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HPRA MEDICAL DEVICES
NEWSLETTER

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In this Issue

Ms Lorraine Nolan has been appointed as the new Chief Executive of the HPRA. Ms Nolan, who takes up office with immediate effect, previously held the position of Director of Human Products Authorisation with the HPRA where she oversaw the evaluation and authorisation of medicines and medical devices for the Irish market. Ms Nolan has extensive experience of the public health sector, the health product sector and the regulatory landscape. She will be responsible for the management of the HPRA whilst leading the organisation nationally and internationally in its ambition to protect and enhance human and animal health.

During her career to date, Ms Nolan has held a number of senior positions within the HPRA spanning the pharmaceutical assessment, products distribution and controlled drugs' departments. Prior to joining the HPRA in 2001, she was Controlled Drugs Manager with the Department of Health and a Forensic Scientist with the Department of Justice, Equality and Law Reform.

Ms Nolan holds a PhD in Chemistry and a Degree in Chemistry from Trinity College, Dublin. Ms Nolan has 20 years of technical and scientific experience attained through working in regulatory (including policy development), technical, senior management, industry and public service areas within the HPRA. She has significant acumen of the public health sector with respect to medicines and health products regulation through managing frontline interaction with manufacturers, distributors, marketing authorisation holders and other stakeholders in this area.

Ms Nolan has an established profile within the national, European and international institutions for medicines, medical devices, cosmetics and controlled drugs regulation. She is a member of the European Medicines Agency (EMA) Management Board; was previously an advisor to the UN's International Narcotic Control Board and represented Ireland at European Committees in the Cosmetics and Drug Precursor areas.

Ms Nolan succeeds Mr Pat O'Mahony who took up the position of Deputy Secretary at the Department of Health in September 2015.

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Clinical investigations of medical devices

Clinical investigations is the legal term for clinical studies or trials conducted in human subjects to verify the safety and performance of a medical device. The HPRA is responsible for reviewing applications to conduct clinical investigations of medical devices in Ireland. The HPRA is keen to ensure that its review of investigations affords for protection of the health of patients enrolled in such studies while also ensuring the process for review is effective and understandable for applicants. In this edition we take a look at Clinical Investigations in order to provide an overview of the relevant guidance available to sponsors intending to submit an application for clinical investigations to the HPRA. To this end we have provided a brief review of the International harmonised Standard EN ISO 14155 Clinical Investigation of medical devices for human subjects – Good clinical practice; an update on the Clinical Investigation guidance in Europe; and an overview of the practical considerations of submitting an application for a clinical investigation to the HPRA. Our focus on clinical investigation within this edition was chosen based on the recent HPRA newsletter questionnaire, to which we received a number of requests for an article on the clinical investigation process in HPRA.

Clinical Investigations and the Role of the HPRA

The aim of a clinical investigation (CI) is to generate data to support the CE marking of a medical device. A CI can be used to verify, under normal conditions of use, that the performance of a device meets that intended by the manufacturer. CI's are also used to determine any undesirable side effects with the device. Investigations should be designed such that they follow a methodologically sound procedure.

Under medical devices legislation the manufacturer, or Authorised Representative, must notify the HPRA if their clinical investigation is to be undertaken in the Republic of Ireland. Only certain types of clinical investigation involving medical devices require notification and review by the HPRA prior to commencement. In general, clinical investigations which require review by the HPRA are proposed by commercial sponsors, typically medical device manufacturers evaluating a new non-CE marked medical device. Where CE marked devices are being investigated for commercial use outside of their intended purpose (for example use of the device for a new function, or modification of the device) an application should be submitted to the HPRA for review. Device investigations solely for the purposes of clinical or academic research, with no commercial intent, may not require review by the HPRA prior to commencement. The HPRA is happy to provide advice on applications on a case by case basis. For further information on when to submit a clinical investigation to the HPRA for review please refer to guidance on our **website**.

The HPRA Clinical Investigation Review Process

Once a completed CI application has been received by the HPRA there is a 60 day review process (as stipulated under medical devices legislation). Proposed investigations are reviewed by the HPRA on considerations of public health and safety. Applications will receive a unique identification number, CIV ID, for the purposes of notification to the EUDAMED database. After an initial 30-day review of regulatory, technical and clinical aspects of the application by the HPRA panel of reviewers, questions relating to the CI may be addressed to the investigation sponsor. The sponsor must provide satisfactory responses to these issues within an allotted timeframe, typically 14 days. By day 60 of the review process the final decision of the HPRA is communicated to the sponsor.

Where there is a favourable outcome a 'Letter of No Objection' is issued and the clinical investigation may proceed. Often there may be specific conditions attached to the 'Letter of No Objection', and the CI should only proceed once all conditions have been satisfied. Occasionally the HPRA may object to the conduct of an investigation on the basis of public health concerns. In this instance the HPRA clearly communicates the reasons for its objection to the sponsor. In circumstances when the HPRA objects to or significantly modifies an investigation or when an investigation is suspended, the HPRA is obliged to communicate this to other Member States and the Commission.

In order for any clinical investigation to commence in Ireland, both the HPRA and the relevant Ethics Committee must have issued a final positive opinion. The HPRA operates a 'parallel review' to the Ethics Committee review i.e. the HPRA application can be made while the ethics review is underway.

The positive opinion of the Ethics Committee must be submitted to the HPRA prior to commencement of the study.

As detailed in the opening article, the HPRA recommends that sponsors submitting clinical investigation applications refer to ISO 14155:2011 *"Clinical investigation of medical devices for human subjects – Good Clinical practice"* for guidance on the documentation to submit as part of the application. The documentation submitted is assessed from regulatory, technical and clinical perspectives by a panel of reviewers within the HPRA. Advice may also be sought from individuals outside the HPRA who have expertise relating to the clinical use of the specific device type. External technical expertise may also be sought for certain devices. When an external expert is utilised by the HPRA our protocols relating to protection against conflict of interest and confidentiality are followed.

The sponsor (i.e. party responsible for the clinical investigation) must be prepared to make all necessary data available during the review process. Sponsors are typically medical device manufacturers. Principal investigators are typically medical practitioners. Principal/clinical investigators must report all adverse events and device effects arising in the course of the study to the sponsor, who in turn should inform the HPRA. A sponsor must submit a report which summarises the results of the clinical investigation within one year of it ending.

How to apply

Applications to conduct a clinical investigation in the Republic of Ireland can be submitted to the HPRA using the application form on our **website**. Applications may be submitted at any stage throughout the month, however the 60 day review process will not start until the subsequent monthly cut-off date. A list of cut-off dates for the submission of clinical investigation applications is available on our website. Prior to submission of an application the HPRA recommends a pre-submission meeting to go through the clinical investigation application process, typically this meeting occurs 1 month prior to submission. Further details regarding fees are available on our website. Please note if an amendment to a clinical investigation, which has previously received a 'Letter of no objection', is required, sponsors must submit an application form for an amendment to a clinical investigation on medical devices. Information on amendments is also available on our website.

If a proposed clinical study aims to generate clinical data on both the medical device and a medicinal product a single application may be submitted to the HPRA using the Clinical Trials application process **(see the HPRA website for further guidance)**. The study is required to comply with the clinical trials legislation for the investigational medicinal product and the medical devices legislation for the device. The application process will follow the timelines set out in clinical trials legislation and no clock-stops are permitted. A single approval decision will be issued for the study. Further advice on clinical investigations involving specific combination products is available from the HPRA on request.

Further information on clinical investigations is available on the HPRA website: **https://www.hpra.ie/homepage/medical-devices/regulatory-information/clinical-investigations**

EN ISO 14155 Clinical Investigation of medical devices for human subjects – Good clinical practice

Clinical investigations are studies conducted in human subjects to verify the safety and performance of a medical device.They are typically carried out by research groups during the design and development of new or modified medical device prototypes and the HPRA is responsible for reviewing the clinical investigation prior to commencement.

EN ISO 14155 is the harmonised standard for clinical investigations of medical devices in human subjects. The standard outlines how to design, conduct, record and report medical device clinical investigations. It defines the responsibilities of the sponsor and principal investigator and assists sponsors, investigators, ethics committees, regulatory authorities and other bodies in the design, assessment and conduct of clinical investigations.

The document gives detailed information about ethical considerations and the responsibilities of the sponsor and investigators. It also details the involvement of the ethics committee during an initial review and the ongoing involvement of the ethics committee during the conduct of the investigation. Key principles of informed consent are also covered in the document. These considerations include information that should be provided to the subject at the start of the investigation, risks and benefits of the trial, who to contact with queries and information about alternative procedures and therapies available.

Considerations for the planning and conduct of a clinical investigation are covered in this document as well. The planning section has an overview of how to proceed with a risk evaluation, the justification for the clinical investigation design, the clinical investigation plan (CIP) and clinical investigation brochure (CIB). The CIP, the CIB and clinical investigation reports are also outlined in greater detail in the annex to the standard.

In relation to the conduct of a clinical investigation, examples are provided as to how to store electronic data, amendments to documentation and auditing investigations are listed. In addition the document covers details relating to the close out, termination or suspension of a clinical investigation. The responsibilities of sponsors are fully reviewed covering everything from quality control to safety evaluation.The principal investigators responsibilities for the investigation and their responsibilities for the medical care of the patients are also explained in detail.

In summary, EN ISO 14155 is a comprehensive good clinical practice document that covers all aspects of clinical investigations of medical devices in humans from the initial design phase to the final close out phase; the HPRA recommends all applications submitted to be in accordance with this standard.

Recent updates to Clinical Investigation Guidance in Europe

MEDDEV Guidelines are developed by European Commission working groups to assist in a harmonised interpretation and application of the Medical Device Directives in Europe. While these guidelines are not legally binding, they are developed in working groups such as the Clinical Investigation and Evaluation working group with intensive collaboration with interested parties in the medical device sector such as Competent Authorities, academic and industry representatives, European Commission services and other interested parties and it is expected that these guidelines will therefore be followed.

A clinical investigation (i.e. trial of a medical device) is a systematic study undertaken on one or more human subjects, in order to assess the safety or performance of a medical device which either does not bear the CE mark or a device which bears the CE mark but is being used outside of the specified indications for use for that device. All clinical investigation applications must be submitted to both a competent authority and the ethics committee responsible for the investigation site and the applications must receive a favourable opinion in order for a study to proceed. Two important updates to MEDDEVs entered into force this year concerning clinical investigations as regulated in the Medical Device Directive 93/42/EEC and the Active Implantable Medical Device Directive 90/385/EEC.

MEDDEV 2.7/2

The first is MEDDEV 2.7/2 Revision 2 concerning the guidelines for competent authorities in the assessment of clinical investigation applications which came into effect in September 2015 and replaces the previous MEDDEV from 2008. The purpose of this revised document is to harmonise the approach taken by competent authorities in different Member States in Europe in their assessment of applications. These guidelines will also inform Ethics Committees throughout Europe as to assessments undertaken and the standards expected in applications.

The revision to MEDDEV 2.7/2 presents far greater clarity, detail and guidance with respect to the types of considerations that are needed with a greater emphasis placed on the type of study planned, for example whether this is an early first in man study or pivotal study etc.

There is much greater alignment and emphasis placed on the harmonised standard EN ISO 14155, which details the general requirements for good clinical practice in the design, conduct, recording and reporting of a clinical investigation. There is also greater device and study specific guidance, for example with regard to justifications of the duration of follow-up, retrieval of implanted investigational devices and a justification of when interim reports should be prepared.

The MEDDEV also provides guidance on the considerations which prompt the suspension by a Competent Authority of a clinical investigation and the communications that are expected to be shared with the Ethics Committee concerned and the other Competent Authorities concerned in the study. Likewise there is guidance on the temporary halting or termination of a study by the sponsor of that study, with guidance on timelines and the type of information that should be shared with interested parties.

It is hoped that this guidance will help to promote and better protect the safety of subjects who decide to take part in clinical investigations in Europe and to provide enhanced predictability to the various stakeholders involved in the conduct and review of clinical investigations.

MEDDEV 2.7/3

A second and related piece of guidance regarding clinical investigation is the MEDDEV document 2.7/3 Revision 3 which provides guidance on the serious adverse event (SAE) reporting of active clinical investigations to Competent Authorities. These guidelines on SAE reporting came into force in May 2015. This document provides guidance and a sample SAE report table. One important development is further detail on the assessment of causality concerning the use of the device in the clinical investigation and the adverse event which occurred. There are now five different descriptors of causality: not related, unlikely, possible, probable and causal relationship. These are defined and greater detail is given for sponsors and investigators in the MEDDEV document. In addition to this, it is necessary to determine if the SAE is related to the device, the procedure or both. It is hoped that this guidance will enhance the oversight and safety of subjects taking part in clinical investigation. In addition a new SAE reporting form has been prepared for the purposes of reporting to Competent Authorities.

Sponsors involved in ongoing studies in Ireland should contact the HPRA regarding the impact of these changes to their study.

Mobile Apps – are they medical devices?

There are many apps readily available that are intended for use within the healthcare setting - are these apps medical devices? In this article we outline some key considerations for the manufacturer in determining the appropriate regulatory framework for their app.

With the advances in mobile technology in recent years, such as smart phone and tablets, there has been a large increase in the use of software both within healthcare facilities and in patient's homes. Mobile devices allow users quick and easy access to the functionality provided by different 'mobile applications' or 'apps'. The range of functions performed by these apps is vast and new apps are appearing on the market at an increasing rate. As with all software, an app may be considered a medical device when it is intended for a purpose that meets the definition of a medical device as defined in S.I. 252 of 1994[1], 'The Regulation', and must then comply with the requirements of the medical device legislation.

Mobile apps and healthcare

Apps are readily available across all platforms such as Android, Windows and IOS. There are many apps readily available that are intended for use within the healthcare setting. However, not all of these apps are considered medical devices, for example apps for general health and wellbeing such as those that record lifestyle habits such as smoking and exercise. Other apps are clearly intended to be used for a medical purpose and as a medical device, for example, apps that claim to diagnose skin lesions or calculate drug dosages.

Medical device regulation and guidance

Under the medical devices regulatory framework, it is the responsibility of the manufacturer to determine whether their app meets the definition of a medical device.

In addition to mobile apps, amendment S.I. 110/2009 to the Regulation[2] recognises that standalone software run on personal computers can also be classified as a medical device in its own right if it fulfils the definition of a medical device.

Mobile apps fulfilling the definition of medical device and intended to be used for the purpose of providing information derived from in vitro examination of a specimen derived from the human body may also fall under S.I 304 of 2001[3], as amended.

Software developers without experience in the field of medical devices may not be familiar with the requirements of The Regulation. For example, the inclusion of a disclaimer on an app stating that the app is for educational purposes does not disqualify an app as a medical device. Users can also be unsure as to whether or not the app they are using is a medical device. It is often assumed that because a mobile app is used within a healthcare setting it automatically qualifies as a medical device. In determining the qualification of an app, as with all software as a medical device, consideration should be given to whether:

[1] S.I. 252 of 1994 European Communities (Medical Devices) regulations, 1994, as amended, transposes Council Directive 93/42/EEC concerning medical devices (MDD 93/42/EEC) into national law and is referred to in this article as 'The Regulation'.

[2] SI 110/2009 amendment transposes amendment 2007/47 to MDD 93/42/EEC into SI 252/1994.

[3] SI No 304/2001 – European Communities (In Vitro Diagnostic Medical Devices) Regulations, 2001

- the app is performing an action on data limited to storage, archival, lossless compression, communication or simple search (in which case it is unlikely to be a medical device)
- the action performed by the app is for the benefit of an individual patient (software cumulative analyses of data from multiple patients may not be a medical device)
- the action performed is for a purpose included in the definition of a medical device in the Regulation
- the app is acting as an accessory to a medical device

These criteria are defined in greater detail in the European Commission guidance document **MEDDEV 2.1/6** 'Guidelines on the qualification and classification of standalone software', which provides additional guidance to manufacturers on determining whether software, including apps, qualify as medical devices.

Key considerations

It is essential that all manufacturers of apps determine whether their app could fall within the remit of the medical device Regulation. As referenced above MEDDEV 2.1/6 is a useful document for determining whether a mobile app qualifies as a medical device. If an app qualifies as a medical device then the obligations of a manufacturer under the medical device legislation apply to the app manufacturer. All medical devices, with the exception of devices that are custom-made or intended for clinical investigation, placed on the market must bear the CE mark.

The Regulation provides clear definitions for a 'manufacturer' and for 'placing on the market'. It is important to note that a person who places an app on the market under their own name, even though they may not have developed the software themselves, is considered the manufacturer under the Regulation. Similarly making a mobile app or any other medical device available for use online or for downloading, whether for a fee or free of charge, is considered to be placing on the market, and therefore the app must comply with the medical device legislative requirements.

Some additional considerations include:

- **Classification**

  Standalone software is treated as an active medical device under the Regulation and must be classified accordingly in accordance with Schedule 9 of the Regulation. Following the classification rules in schedule 9 of the Regulation it is evident that a large proportion of medical device apps fall under the Class I risk classification. As such manufacturers may find the HPRA **Guide for Class I Manufacturers on Compliance with European Communities (Medical Devices) Regulations, 1994** useful. This document provides guidance on the different processes involved in affixing a CE mark to a Class I medical device. However it must be emphasised that every medical device mobile app must be classified in accordance with classification rules in schedule 9 of the Regulation on a case by case basis, taking into consideration the intended purpose and functions of the app.

  The 'Manual on Borderline and Classification in the Community Regulatory Framework for Medical Devices' also includes specific examples of how certain standalone software and medical apps might be classified.

- **Essential Requirements**

  Medical device apps must meet the essential requirements detailed in schedule 1 of the Regulation, taking account of the intended purpose of the devices concerned.

- **Clinical Evaluation**

  In accordance with schedule 1 part 1(6a) of the Regulation the demonstration of conformity with the essential requirements must include a clinical evaluation for all medical devices, regardless of the risk classification. For further information refer to schedule 10 of the Regulation and also **MEDDEV 2.7/1** "Clinical evaluation: Guide for manufacturers and notified bodies" on the European Commission website.

  It is worth noting that, in addition to national and European level guidance, the International Medical Device Regulators Forum (IMDRF) has produced guidance on 'Software as a Medical Device' and is currently in the process of developing guidance on the application of clinical evaluation to medical device software.

- **Technical Documentation**

  A manufacturer or his authorised representative must hold technical documentation that demonstrates the conformity of their device with the provisions of the Irish regulations and related directives that apply to them. This technical documentation must be generated prior to drawing up the EC declaration of conformity.

- **Registration**

  Manufacturers and European Authorised Representatives of certain medical devices including class I medical devices that are based in Ireland must register themselves and their devices with the HPRA. For more information on registration criteria please refer to the **HPRA website**. Medical device apps that meet these criteria must therefore be registered with the HPRA.

For further information or guidance on the application of the medical device legislation to apps please submit all queries to **devices@hpra.ie**

National Medical Device eAlert System

Speakers at the eAlert Launch: From L-R Mr Liam Hackett, National Medical Device Equipment Advisor, Community Services HSE; Dr. Joan Gilvarry, Director of Human Products Monitoring, HPRA; Ms. Caroline Conneely, National Decontamination Quality Lead HSE; Mr. Ronnie McDermott, National Medical Device Equipment Advisor, Acute Services HSE; Ms. Anne Tobin, Medical Device Vigilance Manager HPRA; Ms. Marie Kehoe-O'Sullivan, Director, Safety and Quality Improvement, HIQA; Dr. Philip Crowley, National Director of Quality Improvement, HSE; Mr. Ger Flynn, National Clinical Head of Medical Devices HSE.

A newly developed National Medical Device eAlert System designed to streamline the management of medical device safety notices within the public health system was launched at the Royal College of Physicians in Ireland on November 30th. Developed by the HSE (Health Services Executive) National Medical Devices Equipment Management Committee, in collaboration with the Quality Improvement Division (QID) and with assistance from the Health Products Regulatory Authority (HPRA), the aim of the eAlert system is to provide each HSE or HSE-funded voluntary service location assurance in the management of medical device safety or quality related notices issued by the HPRA.

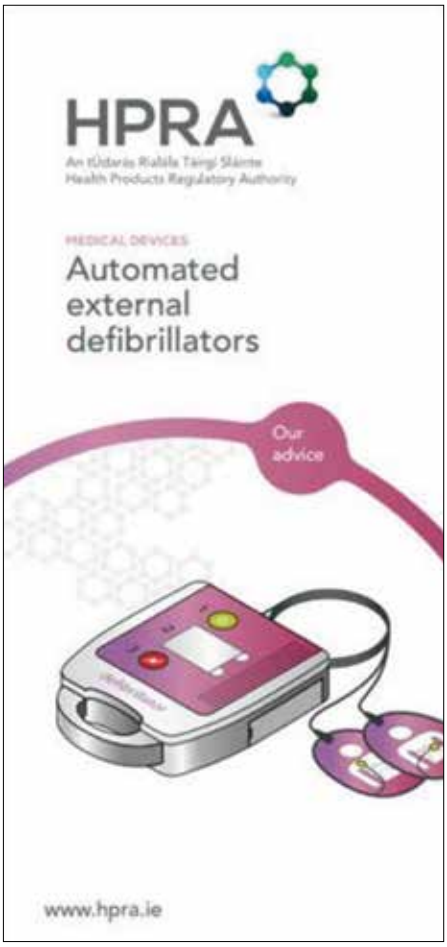
The occasion also saw the launch of a HSE Medical Device Management 'Quality Assessment and Improvement Tool (QA+I tool)' to facilitate assessment against the HSE Medical Device Equipment Management Policy and Best Practice Guidance.

A key component of the medical device vigilance system is the dissemination of information, which may be used to prevent recurrence of an incident or to alleviate the consequences of such incidents. As the national competent authority for medical devices, the HPRA publishes notices relating to the safety and/or quality of medical devices on its website www.hpra.ie. The majority of these notices are for the attention of health professionals including those working in hospitals, community healthcare organisations and other health facilities. The national eAlert system receives notification directly from the HPRA of all safety notices or any internally generated HSE safety notifications for distribution. A priority level is assigned to each alert in accordance with the HPRA traffic light system of red (Priority 1, most urgent), amber (Priority 2) and green (Priority 3, least urgent).

The medical devices eAlert system has been implemented and is available throughout the HSE and voluntary hospitals. The web-enabled system is hosted by the HSE's ICT centre and will facilitate the nomination of a 'designated person / vigilance officer' within hospitals, community healthcare organisations and other health facilities to take responsibility for the receipt of the medical device alert notifications. The 'designated person / vigilance officer' will ensure the further internal facility distribution to the relevant personnel for implementation of the recommended actions where applicable. An automated response timescale (associated with the priority level) is also assigned by the HSE to each notification within which the relevant action must be reported back by the designated person / vigilance officer to the central ICT system as having been completed, or not being applicable, or some other outcome was required. The eAlert system provides for an extremely efficient method of disseminating safety information to key medical device users and will contribute to enhanced patient safety across all the health facilities involved. Healthcare professionals and medical device users are reminded to remain vigilant for field safety notices issued by medical device manufacturers as these will not be circulated via the eAlert system. The HPRA will continue to upload a monthly summary of field safety notices known to affect the Irish market on the website **www.hpra.ie**.

As part of its ongoing work to encourage user reporting, the HPRA in collaboration with the QID and Medical Device Equipment Management Committee developed a Step-by Step guide to facilitate users in reporting medical device adverse events. This guide was also launched on November 30th and will be circulated to all users in the Acute Service and the Community Healthcare Organisation in early 2016. Relevant guidance is available for download from www.hpra.ie.

Automated External Defibrillators – managing your device – important information



An automated external defibrillator (AED) is a medical device that analyses a person's heart rhythm and, when needed, delivers a shock to sudden cardiac arrest (SCA) victims who are in a shockable heart rhythm. A defibrillator can play a potentially lifesaving role. Used correctly, it can improve a person's survival chances following SCA. However, defibrillators need to be accessible and in good working order at all times in the event that they are needed for an emergency situation.

The HPRA recently ran a media campaign centred on AEDs. The aim of the media campaign was to ensure that AED owners were aware of the need to manage these devices appropriately and also to ensure that they cooperated with the manufacturer to ensure that outstanding field safety corrective actions (FSCA's) are completed as appropriate.

The HPRA has been concerned that a number of mandatory FSCA such as software upgrades or devices modifications have not been completed in a timely manner as a result of difficulties for the manufacturer or supplier of the device in contacting the person or organisation to which it was supplied. The HPRA are aware of some 940 defibrillators in Ireland, incorporating five particular models, where a FSCA remains outstanding for these reasons. Certain manufacturers have been unable to complete their actions due to difficulties in locating affected devices.

The HPRA has published a press release calling on all organisations with automated external defibrillators (AEDs) to;

1. Urgently check that the recommended safety and maintenance updates on their device have been undertaken. Updates to these AEDs are needed immediately to ensure that the devices will work as necessary in a life-saving situation. All outstanding field safety notices for defibrillators are listed and linked below. Outstanding Field Safety Notices (as of 10 November 2015)

   Lifepak CR Plus (Physio Control Inc)

   Lifepak 1000 (Physio Control Inc)

   AED Plus (Zoll)

   Samaritan PAD, 300, 300P (HeartSine)

   Samaritan 500P (HeartSine)

2. Ensure that AED owners follow the manufacturer's instructions around device maintenance and storage etc. Further guidance can be found in the HPRA's information leaflet: **Automated external defibrillators - Our advice.** This leaflet provides advice on selecting and purchasing an AED for use in a community setting as well as recommendations for maintaining the device after it has been purchased.

The HPRA developed a 2-pronged approach to help in addressing this. Firstly a press release and dedicated **AED section on the HRPA medical devices website** was created. Secondly, targeted letters to stakeholders were created as well as a list of any group or organisation that could possibly own an AED. The targeted letters were sent out on 19th November to a list of 158 organisations including sporting authorities, local authorities, and retail sector organisations.

In the media campaign the HPRA stressed that if an update or other action is identified and communicated by the manufacturer to the owner, through the publication and distribution of what is known as a 'field safety notice', then this should be undertaken immediately. Otherwise the AED may not work properly when it is needed.

Regulatory updates and developments

Figure 3: November 2015 – Delegates of the 37th CAMD meeting in Clontarf Castle, Dublin.

Proposals for a new regulation on medical devices and in vitro diagnostic medical devices

The final European Council Working Party of the Luxembourgish Presidency took place on 14th December and good progress has been made since June. In September the European Council reached a 'general approach' position on the proposed Regulations for medical devices and *in-vitro* diagnostics. This allowed for the initiation of trialogue with the European Parliament and EU Commission on the dossiers.

The Presidency is negotiating the medical device and *in-vitro* diagnostic proposals in parallel through the trialogue process.

The Dutch are due to assume the Presidency in January 2016 and have a clear plan to progress and finalise the discussions. The HPRA continues to support the work of the Department of Health who head the national delegation at the Working Party discussions to promote agreement on these two proposals.

CAMD

The HPRA hosted the 37th Competent Authority Meeting for Medical Devices (CAMD) on behalf of the Luxembourg Presidency of the European Council, over two days from the 17-18th November. The meeting was attended by over 60 delegates from 25 countries and included representatives from the EU Commission's DG GROW, the FVO and the JRC.

The meeting focused on developing the regulatory system further in preparation for the anticipated revision of the medical device legislation. One of the key focuses was to agree priorities and work plans for co-funded joint actions in medical device market surveillance under the European Health Programme 2014-2020. In addition a workshop was held to focus on a number of operational topics including EU level coordination, communication, information systems, learnings from vigilance taskforces and management of certificate notifications.

EU working groups update

Notified Body Operations Group (NBOG)

The Notified Body Operations Group (NBOG) met in September where the focus of the meeting was on the progress of joint assessments of Notified Bodies to Commission Implementing Regulation 920/2013 and the future tasks resulting from the revision of the medical device Directives. The issue of Notified Body resources was raised in the context of unannounced audits. The Commission highlighted the future implementing acts for the modalities of assessment of Notified Bodies, the first task being the development of the new IVD scope expressions.

IMDRF EU coordination meeting

The International Medical Device Regulators Forum (IMDRF) EU coordination meeting was hosted by the EU Commission in preparation for September's meeting of the IMDRF in Japan. The key topics discussed included the EU pilot for Regulated Product Submissions (RPS) and the EU participation as observers within the Medical Device Single Audit

Programme (MDSAP). A new work item proposed on clinical evaluation principles for Software as a Medical Device (SAMD) initiated by the US FDA was presented. In addition the FDA is seeking to agree a new work item on competency requirements for pre-market reviewers of medical devices. The IMDRF strategy 2016-2020 was also discussed in advance of its finalisation at the September meeting.

MDEG Vigilance

A meeting of the MD Expert Group on Vigilance was held in Brussels on 9th and 10th September 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. Progress updates were provided by the various MDEG Vigilance taskforces including the development of the device specific vigilance reporting guidance for coronary stents.

The Taskforces working on revisions to the MEDDEV 2-12.1; the trending taskforce, the coordination taskforce and the taskforce looking at the Field safety notice template all provided updates on their work. Industry comments were also sought in the open section of the meeting. Further work will be required before the taskforces will be able to merge their recommendations into rev 9 of the MEDDEV 2-12.1.

The MHRA provided a progress report on the MIR form Pilot project. The Pilot will continue to run in order to accumulate more reports for analysis. Updates were provided by the different device specific taskforces: MoM, Radiotherapy and ALCL.

Industry presented a paper on periodic summary reports which proposed that a template document should be developed. This proposal will be given consideration by member states.

New and Emerging Technologies Group (NET)

The New and Emerging Technologies (NET) Working Group met in September 2015 to continue discussions regarding the regulation of novel and new emerging medical devices. Areas discussed at the meeting included:

- Technological and regulatory developments in nanotechnology and applications for medical devices. A report on the potential impact of the proposed Regulation relating to nanotechnology on devices currently on the market was discussed.
- Telemedicine and mobile health which relate to medical practices supported by mobile devices, including the Green Paper on Mobile Health (mHealth).
- Methodologies applied to future horizon scanning.

IVD Technical Group

The IVD Technical Group convened a meeting by Teleconference on 29th September 2015. In the open session, a presentation was given on the overview and outcome of the EQALM questionnaire. A discussion took place on how Competent Authorities and EQA providers could work more closely together. An update was provided on the draft work programme of the group which included Syphilis CTS, Companion Diagnostics, and the new Classification System.

Clinical Investigation & Evaluation (CIE) Working Group

The CIE working group met in Brussels on 9th and 10th of November where the revision of the MEDDEV Clinical Evaluation guidance was discussed. Substantial progress has been made and further consultation will continue in order to finalise this. Two other guidance documents on clinical investigations and serious adverse event reporting are also being finalised.

The European Society of Cardiology (ESC) presented a paper concerning the clinical evaluation of coronary stents. This paper will provide useful material as part of a collaborative approach to assist in updating the current European guidance on the clinical evaluation of coronary stents.

The group was also updated on work being led by the MHRA regarding percutaneous aortic valves (TAVIs). The HPRA is part of this taskforce and it is hoped that this work will add to the guidance available for high-risk devices and will help to establish an approach for common specifications for high risk devices in the Medical Devices Revision.

Representatives of the Italian competent authority presented a mock-up clinical investigation to the members of the group. Interested parties were invited to appraise a mock clinical investigation application and to upload their findings to EUDAMED in order to share experiences. This will hopefully lead to closer cooperation regarding the appraisal of clinical investigation in light of the requirements of the draft Medical Device Regulation (MDR).

Pilot Inspection Programme for Distributors of Medical Devices

The HPRA is responsible for monitoring the safety and performance of medical devices in Ireland throughout the device lifecycle. In discharging our role as market surveillance authority, the HPRA carries out a range of market surveillance activities which also includes auditing medical device manufacturing facilities. The proposals for a regulation on medical devices and in vitro diagnostic medical devices, will introduce new requirements and obligations for all economic operators, including distributors. These are anticipated to essentially constitute Good Distribution Practice (GDP) for medical devices.

In preparation for the adoption and implementation of the new proposed Regulations, the HPRA have invited distributors of medical devices to participate in a pilot inspection programme. The intention of this series of inspections is to promote compliance by facilitating distributors in gaining feedback on the standard of GDP within their facilities as well as an opportunity for HPRA to gain an understanding of current industry practices. The pilot inspections will be fact-finding and the outcomes presented to participants as 'opportunities for improvement' in terms of future requirements for distributors upon implementation of the new Regulations. It is expected that these pilot inspections will take place during Quarter 1, 2016.

Stakeholder survey - Feedback

In our September edition of the newsletter we published a link to our Newsletter Stakeholder Survey in order to ensure we review your needs in terms of our newsletter communications and ensure the newsletter is tailored to meet those needs. The survey has concluded and we received a total of 122 responses – some of the results are summarised below. We would like to thank all of you that participated in the survey and as always we welcome any feedback on the content of our newsletter and encourage our readers to submit suggestions for articles of interest to **devices@hpra.ie**

Figure 1: stakeholder grouping of our readers

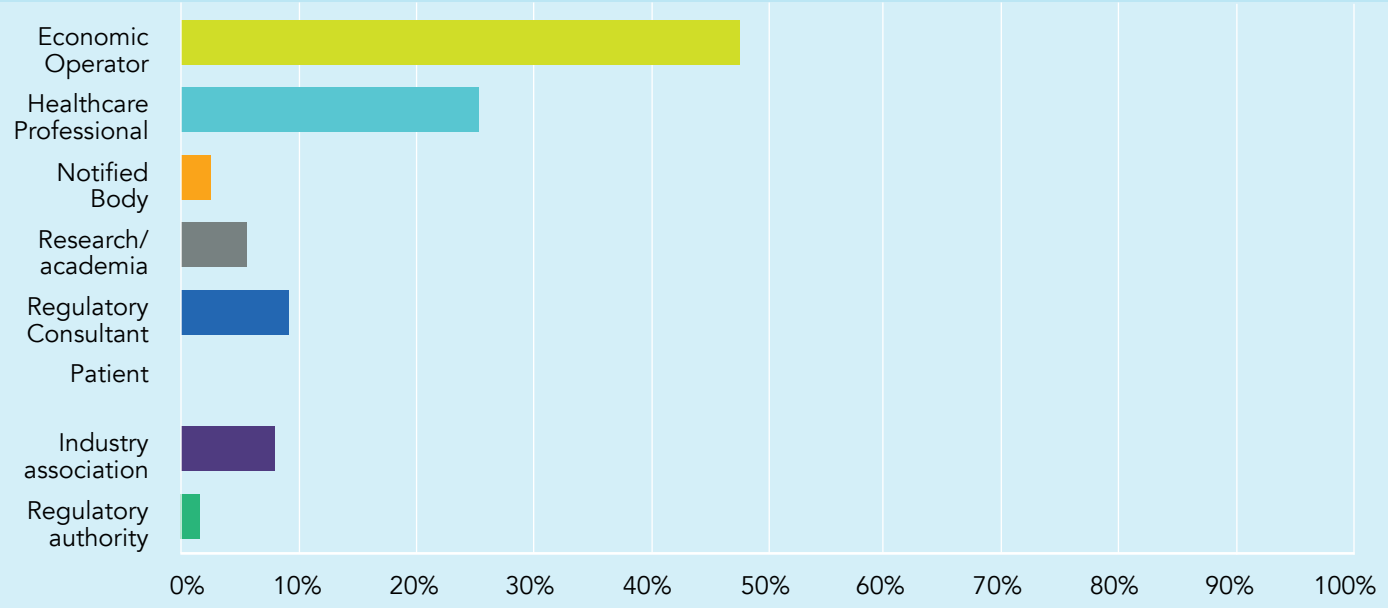


Figure 2: The articles of most interest to our readers

Answer Choices	Responses	
Practical applications of regulations / standards	80.83%	97
Legislative updates and implications	77.50%	93
Technical advancements and new developments in technology	26.67%	32
Updates on EU regulatory meetings	44.17%	53
Total Respondents: 120		

We also received a number of suggestions for articles which will be addressed during 2016. In this edition we featured an article on clinical investigation guidance and the practical considerations for applications to HPRA which was specifically requested through the newsletter stakeholder survey. We would like to take this opportunity to wish all of our readers Happy New Year for 2016.

HPRA
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