IRISH MEDICINES BOARD

news LETTER

MEDICINAL PRODUCTS

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IRISH MEDICINES BOARD, KEVIN O'MALLEY HOUSE, EARLSFORT CENTRE, EARLSFORT TERRACE, DUBLIN 2 TEL: 01 676 4971 FAX: 01 676 7836 EMAIL: FOI@IMB.IE

GENERAL

EU BAN ON MEASURING DEVICES CONTAINING MERCURY

From 3 April 2009 the placing on the market of certain measuring devices containing mercury has been banned under the EU chemical legislation, REACH.

Ban on fever thermometers

It is not permitted to supply or make mercury-containing fever thermometers available to the Irish or EU market, whether for payment or free of charge. This includes fever thermometers supplied or made available to:

- members of the general public e.g. via pharmacies or supermarkets,
- professionals e.g. medical and veterinary practitioners, and
- industrial sectors.

Ban on other measuring devices

It is prohibited to place other mercury-containing measuring devices intended for sale to the general public on the market. Such devices include manometers, barometers, sphygmomanometers and thermometers other than fever thermometers.

This ban only applies to those devices supplied to members of the general public via outlets such as pharmacies and supermarkets. Supply of mercury-containing measuring devices other than fever thermometers to professionals (e.g. medical and veterinary practitioners) and industrial sectors can continue under the current restriction.

There is one exception to this rule in that measuring devices more than 50 years old on 3 October 2007 are permitted to be placed on the market.

The entry into force of the restriction on barometers (other than those more than 50 years old on 3 October 2007) came into effect on 3 October 2009.

Non-compliant stock

If Irish importers, recipients and/or suppliers have non-compliant devices in stock, these cannot be placed on the market. Contact could be made with the suppliers of these devices requesting that this old stock is taken back. Every effort should be made to ensure that mercury does not get into the general hazardous waste stream.

Legislation

Details of the full restriction can be found at entry no. 18a in Regulation EC No. 552/2009, the amended Annex XVII to the REACH Regulation.

It should be noted that the European Chemicals Agency (ECHA) is currently reviewing a proposal to extend the restriction to include certain mercury-containing measuring devices in healthcare and other professional and industrial uses. For further information, please see the ECHA website.

If you have any questions on the above please contact the Health and Safety Authority at REACHRight@hsa.ie.

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HUMAN MEDICINES

PHARMACOVIGILANCE INFORMATION DAY ON FRIDAY 2 DECEMBER 2011

The IMB will hold a Human Medicines Pharmacovigilance Information Day on Friday 2 December 2011 to address issues related to implementation of the new European Pharmacovigilance legislation, which comes into effect in July 2012.

The information day will cover a range of topics including the IMB's implementation plans, progress with the Joint EMA-MS implementation plans, as well as an update on the status of Implementing Measures and Good Vigilance Practice.

There will also be presentations on the pharmacovigilance system master-file, changes to adverse reaction reporting requirements, signal detection and signal management, changes to periodic safety update reports, benefit-risk management planning, requirements for post authorisation safety studies, additional risk minimisation, and activities including educational materials and communications.

Colleagues from the European Medicines Agency (EMA), the Medicines and Healthcare products Regulatory Agency (MHRA) and the European Organisation for Rare Diseases (EURORDIS) will provide presentations and contribute to discussions at the meeting.

A preliminary agenda is available for the meeting on the IMB website, together with information regarding registration arrangements and details of the meeting venue.

SUBMISSION OF RISK MINIMISATION PLANS TO THE IMB

The risk minimisation tools requested in risk management plans (RMPs) must be assessed by the IMB prior to their approval for distribution in Ireland.

Educational materials and other risk minimisation tools intended for healthcare professionals or patients are assessed by the Vigilance Assessment section in the IMB's Human Products Monitoring Department.

A clear distinction is made between risk minimisation tools requiring approval and other information materials which are intended for promotional purposes (i.e. which are not the subject of a RMP). Only educational materials included in an EU-RMP or a condition of the marketing authorisation require IMB approval.

In order to facilitate the assessment process and for optimal efficiency, the following recommendations should be followed:

- Depending on the provisions of the RMP, risk minimisation tools may be conditions of the marketing authorisation, i.e. Annex II requirements, meaning that the risk minimisation tools need to be approved and implemented as a condition for marketing in Ireland. Documentation must therefore be submitted to the IMB with sufficient time for assessment to be concluded (minimum two months, excluding time required for printing and distribution).
- It is important to contact the Vigilance Assessment team directly prior to submission of a risk minimisation plan for a product for which additional pharmacovigilance actions planned in the RMP will be performed in Ireland (post authorisation safety studies, registries etc.). The organisation of a meeting may be necessary.

Submission of a risk minimisation plan

The applicant should submit the risk minimisation plan in electronic format to **vigilance_assessment@imb.ie** together with:

1. An application letter, indicating:
   - The context of the application (launch, update of RMP, follow-up measure);
   - The distribution procedures planned: schedule, distribution list and mode of distribution;
   - Any useful information concerning the elaboration of the document (e.g. reviews by a group of experts, a learned society or patient association).

2. The draft documents or minimisation tools:

   Whenever possible, the documents should be submitted in pdf format, in order to guarantee their readability and the pertinence of the visual aids.

   In order to optimise the efficiency of the assessment and review process, the documents should also be submitted in a modifiable text format (Word).

   For visual or audiovisual documents, apart from the submission of the CD-Rom or DVD, a typed text indicating the scenario, describing or representing the image and transcribing the audio must be attached.

3. Reference documents:
   e.g. Annexes I to III of the marketing authorisation, latest version of the RMP (at least part 2 'Risk Minimisation Plan'), annexes of the RMP describing the minimisation tools, if applicable, the literature references mentioned in the documents, and copies of the relevant version of the SmPC/PL if not already included as part of the specified educational pack.

The IMB may require the company to submit new draft documents if the initial assessment concludes that the documents are not in accordance with the RMP requirements for risk minimisation.

During the assessment procedure, the IMB will send comments to the company. A case reference number will be provided and should be quoted in all subsequent correspondence.

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The final documents must be provided to the Vigilance Assessment section in paper format and in electronic format for filing.

Updates

Following a major variation of the marketing authorsation (with an impact on the key elements of the risk minimisation plan) or an update of the RMP and following agreement with the rapporteur, the updated risk minimisation documents should be submitted to the IMB and will follow the same assessment process.

The application should be submitted as a Word document with track changes (and justification of the modification, for example, indicating in a comment the reference to the variation procedure).

In case of major modifications to the document (paragraphs added, moved or major rephrasing), it is recommended to submit as a three column table (original text, modified text and justification of modification).

Modification of formats, models or following a minor marketing authorisation variation (for example modification of a section of the SmPC without an impact on the body text of the document) should only be provided for information.

In case of submission of an updated document, the company should specify the distribution procedures planned.

Contact:

For paper mailing:

Vigilance Assessment Section
Human Products Monitoring Department
Irish Medicines Board

For electronic submissions or queries:

E-mail to:
vigilance_assessment@imb.ie

HOMEOPATHIC MEDICINES UPDATE

Homeopathic medicinal products currently on the Irish market must be either registered under the Simplified Registration Scheme (SRS) or authorised under the National Rules Scheme (NRS) (see IMB website for details).

Simplified Registration Scheme

All homeopathic medicinal products on the market to which the SRS applies should now be registered.

We are aware that there are a number of SRS applications currently undergoing assessment at the IMB and it is anticipated that all these will be registered over the coming months.

National Rules Scheme

The deadline of 30 April for authorisations of homeopathic medicinal products under the NRS has now passed. This deadline applied only to products that were on the market as of July 2007 {Medicinal Products (Control of Placing on the Market Regulations) 2007}. All other NRS products must have a licence before being placed on the market.

Proposed products which are new to the market can be submitted under either the SRS or the NRS at any time.

In seeking to ensure that all homeopathic products on the market are licensed the IMB is requesting that all manufacturing authorisation holders confirm that, with respect to their products, they are either in possession of a licence (registration or authorisation) or else there is an application currently under assessment at the IMB.

In the case where there is no licence or an application has not been submitted in respect of a product the IMB requests the following from the manufacturing authorisation holder:

1. List of products (which must have been on the market in July 2007).
2. Details of each product including:
   a. Registrations or authorisation in other Member States of the EU.
   b. List of stock(s) present in the product and information as to whether this stock has already been assessed by the IMB in respect of another product.
   c. Letter of intent from the company stating when an application in respect of the product will be submitted to the IMB and under which scheme (SRS or NRS) the application will be made.
3. In the case of a product where the company is not intending to submit an application under either scheme and is in effect taking the decision to cease marketing that particular product, the IMB would like a written statement confirming that this is the company's position.

Requests for information or specific queries should be submitted to **homeopathicmedicines@imb.ie**.

TYPE IA VARIATIONS: EXPERIENCE TO DATE WITH THE NEW VARIATIONS REGULATION

Commission Regulation (EC) No. 1234/2008 became effective on 1 January 2010, replacing 1084/2003/EC and 1085/2003/EC. The purpose of the new regulation was to create a clear structure for managing variations and to reduce the administrative burden on industry and regulators. The new regulation introduced a 'Do and Tell' procedure for Type IA notifications allowing the implementation of minor changes where there is little or no impact on the quality, safety and efficacy of the medicinal product, before the regulatory authorities are informed of this change. The IMB conducts regular audits of Type IA variations in order to confirm that they have been appropriately categorised, to identify any areas of concern arising from the implementation of the new regulation, and to ensure a consistent approach in the processing of new variations both by industry and by the IMB.

The audits have identified a number of deficiencies, some of which required corrective actions from the applicants.

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The most common deficiencies identified were:

- 'EC Classification Guideline' page not submitted.
- Incorrect classification of Type IA variations, where either the wrong Type IA variation subcategory was selected or where a change was incorrectly classified as a Type IA variation when a Type IB or Type II variation was required.
- Missing or incomplete documentation.
- Conditions applying to the chosen Type IA category not met.

To reduce the number of incorrect Type IA submissions, the IMB would like to remind applicants of the following:

- All changes which fall under Type IA are listed in the 'EC Classification Guideline', along with a list of conditions and documentation requirements. These conditions must be met and all necessary documentation must be provided for the variation to be correctly classified as a Type IA. Otherwise, the variation is normally required to be submitted as a Type IB (default category) or as a Type II variation (where the proposed change could have a significant impact on the quality, safety or efficacy of the medicinal product). Careful consideration should be given to the list of conditions to ensure that the variation is appropriately classified as Type IA. Some conditions were found to be not met during the audit and resulted in requests for resubmission as Type IB or Type II variations e.g. 'any change should be within the range of currently approved limits', 'the change is not a consequence of any commitment from previous assessments', 'the method of analysis should remain the same'.

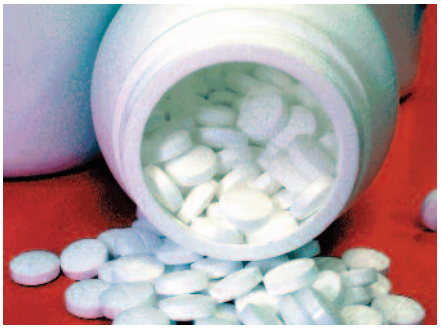
- The relevant page(s) of the 'EC Classification Guideline' including confirmation of compliance with all relevant conditions and documentation requirements must be submitted for each change applied for under a grouped variation.

- Documentation requirements must be met in full, for example, the present and proposed sections of the application form, specifications, amended dossier pages, GMP certificates, etc., as required for each category of change. Updated label mock-ups and/or leaflet text must be submitted with the Type IA variation where the change results in changes to the label and/or leaflet.

- Unforeseen variations are not acceptable as Type IA notifications unless previously classified as such by an Article 5 recommendation published by the EMA, CMDh or CMDv (published recommendations on the classification of unforeseen variations are available on the CMD website).

- As per a published Article 5 recommendation, reduction in the testing frequency for a specification parameter from routine testing to skip or periodic testing, is required to be submitted as a Type IB variation.

- A number of variation categories refer to deletion of a 'non-significant parameter'. Deletion of a specification parameter which may have a significant effect on the overall quality of the finished product is not correctly classified as a Type IA variation. Deletion of 'non-significant parameters' should be limited to situations where it is clear that the test is no longer required in accordance with current requirements. For example, deletion of a test for odour from the specification of a chemical substance that already includes specific identification testing would be considered to be acceptable as deletion of a non-significant parameter. However, deletion of standard tests, for example related substances, based on historical compliance with the specification limits, would not be considered to be acceptable under this category as it would not be considered non-significant. It should also be noted that a 'specification parameter' means the quality and attribute for which a test procedure and limits are set. As such deletion of a parameter implies deletion of the parameter and its corresponding method from the specification in its entirety. It does not allow for the deletion of individual limits from a particular specification parameter.



The EMA has published a 'Pre-notification checklist for Type IA variations' aimed at facilitating submission of complete and correct Type IA notifications; the IMB recommends that applicants consult this checklist, which is available on the EMA website, prior to submission of Type IA notifications.

Further guidance on the variation procedure, including examples of acceptable and not acceptable groupings, best practice guides, and a Q&A document are available on the CMDh website.

CHANGES TO THE SUBMISSION OF PRODUCT INFORMATION TO THE IMB

Current IMB policy is that prior to marketing a new product or a product in amended livery, full colour mock-ups of the labels and package leaflet must be submitted to IMB for approval. The IMB would like to notify applicants of a change to this requirement.

We would like to advise applicants that both a mock-up of the package leaflet and a text-only version of the package leaflet are now required on initial submission of the application. However the submission of a final mock-up of the package leaflet is no longer mandatory for final approval and instead a text-only version of the final package leaflet is required. The applicant may provide a mock-up of the package leaflet in addition to the required text-only version of the package leaflet, if available. Submission and prior approval of colour mock-ups for all labels remains compulsory prior to marketing. Text-only versions of the labels are not required in addition to the final colour mock-ups for labels.

Applicants are advised of the following notable exceptions to the above:

1. Label/leaflet combination style package leaflet: a colour mock-up of the label/leaflet must also be provided in addition to the text-only version of the package leaflet.

2. Products without a separate package leaflet (leaflet information on packaging): a text-only version of the label is required in addition to the mandatory colour mock-up for the label.

3. Package leaflets with sections intended for technical use/ healthcare professional only: two separate documents should be provided, the text-only version of the section of the package leaflet intended for use by the patient and separately the text-only version of the section of the package leaflet intended for use by the healthcare professional. Presentation of the package leaflet as two separate documents is only required for submission of the package leaflet to the IMB; the applicant may provide a single consolidated package leaflet with the medicinal product which contains the information for both the patient and the healthcare professional.

We would also like to advise that it is no longer obligatory for applicants to sign and date mock-ups, whether submitted in hard copy format or electronically submitted as a scanned version of the full colour mock-up or as a PDF document.

The IMB does not object if an applicant wishes to submit signed and dated mock-ups for the applicant's own internal tracking purposes, however the presence of a signature and date is no longer mandatory.

Text-only versions of labels may be submitted instead of mock-ups if the product is not marketed or is not intended to be marketed, in which case the applicant must submit full colour mock-ups of the labels by way of variation or Article 61(3) notification to the IMB for approval prior to marketing the product in Ireland. It is not obligatory for applicants to sign and date text-only versions of product information.

Mock-ups or text-only versions of product information may be submitted in hard copy format (two copies of each mock-up/text), electronically as scanned versions of mock-ups (one copy of each mock up/text) or as PDF documents (one copy of each mock-up/text). In all instances, the applicant should ensure that the text-only version of the package leaflet is provided in MS-Word format, in a separate document from all other product information. The IMB retains the right to request the mock-up of the package leaflet or the licensed version of the package leaflet at any time.

VETERINARY MEDICINES

VETERINARY INFORMATION DAY ON THURSDAY 6 OCTOBER 2011

An IMB Veterinary Information Day meeting will be held on 6 October 2011 in the Radisson Blu Hotel, Dublin Airport. The meeting is intended to update stakeholders on recent regulatory developments and to provide a forum for discussion on such matters with IMB staff and management. A particular focus of this year's programme will be the future EU legislation as it might affect the authorisation, monitoring and supply of veterinary medicines. The registration fee for the event has been held at € 250 with special rates for four or more participants from the same company, as well as for non-profit organisations. Early booking is advised. For more details please visit the IMB website or contact Ms. Michelle Sinnott (michelle.sinnott@imb.ie).

MEMBERSHIP CHANGES IN THE ADVISORY COMMITTEE FOR VETERINARY MEDICINES

The IMB has been notified by the Minister for Health and Children of the appointment of the following experts to the ACVM for the period ending 31 December 2015:

Mr. Patrick Brangan (Chair)
Mr. John Underhill
Ms. Eugenie Canavan
Dr. Ruaidhrí Breathnach
Mr. Des Leadon
Dr. Martin Danaher
Dr. Helena Kelly
Ms. Nola Leonard
Dr. Rhodri Evans
Mr. John Moriarty
Mr Ciaran Mellet
Mr. Michael Clancy

WEBSITE DEVELOPMENTS RELATING TO VETERINARY MEDICINES

Regular visitors to the IMB website will have noticed that the Veterinary Medicines Department now has a direct link from the link bar on the home page website. An online reporting form for the notification of suspected adverse events to the IMB has also been introduced and is available by clicking through the Online Reporting icon on the home page and accessing the veterinary form from the Quick Link menu. Another useful change is that henceforth any new advisory, warning or recall notices relating to veterinary medicines will appear under the 'Safety & Quality' Link, which allows for improved searching of such notices on the site.

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The Veterinary Medicines Department is working to improve the content and layout of the site and improvements are expected imminently. A new feature already introduced is the tabulated listing of new products authorised by the IMB within the previous month. This listing is uploaded manually at the start of each month and contains summary information about

the products concerned. The full details of the Summary of Product Characteristics of new products continue to be added shortly after their authorisation. A listing of frequently asked questions is being updated and rearranged so that topics and content can be accessed more easily in the future. Further developments and features are expected over the coming months. Any comments or suggestions for content should be sent to Ms. Michelle Sinnott (michelle.sinnott@imb.ie).

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This Bulletin is designed by Ashfield Press Publishing Services for

IRISH MEDICINES BOARD, KEVIN O'MALLEY HOUSE, EARLSFORT CENTRE, EARLSFORT TERRACE, DUBLIN 2
tel: +353 1 6764971 fax: +353 1 6767836 email: foi@imb.ie: http://www.imb.ie