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HPRA MEDICINAL PRODUCTS NEWSLETTER

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General

Staff Changes

Ms. Deirdre O'Keeffe, Scientific Officer responsible for review of Product Literature, left the Veterinary Sciences Department to take up a new position within the HPRA's Compliance Department. Deirdre was replaced by Ms. Orla Barry, who took up her appointment on 5 May.

Mr. Darragh O'Hanlon took up an appointment as Veterinary Officer on 13 April. Darragh will be involved in the assessment of the safety and efficacy of veterinary medicines, amongst other duties. We wish all well in their new posts.

Regulatory Science Ireland – working together for better patient outcomes

This recently formed body consists of a network of interested parties from Academia, Government Agencies, Pharmaceutical Industry, Medical Devices Industry and the Health Products Regulatory Authority (HPRA). Its aim is the development of an integrated Irish response in the fields of research, education/training and knowledge sharing that will contribute to the global Regulatory Science effort.

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Introduction

In recognition of the global nature of the life sciences industry, the critical mass of the sector in Ireland, its importance in the Irish economy, the overarching imperative of advancing public health and developments in regulatory science internationally it was agreed to establish Regulatory Science Ireland (RSI). RSI is intended to provide leadership and coordination across the three main pillars of research, education and regulatory awareness to influence and provide a collective and concerted strategic leadership over existing and new initiatives, shared issues and challenges, with the ultimate benefit to patients and the Irish public and to develop the life sciences sector in Ireland and contribute to employment and economic development. The intention is that RSI will become a national body with membership open to all scientists and healthcare professionals working in the field of research, education and training, regulatory science outreach in healthcare products and will encourage these activities as the three main pillars of RSI.

Formation of Regulatory Science Ireland 2014

Following a period of discussion principally between academic colleagues in UCC, DIT and HPRA, an information meeting was held in May 2014 to investigate the possibility of engaging other players from industry and other State agencies in Ireland. Forty representative stakeholders were invited and there was unanimous agreement to the establishment of a body to be known as Regulatory Science Ireland (RSI). The body RSI has now been formally constituted with a Board of Directors and an Advisory Committee structure to advise in specialised areas such as research and education.

The current structure has a Board of 10 Directors representing the different parties involved in the process including HPRA, academia, medical device and medicinal product industries, government agencies such as IDA Ireland, Enterprise Ireland etc;. The Board of Directors will represent the various stakeholders listed above and each Director can nominate an alternate. The Board is chaired by two co-Chairs, in the first instance with one coming from academia and one coming from the industry, to ensure balance and any board decisions will require agreement of both the co-Chairs.

Terms of Reference and Rules of Procedure have been adopted for the operation of the Board of Directors which will meet as often as necessary (currently once a month). The Board of Directors are mandated to issue formal statements at least twice a year to the membership, at least once to be at a general meeting. The intention is that such a meeting will be a science based information forum.

It should be noted that initiatives in this field are already underway in a number of countries including USA, Canada and Singapore and that the regulatory authority in each of these countries is collaborating directly or by way of financial support in these initiatives.

RSI will create, through relevant research, training and communication, an environment that:

- Facilitates Irish contributions to an effective response to the increasing complexity of health products and their associated Regulatory Systems;
- Develops a cohort of Irish based Regulatory Science experts and the life sciences sector in Ireland
- Further strengthens the value proposition of Ireland as an attractive location for Health product related activities.

The focus of the three pillars will be:

- Regulatory Science Research – post-graduate MSc/PhD level. Research will provide the foundation for the other two pillars
- Education and training – the intention is to establish suitable training modules in regulatory science
- Periodic Regulatory Conferences/ Symposia – specific topics with a regulatory science focus

The legal entity of RSI is being established as a company limited by guarantee (not for profit) and once established it is hoped to appoint an Executive Director and to secure future funding.

Research Projects

The HPRA has led on developing certain research projects within RSI, the first of which will consider matters related to biosimilar medicines, including prescribing, dispensing, usage, administration, monitoring and any other aspects. The researcher has been appointed and has commenced working on the project under the guidance of HPRA and will be co-supervised in a postgraduate programme by UCC and HPRA colleagues.

The first project under development on medical devices will look at the topic of medical device registries for certain medical devices.

There are other projects on medicine quality defect reporting being developed.

RSI held its first major symposium on March 26 and 27 2015 in Dublin Castle, on the theme of knowledge management. Further details can be found at www.kmdublin2015.ie

Human Products Monitoring

Electronic Reporting of ICSRs to Marketing Authorisation Holders

On receipt of serious ICSRs from healthcare professionals, members of the public, and other sources, the HPRA has a responsibility to forward cases to the relevant marketing authorisation holder (MAH) of the suspect product(s) on an expedited basis in accordance with EU legislation and guidance. In order to assure a safe and timely transfer to MAHs, cases are forwarded electronically in accordance with E2B standards, via the EudraVigilance gateway. Any MAH who has not already registered to receive their cases electronically is now encouraged to do so.

If you wish to receive ICSRs via E2B, please email ***eudravigilance-test@hpra.ie*** with the following information:

- Contact details for the company representative who will manage the testing phase
- The interchange ID for receipt of ICSRs
- Information on which MAHs with licences in Ireland use this Interchange ID (This will allow the HPRA to identify which cases to send to the Interchange ID)
- Contact details for the MAH's Pharmacovigilance department (for general pharmacovigilance queries including case-related queries)

Testing will typically involve submission of a single test case by the HPRA. Once the HPRA has received an electronic acknowledgement the company may go into production for receipt of electronic cases from the HPRA. For further information please refer to the Guide to Electronic Transmission of ICSRs and SUSARs associated with the use of Human Medicines, available on the HPRA website www.hpra.ie.

Medical Literature Monitoring by the EMA

Preparations are ongoing at the European Medicines Agency (EMA) to launch the Medical Literature Monitoring (MLM) service. As a result of Directive 2010/84/EU there is a legal requirement for EMA to monitor selected medical literature sources for reports of suspected adverse reactions containing certain active substances and to enter individual case safety reports (ICSRs) into the EU adverse reaction database (EudraVigilance). This aims to improve safety monitoring of medicines and reduce the administrative burden on MAHs. MAHs will have access to up-to-date results of MLM activities and ICSRs generated for selected medicinal products. The service will aim to benefit the maximum number of companies by focusing on established substances, i.e those substances in multiple medication products.

The EMA has created a dedicated webpage for information related to MLM services (available on www.ema.europa.eu). This webpage includes the list of active substances that will be covered by its new literature monitoring service and a reference to the journals that will be covered by the service, as well as a detailed guide, a training video and a document detailing the inclusion and exclusion criteria to be used when screening the literature. The MLM service will start with a limited number of active substances on 1 July 2015 and will be fully rolled out in September 2015.

MAHs should review the information published by EMA and consider the impact for their business processes. MAHS should particularly note the provisions set out in Article 107(3) of Directive 2001/83/EC which removes the requirement for MAHs to report ICSRs from the listed medical literature and associated with the relevant active substances to the EudraVigilance database, or to concerned national competent authorities such as the HPRA. All other appropriate medical literature should continue to be monitored and any suspected adverse reactions reported in the usual way. Visit the EMA website www.ema.europa.eu for relevant updates and publications relating to MLM services.

Human Medicines

Human Products Authorisation and Registration

HPRA Guide to Combining Multiple Presentations of a Parenteral Product in One Product Authorisation

The HPRA wishes to announce changes to its previous policy in relation to combining multiple presentations of parenteral products in one Product Authorisation (PA). The revised policy is outlined in the new HPRA Guide to Combining Multiple Presentations of a Parenteral Product in One Product Authorisation which has been published on the HPRA website.

The main change introduced in this guide is that it will no longer be an absolute requirement for different presentations of a parenteral product to be presented in the same type of container that is made from the same materials to be listed on a single PA. This will mean that it will be possible for different container types (e.g. ampoules and vials) to be listed on the same PA provided that all other criteria outlined in the guide are met. Similarly it will be possible for bags manufactured using different types of plastic to be listed on the same PA if all other requirements are met.

The new guide will apply immediately for all new applications and variations to add additional presentations of a parenteral product. The guide also provides information for MAHs on how to proceed if they wish to apply to merge existing PAs for authorised medicinal products where the new criteria for merging such PAs are met.

Veterinary Medicines

Planning for new work as Reference Member State

The Veterinary Sciences Department has been successful in serving the needs of the Animal Health industry in Ireland as well as in other EU countries in acting as Reference Member State for outgoing applications over the last several years. We intend to build on this service in the coming years, and would wish your assistance in advising us if you wish us to act in this capacity in the next year, or if there should be changes to plans that have been previously advised to us. Please contact Ms. Elaine Hynes, Planning & Authorisation Manager, (***Elaine.hynes@hpra.ie***) in the first instance.

Raising awareness of updates to summary of product characteristics

Following feedback from stakeholders that it would be useful to alert website users to changes in the authorisation status or significant changes in the conditions of use of veterinary medicinal products listed in the HPRA website, we have introduced a new system to flag certain changes. The system is akin to the monthly update of new products; separate listings will in future be given in relation to withdrawn authorisations and in relation to the updating of certain information in the SPC.

We encourage users of our website to provide us with feedback, both in relation to the user experience and in relation to useful content that we might add. Please email any suggestions to ***michelle.sinnott@hpra.ie***.

Methylisothiazolinone (MI)
in Cosmetic Products

Methylisothiazolinone (MI) is a preservative permitted for use in cosmetic products. It is also used as a preservative in many other products such as household detergents. Preservatives are important in cosmetics in order to prevent their spoilage and enable their safe use by inhibiting the growth of harmful microorganisms that may otherwise pose a risk to the health of consumers.

Regulation (EC) 1223/2009 Annex V/57 currently permits the use of MI as a preservative up to a maximum concentration of 0.01% (100ppm).

There are currently only a limited number of preservatives approved for use in cosmetic products and, due to its broad spectrum of activity, MI has proven a popular choice of preservative for the cosmetics industry over the last decade. While the vast majority of people are not sensitive (allergic) to MI, the continued use of this preservative can result in sensitivity in a small percentage of the population. Indications are that the level of sensitivity to MI is increasing. Symptoms reported include skin dryness, redness, stinging and swelling.

Because of this, European regulations have been, and are currently being, drafted that are aimed at reducing the risk from MI and the incidence of skin sensitivity.

Changes in European Regulations on Methylisothiazolinone

(1) Methylisothiazolinone (MI)

MI is used alone as a preservative, normally at a concentration of 0.01%. The European Commission has proposed a change in the law to remove MI from leave-on cosmetic products. This will be available for public consultation over the coming weeks.

Furthermore, the Scientific Committee on Consumer Safety (SCCS) has been mandated by the European Commission to investigate safe levels of MI in rinse off products following submission of additional safety data on the substance. This SCCS opinion is expected in the coming months.

(2) Methylchloroisothiazolinone (MCI) / Methylisothiazolinone (MI) Mixture

MI often forms part of a mixture with a similar substance, Methylchloroisothiazolinone (MCI), which is used as a preservative in cosmetics. The mixture is deemed not to pose a risk to the health of the consumer when used as a preservative up to a maximum concentration of 0.0015% in rinse-off cosmetic products.

With effect from 16 July 2015:

- The European Commission has banned the mixture of MCI/MI from leave-on cosmetic products that are placed on the EU market;
- Only cosmetic products containing the restricted levels of 0.0015% MCI/MI mixture in rinse -off products will be allowed to be placed on the market.

With effect from 16 April 2016:

- Only cosmetic products containing the restricted levels of 0.0015% MCI/MI mixture in rinse- off products will be allowed on the market.

Consumer Advice

The HPRA advises anyone who experiences any undesirable effects relating to a cosmetic product, to stop using the product immediately and report the incident to their healthcare professional, the responsible person for the product (whose contact details are found on the product packaging) and to ***cosmetics@hpra.ie***

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