third countries.
- Following a request for GMP documentation, each party shall endeavour to transmit the document within 30 calendar days of the date of the request.
- Under specific circumstances, each party may opt not to accept an official GMP document issued by the other party's authority.
- Each party has the right to conduct its own inspection of manufacturing facilities that have been certified as compliant by the other party.
- Each party shall notify the other party at least 60 days before adopting any new measures or changes relating to GMP, concerning any of the relevant laws, regulations and technical guidelines.
- As a result of any of the new measures or changes, a party can consider that it can no longer recognise inspections or accept official GMP documents issued by the other party and the parties shall enter into consultations within the working group on medicinal products.
- Each party has the right to suspend totally or partially the recognition of inspections of the other party for all or some of the products.
- The parties shall cooperate with a view to strengthening, developing and promoting the adoption and implementation of internationally agreed scientific or technical guidelines.
- The working group on medicinal products shall assist the Trade Specialised Committee on Technical Barriers to Trade in monitoring and reviewing the implementation and ensuring the proper functioning of this Annex.

An Údarás Rialála Táirgí Sláinte
Health Products Regulatory Authority