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HPRA MEDICAL DEVICES NEWSLETTER

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Letter from the editor

Welcome to the first edition of the medical devices newsletter for 2015. In this edition, we introduce an article from our Director of Scientific Affairs, Dr J. M. Morris on a new regulatory initiative, Regulatory Science Ireland (RSI). RSI is a network comprised of academia, industry, regulators and government agencies involved in health products that are committed to the development of an integrated response in the fields of research, education and leadership in the global regulatory science effort. RSI strives to: create an environment that facilitates Irish contributions to an effective response to the increasing complexity of health care products and their regulatory systems; create a cohort of Irish based regulatory science experts; and strengthen the value proposition of Ireland as an attractive location for health care product related activities.

We feature an article from Ms Kimberly Trautman, Chairperson of the working group of the Medical Device Single Audit Program (MDSAP) of the International Medical Device Regulators Forum (IMDRF) and the US Food and Drug Association's (FDA) Associate Director of International Affairs at their Centre for Devices and Radiological Health (CDRH). The working group is developing a system and standard set of requirements for third party auditing organisations to conduct regulatory audits of medical device manufacturers' quality management systems on behalf of multiple regulatory regions. In February 2015, the HPRA as members of the IMDRF Management Committee hosted a meeting of the working group in Dublin.

We would also like to raise awareness to the communication of information notices to stakeholders. To this end we feature two information notices recently published on our website regarding food intolerance testing and guidelines regarding the use of medical devices in the home.

The discussions on the revision of the medical devices legislation are continuing to progress at the European Council Working Party and we provide an update on its progress in this newsletter. Additionally, we have included regulatory updates on the recent European working group meetings namely the Medical Device Expert Group, MDEG Vigilance, Compliance and Enforcement Group, the *In-vitro* Diagnostics Technical Group and also on the activities at the International Medical Devices Regulators Forum.

As always, the HPRA welcomes feedback on the content of our newsletter and encourages readers to submit suggestions for articles that would be of interest by contacting us at **devices@hpra.ie**

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Regulatory Science Ireland - working together for better patient outcomes

RSI
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.

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**

How RSI Works

The RSI Board of Directors creates an annual work plan in the following three areas.

Research

Education and Training

Regulatory Symposia

The Medical Device Single Audit Programme (MDSAP) – a global approach to quality management system auditing.

In February 2015 the HPRA hosted a meeting of the International Medical Device Regulators Forum (IMDRF) Medical Device Single Audit Programme (MDSAP) working group. This working group, chaired by Ms. Kim Trautman of the US FDA, included participants from Australia, Brazil, Canada, Europe, Japan and observers from the World Health Organisation and the Asian Harmonisation Working Party (AHWP). In addition to HPRA, Europe was represented at the meeting by colleagues from the UK's MHRA and from the European Commission's medical devices unit and from the Food and Veterinary Organisation (FVO). Arising from this the HPRA has invited Kim Trautman to write an article on the MDSAP for our newsletter.

The FDA and its regulatory counterparts abroad have the weighty responsibility of ensuring the safety of the thousands of regulated medical devices imported in their countries each year. To make this task more manageable, FDA and regulatory agencies in Australia, Brazil, Canada, and Japan embarked in 2014 on a pilot called the Medical Device Single Audit Program (MDSAP). Its goal is to develop a process that allows a single audit, or inspection to ensure the medical device regulatory requirements for all five countries are satisfied, in an efficient yet thorough manner.

On January 1, 2015 the MDSAP pilot reached a major milestone – manufacturers around the globe interested in marketing medical devices in Australia, Brazil, Canada, and the U.S. were invited to participate in the program. This summer, when Japan enters the MDSAP as a full member, the same invitation will be issued also to medical device manufacturers interested in marketing in Japan.

February 2015 – IMDRF Medical Device Single Audit Program (MDSAP) Working Group

Under this pilot, audits will be conducted by recognised third-party organisations, and medical device regulators in the participating countries will be able to use these inspection reports when making their regulatory decisions. Not only does this program reduce the participating regulators' need to individually perform routine inspections; it allows them all to have the same reliable information about inspectional findings. Manufacturers, too, can benefit from the MDSAP pilot by cutting down on the number of regulatory audits they have to host, thereby minimizing manufacturing plant and personnel disruptions. This form of international and standardised oversight lessens the burden on manufacturers by bringing more consistency and transparency to the regulatory process.

The MDSAP pilot does not increase regulatory requirements for medical device manufacturers – the audits cover only existing requirements of the regulatory authorities participating. In many cases, these requirements are already harmonised or very similar to one another, such as the international standard for medical devices quality management systems (ISO 13485:2003), the Brazilian Good Manufacturing Practices (RDC ANVISA 16/2013), the U.S. Quality System Regulation (21 CFR Part 820), and other specific pre- and post-market regulatory requirements of the authorities participating in the MDSAP pilot.

The FDA will accept MDSAP audits as a substitute for routine FDA inspections, typically done every two years for all classes of medical devices and including in vitro diagnostic devices. Pre-approval inspections for devices requiring premarket approval applications (PMAs) and "for cause" compliance inspections will not be part of the MDSAP pilot.

Manufacturers that choose to participate in the pilot program will help to shape the policies and procedures of the fully operational MDSAP, which is scheduled to begin in 2017. We expect that the MDSAP pilot will enhance confidence in third party audit programs, increasing the footprint of this global endeavor. The EU Commission is now an Observer to the MDSAP pilot and attended the latest meeting of the MDSAP held at HPRA offices in February.

New information about how countries will participate in the **MDSAP pilot** is available on the FDA's **MDSAP pilot web page**. Manufacturers can find additional information on the **MDSAP web page** which provides information on the auditing organisations involved in the pilot for interested manufacturers to contact directly.

HPRA Communications

HPRA would like to raise awareness to two recent notices published on our website. The first is an information notice relating to the increasing number of food intolerance tests and services being made available in Ireland. These include testing services offered through nutritional and food intolerance centres, certain pharmacies, test kits for people to use in their own home and postal based services where people send blood specimens to a company's laboratory and receive a result through the post or through an online service.

The diagnosis of any condition relating to ability to digest or "tolerate" foods and the level of clinical significance of this including any planned actions, such as dietary restriction, should be made only after careful consultation with your doctor and should not be based on the use of self testing alone and/or use of testing services that have not been recommended by your doctor. The full information notice is available for download **here**.

The second is a safety notice relating to the safe use of medical devices in the home with particular emphasis on users, carers/ family members and healthcare professionals who come into contact with devices on a daily basis. Medical devices used in the home are becoming more complex and sophisticated. There are many potential benefits including improved quality of life and reduced cost of care, however it is fundamental that good medical device management is adhered to in order to reduce the potential for harm associated with the use of medical devices in this environment. The full safety notice is available for download **here**.

Proposals for new regulation on medical devices and *in vitro* diagnostic medical devices – state of play

The first European Council Working Party of the Latvian Presidency took place on the 9th January where the work plan for medical devices was presented. The Latvians have developed a well structured plan of review in order to progress the proposals for a regulation on medical devices and *in vitro* diagnostic medical devices, with an objective of seeking agreement by June at the European Council of Ministers meeting. This would facilitate commencement of discussions with the European Parliament and hopefully final agreement by the end of 2015.

The HPRA continues to support the Department of Health, who head the national delegation, at the Working Party discussions to promote development, achieve compromise and agreement on these two proposals and we are optimistic that a general approach agreement of the European Council will be achievable during the Latvian Presidency.

Regulatory Updates

February 2015 - Participants of the CAMD meeting in Riga, Latvia

CAMD

The State Agency of Medicines of Latvia (SAM) welcomed representatives from the medical device Competent Authorities from the EU Member States, the European Economic Area, and European Free Trade Association countries and representatives from the European Commission to the 36th meeting of the Competent Authorities for Medical Devices (CAMD) on February 24th – 25th in Riga, Latvia.

An update was given by the Chair of the European Council's working party on the revision of the medical device legislation and the Latvian Presidency's plans to progress the discussions to a final agreement. The Latvian authority, SAM, gave an overview of their approach to and experience of medical device regulation.

The main plenary sessions focussed on market surveillance of medical devices and included small group workshops to discuss systems, resources and activities involved in market surveillance. There discussions were based on the European Commission's 20 principles for market surveillance and cross cutting and emerging issues as seen by the chairs of the CIE, NBOG and COEN working groups.

An update was given by the Chair of the CAMD Executive on meetings and priorities to date. The CAMD Executive was established last year to improve the operational effectiveness, communication and coordination of the regulatory system for devices at European level.

Updates were also provided on the work of the COEN, NBOG and CIE working groups. Specific discussions took place on joint market surveillance projects and their planning at European level and on the need for cooperation between the NBOG and CIE to develop guidance relating to clinical aspects for the oversight of notified bodies by authorities.

Clinical Investigation and Evaluation (CIE) Working Group

A meeting of the CIE working group was held on 12 and 13th of March in Brussels. A number of EU Commission guidance documents (MEDDEV) were discussed. With regard to MEDDEV 2.7.1 on clinical evaluation, this guidance is at an early stage of redrafting with comments for change invited from Member States. The MEDDEV 2.7.2 concerning competent authority assessment of a clinical investigation was discussed by Member States and a final draft is nearing completion.

The topic of serious adverse event (SAE) reporting arising from clinical investigations was also the subject of constructive discussion. A revision of the Commission guidelines on this, MEDDEV 2.7.3 was discussed and final amendments were proposed. Representatives of the German competent authority BfArM also presented their work on the development of automated SAE reporting. A number of pragmatic difficulties in automating SAE reporting were discussed. It was agreed to amend draft MEDDEV 2.7.3 regarding SAE reporting to ensure that SAE reports are easier to analyse and that competent authorities adopt similar requirements for reporting standards.

In the plenary session, a representative of the international organisation for standardisation (ISO) updated the group on their progress in drafting a revision to ISO 14155 concerning the clinical investigation of medical devices. A number of ISO working groups are examining topics such as study design, gap analysis and data protection. It is envisaged that the revision will take approximately 2 years to finalise.

Finally the topic of developing Common Technical Specifications for a number of high risk devices was discussed. The benefits of such a system were widely acknowledged by the group and a subgroup will look at the parameters of this prior to the next meeting.

New and Emerging Technologies (NET) Working Group

The New and Emerging Technologies (NET) Working Group met in February 2015 to continue discussions regarding the regulation of novel and new emerging medical devices. Innovative developments in medical device technology present opportunities for increased patient benefit but must also be assessed to ensure that any new associated risks to patients, users and third parties are captured within the regulatory framework. Areas discussed at the February meeting included:

- Discussion of technological and regulatory developments in nanotechnology and applications for medical devices. Items discussed included the finalised SCENIHR opinion and developments of standards in the area.
- Telemedicine and mobile health which relate to medical practices supported by mobile devices were also discussed. The commission (DG CONNECT) launched a broad stakeholder public consultation on the Green Paper on Mobile Health (mHealth) as part of the eHealth Action Plan 2012-2020. The results of this consultation were summarised at this meeting and further discussions were proposed with the Software Working Group.
- The integration of telemedicine and IVDs was discussed along with new developments in the area of companion diagnostics.
- New radiotherapy modalities were highlighted and further discussions with academic researchers in the area were proposed.

Medical Device Expert Group (MDEG) - Vigilance

A meeting of the MD Expert Group on Vigilance was held in Brussels on 2nd and 3rd March 2015. The first day of the meeting involved a closed session attended by Member States and the European Commission with the second day of the meeting also attended by representatives of the medical devices industry.

Brief updates were provided on the proposed new medical devices regulation and the status of IMDRF work items. A progress update was provided on the various MDEG Vigilance taskforces including the development of the device specific vigilance reporting guidance for coronary stents. HPRA is a member of the taskforce developing this guidance and it is hoped that a final document will be published by mid to late 2015. Templates for periodic summary reporting and a new field safety notice form were also discussed.

Discussions included future developments of the medical devices vigilance system, with specific emphasis on the development of a centralised vigilance data bank. Significant progress has been made since the last meeting of the working group and a pilot phase of this project will commence in May 2015. Manufacturers who are participating in the pilot phase will be requested to supply additional information to competent authorities including codes for adverse events and similar incident data. It is hoped that the introduction of standard coding nomenclature will allow for earlier detection of adverse signals. The definition of the term similar incidents was also discussed and EDMA presented a paper on this item.

Promoting user reporting and stakeholder engagement are recognised as key cornerstones of the vigilance system. The HPRA delivered a presentation on national initiatives being undertaken to encourage and empower healthcare professionals to report incidents involving medical devices. The UK Competent Authority, the MHRA, also provided an overview of a proposed European transparency initiative; competent authorities agreed to convene a taskforce to explore this item in further detail.

Working Group on Qualification and Classification of Software

The Borderline and Classification - Software Working Group, consisting of competent authority and industry representatives, met in February 2015. The group discussed, amongst other items, the development of the European Commission guidance on software as a medical device (MEDDEV 2.1/6) and the Manual on Borderline and Classification as tools for providing guidance to developers of software as a medical device. The group discussed some of the recent software entries to the Manual on Borderline and Classification that had been agreed by the group. Also discussed was the recently published Green Paper on mobile health (mHealth) in the EU and documents developed by the IMDRF Software working group.

Compliance and Enforcement (COEN) Working Group

The Compliance and Enforcement Group (COEN) met in Brussels in January 2015. During the meeting there were discussions around the development of guidance documents on market surveillance. Specific market surveillance activities and projects were also discussed. The development of a joint project on market surveillance involving a number of European countries was further discussed.

The IMDRF Management Committee Meeting

The IMDRF Management Committee met in Tokyo from 24-26th March. The seventh meeting of the Management Committee included regulator members from Australia, Brazil, Canada, China, the European Union, Japan, the Russian Federation, and the United States of America. The EU delegation was led by the EU Commission and includes three Member State representatives from France, Germany and Ireland (HPRA).

The Management Committee discussed ongoing work in relation to the Medical Device Single Audit Program (MDSAP), National Competent Authority Report (NCAR) exchange programme, developing a list of Recognized Standards in each global region, finalising a pilot for Regulated Product Submission (RPS) for medical devices and developing guidance on Software as a Medical Device (SaMD). An update on Medical Device Patient Registries was also communicated to attendees. A new item on adverse event coding and nomenclature was also agreed and initiated.

The stakeholder session involved over 200 participants primarily from industry. Representatives from each regulatory region made presentations about regulatory development. The industry provided feedback on their perception of IMDRF work items and operations. The Global Medical Technology Alliance (GMTA) presented a proposal for a New Work Item on acceptance and barriers to acceptance of standards. Industry expressed concern about the implementation of IMDRF decisions and initiatives in each regulatory region. In addition they also flagged their wish to become more engaged and involved in IMDRF work and strategy.

Outcome statements and further information on the IMDRF Management Committee meeting can be found at **www.imdrf.org.**