

HPRA MEDICINAL PRODUCTS

NEWSLETTER

ISSUE
66

In this Issue

Human Medicines

- COVID-19: Queries and Updates
- COVID-19 Update
- Getting Brexit Ready
- Nitrosamine Impurities: Conclusion of Nitrosamines 5.3 Review and Requirements for Chemical and Biological Products
- Interchangeable Medicinal Products
- IE Requirements Regarding Release of Batches of Vaccines or Blood-Derived Medicinal Products
- Multilingual Packaging Update

Veterinary Medicines

- Brexit Implications for Veterinary Medicinal Products on the Market in Ireland
- Changes to Submission Requirements of Joint-labelled Mock-ups Post Renewal Procedures
- Ongoing Operations during the COVID-19 Pandemic
- HPRA Input into Revision of National Legislation on Veterinary Medicinal Products

Compliance

- Controlled Drugs: Notice Regarding PharmaTrust
- Inclusion of Postcodes (Eircodes) on MIAs and GMP Certificates
- European Commission Call for Data on Prostaglandins and their Analogues used in Cosmetic Products
- Brexit Transitional Period: Implications for Cosmetic Product Companies up to 31 December 2020
- Addition of Imported Medicinal Products to Annex 8 of a Manufacturer's / Importer's Authorisation (MIA)
- Distant Assessments (Remote Inspections)

Human Medicines

COVID-19: Queries and Updates

If you have any regulatory queries specific to this issue, please e-mail covid19@hpra.ie.

For further information on the HPRA response to COVID-19, see our [dedicated webpage](#).

Queries to Receipts and Validation

We continue to operate our standard service for the receipt and validation of applications with all mailboxes closely monitored. To ensure the efficient processing of your query, please provide:

- PA number
- Procedure Number
- CESP submission number

within the body of your query to facilitate our prompt follow up.

COVID-19 Update

The HPRA continues to support companies throughout the COVID-19 pandemic regarding the regulation of medicines and maintaining supply. We would like to highlight the latest version of *Questions and Answers on Regulatory Expectations for Medicinal Products for Human Use during the COVID-19 Pandemic* (now version 3, 1 July 2020), published by the European Commission, the Heads of Medicines Agencies and the European Medicines Agency. It has been updated to cover GMP and Pharmacovigilance issues.

This Q&A and the associated CMDh practical guidance for facilitating the handling of processes during the COVID-19 crisis are available on the HMA website on the [CMDh COVID-19 webpage](#).

Regulatory flexibilities which the HPRA can consider include Exceptional Change Management Process (ECMP) requests (using the associated templates published in June); submission of batch-specific requests to address labelling issues; notification of Exempt Medicinal Products; and expediting regulatory procedures such as MR and DCP new applications (through zero day procedures) and variations.

A full list of contact points for such requests is available on the [HPRA website](#).

We are requesting that marketing authorisations holders (MAHs) intensify Brexit readiness work in advance of the end of the transition period on 31 December 2020. Stakeholders should prepare to ensure their authorised medicines comply with EU law and avoid unnecessary disruption to market supply after the transition period as a result of Brexit.

Outstanding regulatory actions should be completed urgently. This includes, for example, transfer of outstanding MAHs, batch control sites, batch release sites, local representatives, QPPV or PSMF to EU/EEA sites to ensure supply to the Irish market is maintained. It is also important that you engage with Irish Revenue Customs to understand how your products are imported into Ireland, to ensure that appropriate arrangements are in place to replenish Irish stocks in a timely manner well before they are exhausted, to allow for any unexpected delays during transportation and to avoid any interruption to supply to patients.

In the coming weeks, the HPRA will directly seek specific assurances with regard to particular supply and regulatory matters and how these relate to your product(s) marketed in Ireland. We look forward to your cooperation and remain available to discuss particular challenges presenting to stakeholders and to clarify any aspects, as required.

The European Commission has published Brexit readiness notices [at this link](#).

Further information on the Withdrawal Agreement is available [here](#).

MAHs should also review the European Commission's [Notice to Stakeholders: Withdrawal of the United Kingdom and EU rules for Medicinal Products for Human Use and Veterinary Medicinal Products](#) (13 March 2020) for further detail on aspects of medicines regulation that will arise at the end of the transition period, including the Northern Ireland protocol.

A CMDh document provides practical guidance on the regulatory scenarios for MR/DCP applications, which may be encountered by applicants now and at the end of the transition period, and the required approach. [Download it here](#).

If you are aware of a Brexit-related issue that could potentially affect the supply of a medicine to Ireland, we would request that you engage with the HPRA immediately at brexit@hpra.ie for Human Medicines and vetinfo@hpra.ie for Veterinary Medicines.

The HPRA will continue to highlight further guidance in relation to the impact on medicinal products as it becomes available.

We encourage you to consult www.hpra.ie/brexit regularly and to sign up for website alerts at www.hpra.ie/register to receive up-to-date information and guidance.

Nitrosamine Impurities: Conclusion of Nitrosamines 5.3 Review and Requirements for Chemical and Biological Products

As previously highlighted on the [HPRA website](#), the EMA's human medicines committee (CHMP) commenced an Article 5(3) review into nitrosamine impurities in human medicinal products in September 2019. This review, which built on previous specific assessments, such as the Article 31 referral for tetrazole sartans, has now been finalised. The requirements, such as the 'call for review' published previously by CHMP in Sept 2019, have been integrated into the final assessment report. The published assessment report provides a comprehensive insight into the issue of nitrosamine impurities and outlines a number of conclusions and recommendations. The

assessment report, the outcome of the Article 5(3) review, and an associated EMA Q&A document can be accessed from the [EMA website](#).

As outlined in the above documents, the recommendations are applicable to all human medicinal products. All MAHs/applicants of human medicinal products should continue to work with the manufacturers of their active pharmaceutical ingredients and finished products to mitigate and control the presence of such impurities in their medicinal products.

Additionally, a separate exercise known as the 'call for review' is being conducted for specific categories of

products. In line with the requirements of the 'call for review', marketing authorisation holders of human medicinal products containing chemically synthesised or biologically derived active substances are required to review their medicinal products and complete the required risk evaluation and, where applicable, risk assessment and control steps. Please note that biological products have now been added to the 'call for review' following the outcome of the Article 5(3) review. The deadlines for completion of the various steps have been amended and the following dates apply. These differ between chemical and biological medicinal products.

Step Number	Chemical Medicinal Products	Biological Medicinal Products
Step 1 – Risk Evaluation	31 March 2021	01 July 2021
Step 2 – Confirmatory Testing	26 September 2022	01 July 2023
Step 3 – Submission of relevant changes	26 September 2022	01 July 2023

Nitrosamine Impurities (cont'd)

Guidance on the procedural requirements for these steps is available and has been published by the EMA and CMDh to facilitate the submission of the required information. Links to this guidance are outlined at the end of this article. A number of templates, which should be used when submitting a response under steps 1 and 2, have also been prepared. The guidance also highlights that updates of Step 1 responses to reflect 'no risk' are not accepted. In such cases, the applicant must proceed to submission of a Step 2 response. The [HPRA has published information on its website](#) related to the format and contact point for submission of responses to steps 1 and 2.

Applicants / MAHs are required to ensure their reviews are concluded as soon as possible, within the timeframe outlined above, and to communicate detections of nitrosamines to the competent authorities. The guidance additionally outlines the approach to be taken for new and ongoing applications for marketing authorisations, where nitrosamine impurities must be fully evaluated by the applicant during the procedure.

Relevant EMA and CMDh guidance

Assessment report Procedure under Article 5(3) of Regulation EC (No) 726/2004 Nitrosamine impurities in human medicinal products - EMA/369136/2020

Questions and answers for marketing authorisation holders/applicants on the CHMP Opinion for Article 5(3) of Regulation (EC) No 726/2004 referral on nitrosamine impurities in human medicinal products - EMA/409815/2020

CMDh practical guidance for Marketing Authorisation Holders of nationally authorised products (incl. MRP/DCP) in relation to Article 5(3) Referral on Nitrosamines - CMDh/412/2019

Requirements Regarding Release of Batches of Vaccines or Blood-Derived Medicinal Products

This is a reminder to holders of marketing authorisations (MA) in Ireland for vaccines or blood-derived medicinal products.

For each batch of marketed product, a Marketing Information Form and an Official Control Authority Batch Release certificate should be submitted to CACerts@hpra.ie.

In reference to Article 5 of the EU Administrative Procedure for Official Control Authority Batch Release (which can be found [here](#)), the MA holder can proceed to market a batch of these products in Ireland on the eighth day following submission, provided within the intervening seven working days the HPRA has not

raised an objection. For example, if these documents are submitted on a Monday the batch can be released on the Wednesday of the following week. MAHs are reminded to account for the impact of Irish public holidays on this.

By default, there is no formal approval of these documents unless a waiver of the above eight day procedure is requested. Therefore, should there be a requirement to market a batch before the end of this hold period, this should be clearly stated in the cover letter / email upon submission of the documents and a case will be created. The HPRA will then endeavour to review this case by the next working day.

Multilingual Packaging — Update

We would like to highlight the [CMDh Best Practice Guide on Multilingual Packaging revision 2](#), which has been published on the HMA website. The guidance contains useful information on the procedures and principles associated with the preparation of multilingual packs. The templates for the cover letter for submissions for new applications, variations and Article 61.3 notifications for the MR/DCP procedure now include a section so the MAH can highlight their proposed Member State clusters for multilingual packaging in advance. This should improve visibility to and promote the involvement of the affected Member States in MR/DCP procedures. The CMDh is currently undertaking a pilot exercise to implement a coordinated approach to the preparation of multilingual packaging in MR/DCP procedures. This works as follows: Ongoing new applications may be included in the pilot with the agreement of

the RMS, who will be supported by the Multilingual Packaging Working Group as necessary. A template for the EU harmonised text for the labelling is prepared by the applicant and agreed during the procedure, and may include text reductions (in grey shading) where there is space restriction for multilingual packs. Finalisation of the new application with the agreed template will then facilitate future preparation of multilingual packs between different MS. The HPRA encourages applicants to participate in this pilot and will assist as RMS in discussions with other MS or as necessary. Please also note that the HPRA continues to accept article 61.3 notifications as usual where applicants wish to prepare new multilingual packs for existing authorisations. This combination of measures to support multilingual packaging aims to improve availability of medicines in smaller markets.

Interchangeable Medicinal Products

Information relating to ongoing consultations and updates to existing Groups of Interchangeable Medicinal Products is available on the HPRA

website under [Medicines Information – List of Interchangeable Medicines – Consultations and Updates to the List](#).

Veterinary Medicines



Brexit Implications for Veterinary Medicinal Products on the Market in Ireland

The UK departed the EU on 31 January 2020 and the current transition period is scheduled to end on 31 December 2020. Marketing Authorisation Holders will be aware that this necessitates several changes to products for which key regulatory activities are located in the UK. In particular, any veterinary medicinal products marketed in Ireland that are still quality control (QC) tested and batch released in the UK will need to transfer QC and batch release to an appropriately authorised manufacturing site in the EU/EEA as soon as possible and no later than 31 December 2020. Products that have been QC tested, batch released and imported into Ireland from the UK prior to 31 December will remain acceptable to be used until their shelf life expires.

From the end of the transition period, the Northern Ireland Protocol (NIP) applies. Under the protocol, QC testing and batch release conducted in Northern Ireland will be recognised by the EU member states. Further guidance in relation to the protocol is available on the [EMA website](#).

At the time of writing, the HPRA is in discussions with the Department of Health, the Department of Agriculture, Food and the Marine and the EU Commission regarding the practical operation of the Northern Ireland Protocol. Developments in this area can be followed on the [HPRA website](#).

The HPRA encourages marketing authorisation holders and veterinary wholesalers to ensure that adequate supplies of veterinary medicinal products for the Spring 2021 period are imported into the country ahead of the year-end deadline to mitigate against possible congestion at UK and Irish ports. The Department of Health has advised that disruption is inevitable on 1 January 2021 and all stakeholders should prepare for this eventuality. Even where the transport cargo contains only medicinal products and should therefore need minimal inspection by port authorities, it is expected that the movement of all goods will be affected if the transport infrastructure leading to the ports become log-jammed.

Ongoing Operations during the COVID-19 Pandemic

The Veterinary Sciences department remains open for business during the current COVID-19 emergency with all work and services continuing as normal. Staff are primarily working remotely but all normal channels of communication remain available. Our order book for applications as Reference Member State is open for bookings for 2021. If you are interested in finding out more, please contact Ms Elaine Hynes, Planning and Authorisation Manager (elaine.hynes@hpra.ie).

Please note that requests for meetings, including those to discuss

planned applications with assessment team members, are still possible. However, given the current pandemic, these meetings will be held virtually by video-conferencing. In the exceptional circumstance where a physical meeting is requested, this will be considered in light of public health advice on the state of risk of the pandemic and risk management measures in operation at the time. However, in this case, advance notice and agreement is required, as the capacity of the HPRA meeting rooms has been reduced based on COVID-19 public health guidance.

Changes to Submission Requirements of Joint-labelled Mock-ups Post Renewal Procedures

In line with the HPRA Guide to Renewal of Veterinary Product Authorisations, on completion of a renewal procedure, it is the MAH's responsibility to incorporate any approved changes into the previously approved mock-ups. Until recently, where the product was joint-labelled with the UK, and the UK's Veterinary Medicines Directorate (VMD) requested colour mock-ups, the applicant was required to submit colour mock-ups simultaneously to the HPRA to facilitate the joint-labelling process. The HPRA wishes to inform applicants that this requirement will now change with immediate effect.

In instances where the product is joint-labelled with the UK and the VMD request a review of mock-ups, the VMD will now perform an independent assessment of the mock-ups. After VMD assessment, the MAH should provide the HPRA with a copy of the agreed mock-ups accompanied by a declaration that no changes have been made, other than those arising from revisions to the QRD texts approved during the renewal assessment. This procedural update has been communicated to our colleagues in the VMD and the applicant is reassured that this does not affect the joint-labelling status of the veterinary medicinal product.

HPRA Input into the Revision of National Legislation on Veterinary Medicinal Products

Although HPRA personnel have been working remotely since March, work continues on the revision of the national legislation being developed by the Department of Agriculture, Food and the Marine (DAFM). The revision of SI No 786 of 2007 is required to complement the implementation of Regulation 2019/6 in January 2022, as some of the current national requirements will no longer be compatible with the new legislation.

The HPRA has set up an internal project team to examine where changes to the national legislation are needed and to review how they might impact the authorisation and monitoring processes for veterinary medicines. This group is engaged in regular dialogue with the DAFM regarding changes expected to impact areas within the responsibility of the HPRA. The HPRA understands that the new legislation will be available towards the end of 2021.

Once the HPRA has certainty over the new legislative requirements, we will launch a communications campaign to alert stakeholders to those changes that affect the regulation of veterinary medicines within the remit of the HPRA. In the meantime, it is recommended that stakeholders keep in touch with developments by consulting the [DAFM website](#).

Compliance

Controlled Drugs: Notice Regarding PharmaTrust

Over the last number of months, the HPRA has been working on a project with the United Nations Office on Drugs and Crime (UNODC) to upgrade the software systems used to issue licenses for the import and export of controlled drugs in Ireland. A significant amount of work has already been completed and the HPRA's internal software system has been updated.

As of July 2020, the HPRA has moved to the final phase of the project and stakeholders are actively transitioning to the new stakeholder interface known as NDSWeb. This interface offers enhanced functionality and usability to support the licensing of controlled drugs. The transitioning of existing Pharmatrust users to NDSWeb is occurring on a phased basis. Once all existing users have transitioned over to NDSWeb, Pharmatrust will be retired.

What does this mean for stakeholders?

Firstly, until a member of the HPRA Controlled Drugs team makes contact, stakeholders should continue to use PharmaTrust to apply for controlled drugs import and export licences as normal. Once our team has contacted you, there will be several steps to be completed to ensure that you have a

smooth transition to the new system. These steps are summarised below.

Please be assured that instructions will be provided at each step and our controlled drugs team will be available to guide you through the process.

Registration

Stakeholders will be asked to register for a NDSWeb account and will be required to review the controlled drug preparations and foreign establishments linked to their new NDSWeb account to ensure that all required preparations and establishments are available.

Stakeholders should inform us if additional preparations or foreign establishments need to be added to the account. These requests can be made through NDSWeb itself or by email.

Applying for a licence

Upon confirmation that all the required preparations and foreign establishments are available, stakeholders will be asked to apply for an actual import or export licence, using NDSWeb. A member of our Controlled Drugs team will be available to provide support during this process. Following the successful receipt of the

first import or export licence through NDSWeb, stakeholders will transition permanently to the new system.

Hard copy licences and endorsing

The process for the issuing of hard copies of the licences remains the same and stakeholders will receive a signed hard copy of the import and/or export licence in the post. Once a shipment has been received or sent, the licence should be endorsed by the stakeholder. The endorsed quantity of controlled drug imported/exported should be submitted through NDSWeb under the corresponding licence number and the hard copy licence should be returned to the HPRA.

Your processes and documents

Stakeholders are expected to review and update internal processes and controlled documents such as procedures, work instructions and forms in line with the new system.

We look forward to working with you on NDSWeb and we hope that you will find the new system efficient and user-friendly. A 'Guide to NDSWeb' will be published on our website soon. If you have any questions, please contact controlledddrugs@hpra.ie.

Inclusion of Postcodes (Eircodes) on MIAs and GMP Certificates

In recent years, we have reformatted Manufacturer's / Importer's Authorisations (MIAs) for all manufacturing sites located in Ireland so that these authorisations could be electronically uploaded to the central European database (EudraGMDP), which is managed by the European Medicines Agency. Postcodes (also referred to as Eircodes) were introduced in Ireland in 2015 and, during the reformat of existing MIAs, we included details of the postcodes on MIAs.

The postcode is now also required as standard in applications for new authorisations. It appears on all MIAs viewed electronically on the EudraGMDP database and on any hard

copies of the MIA issued by the HPRA. As the same manufacturer's address details appear on GMP Certificates, the postcode is now also visible on GMP certificates for Irish manufacturing sites when viewed on the EudraGMDP database, as well as on authenticated paper copies of GMP certificates issued by the HPRA under the Export Certification process.

The HPRA is aware of the fact that previous versions of GMP certificates, which may have been used for regulatory submissions in third countries, may not have included postcode details. The appearance of the postcode on new versions of the GMP certificates may give rise to queries relating to the site address

from authorities in those countries. We can confirm that the inclusion of this postcode on the MIAs, or on the associated GMP certificates, without change to other address details (e.g. street number, street name etc.), serves only as additional locator information and does not reflect any change in the location of the manufacturing site or any material change to the official address of the site. The inclusion of the postcode does not require any variation to medicinal product Marketing Authorisations in the EU. Any queries about inclusion of the postcode on MIAs and GMP certificates should be addressed to compliance@hpra.ie.

European Commission Call for Data on Prostaglandins and their Analogues used in Cosmetic Products

The European Commission has issued a call for data on the safety of **prostaglandins and their analogues** as cosmetic ingredients in the framework of Regulation (EC) 1223/2009.

The Commission has concerns about the use of such ingredients in cosmetic products. Several countries have recorded serious undesirable effects caused by the use of cosmetic products containing prostaglandins and/or their analogues for eyelash growth.

The Commission will mandate the EU Scientific Committee on Consumer Safety (SCCS) to assess the safety of the above-mentioned ingredients when used in cosmetic products. In preparation, interested parties have been invited to submit relevant scientific information on the safety of prostaglandins and their analogues.

More information in relation to the requirements for the submission of data and the background to this topic,

as well as a non-exhaustive list of the ingredients in question, can be found on the [European Commission website](#).

The last date for submission of relevant information to the European Commission is 21 October 2020.

Brexit Transitional Period: Implications for Cosmetic Product Companies up to 31 December 2020

The UK left the European Union on 31 January 2020 on the basis of the [Withdrawal Agreement](#), which was agreed by the European Council on 17 October 2019. The agreement includes a [transition period](#) until at least 31 December 2020.

The EU and the UK have begun negotiations on a new future relationship agreement, which, if agreed, is due to come into effect from 1 January 2021. EU law in its entirety

applies to, and in, the UK during the transition period.

The HPRA wishes to highlight that the European Commission published two *Readiness Notices* in the form of Notice to Stakeholders on 13 March 2020 that are relevant to cosmetic products.

The Notice to Stakeholders regarding the [Withdrawal of the UK and EU rules in the field of cosmetic products](#)

replaces that previously published on 18 July 2019.

- This document outlines the legal situation applicable as of the end of the transition period, particularly advising to:
 - establish a Responsible Person in the EU and reflect this in the corresponding labelling;
 - ensure compliance of the safety assessment in relation to

qualifications of the safety assessor; and

- take the necessary steps to update the Cosmetic Product Notification Portal (CPNP).
- This notice also discusses cosmetic products placed on the EU or UK market before the end of the transition period and provides information in relation to the applicable rules in Northern Ireland after the end of the transition period.

The Notice to Stakeholders regarding [Withdrawal of the United Kingdom and EU rules in the field of industrial products](#) replaces previous publications by the European Commission: the Notice to Stakeholders of 22 January 2018 and the Q&A document dated 1 February 2019.

- This notice provides further information on the legal situation at the end of the transition period, on certain separation provisions of the Withdrawal Agreement and the rules applicable to Northern Ireland as of the end of the transition period for cosmetic products (and other products covered under the New Approach legislation).
- The notice also provides examples of when goods are considered to have been placed on the market and information regarding products placed on the EU or the UK market before the end of the transition period, including the obligation to appoint a new RP in the EU where the current RP is based in the UK.

The HPRA encourages responsible persons, distributors, manufacturers

and retailers of cosmetic products to consult the details of both published Notices to Stakeholders and to take the appropriate steps in preparation for the end of the transition period to ensure supply of compliant cosmetic products to the Union market. If there are any specific queries, these can be sent to cosmetics@hpra.ie.

The HPRA is continuing to work with the European Commission and other Member States in relation to cosmetic product issues arising from Brexit.

Both Notices to Stakeholders regarding Withdrawal of the United Kingdom and EU rules in the field of industrial products and in the field of cosmetic products are available for download from the [European Commission website](#).

Addition of Imported Medicinal Products to Annex 8 of a Manufacturer's / Importer's Authorisation (MIA)

The purpose of Annex 8 of the MIA is to identify products which are imported from outside the European Economic Area (EEA) and for which the manufacturing authorisation holder is the named site of batch release in a marketing authorisation, i.e. the manufacturing address where certification of each batch by a Qualified Person (QP) takes place prior to its release to market. Only those medicinal products imported either as a bulk dosage form (e.g. bulk tablets or bulk nude vials) or as a finished packed product should be listed in Annex 8.

Annex 8 is not required to reflect the following:

- Intermediates which undergo further processing within the European Union (EU).
- Medicinal products for which physical importation is the only activity performed by the MIA holder.
- Certification of imported Investigational Medicinal Products (IMPs) under an MIA for IMPs.

To add an imported medicinal product to Annex 8 of an MIA, application form AUT-F0211 '[Application Form for Variation to a Manufacturer's](#)

[Authorisation](#)' must be completed and should contain the name and address of the non-EEA site from which the medicinal products will be imported, as well as information relevant to the medicinal products to be listed. AUT-G0140 '[Guide to New Applications and Variations to Manufacturer's Authorisations](#)' should be consulted.

The applicant should consider the points outlined below when submitting variation applications to update Annex 8 of the MIA:

- The non-EEA site from which the applicant wishes to import the medicinal product should be already listed in Annex 3. Otherwise, a variation must be submitted to add this site to Annex 3 of the MIA.
- The dosage forms included in Annex 8 should be aligned with the dosage forms listed in Annex 3 for that particular non-EEA site.
- In the event that the manufacturer and the packer are separate sites located in a third country, the last site from which the product is imported is the one required to be included in Annex 8.

- Non-EEA sites involved in storage operations only, prior to importation, should not be listed in Annex 8.
- The activity to be performed by the MIA holder must be specified, i.e. batch certification and/or site of physical importation. If the MIA holder is also the site of physical importation, operation 2.3.1 should be included in Annex 1. If physical importation is outsourced to a contract manufacturer, this activity should be recorded under operation 1.4.3 in Annex 3 for the relevant contract manufacturer.

Some examples of common errors in applications received, which have required further correspondence with the applicant, are detailed below:

- The trade name of the product should not be included under the 'Product Description' heading in the table in Annex 8. This is to avoid multiple entries when the same product is marketed under a number of trade names throughout the EU. It also prevents the need for variations to the MIA should the trade name of the product change. Examples of what might be appropriate entries under 'Product Description'

- for a number of dosage forms are suggested in the table below.
- If there is no additional relevant information, then it is acceptable to just repeat the dosage form under the product description heading, e.g. 'Hard Shell Capsules'.
 - Each table for inclusion in Annex 8 should be specific to the non-EEA site in question. In situations where the same products are imported from multiple non-EEA sites, a separate table for each of these sites is required in Annex 8.
 - Separate tables are required where the 'Product type' and 'Dosage form' fields for products are not the same. For example, when a product type refers to a non-sterile product and dosage forms are both hard and soft shell capsules, two separate tables should be appended to Annex 8.
 - Where the products are imported as bulk dosage forms, a reference to this should be made in the 'Product description' field of the table (e.g. 'Bulk tablets').

Approval of a product entry in Annex 8 of the MIA does not infer that the product is approved for any particular market. The Qualified Person should ensure that the product has received relevant market approvals prior to certification of batches.

Dosage Form	Product Description
Aseptically Prepared Small Volume Liquid	Vials Pre-filled syringe Autoinjector Vial containing concentrate for solution for infusion
Aseptically Prepared Lyophilisate	Vial containing powder for solution for infusion
Non-sterile Tablets	Enteric coated tablets Sustained release tablets Tablets
Non-sterile semisolid	Ointment Cream Gel Paste
Non-sterile liquid for internal use	Oral suspension Oral liquid

Distant Assessments (Remote Inspections)

Introduction

Due to the COVID-19 pandemic and the associated restrictions, standard onsite GMP/GDP/GCP/ Pharmacovigilance/Blood, Tissues, Organs (BTO)/Cosmetic/Controlled Substance inspections are not possible for the foreseeable future. Accordingly, the HPRA has introduced a process for distant assessments (remote inspections). This is aligned with the approach agreed by the EU working groups coordinated by the European Medicines Agency. The process will be utilised for both routine and non-routine assessments while the current restrictions pertain.

The distant assessment process, in general, will follow a similar format to that for an onsite inspection. However,

the inspector(s) will conduct discussions with site representatives and review documentation remotely. In certain limited cases, an element of onsite inspection may be deemed necessary as part of the assessment.

Communication prior to the assessment

The site will be notified of the distant assessment via email in the normal manner. It will be requested to contact the Lead Inspector directly to arrange an initial virtual meeting to agree key logistics regarding the assessment and expectations in terms of sharing of documents, interviews with subject matter experts (SMEs) and the conduct of virtual tours.

Sites will be required to propose either Skype or Microsoft Teams as suitable remote communication platforms for the distant assessment and the site will be responsible for considering any associated security requirements.

The HPRA will provide access to a One Drive shared folder system to facilitate the provision of electronic copies of documents and other information to the inspector(s). Access to One Drive will be granted to a number of site personnel and this will be agreed with the inspector in the initial meeting.

The inspector will also discuss with the site a suitable mechanism to facilitate virtual site tours including options for live camera streaming or elements of recorded footage. The capability for live sharing of screens displaying

computerised systems such as SAP, Track wise, LIMS etc., will also be discussed.

Follow-up calls with the Lead Inspector may be necessary to test the equipment, software and internet connection to ensure that any potential technical issues are resolved in advance of the assessment.

Provision of documents prior to the assessment

The site will be requested to provide certain documents before the assessment. Requests may include 'Excel' lists of deviations, complaints, laboratory investigations etc. and relevant site procedures. A site presentation for the opening meeting may also be requested in advance.

The Lead Inspector will provide a summary draft agenda to the site prior to the distant assessment indicating which topics are scheduled to be addressed on each day of the assessment, if relevant. The intent of the summary agenda is to facilitate the site in having the appropriate SMEs available at the appropriate time.

Distant assessment

The distant assessment will commence with an opening meeting on the first day and end with a closing meeting on the last day. It is the responsibility of the site to organise the opening and closing meetings, via either Skype or Microsoft Teams.

The mechanism and format to provide feedback and communicate any deficiencies throughout the distant assessment will be confirmed at the opening meeting.

The site will be required to monitor and respond to HPRA requests at all times during the course of the distant assessment. At various stages during the assessment, the inspector may request to speak directly to relevant SMEs concerning documents/topics under review.

At the end of each day of the assessment, the inspector will confirm a list of topics and a list of documents, to be reviewed on the following day.

The closing meeting will address the draft deficiencies and provide an outline of the post-assessment process.

Distant assessment combined with onsite elements

Although primarily conducted remotely, in some cases an element of inspection may be required where it is decided that the compliance of some processes cannot be determined remotely.

Elements of an onsite inspection will be agreed with the site in advance and will only be conducted where it can be completed safely and aligned with current public health and government advice including travel restrictions, working protocols, requirements for physical distancing.

Any agreed onsite elements will be subject to risk assessment and the Lead Inspector will request relevant information including numbers of confirmed COVID-19 cases, if any, at the site, corrective measures implemented and precautions in place. Relevant health questionnaires and guidelines for visitors may be requested.

Specific precautions for the onsite assessment elements will be agreed on a case by case basis but, in general, these will be focused on maintaining two metres distancing at all times, minimising the number of personal interactions and limiting the timing of those interactions to no more than 15 minutes, where possible.

Queries regarding distant assessments

Any queries with respect to this article or general queries regarding distant assessments should be submitted to inspect@hpra.ie