ANNUAL REPORT 2015

HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

CONTENTS

2015 Statistics at a Glance

7th

HPRA RANK IN EU FOR RAPPORTEURSHIPS FOR CENTRALLY AUTHORISED HUMAN PRODUCTS

806

THE TOTAL NUMBER OF NEW HUMAN MEDICINES AUTHORISED

17,122

VARIATIONS TO MARKETING AUTHORISATIONS ISSUED FOR HUMAN AND VETERINARY MEDICINES

83

NEW MEDICINES FOR VETERINARY USE AUTHORISED

10

APPLICATIONS FOR CLINICAL INVESTIGATIONS OF MEDICAL DEVICES TO BE CONDUCTED IN IRELAND

120

MANUFACTURING LICENCES IN PLACE AT YEAR END FOR HUMAN AND VETERINARY MEDICINES

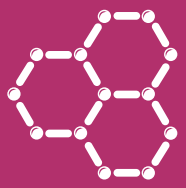
4,346

EXPORT CERTIFICATES ISSUED

108

CLINICAL TRIALS WERE APPROVED TO COMMENCE IN IRELAND ON MEDICINES FOR HUMAN USE

2,810



SUSPECTED ADVERSE REACTIONS REPORTS FOR HUMAN MEDICINES RECEIVED

435

REPORTS OF SUSPECTED ADVERSE REACTIONS ASSOCIATED WITH USE OF VETERINARY MEDICINES RECEIVED

2,126

MEDICAL DEVICE VIGILANCE REPORTS RECEIVED AND ASSESSED

356

RMPs FOR HUMAN MEDICINES SUBMITTED VIA NATIONAL, MUTUAL RECOGNITION, DECENTRALISED AND CENTRALISED PROCEDURES

116

RECALLS OF HUMAN MEDICINES AND VETERINARY MEDICINES

344

NATIONAL AND FOREIGN INSPECTIONS AND AUDITS PERFORMED

107

COMPLIANCE CASES OPENED UNDER COSMETIC PRODUCTS MARKET SURVEILLANCE PROGRAMME

3,677

ENFORCEMENT CASES WERE INITIATED IN RESPECT OF POTENTIAL BREACHES OF HEALTH PRODUCTS LEGISLATION

206,000

THE NUMBER OF UNIQUE VISITORS WHO ACCESSED THE NEW HPRA WEBSITE

6th

YEAR OF HPRA PARTICIPATION AT THE BT YOUNG SCIENTIST AND TECHNOLOGY EXHIBITION

Chairman's Statement

The annual report of the Health Products Regulatory Authority (HPRA) details the extensive work programme undertaken by the national regulator during 2015 to deliver on its role to protect public and animal health.

The 12 months in review also represented the final year of the HPRA's ambitious strategic plan for the period 2011 to 2015 which set out clear goals and objectives to govern the organisation's strategic direction and work programme. The development of a new plan, which outlines the strategic focus of the HPRA for the next five-year period, was overseen by the Authority in 2015 and, importantly, involved extensive stakeholder consultation.

The HPRA has a well established reputation as a highly capable and effective regulatory authority both internationally and at home. It has been a pleasure, along with my fellow Authority members, to support its operations and development over the past number of years as it continued to successfully deliver a world class regulatory regime for the health products sector in Ireland.

This report highlights the many achievements delivered during the past year as a result of the commitment and hard work of HPRA staff, the active contributions of its Authority and advisory committee members, as well as the support of the many stakeholders who actively engaged with our organisation.

In carrying out its regulatory remit, the HPRA puts the safety and health of people and animals at the centre of all its activities and areas of remit. These include an extensive range of primary functions such as product authorisation, manufacturing and market compliance, product monitoring and safety communications. All of this work incorporates continued risk management and assessment across thousands of products on the market with the same overarching objective to protect and enhance public and animal health.

We operate in a changing world where advances in medicines and new technologies are rapidly transforming treatments and ultimately leading to new health products. There is no doubt that these new products, whether medicines or medical devices, can improve the quality of life, and in many cases, extend the life expectancy of those who use them. Our important role is to ensure that these products are as safe as possible and that they work as intended. We do this through reviewing the pre-market evidence and data and by continuously monitoring the products once they are in actual use. In tandem, our organisational capabilities and skills must continue to keep pace with product innovation, new scientific data and developments in the regulatory environment so as to ensure the best possible health outcomes. The HPRA's strategic plans over the last decade have acknowledged this and made provisions to ensure that the organisation continually has access to the most up-to-date information and expertise to appropriately support these continually evolving industries.

Market diversification and reconfiguration also continues to be a feature of the pharmaceutical, medical device and cosmetic product sectors. In addition to the continuous up-skilling of the required expertise, and an efficient and robust risk-based regulatory model, the effective oversight of these areas requires co-operation at an EU and global level to enable both the sharing of safety information and the development of consistent regulatory practices. During 2015, the HPRA continued to actively participate and provide its expertise and inputs into the European regulatory network where strategic decisions and actions are undertaken in respect of a huge number of health products on the Irish market. The HPRA contributes significantly to the work of the European Medicines Agency, where it is represented on all major decision-making committees, and we are also heavily active at the Heads of Medicines Agencies. In relation to medical devices, and specifically the new legislation being devised at EU level, the HPRA is playing a significant role through the contribution of our national experts. When completed, the recast of this legislation will provide significantly enhanced safeguards for users of medical devices across Europe. The HPRA is also very active within the network for medical devices in Europe and is a key participant through its experts

within the many committees and working groups which have a role in the regulation of devices. At an international level, our agency continues to be one of the lead partners in the ongoing development of the International Coalition of Medicines Regulatory Authorities (ICMRA) and the International Medical Device Regulator's Forum (IMDRF).

Our remit is comprehensive with responsibility for the regulation of clinical trials, human and veterinary medicines, medical devices, blood and blood components, tissues and cells, and cosmetic products. We play a role in the regulation of controlled substances and of organs intended for transplantation while also overseeing the regulation of animals used for scientific purposes. Looking at the key data from the HPRA's 2015 output gives just some indication of the level of authorisation, assessment and safety monitoring work that is carried out across the organisation with increases in a number of work areas witnessed during the year. Close to 900 new human and veterinary medicines were authorised while over 17,000 variations to market authorisations were evaluated. We completed more than 370 inspections and audits across a range different sites and facilities to ensure that there was compliance in respect of relevant standards and legislation.

A significant area of our work is the continuous monitoring of the safety and quality of products on the market. With many thousands of products available this involves our post market teams proactively and reactively taking action when appropriate to minimise risk for patients and consumers. In 2015, the HPRA assessed some 3,200 adverse reaction reports in relation to human and veterinary medicines. Our risk based sampling and analysis programme resulted in the assessment of 480 product samples with a total of 772 quality defects relating to medicines reported to, or identified by, the HPRA. As regards medical devices, over 2,100 vigilance reports were received. Each individual case arising from of our monitoring and vigilance activities is assessed by appropriate experts to review risks and actions if required. Where action is deemed necessary, the HPRA has a range of tools it can use to protect public and animal health. In 2015, for example, 116 medicine recalls were completed including the issuing of targeted safety communication to ensure that where stakeholders needed to be informed of new information, this was done so swiftly. The HPRA is grateful to those members of the public and healthcare professionals who take the time to inform us of their experiences, observations or concerns in respect of health products.

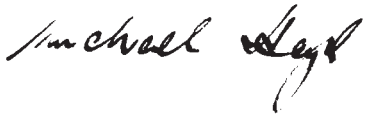
During 2015, our Chief Executive, Mr Pat O'Mahony, moved to the Department of Health to take up the position of Deputy Secretary, Governance and Performance. On behalf of the outgoing Authority, I wish to express our sincere gratitude to Pat for his visionary leadership of this organisation for over a decade, during which time the HPRA's remit expanded significantly. The Authority members wish his successor as Chief Executive, Ms Lorraine Nolan, former Director of Human Products Authorisation and Registration, well in her new role and are confident that under her leadership the HPRA will continue to be a highly effective regulatory agency. Particular thanks are due to Ms Rita Purcell who acted as Chief Executive during the interim period.

On behalf of the Authority, I would like to take this opportunity to thank the Minister for Health, the Minister for Agriculture, Food and the Marine, and the staff of their departments for their continued support of the HPRA in its endeavours and actions.

Behind the extensive work outputs detailed in this report, are the highly skilled and experienced staff of the HPRA. At the beginning of my tenure as Chairman, I noted the vigour, passion and enthusiasm with which they approach their individual roles. I can assure all our stakeholders that this very much remains the case and on behalf of the Authority I thank all staff for their ongoing contribution and commitment.

Additionally, on a personal note, I would like to thank my fellow Authority members, past and present, for their tremendous contribution to the strategic direction of the HPRA. I also wish to express my appreciation to those who have chaired the HPRA advisory committees and sub-committees. The contribution of all Authority and committee members is of huge value to the HPRA as it works to carry out its broad public and animal health remit.

As outgoing Chairman of the Authority, I am pleased to have played my part in supporting everyone at the HPRA as we sought to drive high quality outputs across all areas of the organisation. It has been a privilege to serve as Chairman of this highly regarded public body and I wish my successor, Ms Ann Horan, the very best in her new role.



Michael D. Hayes
Chairman

Authority Members

The Authority of the HPRA is appointed by the Minister for Health in accordance with the powers conferred by subsection 2 of section 7 of the Irish Medicines Board Act, 1995. There were nine Authority members up to 31 December 2015.

Mr. Michael D. Hayes (Chairman)*

Mr. Pat Brangan

Mr. Wilfred J. Higgins

Ms. Ann Horan

Prof. Mary Horgan

Dr. Elizabeth Keane

Mr. Noel O'Donoghue*

Prof. Caitriona O'Driscoll

Dr. Diarmuid Quinlan

* Term ended 31 December 2015

Management Committee

Ms. Lorraine Nolan
Chief Executive

Ms. Rita Purcell
Deputy
Chief Executive

Dr. J.G. Beechinor
Director of
Veterinary Sciences

Dr. Jayne Crowe
Director of Human
Products Authorisation
and Registration

Dr. Caitríona Fisher
Director of Quality,
Scientific Affairs and
Communications

Dr. Joan Gilvarry
Director of Human
Products Monitoring

Mr. Kevin Horan
Director of ICT and
Business Services

Mr. John Lynch
Director of Compliance

Ms. Lynsey Perdisatt
Director of Human
Resources and Change

Management Committee as of June 2016

Chief Executive's Report

It is a great pleasure to present my first Chief Executive's Report on the annual activities of the Health Products Regulatory Authority (HPRA).

While I have written the report, I wish to acknowledge that it outlines the activities of a year under the leadership of my predecessor, Pat O'Mahony, and my colleague, Rita Purcell, who served as Acting Chief Executive during an interim period.

The report, which is also the first full-year review under the HPRA name, outlines another year of high performance for our organisation and demonstrates again our absolute commitment to the protection and enhancement of public and animal health.

Strategic Plan 2011 – 2015

The layout of the annual report for 2015 is structured to ensure that the main chapters are closely aligned with the HPRA's five high-level strategic goals.

These goals are to:

1. Enhance healthcare product safety and patient outcomes by effective risk management and market surveillance.
2. Deliver clear, relevant and timely communications to patients, consumers and healthcare professionals.
3. Improve service delivery within a high quality, risk-based regulatory framework.
4. Influence legislation and policy development at European and international levels for the benefit of public and animal health.
5. Build future capabilities to meet evolving regulatory requirements, and scientific and technological advances.

Significantly, the past year marked the end of our existing strategic plan for 2011 to 2015. The final implementation report showed significant achievements in respect of each of the five strategic goals, something that is reflected throughout this and previous annual reports. During the past year, we also commenced the process for developing our next strategic plan which covers the period from 2016 to 2020. This plan was launched early in 2016 with the intention of building on the achievements of the past, while at the same time addressing future requirements and opportunities.

Authorisation, Registration and Licensing Activities

Our pre-market activities are a core regulatory function of the HPRA. They include the authorisation and registration of healthcare products, as well as the licensing of manufacturing, wholesaling and related activities. Our focus is on providing an effective and efficient regulatory framework that ensures the timely availability of appropriate health products. Among the activities and achievements of note during 2015 were the following:

- A total of 108 clinical trials for human medicines were approved to commence in Ireland compared with 80 the previous year. There were 10 applications for clinical investigations of a medical device, which was the same number recorded in 2014.
- In respect of human medicines, the HPRA assessed 137 new national applications (including parallel product authorisations), 67 applications via mutual recognition procedures (MRP) and 372 via decentralised procedures (DCP).
- In continuing our active contribution to the European human medicines licensing system, we acted as reference (lead) Member State for the assessment of 17 MRP and DCP procedures. The HPRA was also allocated as rapporteur or co-rapporteur for 12 new marketing authorisation applications by the European Medicines Agency (EMA). Based on allocations for the year, the HPRA ranked as joint seventh in the EU for rapporteurships for centrally authorised human products. We acted as lead in 39 scientific advice procedures for medicines proposed for the treatment of a broad range of conditions.
- During the 12 months in review, the HPRA issued 15,691 variations to marketing authorisations for human products authorised through the national or MR procedures. Of note, at a European level, we acted as rapporteur for one Article 45 procedure and nine procedures relating to Paediatric Investigational Plans (PIPs).
- In the area of veterinary medicines, we authorised a total of 83 new product applications and 1,431 variations to existing authorisations.
- A total of 371 notifications of medical devices to the medical device register were recorded while 43 organisations registered with the HPRA as Irish based manufacturers of medical devices.
- The number of manufacturing licences in place at year end for human and veterinary medicines was 120 while there were 287 wholesale distribution authorisations for human medicines.
- There were 323 individual authorisations and 114 project authorisations issued in respect of the use of animals for scientific purposes.

Safety and Compliance Monitoring

Monitoring the safety and quality of medicines, medical devices and other health products that have been licensed or registered for use in Ireland is a core public health function of the HPRA. Our regulatory decisions and actions in this regard are based on the best available information regarding benefit and risk.

It is also a function of the HPRA to monitor and inspect industry compliance with legislation, policies and procedures. Our focus is to make sure that all health products manufactured, processed or distributed in Ireland meet essential quality standards.

- A key part of our monitoring activity is the operation of a national pharmacovigilance scheme for adverse reactions, or side effects, associated with the use of human medicines. In the past year, the HPRA received a total of 2,810 valid new adverse reaction reports which is a figure broadly consistent with the reporting rates seen in the recent past.
- In respect of human medicines, the HPRA again contributed to the work-sharing programme for signal detection within the EU. We acted as lead Member State for the detection and management of signals for 54 active substances authorised nationally. We also retained responsibility for assessing any signals arising as a result of signal detection for 27 centrally authorised active substances (or combination of active substances). In addition, the HPRA acted as concerned Member State in five newly initiated EU safety-related referrals.
- Periodic safety update reports (PSURs) are vigilance reports submitted by marketing authorisation holders. For human medicines, as part of its contribution to the EU PSUR single assessment procedure, the HPRA contributed to the evaluation of 1,002 PSURs in 2015.
- The upward trend in the number of national reports of suspected adverse events to veterinary medicines continued in 2015 with 437 reports received by year end. We also completed the evaluation of 1,205 PSURs for veterinary medicines.
- Post-market surveillance and vigilance activities are employed to monitor the safety and quality of medical devices. A total of 2,126 medical device vigilance reports were received and assessed during 2015 while we also commenced 324 market surveillance cases. Both figures represented a slight increase compared to 2014.
- Over the course of 2015, 344 inspections and audits were performed compared to 260 in 2014. The figure for the past year included 124 Good Manufacturing Practice (GMP) inspections, 126 Good Distribution Practice (GDP) inspections, 15 Good Clinical Practice (GCP) inspections, 16 medical device audits and 26 covering blood, tissues and organs. A full re-designation assessment of the Irish notified body, the National Standards Authority of Ireland, was also completed.
- As part of our risk-based sampling and analysis programme, we sent a total of 297 product samples for analytical testing while the packaging and labelling of a further 156 medicines and other products from the Irish market were examined.
- In certain cases, it may be necessary to withdraw, or recall, products from the Irish market in order to protect public health. In 2015, 116 medicine recalls occurred.
- In total, 3,677 enforcement cases were initiated with 1,136,494 dosage units of medicines being detained.
- The national sampling and analysis programme for cosmetics, which involves close co-operation with the Health Service Executive (HSE), resulted in the sampling of 469 such products. Of these, 398 were analysed by year end with 71 being found to be non-compliant.

Legislative and Regulatory Developments

The regulatory role of the HPRA continues to evolve and grow in line with new national and European legislation and in response to other changes and developments in our operating environment.

Legislative Changes and Updates

During the past year, representatives from across the HPRA were heavily involved in implementing, or preparing for the implementation of, new and updated EU directives which will typically result in significant changes to how specific health products are regulated across Europe.

- As regards the ongoing implementation of the remaining aspects of Directive 2011/62/EU on falsified medicines, the HPRA continued to participate in the expert group convened by the Commission to assist with drafting of the Delegated Regulation in respect of proposed safety features on specified human medicines. It is expected that the Regulation will be finalised early in 2016 with a three-year period thereafter for implementation. We also liaised with industry and other stakeholder organisations in Ireland in relation to the establishment of a National Medicines Verification Organisation.

- New clinical trials legislation (Regulation (EU) No. 536/2014) will come into effect in Europe in mid-2016. During the past year, the HPRA continued to progress the development of systems and procedures necessary to meet the new requirements.

- The HPRA continued its work to support the phased implementation of EU pharmacovigilance legislation. This included participation in a pilot of a PSUR repository as well as user acceptance testing in preparation for mandatory use of the repository from June 2016. During 2015, the HPRA continued to contribute to three EMA / Member State project teams concerned with collection of key information on medicines, better analysis and understanding of data and information, and committees and communications with stakeholders.

- Negotiations in respect of the European Commission's proposals for Regulations on medical devices and *in vitro* diagnostic (IVD) medical devices reached a new phase with the adoption of a 'General Approach' on the legislative texts by the European Council. This allowed for the initiation of trialogue discussions with the European Parliament and the EU Commission on the dossiers, which is one of the key elements of the ordinary legislative process. The HPRA strongly supports the introduction of the revised legislation which we believe will represent a significant improvement and strengthening of the regulatory system for devices. Throughout 2015, the HPRA provided significant support to the Department of Health and the Permanent Representation of Ireland in Brussels for the purposes of negotiation of the legislation at the European Council Working Party and at various expert working groups.

SCOPE Joint Action

The Strengthening Collaboration for Operating Pharmacovigilance in Europe (SCOPE) Joint Action is intended to support the operation of pharmacovigilance in Europe in light of requirements introduced by new pharmacovigilance legislation.

During 2015, the HPRA contributed to both risk communications and lifecycle pharmacovigilance which are two of the eight work packages being implemented under SCOPE. The HPRA is the topic lead in respect of carrying out an impact assessment of risk communications under work package 6 (WP6). This incorporates the collection of information on risk communications practice in the EU network to better understand the communication channels and tools used. We also contributed in 2015 as a partner under work package 8 (WP8) relating to lifecycle pharmacovigilance.

Existing Medical Devices Regulatory Framework

The HPRA has taken a leading role, along with a number of other European competent authorities and the European Commission, in enhancing the existing regulatory framework for medical devices in advance of the introduction of the revised legal framework. A key focus has been to improve the performance of notified bodies and their oversight by authorities. This was achieved by the development of an EU wide joint assessment scheme for notified body oversight by authorities and the HPRA continues to be part of a small expert group which oversees and co-ordinates its implementation. During 2015, the HPRA directly participated as experts in six joint assessments of EU notified bodies while the Irish notified body was also subject to an EU joint assessment.

In addition, throughout 2015, we progressed a number of initiatives to further enhance and strengthen our market surveillance and vigilance activities.

Participation in the European and International Regulatory Systems

The health products and associated areas regulated by the HPRA are part of a dynamic and developing international industry. The HPRA is committed to playing its part in the global regulatory network thus ensuring that we represent and protect the interests of Irish patients and consumers.

Our participation and contribution at a European level continues to be significant with HPRA scientific and technical staff contributing to a broad range of committees and working parties at the EMA, the European Commission, the Heads of Medicines Agencies (HMA) and via other platforms. We also contribute where appropriate to relevant international organisations and initiatives.

The following are some of main developments and HPRA contributions from the past 12 months which are in addition to those already outlined in my report.

- The HPRA continued in the role of Vice-Chair of the International Coalition of Medicines Regulatory Authorities (ICMRA). This group acts as a forum to support international co-operation among medicines regulatory authorities. It aims to avoid duplication and promote informed, risk-based allocation of resources.
- Our Pharmacovigilance Manager for human medicines continues to represent the World Health Organization (WHO) as a member of the Board of the Uppsala Monitoring Centre (UMC) and WHO Collaborating Centre for International Drug Monitoring.
- The HPRA again served as a member of the European delegation on the Management Committee of the International Medical Device Regulators Forum (IMDRF). This forum seeks to promote the harmonisation of medical device regulation across the globe. In 2015, the HPRA hosted a meeting of the IMDRF Medical Device Single Audit Program (MDSAP) working group in Dublin.
- In July, the Irish Pharmacovigilance Risk Assessment Committee (PRAC) delegate was elected to serve a further three years as Vice-Chair of this important EMA public health committee.
- The Pharmacovigilance and Risk Management Lead contributed to a number of strategies to support stakeholder engagement as well as to a range of other specialist topics at a European level. She also participated in a number of initiatives exploring development of the regulatory environment, strategies to facilitate access to innovative medicines for patients in need, and benefit-risk management through the product lifecycle.
- As a member of the Benchmarking of European Medicines Agencies (BEMA) steering group, the HPRA continued to work with other Member States to prepare for the fourth benchmarking cycle which is due to begin in 2016.
- Our contribution to the veterinary medicines regulatory network is primarily through our involvement at the EMA, where our Veterinary Assessment Manager is the Vice-Chair of the Committee for Medicinal Products for Veterinary Use, and at the HMA.
- The revision of the legal framework for veterinary medicines was again a key focus in 2015 and the HPRA provided practical support and advice to the Department of Agriculture, Food and the Marine during Council Working Party discussions.
- The HPRA contributed to deliberations in respect of a number key topics as part of the EU National Committees for the Protection of Animals used for Scientific Purposes.

- At a European level, the HPRA was an active participant in the Medical Devices Expert Group (MDEG) and is the chair of three taskforces including the vigilance co-ordinating competent authority role.

- The HPRA is an elected member of the Executive Group of the Competent Authority for Medical Devices (CAMD). In November 2015, the 37th CAMD meeting was hosted in Dublin by the HPRA on behalf of the Luxembourg Presidency of the European Council.

Interchangeable Medicines

Under the Health (Pricing and Supply of Medical Goods) Act in June 2013, the HPRA was tasked with publishing a list of interchangeable medicines to facilitate generic substitution by pharmacists and to allow for the introduction of a reference pricing system by the HSE. This work continued during 2015 and by year end there was a total of 44 active substances included on the list.

Legal Classification of Medicines

The HPRA has taken a proactive approach to the reclassification of the legal status of medicines. We have identified products which we consider could be safely made available without prescription in pharmacies, or made more widely available in general retail outlets such as supermarkets. Companies have been invited to make applications to have these medicines reclassified and, on foot of this proactive approach, a number of reclassification applications were completed in 2015. Further progress is anticipated during 2016.

Responding to Medicines Shortages

We continue to work closely with the Department of Health and other stakeholders in relation to the management of shortages of medicines impacting the Irish market. One mechanisms used by the HPRA to help alleviate shortages is the granting of a temporary authorisation for a batch of a product known as a 'batch specific request'. During 2015, the HPRA reviewed 115 such requests.

Stakeholder Engagement and Communications

The HPRA is committed to ensuring that all our stakeholders have timely access to relevant safety and regulatory information and we continue to expand and develop our communications and engagement activities. In addition to ongoing meetings with key stakeholders, we implemented and further developed a number of significant communications programmes and initiatives during 2015.

Events

HPRA information events and seminars, which are all organised and managed by an in-house events team, provide regulatory guidance and updates to a range of stakeholders and include presentations from HPRA staff and, where appropriate, external contributors. These events also enable attendees to submit questions, seek clarifications and network with colleagues. A number of information seminars were hosted during 2015 focused on topics such as herbal medicines, cosmetic products and the regulation of human tissues and cells. An animal welfare body training workshop and seminar was also organised on behalf of the National Committee for the Protection of Animals used for Scientific Purposes. Additionally, the HPRA also hosted one European and one international meeting focused on the regulatory system for medical devices.

In January 2015, thousands of students as well as teachers, parents and members of the general public from all over Ireland, visited the HPRA's exhibition stand at the BT Young Scientist and Technology Exhibition 2015. This was the sixth year of HPRA participation and our stand again focused on building awareness of the significant role the HPRA plays in protecting public and animal health.

Publications

The HPRA continued to produce an extensive range of publications during 2015. As well as new and updated regulatory guides, we continued to publish our drug safety, medical devices and medicinal products newsletters which are focused on updating stakeholders in respect of key safety and regulatory issues. We also published specific safety warning and notices as required in respect of human and veterinary medicines, medical devices and cosmetic products. All these documents and notices are published online and we encourage stakeholders to subscribe to our e-mail alerting system to receive notifications of new content and information published on our website.

During 2015, the HPRA also published an information leaflet highlighting the importance of reporting suspected adverse events following the use of veterinary medicines. Details on what information should be included in a report are also provided as are instructions on how to report. We also published a leaflet, developed with the input of the National Committee for the Protection of Animals used for Scientific Purposes, which is intended to support the work of the Animal Welfare Body in each research establishment in promoting the 3R principles (replacement, reduction, refinement), which provide a framework for humane scientific research.

HPRA Website

Our website continues to be a critical component of our communications programme and we are committed to its ongoing development and enhancement to ensure it remains an attractive and user-friendly resource. Over 200,000 unique visitors accessed the HPRA website during 2015 while there were in excess of 536,000 visits in total.

As well as the addition of new content and sections during the past year, we also implemented a search engine optimisation (SEO) and pay-per-click (PPC) campaign which resulted in both increased traffic to the HPRA website and improved rankings for the HPRA in search results. In addition, an online survey among the users of our website was completed in August. While the user satisfaction levels were at a high level overall, the specific feedback received will be used to guide the future development of our online presence.

Parliamentary Affairs

The HPRA engaged significantly with elected representatives and government officials throughout 2015. We responded to 125 parliamentary questions during the year while more than 100 further requests for information were received from the Department of Health, other government departments and members of the Oireachtas. We also addressed the Oireachtas Joint Committee on Health and Children in December during a meeting to discuss the safety of the HPV vaccine.

Organisational Management and Development

It is vitally important that our organisational capabilities continue to expand and evolve in line with regulatory and scientific developments while we must also display the flexibility required to adapt to changes in the environment in which we operate.

Change is something that we have constantly embraced in the HPRA and we are committed to ensuring that we have the requisite structures, systems and processes in place to deliver on our public health mission.

Human Resources and Change

The retention, engagement and continuing development of our highly skilled employees, is central to the HPRA delivering on its public health remit. Our new organisational competency of innovation and creativity, launched as part of the 2015 Performance Development Programme (PDP) process, framed our approach to the development of many of our human resources initiatives during the past year.

PDP continues to be one of our core platforms to support high performance, superior service delivery and the development of our staff. The programme was enhanced during 2015 with the full implementation of a range of tools designed to support employees and people managers in using the programme.

Our learning and development strategy continued to focus on staff development as one of our key motivation and retention tools. A full range of developmental in-house programmes were delivered in addition to new manager and PDP training. A group of HPRA managers also completed our externally accredited Leadership Development Programme.

During 2015, a number of projects requiring change management support were commenced. This included the creation of the Quality, Scientific Affairs and Communications directorate and the ongoing development of the EOLAS workflow system. The human resources and change team were also involved in the capacity building project that sees the HPRA contributing to the development of the Zambian medicines agency. As regards the public sector reform agenda, a comprehensive communications programme outlining the detail of the reforms and the associated impact on individuals was delivered to our employees.

The HPRA continues to recognise the importance of supporting employee engagement and commitment. Building on the previous success of our wellness and health initiatives, we further developed this programme to deliver a range of initiatives during the year, with staff engagement levels for the programme remaining high. Our lunchtime learning programme operated in tandem with the wellness initiatives while we also reintroduced our organisational awareness programme with the purpose of highlighting the role and activities of individual departments and sections within the HPRA.

We are committed to managing our resources in line with public sector policy with a focus on internal skills development and the reallocation of tasks and responsibilities where possible. When required, recruitment of staff in specialist areas was completed in line with Department of Health approvals.

Information Technology and Business Services

Technology is recognised as a key component in supporting the regulatory activities of the HPRA at both national and international levels. We continue to actively contribute to, and in certain cases lead, a number of key national and pan-European technology projects. This includes the ongoing development and management on behalf of the wider EU regulatory community of the Common Electronic Submission Portal (CESP). The CESP activity levels again grew substantially in 2015, handling over 350,000 submissions on behalf of more than 30 European regulatory organisations and the pharmaceutical industry.

The HPRA is also actively engaged at national level through its involvement with the National Health Data Standards Committee and we work closely with other relevant agencies including the HSE, NSAI, HIQA and eHealth Ireland on a number of mutually beneficial projects. During 2015, the HPRA also commenced development of a new registration system to support the implementation of new legislation to provide emergency access to certain prescription-only medicines.

An area of significant focus for our information technology and business services team, as well as many other colleagues across the organisation, is the ongoing development of a new workflow technology solution, known as EOLAS. The new system will enable the consolidation and replacement of a number of legacy solutions and will provide a new workflow and data management platform for the entire organisation. Considerable progress was achieved in respect of the the design and build of the system during 2015 with an initial launch expected in the second half of 2016.

Financial Performance

In common with many of its peers internationally, the HPRA is primarily self-funded through a regulatory fee system. Fees are approved each year by the Minister for Health following a public consultation. The HPRA is committed to the highest standards of independence and governance so as to ensure quality of service combined with value for money. Throughout the past 12 months, we continued to successfully manage the affairs of the HPRA in line with our statutory obligation that income at least meets costs.

The Future

To ensure that we continue to deliver on our mission to protect and enhance human and animal health, the HPRA must be prepared for both the challenges and opportunities that will no doubt arise during 2016 and beyond. Our new strategic plan for the years 2016 to 2020, which was launched early in 2016, will be central to our future planning and provides a clear roadmap for the future focus and development of the HPRA. The strategy also reflects the key issues and work areas highlighted during an extensive consultation process and we look forward to working in collaboration with all our stakeholders to deliver on our plan in the years ahead.

As regards 2016 specifically, we can expect that the overall workload for the organisation will continue to expand and diversify in response to legislative and regulatory developments as well as advances in new innovative products and technologies. The former includes the ongoing development of new legislation in respect of both veterinary medicines and medical devices which we know will result in quite significant changes to how these product areas are regulated.

We will maintain a risk-based approach to our regulatory work. We will continue to review and assess our own processes and will adopt changes across the organisation where these are deemed necessary and beneficial. We will continue to enhance our quality management systems and our IT capabilities with the latter incorporating the launch of the HPRA's new workflow and data management platform. A new communications strategy will also be developed to support our stakeholder engagement activities and to build further awareness of our public health role. There will be an ongoing review of our funding provision and management of our cost base so as to ensure optimal use of resources. Of note, we anticipate that a fee model that reflects our regulatory role in respect of medical devices, will be introduced.

Finally, in parallel with the development of our new strategic plan, we will also finalise and launch a new human resources strategy. This broad, long-term plan will focus on a number of key elements including the critical area of staff retention and engagement. Learning and development will also be a priority area as we endeavour to maintain and enhance the skills that are required in an increasingly complex regulatory environment.

Acknowledgements

I wish to thank and acknowledge the Ministers and staff of the Department of Health and of the Department of Agriculture, Food and the Marine for the support and co-operation afforded to the HPRA during 2015.

On behalf of the Management Committee and all our colleagues, I want to sincerely thank the outgoing members of the Authority and advisory committees for their valuable contribution and commitment to the HPRA over a number of years. Their independent expertise and advice has been of immense value to the workings of our organisation. In particular, I wish to acknowledge the strategic input of the outgoing Authority Chairman, Michael Hayes, and thank him for the considerable time and energy he devoted to the role during his term of office.

I also wish to express my personal appreciation to all colleagues, not just for the significant programme of work delivered in 2015, but for your continued professionalism and commitment to both your individual roles and the overall remit of the HPRA. After over 14 years working in this highly regarded and progressive organisation, I was hugely honoured to be appointed its new Chief Executive. I look forward to working with you all, as well as our new Chairperson, Authority and committee members, as we focus all our efforts on the continued protection and enhancement of public and animal health.

Finally, on behalf of everyone associated with the HPRA, I must also acknowledge the huge contribution of my predecessor, Pat O'Mahony. The role, functions and responsibilities of our organisation expanded significantly across the health products sector under his dynamic leadership, culminating in the adoption of our new HPRA name in 2014. We all wish Pat well in his new role and thank him for his transformative work as Chief Executive of the HPRA.

Lorraine Nolan
Chief Executive

AUTHORISATION, REGISTRATION AND LICENSING ACTIVITIES

The authorisation and registration of health products is a core public health function of the HPRA. These are the regulatory actions which are carried out before a health product can be marketed and supplied in Ireland. Ensuring timely approval of new product applications in particular, following a positive assessment of safety, quality and effectiveness, gives patients and users access to a range of appropriate treatments.

The HPRA is responsible for the authorisation of human and veterinary medicines, of clinical trials and for the registration of certain medical devices. We licence manufacturers and wholesalers of human medicines, manufacturers of veterinary medicines as well as blood and tissue establishments and organ transplant centres. We also grant relevant authorisations under scientific animal protection legislation and we are responsible for issuing export certificates for medicines, medical devices and cosmetics.

In addition, the HPRA provides a classification service to assist stakeholders in clarifying whether products should be categorised as human medicines, veterinary medicines, medical devices, cosmetics or none of these.

Human Medicines

Borderline Product Classification

The HPRA regularly receives queries in regard to the correct classification of human medicines, veterinary medicines and medical devices. Products in these categories fall under the remit of the HPRA from a regulatory perspective and are distinct from other products which are outside the HPRA's remit. For products for human use, a classification service is operated for products which are on the borderline between medicines and other products such as food supplements, cosmetics and medical devices.

Requests for classification, whether external or internal, are presented to an internal, multi-disciplinary, human medicine classification committee. This committee met 11 times in 2015 and considered a total of 80 new products. In addition, there were 16 products revisited from pre-2015.

The committee has a close working relationship with the Food Safety Authority of Ireland (FSAI). During the course of 2015, the FSAI notified the HPRA of 59 products which had been brought to its attention and which it considered to fall more appropriately under the HPRA's remit. Where this turned out to be the case, these products were followed up by the HPRA.

Clinical Trials

The role of the HPRA is to assess applications from sponsors to conduct clinical trials in Ireland. Sponsors include pharmaceutical companies and / or research institutions. The HPRA approves the clinical trial protocols which describe in detail how each trial is to be conducted and outlines the steps that will be taken to protect the health of volunteers or patients.

In 2015, 108 clinical trials were approved to commence in Ireland. This is an increase compared with the total of 80 trials approved in the previous year. The key areas of interest for clinical research continue to include cancer and blood disorders.

Voluntary Harmonisation Procedures

A voluntary harmonisation procedures (VHP) is a co-ordinated work sharing assessment procedure for multinational clinical trials. This procedure was established by the national competent authorities for clinical trials from across the EU.

The HPRA participated in 15 VHPs for clinical trials during 2015, compared with seven during the previous year. The HPRA acted as lead Member State for the assessment of eight of these VHPs in 2015. This compares with a figure of two in the previous year.

The VHP is similar to the approval process for clinical trials under planned new legislation. For this reason, it is popular with sponsors wishing to gain experience and the HPRA continues to actively participate in this procedure.

New Marketing Authorisation Applications

Prior to a new medicine being placed on the Irish market, it must be assessed and authorised (licensed) by the HPRA or by the European Medicines Agency (EMA) in conjunction with the European Commission. The assessment involves establishing that a medicine's health benefits outweigh its known risks. Where this is the case, it may be granted a marketing authorisation.

There are a number of routes through which a product can be authorised by the HPRA. These include the national procedure, the mutual recognition procedure (MRP) and the decentralised procedure (DCP). Both MRP and DCP involve the simultaneous submission of applications in a number of EU Member States. The

assessment involves the input from all of the relevant competent authorities in evaluating the benefit / risk of the product(s). The DCP route differs from the MRP in that the product has not previously been authorised within the EU.

The following applications were assessed by the HPRA during 2015:

- 137 new national applications (including parallel product authorisations);
- 67 applications made under the MRP;
- 372 applications made under DCP.

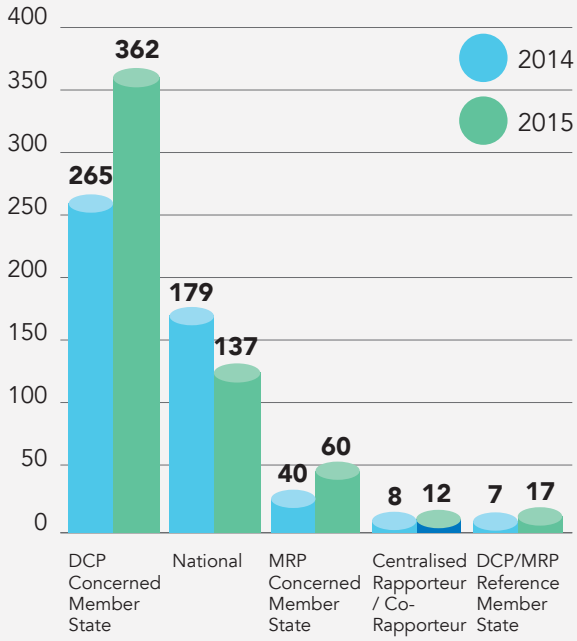
The HPRA acted as reference (lead) Member State for the assessment of 17 of the MRP and DCP procedures.

The centralised route is another mechanism whereby products can be authorised in Ireland. In this procedure, the assessment is carried out by Member States (MS) appointed as lead assessor (rapporteur) and joint lead assessor (co-rapporteur), with input also from all other Member States and is co-ordinated by the EMA. The authorisation is granted by the European Commission. The centralised route involves the submission of a single application to the EMA, and the authorisation once granted is valid in all Member States. In 2015, the HPRA was allocated as rapporteur / co-rapporteur for 12 new marketing authorisation applications by the Committee for Medicinal Products for Human Use (CHMP) at the EMA. These included treatments for respiratory, musculoskeletal and orphan diseases, such as Cushing's syndrome, as well as for rare corneal diseases. The HPRA was also responsible for the assessment of radiopharmaceutical products.

Based on 2015 allocations, the HPRA was ranked joint seventh in the EU for rapporteurships for centrally authorised human products.

The total number of new products authorised in 2015 was 806. This figure also includes 218 products authorised through the centralised route where the HPRA was not rapporteur or co-rapporteur. In overall terms, the number of products authorised has increased relative to 2014 when the total number of new products authorised was 615.

New Applications



Traditional Herbal and Homeopathic Medicinal Products

During 2015, seven traditional herbal medicinal products (THMPs) were authorised by the HPRA. This is a simplified registration scheme which takes into account the tradition of use of these products. Legislation requiring registration for THMPs came into effect in full in 2011. The number of applications received by the HPRA since that time has remained low. A total of 40 THMPs are now authorised for sale.

There were no homeopathic medicinal products authorised during 2015 under the simplified rules scheme. As a result, the total number of products registered remained at 98.

Transfer Applications

The HPRA processed a total 245 human medicine transfer applications in 2015. Of these, 197 related to the transfer of an existing marketing authorisation to a new marketing authorisation holder while the balance related to a transfer of a marketing authorisation holder prior to authorisation.

Variations

After a medicine has been authorised, the terms of its marketing authorisation may need to be changed and the process whereby such changes are implemented is known as a "variation". Examples of variations include the addition of a new indication, a new potential side effect, or updates to the company's manufacturing or contact details. In the past year, the HPRA issued 15,691 variations to marketing authorisations for products authorised through the national or MR procedures. The figure compared with a total of 13,205 variations during the previous year. The HPRA also issued 283 work-sharing variations in 2015 through national or MR procedures. For five of these procedures, the HPRA acted as lead Member State.

Articles 45 and 46 - Variations to Update Product Information

During the past 12 months, the HPRA acted as rapporteur for one paediatric Article 45 procedures and nine procedures relating to Paediatric Investigational Plans (PIPs). These are important procedures from a public health viewpoint as they increase the availability of medicinal products specifically indicated for use in children.

39

EMA SCIENTIFIC ADVICE PROCEDURES FOR HUMAN MEDICINES LED BY THE HPRA

Renewals

A total of 108 renewals to marketing authorisations for products authorised through the national (43), MR (19) or centralised (46) procedures were assessed in 2015. In general, the numbers of renewals are decreasing, reflecting the lifecycle of the products in question.

Scientific Advice

Scientific advice is a pre-authorisation activity which assists product and technology innovation and development. The EMA operates a scientific advice system for innovative products which will ultimately be the subject of applications under the centralised authorisation system. During 2015, the HPRA acted as lead in 39 EMA scientific advice procedures for medicines proposed for the treatment of a broad range of conditions. Areas of focus included medicines to treat respiratory disorders, inflammatory diseases, cancers and blood disorders.

Veterinary Medicines

The HPRA, through its veterinary medicines licensing activities, is committed to protecting the welfare of treated animals, including fish, poultry, bees and domestic animals, as well as ensuring the safety of foodstuffs obtained from animals treated with veterinary medicines. The assessment of veterinary products also includes an evaluation of any possible risks to the user as well as the elaboration of risk-management measures to control any risks. Finally, we also evaluate the potential impact of new veterinary medicines on the environment.

83

NEW PRODUCT APPLICATIONS FOR VETERINARY MEDICINES

Product Classification Requests

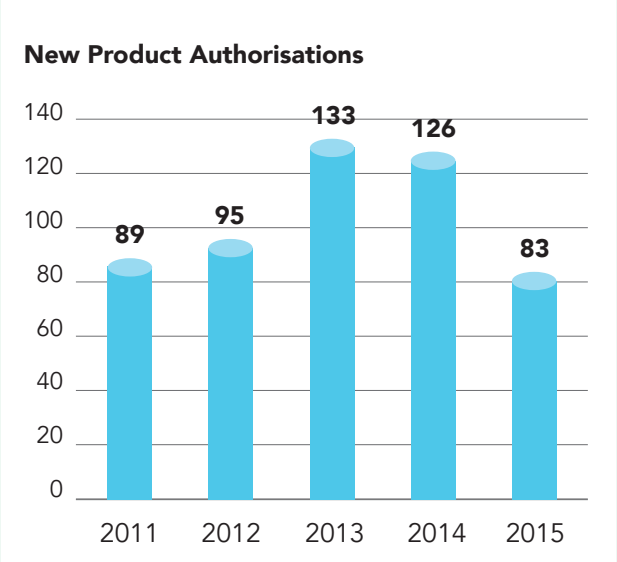
As the competent authority, the HPRA has an important role in deciding which types of products fall within the scope of the veterinary medicines legislation. Products that are regarded as medicinal but which do not have a marketing authorisation are deemed illegal in Ireland and may be seized by the Department of Agriculture, Food and the Marine. HPRA work in this area is largely driven by the monitoring activities of the Department which polices the market.

During 2015, 21 product classification queries were received in respect of veterinary medicines. A total of 49 queries had been received the previous year.

New Applications

Ensuring timely approval of new products applications, following a positive assessment of their safety, quality and effectiveness, ensures a range of medicines and vaccines are available to prevent and treat diseases in animals. The HPRA is responsible for authorising the majority of new products coming to

the market in Ireland, with a smaller number (relating to innovative or high-tech veterinary medicines) being authorised centrally under the responsibility of the EMA.

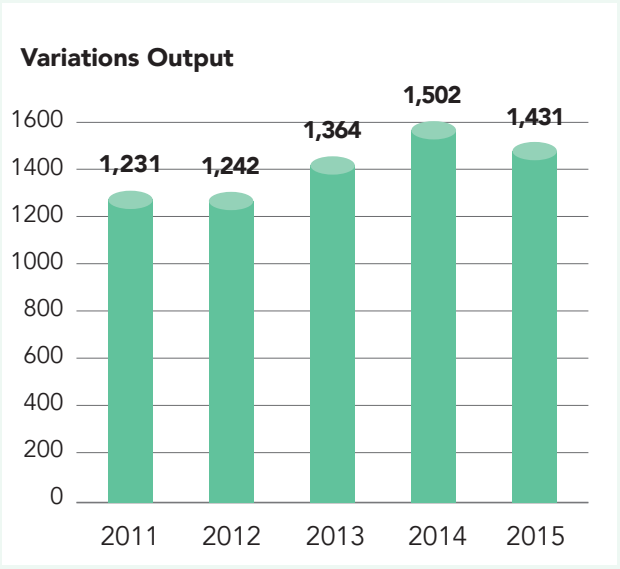


The accompanying graph shows new product authorisations in respect of veterinary medicines during the past five years.

Variations

After a medicine has been authorised, the terms of the marketing authorisation may subsequently be varied. Examples of variations include the addition of a new indication or potential side effect, an alteration to the method of manufacture or a change in active substance suppliers.

Under European legislation, such variations must be notified to the competent authority which must evaluate and approve any significant changes. The goal is to ensure that medicines are produced in a robust and standardised manner, thus safeguarding against sub-standard products. This requirement, together with a more global manufacturing environment, has led to in an increasing number of variations in recent years as shown in the accompanying graph. This activity now represents approximately half of the total number of applications for veterinary medicines processed annually.



Work-in-Progress Applications

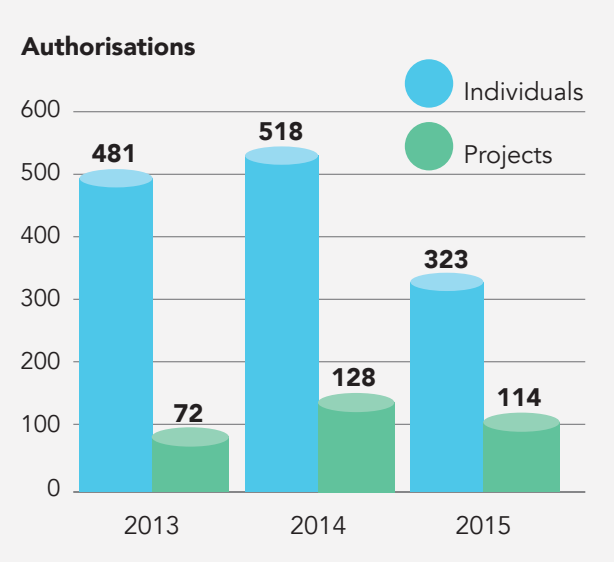
The HPRA actively monitors work-in-progress data as an important indicator of our customer service levels. The overall figure for work-in-progress at the end of the year relevant to veterinary medicines was 621 units (comprising various application types). The overall work-in-progress overdue figure was down to 24. It follows that, everything else being equal, the greater the volume of business being conducted, the greater will be the levels of work-in-progress.

Scientific Animal Protection

This relatively new area for the HPRA represents a very important opportunity to improve the welfare of animals used for scientific purposes and to ensure that animals are used only when there is no alternative to their use and the use itself is properly justified. Our regulatory approach is specifically focused on adherence with the 3R principles (reduction, refinement and replacement of animal testing).

One of the primary functions of the HPRA is to perform evaluations of applications for the authorisation of research establishments and projects. The HPRA also evaluates applications from individuals to allow them to conduct procedures or euthanasia of animals.

While the total number of projects authorised during 2015 was similar to the previous year, there was quite a significant fall in the number of applications for individual authorisations. This reduction was anticipated and was due to the legal requirement for existing establishment personnel to apply for individual authorisations before the end of 2014. Hence, there were a large number of applications for individual authorisations, which are valid for five years, during the previous 12-month period. It is likely that the application numbers for 2015 mainly reflect new individuals joining the sector.



Medical Devices

Classification Requests

The HPRA received 35 applications for classification of medical devices or products queried as medical devices in 2015. The queries emanated from other medical device competent authorities in Europe / the European Commission, from medical device manufacturers and from distributors.

The HPRA circulated one enquiry relating to a medical device classification issue to other European medical device competent authorities with a view to seeking a consensus opinion in Europe on the classification or qualification of a specific product.

Clinical Investigation Applications

The HPRA received 10 applications for clinical investigations of a medical device to be conducted in Ireland in 2015. The investigations were received in areas such as closure devices, cardiac and software. This level of activity was broadly similar to the previous 12-month period.

In addition, three compassionate use procedures were completed during 2015.

Product Registrations

The HPRA received 371 notifications of medical devices to the medical device register. These relate to class I, *in-vitro* diagnostic and custom made medical devices and to system and procedure packs. Registration of these devices in the Member State in which the manufacturer or their authorised representative is based is required by legislation as there is a self-declaration of conformity made by the manufacturer.

During 2015, 43 organisations registered with the HPRA as Irish based manufacturers or authorised representatives of class I, custom-made, *in-vitro* diagnostic medical devices, as manufacturers of system or procedure packs, or as sterilisers of medical devices. This was an increase of over 60% on the number of organisations registered in 2014.

Controlled Substances

Controlled Drugs

Import, export and holding of controlled drugs (for legitimate purposes) are subject to licensing. The Department of Health is the licensing authority while the HPRA handles the administrative aspects of the application and licensing process.

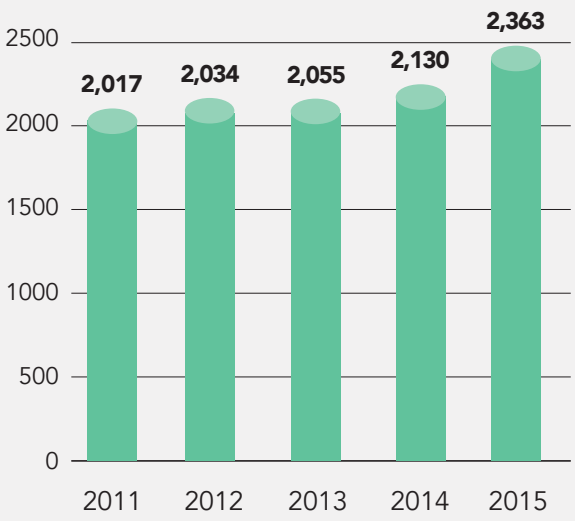
Licensing activity, which consists primarily of export and import licences and letters of no objection, has increased somewhat during recent years.

Precursor Chemicals

Precursor chemicals are legally used in a wide variety of industrial processes and consumer products, such as medicines, flavourings and fragrances.

The HPRA has been the licensing authority for precursor chemicals since 2010. Precursor chemicals are subject to different licensing requirements, dependant on the category.

Controlled Drugs Licensing



Precursor Chemicals Licensing Activity	2011	2012	2013	2014	2015
Total	67	70	27	46	32

Authorisation / Licensing of Sites and Facilities

The authorisation / licensing of manufacturers and wholesalers of medicines, of blood and tissue establishments and the approval of contract laboratories permits those facilities to carry out specified activities. The authorisation is based on satisfactory outcomes to HPRA inspections (see also under Safety Monitoring and Surveillance) during which adherence to relevant European guidance is evaluated.

The total number of licences / authorisations in place at year end for the past five years is presented by category in the accompanying table.

Variations to authorisations / licences for sites and facilities

Applications from authorisation and licence holders to vary the information on which the authorisation / licence is based are processed regularly by us. These variations, including updates and amendments, are classified as either administrative or technical.

Total Number of Licences/Authorisations (Sites)	2011	2012	2013	2014	2015
Manufacturers of Medicines for Human Use	88	87	89	92	95
Manufacturers of Veterinary Medicines	24	23	24	25	25
Investigational Medicinal Products for Human Use	50	47	49	53	52
Wholesalers of Medicines for Human Use	243	258	269	272	287
Blood Establishments	4	3	4	4	3
Tissue Establishments	22	21	23	24	24
Laboratory Approvals	16	17	16	16	12
Total	447	456	474	486	498

Total number of Variations	2011	2012	2013	2014	2015
Total	684	1068	947	815	1091

Registrations for Active Pharmaceutical Ingredients and Brokers of Medicinal Products

Under amendments (via the so-called 'Falsified Medicines Directive') to the Medicines Directive, 2001/83/EC, that came into force at the beginning of 2013, manufacturers, importers and distributors of active substances are required to register with us.

The total numbers of registrations in place at year end is outlined by category in the accompanying table.

Brokers of medicines for human use are also required to register with us. One new broker registration was issued, meaning that there was a total of two registrations in place at year end.

Total Number of Registrations for Active Pharmaceuticals Ingredients	2013	2014	2015
Manufacturers	22	22	22
Importers	35	37	37
Distributors	38	36	37
Total	95	95	96

Export Certificates

Export certificates are required by health authorities in many so-called third country markets as an indication that a product registered, authorised and / or manufactured in the country of origin is of appropriate quality. The inspection and authorisation / registration programmes operated by us form the basis on which certificates are issued. Where possible, certificate formats, as published by the World Health Organisation, are used.

There was an output of 4,346 export certificates as set out below.

Product Certification Activity	2011	2012	2013	2014	2015
Certification of Documents	239	272	223	231	134
Certificates of Good Manufacturing Practice for Active Substance and Finished Product Manufacturers	272	276	252	255	221
Certificates for Medicinal Products	1416	1350	1510	2112	1358
Medical Device Free Sale Certificates	1780	1522	1987	2535	2601
Other	51	16	50	86	32
Total	4146	3436	4022	5219	4346

Export certificates can also be required to facilitate the registration of cosmetics in third countries. The certificates issued by us are based on the product concerned having a valid registration in the EU.

Product Certification Activity	2011	2012	2013	2014	2015
Cosmetics Free Sale Certificates	388	210	242	246	216

4,346

EXPORT CERTIFICATES ISSUED

SAFETY AND COMPLIANCE MONITORING

Post-market surveillance, which refers to the safety monitoring of medicines, medical devices and other healthcare products that have been authorised, licensed or registered for use in Ireland, is a primary function of the HPRA.

There are a range of tools employed to monitor the safety of health products while quality issues may also arise at the post-market stage. Where changes to how a product is used are required to enhance safety, we work closely with stakeholders to ensure such changes are introduced in a timely and effective manner.

Human Medicines

Pharmacovigilance

Pharmacovigilance is defined as the science and activities relating to the detection, assessment, understanding and prevention of adverse reactions, or side effects, associated with the use of medicines.

The HPRA, in co-operation with pharmacovigilance professionals in Europe and further afield, monitors adverse reaction reports to look for new types of reactions or changing trends in reporting. If there appears to be a new and serious risk emerging, the issue must be assessed to determine the impact on the overall benefit-risk profile of the medicine concerned and consideration is given as to how any new risks should best be managed and communicated to healthcare professionals and patients.

During 2015, the HPRA received a total of 2,810 new adverse reaction reports associated with the use of human medicines in Ireland. While this represents a slight decrease when compared with the 2,884 reports received in 2014, overall reporting rates have remained quite consistent in recent years. In addition, 2,615 follow-up reports were also received during the past 12 months with any duplicate case reports reconciled with previously submitted cases and invalid / nullified reports managed appropriately.

Source of Suspected New Adverse Reaction Reports	%
Pharmaceutical company	67
Patient/Consumer	8
Community Care doctor	4
Community Pharmacist	4
General Practitioner	4
Hospital Pharmacist	4
Nurse	4
Hospital Doctor/Specialists	3
Clinical Trial reports	1
Other	1

The majority of adverse reaction reports are notified to the HPRA by pharmaceutical companies marketing the medicines, also known as marketing authorisation holders. It is important to note that reports submitted by pharmaceutical companies to the HPRA, in the context of their regulatory reporting obligations, will have initially been notified to them by healthcare professionals, patients or consumers.

Medicines subject to additional monitoring accounted for 25% of the reports submitted during 2015. The requirements for additional monitoring, introduced in the context of the pharmacovigilance legislative revisions in 2012, highlight the importance of reporting all suspected adverse reactions associated with the use of these products which are identifiable by a black inverted triangle included on the accompanying package leaflet (PL) and the summary of product characteristics (SmPC).

Reports submitted to the HPRA in many instances arise from suspicions occurring during observation of an unexpected and / or unwanted event, in the context of use of a medicine. They also include adverse reactions known to occur in association with medicines such as those described in the product information.

The medicines most frequently included in reports to the HPRA accounted for over 55% of the adverse reaction reports received during 2015 (see table). It is important to note that the place of a medicine on this list cannot be taken as an indicator of safety or risk. The number of reports received cannot be used as a basis for determining the incidence of a reaction as neither the total number of reactions occurring, nor the number of patients using a medicine, is known.

Suspect Medicine(s)/ Class of Medicines	Number of Reports in 2015
Protein kinase inhibitors	258
Antipsychotic medicines	223
Selective immunosuppressant medicines	207
Antithrombotic agents	181
Systemic antiviral medicines	158
Anti-TNF inhibitors	156
Vaccines used in the primary immunisation programme	148
HPV vaccine	112
Medicines used in the treatment of bone disease	87
Systemic antibiotics	87

Of the reports received by the HPRA, 147 patients were reported to have died while on treatment. The accompanying table outlines the medicines / class of medicines associated with the highest number of reports.

In many of these cases, the patients concerned had significant underlying illness and were treated with multiple medicines and / or surgery, which may also have contributed to the outcome. In addition, many of these cases were influenced by disease progression or other complications unrelated to the medicine. The majority were associated with medicines used in the context of products subject to close monitoring, those used in the management of severe underlying medical conditions, in patient support programmes and special patient monitoring programmes.

Suspect Medicine(s)/ Class of Medicines	Number of Reports in 2015*
Antineoplastic medicines	50
Antipsychotic medicines	22
Antithrombotic agents	19
Systemic antiviral medicines	16
Selective immunosuppressant medicines	15
Systemic antibiotics	9
Analgesics (including NSAIDs and Opioids)	9
Antiepileptic medicines	7
Medicines used in the treatment of bone disease	5
Immunostimulant medicines	4

* Please note that in some cases treatment may have involved more than one medicine from the above groups.

Online and Electronic Reporting

The online reporting system, available to healthcare professionals and patients / consumers, continued to be used during 2015 with some 484 reports submitted via our website by year end. This was a significant increase when compared to the 391 reports submitted online during the previous year. As part of this increase, the submission of reports directly by patients and consumers grew in annual terms by over 5%.

The HPRA continued to increase both receipt and transmission of individual case safety reports (ICSRs) electronically during 2015 and actively engaged with companies to encourage and facilitate testing to support additional electronic reporting throughout the year.

Monitoring Compliance with Pharmacovigilance Obligations

Company / sponsor compliance with pharmacovigilance obligations continued to be monitored throughout 2015, with follow up and feedback provided as appropriate. See Inspections and Audits on page 49 for details of the associated inspection programme.

Vigilance Assessment and Risk Management

The HPRA plays a key role in monitoring the safety of medicines available on the Irish market through the regular assessment of signals and emerging safety issues, and via routine and urgent benefit-risk evaluations. The HPRA also proactively participates in evaluating and approving risk management plans for medicines throughout their life cycle and serves as a key source of advice and information on the safe and effective use of medicines. The HPRA is represented at a European level on the Pharmacovigilance Risk Assessment Committee (PRAC) and works continuously with the EMA and other Member States within the EU to ensure robust and timely decision-making on safety-related issues.

Signal Management Activities

Signal detection and management activities allow for enhanced detection of new or changing safety issues relating to medicines thus allowing for more rapid action when necessary to protect public health. Throughout 2015, the HPRA continued its participation in the work-sharing initiative for signal detection within the EU acting as lead Member State in the detection and management of signals for 54 active substances authorised nationally. Serving as the PRAC rapporteur, the HPRA was also responsible for the further management of any signals detected in relation to 27 centrally authorised active substances / combination of active substances. Labelling changes were also implemented for nationally authorised products during the past year following PRAC recommendations thus ensuring improved medicines information was provided to healthcare professionals and patients.

The HPRA continued its participation in the Signal Management Review Team at the EMA which focuses on improving tools, methods and processes for signal detection as well as developing methodological guidance.

Periodic Safety Update Reports

Periodic safety update reports (PSURs) are pharmacovigilance documents submitted by marketing authorisation holders at defined time points following authorisation of products. PSURs are intended to provide a continuous cumulative update and analysis on the benefit-risk profile of a medicine throughout its lifecycle. The outcome of these procedures may lead to automatic harmonised regulatory action if considered necessary such as a variation, suspension or revocation. During the year in review, the HPRA contributing to the evaluation of 1,002 EU PSUR single assessment (PSUSA) procedures and consistently ranked in the top 10 for appointments as lead Member State for PSUSA evaluation for nationally authorised products at EU level.

Safety Referrals

In a safety related referral, the EMA conducts a scientific assessment of a particular medicine or class of medicines, through the PRAC, on behalf of the EU. Following this assessment, PRAC makes a recommendation for a harmonised position across the EU which is ultimately implemented nationally by the HPRA.

The HPRA participated as concerned Member State in five newly initiated safety referrals in 2015 and a further four safety referrals which reached a conclusion during the year. The HPRA ensures that the final outcomes of referrals are implemented nationally and communicated to stakeholders.

1,002

THE NUMBER OF EU PSUR SINGLE ASSESSMENT PROCEDURES EVALUATED WITH HPRA INPUT

Risk Management Plans and Post Authorisation Safety Studies

All new applications for drug marketing authorisations now include a risk management plan (RMP) documenting the proposed risk management system to be implemented once a marketing authorisation is granted. During 2015, the total output was 356 RMPs (newly approved or updated) submitted via national, mutual recognition, decentralised and centralised procedures. The HPRA ranked 10th amongst the EU Member States for PRAC rapporteurship / co-rapporteurship appointments for initial marketing authorisation applications. These products include treatments for orphan diseases including cystic fibrosis as well as other innovative products.

The HPRA also provided assessment input to 263 post authorisation safety study (PASS) procedures (protocols, reports and other post authorisation safety-related measures). PASS are non-interventional studies carried out as part of a risk management plan in order to further evaluate the safety and benefit-risk profile of a medicine in the post-authorisation phase, or to measure the effectiveness of risk minimisation activities that have been introduced.

Risk Communications

As part of its role to promote and support the safe and effective use of medicines, the HPRA reviewed and approved 21 direct healthcare professional communications (DHPCs) which provided new safety information or risk minimisation advice to prescribers and published these on the HPRA website. During 2015, the HPRA also commenced online publication of educational materials and tools which have been developed by marketing authorisation holders as additional risk minimisation measures for their medicines. In total, 70 suites of educational materials were approved by the HPRA by year end.

Blood, Tissues and Cells, Organs

Haemovigilance

The HPRA is the competent authority for legislation concerning blood and blood components. Haemovigilance refers to a set of organised surveillance procedures relating to serious adverse or unexpected events or reactions in donors or recipients and the epidemiological follow-up of donors.

The HPRA continued its interaction with the National Haemovigilance Office (NHO) during 2015, including discussion of issues of mutual interest and concern at bilateral quarterly meetings.

Following collaboration with the NHO, the HPRA submitted an annual report of serious adverse reactions and events to the European Commission during 2015. The report reflected information received from January to December 2014 and included information on 64 serious adverse reactions and 201 serious adverse events which met the mandatory legislative reporting requirements.

The HPRA continued to work closely with the Irish Blood Transfusion Service (IBTS) and the Department of Health in respect of haemovigilance activities and developments. This included a contribution to the review of options proposed by the IBTS / NHO for the online reporting system to facilitate simultaneous submission of mandatory reports to both the NHO and HPRA. Pending finalisation of these formalised arrangements, and access to an online reporting system, the interim arrangements, first agreed for reporting to the HPRA in 2008, continued to operate throughout the past year. These arrangements have facilitated consistency and timeliness in reporting allowing appropriate regulatory oversight.

Tissue and Cell Vigilance

The HPRA is the competent authority in Ireland for the purposes of the EU tissues and cells legislation. The legislation focuses on standards of quality and safety for donations, procurement, testing, processing, preservation, storage and distribution of human tissues and cells.

The HPRA submitted an annual report on serious adverse reactions and events associated with tissues and cells to the EU Commission during 2015. The report reflected information received in 2014 and consisted of some 42 reports, 29 of which met the legislative reporting requirements, including two serious adverse reactions and 27 serious adverse events.

Human Organs for Transplantation

During 2015, the HPRA continued to liaise closely with the Health Service Executive (HSE) lead and colleagues responsible for this area in relation to the development of report forms and guidance to facilitate serious adverse reaction and event reporting.

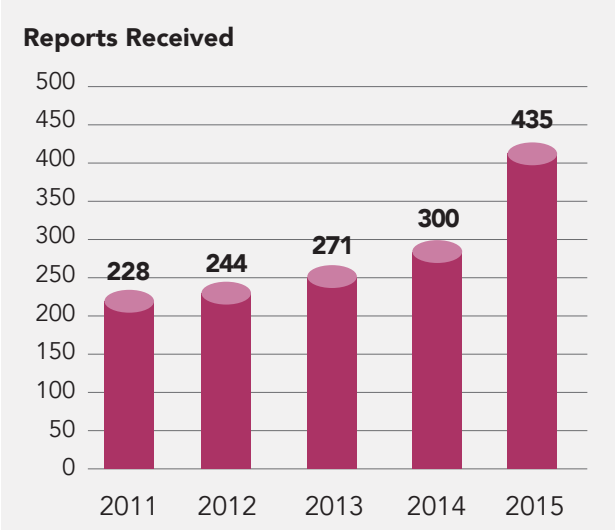
During the past year, the HPRA received 12 reports of serious adverse reactions and events associated with organ donation / transplantation. These reports have been followed up with the HSE in the context of its regulatory role as the competent authority for clinical and transplant related matters.

Veterinary Medicines

Pharmacovigilance

The operation of a national pharmacovigilance system which is based on the receipt and review of reports of suspected adverse events is a primary role of the HPRA. An effective system enables us to monitor the continued safety and efficacy of veterinary medicines under actual use conditions. Where necessary, the HPRA will intervene and introduce new risk management measures for a product. In so doing, we strive to prevent adverse effects in other animals as well as in humans exposed to the medicine.

The effectiveness of the system is dependent on the submission of reports by veterinarians, pharmacists, licensed merchants and others involved in dispensing or using the products concerned. These reports may be submitted either directly to the HPRA or to the companies' marketing the products. The companies, in turn, must relay the data to the HPRA.



During the 12 months under review, the HPRA received 437 national reports of suspected adverse events to veterinary medicines. The vast majority of reports (95%) were received from pharmaceutical companies.

The quite significant increase in the number of reports received in 2015 is due to greater reporting of suspected lack of expected efficacy. One of the factors for the increase in such reports is a change in reporting practices whereby a number of companies marketing products are now reporting non-serious reports in addition to the serious reports required under legislation.

Periodic Safety Update Reports

Evaluating PSURs on individual products accounts for approximately 38% of the HPRA's overall veterinary medicines workload currently and is evidence of our commitment to the ongoing assessment of benefits and risks. Our work includes the assessment of individual medicines on the market in Ireland as well as a work-sharing initiative where we lead, or contribute to, the assessment of a class of veterinary medicines for the European Union.

The HPRA completed the evaluation of 1,205 PSURs in 2015 which was a notable increase on the figure of 852 in the previous 12-month period.

Use of Veterinary Antimicrobials in Ireland

The HPRA collects annual information on the consumption of veterinary antibiotics from each marketing authorisation holder. This information is important as it allows us to benchmark our usage rate against those of our European neighbours. The data for the period 2009 to 2014 show that there are significant fluctuations in consumption levels annually and, consequently, that a clear trend is not yet evident. This is likely due to a variety of factors, such as seasonal disease patterns, fluctuations in the classes of antibiotics being prescribed, end of year sales activities, the numbers of animals slaughtered and exported as well as changes in breeding policy for the national herd.

The HPRA continues to work with other EU veterinary medicines agencies and the EU Commission to help ensure that veterinary antibiotics are used responsibly in accordance with their approved conditions of use.

Consumption of Antibiotics	2009	2010	2011	2012	2013	2014
Tonnes sold	88.3	93.9	85.2	97.4	100.2	90.2

Scientific Animal Protection

This relatively new area represents a very important opportunity to improve the welfare of animals used for scientific purposes and to ensure that animals are used only when there is no alternative to their use and the use itself is properly justified.

Inspection Programme

A key component of our work involves inspection of animal facilities to monitor animal welfare standards and compliance with legislation. Our inspections, which may be announced or unannounced, follow a risk-based approach.

During 2014, the focus of the HPRAs inspection programme had been determined by the legislative requirement to complete the authorisation of all relevant national establishments previously licensed by the Department of Health. There were therefore a particularly high number of inspections conducted in 2014, as, in addition to the compliance inspections conducted that year, every establishment (including those deemed to be very low risk) had to be inspected for the purposes of granting an establishment authorisation. The focus for 2015, however, was on carrying out compliance inspections, a significant proportion (28%) of which were unannounced inspections. These inspections help us to ensure the welfare of animals used in scientific studies as well as ensuring that unauthorised animal experiments cannot take place in this country.

Number / Category of Inspections	2013	2014	2015
Total	30	38	29
Advisory inspections	22	1	0
Establishment authorisation inspections	1	23	0
Announced compliance inspections	2	11	21
Unannounced compliance inspections	3	3	8
% of unannounced inspections	10%	8%	28%

Market Compliance – Human and Veterinary Medicines

The HPRA is responsible for a number of risk-based market surveillance programmes. These include proactive activities such as the sampling and analysis programme and the advertising compliance programme, and reactive activities such as the quality defect and recall programme.

We also operate an exempt medicines notification scheme designed to monitor the importation and supply of unauthorised medicines. In addition, we carry out a programme of regulatory compliance inspections at the premises of marketing authorisation holders. The latter is designed to assess the level of compliance against national legislation relating to the placing on the market and advertising of medicines.

Sampling and Analysis Programme

The risk based sampling and analysis programme is part of our monitoring of the quality and safety of medicines and our identification of borderline medicinal / non-medicinal products that may be on the Irish market. This is achieved through analytical testing and / or examination of packaging and labelling of medicines, active substances, borderline medicinal / non-medicines and enforcement-related samples.

A total of 480 product samples were sent for analytical testing / examination work. Details are provided in the accompanying tables.

Examination of Packaging and Labelling

The packaging and labelling of 156 medicines and other products available on the Irish market were examined. Individual checks were carried out on the samples including reviews of the safety information contained in the package leaflets.

Authorised medicines accounted for 96% of the products examined and all of these were examined for signs of falsification and tampering. No issues were identified. Of the products examined, 30% were parallel imported or parallel distributed products and a small number were products supplied via the exempt medicines route. Braille compliance checks were also carried out on 31% of the products.

The following table outlines the type of examinations that were carried out:

Categories of products examined for packaging and labelling attributes	Number of samples examined
Authorised medicines (including samples for Braille compliance checks)	102
Authorised parallel imported and parallel distributed medicines	47
Exempt medicines	7
Total	156

Analytical Testing

During the past year, 297 medicinal and other product samples were sent for analytical testing. These included 234 samples sent to governmental laboratories in Ireland and 69 samples sent to governmental laboratories in other countries as part of European working-sharing arrangements.

A breakdown of the types of samples tested is outlined in the accompanying table. In summary, 53% were authorised medicines, 27% related to enforcement and borderline medicines / non-medicines, while 19% were actives and other substances.

Product categories selected for analytical testing in 2015	Number of samples analysed
Physico-chemical Analysis / Biological Analysis:	
Enforcement-related products for human use	83
MRP / DCP authorised medicines for human use	61
Centrally authorised medicines for human use	36
Nationally authorised medicines for human use	35
Active / Intermediate pharmaceutical ingredients	33
Parallel imported medicines for human use	10
Other product categories	23
Microbiological Analysis:	
Nationally authorised medicines for human use	10
Other product categories	6
Total	297

Participation in EU Co-ordinated Market Surveillance Activities

The HPRA is an active participant in EU surveillance programmes that involve the sampling and analysis of medicines. This is achieved by its active participation in the Official Medicines Control Laboratories (OMCL) network, co-ordinated by the European Directorate for Quality of Medicines (EDQM) in Strasbourg.

The 2015 programmes included:

- Centrally authorised medicines: 29 sampled in Ireland for testing at OMCLs in other Member States and seven tested at the HPRA's OMCL (Public Analyst's Laboratory, Galway).
- MRP / DCP: 11 medicines sampled in Ireland and analysed at other Member State OMCLs.
- Other products: A number were analysed at our request at OMCLs in other Member States. For example, 16 products underwent microbiological analysis at the Finnish and Czech OMCLs.

Principal Findings

Analysis	Findings
Laboratory analysis	While the majority of samples tested were compliant with their specifications, 12 of out-of-specification results were obtained. Nine deficiencies were identified in the analytical methods and specification documents used by manufacturers of medicines.
Packaging and labelling	In total, 15 non-compliances, including 11 braille-related issues, were identified across samples of a number of human and veterinary authorised medicines.

Appropriate follow-up actions were taken in each case.

Acknowledgements

The HPRA would like to thank the staff of the Public Analyst's Laboratory, Galway, and the staff of the State Laboratory, Young's Cross, Celbridge, Co. Kildare, for their invaluable contributions to the HPRA's sampling and analysis programme in 2015.

Quality Defects and Recalls

The HPRA's quality defects and recalls programme investigates, on the basis of risk to public and animal health, reports of suspected quality defects in both human and veterinary medicines and in their related active substances. We also co-ordinate any subsequent recall actions on the Irish market.

Number and Types of Quality Defects

A total of 772 quality defects were reported to, or identified by, the HPRA during the past 12 months representing a decrease of 5% on the figure for 2014. The accompanying table outlines the corresponding risk classification applied to each report.

Overall, 633 reports (82%) were determined to affect Ireland meaning that the defective batch or batches were either on the Irish market and / or were manufactured in Ireland. Medicines for human use accounted for 737 quality defect reports with 35 reports concerning veterinary medicines.

Critical quality defects, which are those defects defined as potentially life-threatening or a serious risk to health, accounted for 214 of the total reports received. Of these, 118 were deemed to affect Ireland. These included 49 reports relating to lack of sterility assurance, 41 reports of potential contamination and 14 reports of a falsified medicine.

The most common categories / causes of defects were:

- Stability issues (150 reports)
- Contamination issues (125 reports)
- SmPC / printed artwork issues (68 reports)
- Lack of sterility assurance (57 reports)

Of the 150 stability issues investigated, 124 cases affected Ireland, with 61 of those products having been manufactured in Ireland for the home and other markets. The figures for lack of sterility assurance and contamination include four separate events at one compounding facility that affected 85 products.

In relation to each instance of lack of sterility assurance / potential contamination, it was subsequently confirmed that there was no evidence of contamination in any of the concerned medicines. The 14 falsified medicine issues were classified as affecting Ireland because in each case the genuine products, of which falsified representations were detected on other markets, were manufactured in Ireland.

Year	2011	2012	2013	2014	2015
Minor Quality Defects	314	236	230	248	214
Major Quality Defects	364	303	300	199	226
Critical Quality Defects	231	189	235	365	326
Number of Quality Defect Reports Not Justified	8	13	9	4	6
Total Number Quality Defects	917	741	774	816	772

Sources of Quality Defects

As in previous years, pharmaceutical companies and other competent authorities accounted for the majority of reports of quality defects received.

Source of Reports	Human Medicines	Veterinary Medicines
Companies (Manufacturers, distributors and / or authorisation holders)	490	32
Other Competent Authorities (Regulators)	147	3
HPRA Staff Members	41	
Community Pharmacists	32	
Hospital Pharmacists	20	
Other Health Care Professionals	4	
Patients and / or Members of the Public	2	

Recalls of Human and Veterinary Medicinal Products

In certain cases, so as to protect public or animal health, it is deemed necessary to withdraw, or recall, products from the Irish market. During the year in review, 116 medicine recalls occurred. Of these, 113 related to human medicines and three to veterinary medicines.

As regards the level of recall, 44% were to patient / user level, 22% to pharmacy / retail level and 34% to wholesale level. The proportion of recalls to patient level is high compared with recent years. This can be attributed to four recalls of compounded products affecting 48 different products (41% of all recalls). Consequently, 67 (58%) of the products recalled from the Irish market were manufactured in Irish manufacturing facilities, compared with 24 (24%) in 2014. These were mainly precautionary recalls of compounded products for human use. Exempt medicines accounted for 12% of human medicine recalls.

The most common causes of a human medicine recalls were:

- Lack of sterility assurance (27)
- Contamination issues (25)
- SmPC / printed artwork issues (11)
- Cold-chain issues (8)
- Stability issues (8)
- Non-compliance with GMP (6)

In respect of veterinary medicines, two of the recalls related to stability issues while the remaining recall was due to a lack of therapeutic efficacy.

Retail Sales Monitoring

General Retail Sale Investigations

The sale of consumer healthcare products by retail outlets such as grocery shops, health food shops and, where necessary, pharmacies, is monitored by the HPRA using a proactive and reactive, risk based, retail monitoring programme. During 2015, 69 cases, some of which involved multiple products, were investigated. Of these, 36 related to the sale of medicines that did not carry a valid registration number or authorisation number for the Irish market. An additional 32 cases related to the sale of medicines that had been incorrectly classified as non-medicines by those placing them on the market while one case related to the sale of a pharmacy-only medicine by a non-pharmacy retailer. A total of 143 products that did not carry a valid registration or authorisation for the Irish market were removed from sale.

Exempt Medicines Programme

Medicines placed on the Irish market must be authorised by the HPRA or, in the case of centrally authorised products, by the European Commission. However, European and Irish legislation provide for an exemption to this rule. In this case, authorised healthcare professionals are permitted to prescribe unauthorised medicines for individual patients under their direct responsibility in order to fulfil the special needs of those patients. Such products are referred to in Irish law as 'exempt medicines'. Under Irish medicines legislation, wholesalers and manufacturers of medicines are obliged to notify certain information to us in relation to any exempt products that they source. This is done by submitting electronic notification to a HPRA database. This information facilitates, when required, the effective recall of any defective exempt medicine from the Irish market.

In 2015, 1,639,312 packs of exempt medicines were notified to us. In addition, we responded to approximately 200 queries related to the exempt medicinal products programme.

Note: The figure in the 2014 Annual Report for the number of packs notified during that year was significantly higher than that for 2015. However, the HPRA has since become aware that the 2014 figure, which was in excess of three million packs, was overstated due to an error in the way that the database counted pack numbers.

Regulatory Compliance Inspections

These risk-based inspections are carried out at the premises of marketing authorisation holders. The inspection seeks to determine the level of compliance with the legal requirements for the marketing and advertising of medicines. Three inspections were carried out at the premises of marketing authorisation holders and a number of non-compliances were identified. These were followed up and we monitored the implementation of corrective actions at the companies concerned. This inspection activity is linked to the HPRA's advertising compliance programme.

Human Medicines Advertising Compliance Programme

It is the role of the HPRA to monitor and review advertising and promotion activities by the industry for compliance with the requirements of the Medicinal Products (Control of Advertising) Regulations, 2007. Some 152 advertisements were reviewed for compliance.

The five aspects to the programme are shown in the table below:

In all cases of non-compliance identified under the different elements of the programme, the HPRA supervised the adoption of the necessary corrective and / or preventative actions by the marketing authorisation holder.

	Total	Advertisements Reviewed	Non-Compliances Identified
Proactive Monitoring: Pre-planned Projects	4	48	Seven individual advertisements were non-compliant.
Proactive Monitoring: Includes Randomly Selected Projects	1	1	This advertisement was found to be compliant.
MAH Inspections Performed	3	Multiple	Five major and other deficiencies identified across a number of areas with one major deficiency related directly to advertising activities.
Complaints Received	22	45	14 with seven complaints upheld as being valid. Six advertisements in total were non-compliant.
Queries Received	66	58	18 advertisements were non-compliant.

*Note: Some of these figures are approximate. They may include website advertisements, and each page of a website is counted as one advertisement, because multiple pages can have multiple advertisements. Additionally, the data exclude advertisements that were reviewed during the regulatory compliance inspections work. Numerous advertisements were reviewed during those inspections.

Medical Devices

Vigilance

The medical devices vigilance system which was established under European medical device directives aims to minimise risks to the safety of patients, users and others. Vigilance activities include the following:

- The submission of vigilance reports by manufacturers and users to the relevant competent authorities (the HPRA in Ireland);
- The evaluation of reported incidents by the competent authorities;
- The dissemination of information, which may be used to prevent recurrence of the incident, or to alleviate the consequences of such incidents, in cases when it is necessary to do so;
- A device being updated, modified or taken off the market in cases when it is necessary to do so.

In 2015, there was a particular HPRA focus on the dissemination of medical device safety communications.

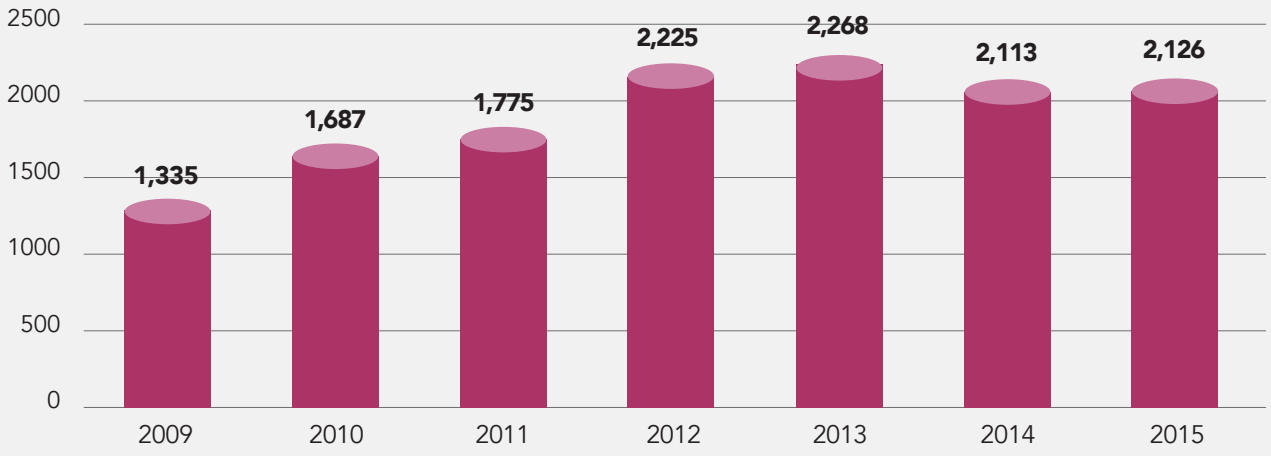
2015 Reports in Summary

A total of 2,126 medical device vigilance reports were received and assessed representing a slight increase on 2014. Manufacturers accounted for 57% of all vigilance reports received in 2015 while 24% were received from competent authorities. Of the incidents reported, 35% were as a result of an incident on the Irish market. Of the Irish Incidents, 30% were related to an ongoing field safety corrective action.

Concerning the regulatory response to the reports received, 62% resulted in an action being taken in Europe. In Ireland, the HPRA published online 474 manufacturer's field safety notices directly affecting the local market. These notices are intended to inform users of safety issues relating to medical devices. In addition, there were 160 product removals conducted in Ireland in 2015.

Safety information was also highlighted to the public through HPRA safety notices. There were 33 such notices sent to relevant interest groups and published on our website. During the year in review, we issued 76 national competent authority reports.

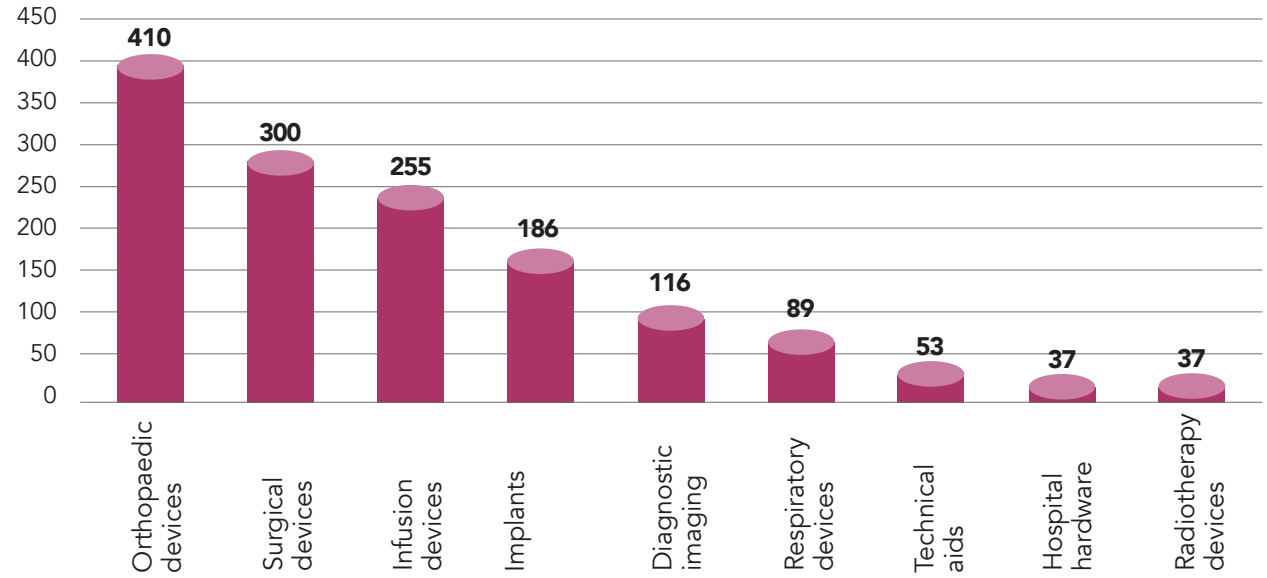
Number of Vigilance Reports



2015 Reports by Product Type

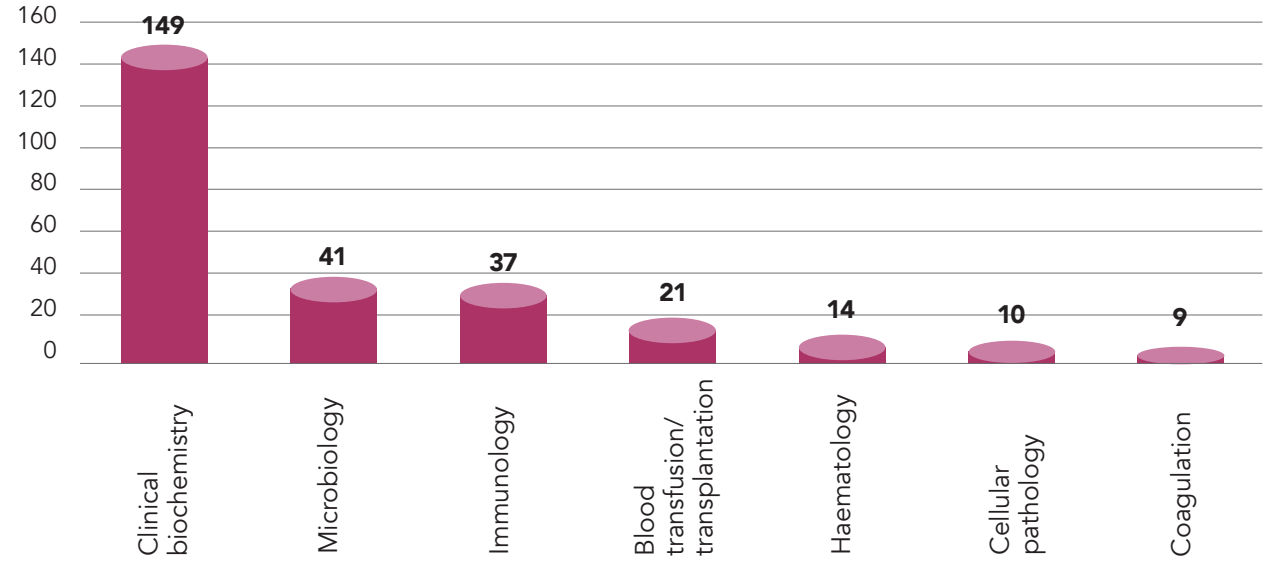
Orthopaedic, surgical devices and infusion devices accounted for a large proportion of vigilance reports received. Reports were again received relating to software issues associated with medical devices. The HPRA continued to receive reports relating to revision procedures associated with the ASR Articular Surface Replacement and ASR XL Acetabular system manufactured by DePuy.

Vigilance Reports Received – General Medical Devices



In the area of *in-vitro* diagnostic (IVD) devices, the largest number of vigilance reports received related to clinical biochemistry. Field safety corrective actions relating to clinical biochemistry reagents and analysers continued to have a high impact on the number of IVD vigilance cases.

Vigilance Reports Received – *In Vitro* Family Group



Market Surveillance

Medical device surveillance activities are focused on protecting the health and safety of those who use medical devices. Our role includes continuous surveillance of the market to monitor the regulatory compliance of medical devices after they are placed on the market.

Surveillance Cases

During 2015, the HPRA continued to develop its lifecycle approach to market surveillance and investigated 324 market surveillance cases. It is expected that market surveillance activity will increase further in the future due to ongoing increases in both the number of European Compliance and Enforcement (COEN) requests from other Member States and the number of certificate notifications from notified bodies. COEN requests serve as a method for communication between European authorities on market surveillance issues.

Other market surveillance activities conducted in 2015 include:

- The development of the system and procedure guidance pack;
- The development of a Medical Device Information Notice for communicating market surveillance issues;
- Review of food intolerance products available on the Irish market;
- Review of the standalone software on the HPRA register;
- Proactive reviews of respiratory and ophthalmic manufacturers based in Ireland;
- Review of bio resonance products;
- Development of specific test methods implant analysis;
- Reviews of clinical data presented as part of clinical evaluations of high risk medical devices.

The HPRA also initiated a program of sampling and analysis in 2015 which included testing of several types of implants.

Certificate Withdrawals

There was an increasing trend of certificate refusals, withdrawals and suspensions from notified bodies during 2015 reaching 959 by year end. The number of notifications received highlights the impact of the joint assessment process for notified bodies which may affect the scope of activities and potentially the ongoing validity of certificates issued. The number also reflects the continued improvements in performance and consistency of notified bodies. The HPRA investigated those certificate notifications with implications for the Irish market, those arising from identified safety concerns and major non-compliances, and those arising from a reduction in the designation scope or de-designation of notified bodies.

Technical File Reviews

In 2015, the HPRA continued its increased focus on review of technical documentation both in the context of market surveillance activities and notified body oversight. A total of 17 technical file reviews were completed in 2015. The proactive technical file reviews were requested as part of reactive market surveillance with a particular emphasis on the areas of software, respiratory and ophthalmic devices as well as files associated with the Irish notified body.

Clinical Evaluation Review

During 2015, the HPRA increased its activities further in the assessment of clinical data presented by manufacturers to support the safety and performance of their device. A total of 32 clinical evaluation reviews were conducted. This work was undertaken reactively in response to a number of specific device issues highlighted during the year and proactively as part of our ongoing market surveillance activities. This work also formed a significant part of our notified body designation and oversight activities both at national level and European level as part of EU joint assessment activities.

Designation and Monitoring of the Irish Notified Body

A key activity for the HPRA in 2015 was the assessment of an application from the NSAI which resulted in the renewal of its designation as a notified body for medical devices in accordance with the new European Regulation (920/2013). The assessment was conducted as part of a joint assessment team led by the European Commission's Food and Veterinary Office (FVO). National experts from the Turkish and UK regulatory agencies also participated. Both the HPRA and NSAI received positive feedback from the FVO following the assessment.

In addition, one observed audit was conducted by the HPRA of NSAI staff auditing medical device manufacturing sites.

The HPRA provided technical, clinical and quality system experts to support six joint assessments of medical device notified bodies in other European countries during 2015.

The HPRA received 69 certification notifications from NSAI during the past year. These notifications were uploaded, as required, to the European EUDAMED database.

324

MARKET SURVEILLANCE CASES INVESTIGATED

Market Compliance of Cosmetics

Proactive Market Surveillance

Post market surveillance of cosmetic products includes a national sampling and analysis programme and involves close co-operation between the HPRA and the HSE's Environmental Health Service and Public Analyst Laboratories in Galway, Cork and Dublin. During 2015, 469 cosmetic products were included in the sampling programme. Analysis was carried out in respect of 398 of these products by year-end with 71 (18%) found to be non-compliant. The largest areas of non-compliance related to skin whitening products containing prohibited substances, sunscreens containing undeclared UV filters, hair dyes missing appropriate label warnings and microbial contamination of baby powders, face paint creams and hand cleaning products.

Reactive Market Surveillance

Reactive surveillance includes investigation of quality related complaints (compliance cases), reports of adverse events relating to the use of cosmetics (vigilance cases) and RAPEX serious risk alerts.

During the past year, 107 compliance cases were opened and 99 closed. Of these, 90 involved cosmetic products that were deemed to be non-compliant with the EU Cosmetics Regulation 1223/2009. The majority of non-compliances were in the areas of labelling, the presence of prohibited substances, contamination (mainly microbiological or heavy metals) and unsupported efficacy claims. A total of four products were withdrawn from the Irish market as a result of stability issues, contamination or the presence of prohibited substances.

Eleven vigilance cases were investigated relating to different product types such as hair dyes, face masks, moisturisers and shampoos.

During the year, 55 RAPEX serious risk alerts were received from other European Member States regarding non-compliant cosmetic products. One of these products was found on the Irish market and removed from sale.

Reactive Market Surveillance	2013	2014	2015
Compliance cases opened	145	105	107
Compliance cases closed	139	109	99
Vigilance cases opened	17	21	11
Vigilance cases closed	19	14	20
RAPEX alerts received	102	100	55
Recalls / withdrawals from the Irish market	-	1	4

Inspections and Audits

As part of our regulatory role, the HPRA is focused on ensuring industry compliance with relevant standards and legislation. Our inspections and audits work programme includes:

- Regular inspections of manufacturers and wholesalers of medicines to check for compliance with EU guidelines on Good Manufacturing Practice (GMP) and Good Distribution Practice (GDP), respectively.
- Inspection of manufacturers of active substances for compliance with EU guidelines on GMP.
- Inspection of clinical trial sites for compliance with EU and International Conference on Harmonisation (ICH) guidelines on Good Clinical Practice (GCP).
- Inspection for compliance, by marketing authorisation holders, with Good Pharmacovigilance Practice.
- Regular audits of the NSAI, the notified body for medical devices that is designated by the HPRA.
- Proactive audit of manufacturers of Class I devices and 'for cause' audits as required, for example, as part of the follow-up to a defect.
- Inspection of blood, tissue and cells, and organ establishments for compliance with applicable EU guidelines on the quality and safety of blood, blood products, tissues and cells, and human organs intended for transplantation.
- Inspection, often in conjunction with the Garda National Drugs Unit, of manufacturers and wholesalers of medicines containing controlled drugs (CD) and of precursors (chemicals that can be used in the preparation of illicit drugs).
- Inspection, primarily based on risk assessment, of manufacturers of cosmetic products.

Overview of the 2015 Inspection Programme

During the 12 months under review, 344 inspections and audits were performed compared to 260 in 2014 and 313 in 2013. The average number of days required to close-out inspections and audits was 106.

Performance Results and Statistics	2011	2012	2013	2014	2015
No. of national inspections and audits performed	271	289	279	229	319
No. of foreign inspections and audits performed	29	26	34	31	25
% inspections and audits closed on time (≤ 90 days)	66	61	63	61	67
Average time for close-out (days)	79	76	103	112	106

In the past year, there were:

- 124 GMP inspections carried out at manufacturing sites. These included 21 inspections in non-EEA countries, 14 of which were carried out at the request of the EMA for centrally authorised products. Of the GMP inspections carried out, 15 were of active substance manufacturers.
- 126 GDP inspections of wholesalers were performed. There were also 26 inspections of sites that handled controlled substances (controlled drugs or precursor chemicals), two inspections of medicines brokers and two inspections of registered distributors of active substances.
- 15 GCP inspections were carried out at investigator sites in Ireland.
- Two pharmacovigilance inspections were conducted. The first was at the facility of an Irish based marketing authorisation holder while the second inspection, relating to centrally-authorised medicines, was conducted at the request of the EMA.
- Medical devices / Notified Body Assessment: A full re-designation assessment of the Irish notified body, the NSAI, was completed. This assessment was also part of the EU joint assessment program and was carried out alongside representatives of the European Commission's Food and Veterinary Office and national experts (as outlined earlier on page 47).
- An observed assessment of an NSAI auditor at a class III implantable medical device manufacturer based in the US was also conducted.
- 16 audits were performed at both medical device manufacturer and authorised representative facilities. Of these, two were for-cause audits (one of which was at a US based facility), eight were reactive audits based on vigilance / market compliance issues, four were proactive audits based on proactive market surveillance projects while the remaining two audits were of authorised representatives of medical device manufacturers.
- Seven blood establishment inspections were completed. These included six inspections of facilities maintained by the IBTS and one routine inspection of a holder of blood and tissue establishment authorisations.
- 16 tissue establishment inspections were carried out.
- Three inspections were carried out to assess applications for authorisation for establishments involved in organ transplantation.
- Three inspections were also carried out under cosmetic products legislation. Two of these inspections were of distributors while one was of a manufacturer. These were the first cosmetic product inspections to be carried out by us.

Enforcement

Illegal activity involving the manufacture, supply and sale of medicines or medical devices can have adverse consequences for public health. It is the role of the HPRA to investigate potential breaches of human medicines, medical device and the majority of other legislation within its remit. Where necessary, we will take the appropriate corrective action, including the possibility of legal proceedings.

Enforcement Cases and Medicines Detained

During 2015, 3,677 enforcement cases were initiated, compared to 3,703 in the previous year. There were a total of 1,136,494 dosage units detained, an increase from 730,056 units in 2014.

Sedative products accounted for almost two-thirds (64%) of all detentions. Erectile dysfunction products and illegal cosmetic products accounted for 9% and 6% of detentions, respectively. Other categories of products detained in smaller quantities included anabolic steroid, slimming and pain relief.

A summary of the HPRA enforcement data is provided in the accompanying table.

Inter-Agency Co-operation and Pangea VIII

The HPRA continues to liaise and work closely with other enforcement agencies both nationally and internationally, in combating, detecting and preventing the unauthorised flow of medicines, medical devices and other health products.

National co-operation between the HPRA, the Revenue's Customs Service and An Garda Síochána continued in 2015 incorporating Operation Pangea VIII. During this operation, the inter-agency approach resulted in the detention of 142,000 tablets and capsules, with an estimated value of over €430,000. Pangea VIII was a global initiative which involved 236 agencies drawn from health product regulatory authorities, police and customs across 115 countries. The operation, which was co-ordinated by INTERPOL, targeted criminal networks behind the sale of falsified and illegal medicines via illicit websites.

Throughout 2015, the HPRA worked in co-operation with the Pharmaceutical Society of Ireland, the HSE and the Food Safety Authority of Ireland across areas of common interest to address offending behaviours in the market. The HPRA also liaised with Sport Ireland regarding substances that could be used in doping.

Prosecutions

The policy of the HPRA is to prosecute where it is considered necessary in order to protect public health and where a compliance based approach is not considered appropriate.

During the past year, one prosecution was initiated while four prosecutions that commenced prior to 2015 were concluded. These cases related to products containing active substances that had the potential to be used for mood stabilisation, sports performance enhancement, erectile dysfunction and weight loss.

Year	2011	2012	2013	2014	2015
Product detained (dosage units)	762,641	758,276	919,965	730,056	1,136,494
Cases Opened	4,549	3,911	3,932	3,703	3,677
Prosecutions	9	11	9	10	1
Product destroyed	4,519kg	1,065kg	4,194kg	3,440kg	0kg (at year end)
Voluntary Formal Caution (VFC)	12	6	27	13	14

LEGISLATIVE AND REGULATORY DEVELOPMENTS

The remit and role of our organisation continues to develop and expand in line with national and European legislative changes and in response to the addition of further competencies.

This section of the 2015 annual report outlines the most significant legislative and regulatory developments during the past year by product type, how these changes influenced the work of the HPRA and, where relevant, the associated impact on stakeholders.

Human Medicines

Falsified Medicines

Work continued towards implementation of the remaining aspects of Directive 2011/62/EU on falsified medicines, which amended Directive 2001/83/EC (relating to medicinal products for human use).

Of note, the European Commission issued a draft Delegated Regulation for consultation in respect of proposed safety features on specified human medicines. It is expected that this will be finalised early in 2016 with a three-year period thereafter for implementation. The HPRA continued to participate in the expert group convened by the Commission to assist with drafting of the Delegated Regulation. We also liaised with industry and other stakeholder organisations in Ireland in relation to the establishment of a National Medicines Verification Organisation. The tasks of this organisation will include development of a repository system to hold batch data and permit authentication of packs of medicines carrying safety features at point of dispensing and at earlier points in the distribution chain.

Also during 2015, regulations amending the Medicinal Products (Prescription and Control of Supply) Regulations 2003 and the Pharmacy Act 2007, were put in place. These provide for legitimate supply of authorised non-prescription medicines by entities that apply, and are listed by, the Pharmaceutical Society of Ireland.

New Clinical Trials Regulation

The new clinical trials legislation (Regulation (EU) No. 536/2014) was adopted and published in May 2014. It will come into effect in Europe in 2018. The new Regulation is intended to increase the number of clinical trials conducted in Europe and provide for improved transparency.

The HPRA has been working to progress the development of systems and procedures to meet the new requirements. The existing voluntary harmonisation procedure (VHP) is similar to the approval process for clinical trials under the new legislation and the HPRA continues to increase its involvement in this procedure.

Interchangeable Medicines

Following commencement of the Health (Pricing and Supply of Medical Goods) Act in June 2013, the HPRA was tasked with publishing a list of interchangeable medicines to facilitate generic substitution by pharmacists and to allow for the introduction of a reference pricing system by the HSE. By the end of 2015, the list included a total of 47 active substances.

Legal Classification of Medicines

Medicines are classified, in law, as prescription or non-prescription. Since 2014, the HPRA has taken a proactive approach to the reclassification of the legal status of medicines, with the aim of increasing the number of medicines available without prescription, where it is safe to do so. The HPRA has identified medicines which we consider could be safely made available without prescription in pharmacies, or made more widely available in general retail outlets such as supermarkets, and has invited the industry to make applications to have these medicines reclassified. On foot of this proactive approach, a number of reclassification applications were completed in 2015 and further progress is anticipated during 2016.

Responding to Medicines Shortages

The HPRA works closely with all relevant stakeholders to limit the impact of human medicines shortages on the Irish market. One of the mechanisms used by the HPRA to aid continuity of supply to the market place in the event of a shortage includes the granting of a temporary authorisation for a batch of a product known as a 'batch specific request'. During 2015, the HPRA reviewed 115 batch specific requests to facilitate continuity of supply of medicinal products in Ireland and prioritised other applications where expedited review was required to avoid shortages. It also worked with marketing authorisations, including suppliers of alternative products, to avoid or mitigate shortages.

Innovative Medicinal Products and New Manufacturing Technologies

The HPRA continues to support the development of innovative medicinal products and new manufacturing technologies, and recognises the need to ensure the appropriate regulation of such products. In the past year, it was an active participant in European groups which aim to support such innovation and the ongoing training and development of staff in these areas remains a priority for the HPRA.

Working towards Full Implementation of EU Pharmacovigilance Legislation

The HPRA continued its work with stakeholders including the EMA, other national regulators and industry to support the phased implementation of EU pharmacovigilance legislation.

Under this legislation, there is a requirement for the EMA to set up a repository of PSURs and assessment reports. This allows for centralised PSUR reporting and enhances access to data and information, thereby supporting benefit / risk assessments of medicines. During 2015, the HPRA participated in a pilot of the PSUR repository with the EMA and other Member States as well as user acceptance testing in preparation for mandatory use of the repository in June 2016.

The HPRA continued to contribute to three EMA / Member State project teams (PT) concerned with:

- collection of key information on medicines (PT1);
- better analysis and understanding of data and information (PT2);
- committees and communications with stakeholders (PT3).

The HPRA's Pharmacovigilance and Risk Management Lead contributed to the project oversight governance through membership of the Project Co-ordination Group and the European Risk Management Strategy Facilitation Group.

SCOPE Joint Action

The Strengthening Collaboration for Operating Pharmacovigilance in Europe (SCOPE) Joint Action was established to optimise the operation of strengthened pharmacovigilance legislation in Europe which was brought into effect in June 2012. The SCOPE Joint Action is being implemented via eight work packages which target discrete elements to support the overall project. During 2015, the HPRA contributed to the risk communications and lifecycle pharmacovigilance work packages.

The HPRA is the topic lead in respect of carrying out an impact assessment of risk communications under work package 6 (WP6). Information is being collected on risk communications practice in the EU network to better understand the communication channels and tools used. During 2015, a web-based survey on safety communications and their effectiveness for healthcare professionals was delivered and distributed to general practitioners, cardiologists and pharmacists across the Member States which are partners in WP6, including Ireland. The survey was designed to assess different means of communicating drug safety updates with particular focus on Direct Healthcare Professional Communications (DHPCs), national competent authority communications and product specific educational materials. Analysis of results has commenced with a consolidated report anticipated by the final quarter of 2016. These results, together with input from patient organisations, consumer groups and national regulators, will inform the development of good practice recommendations for use in EU Member States.

The HPRA also actively contributed in 2015 as a partner under work package 8 (WP8) relating to lifecycle pharmacovigilance. A survey of national competent authorities was undertaken in 2015 and the results will be used to develop recommendations, guidance and training for regulators to support EU pharmacovigilance work.

Contributing to the European and Global Regulatory Network

Europe

The HPRA continues to actively participate across the European medicines regulatory network. HPRA scientific and technical staff contribute to a broad range of committees and working parties, preparing papers as appropriate, at the EMA, the European Commission, the HMA, and at other fora.

In addition to our regular participation at a European level, highlights from the past year included the following:

- An active contribution to the work of the PRAC, with the Irish PRAC delegate being re-elected as Vice-Chair of the committee for a further three-year term.
- The Pharmacovigilance and Risk Management Lead participated in a number of initiatives exploring development of the regulatory environment, strategies to facilitate access to innovative medicines for patients in need and benefit-risk management through the product lifecycle.
- The Pharmacovigilance and Risk Management Lead contributed to a number of strategies to support stakeholder engagement and to specialist topics such as risk management planning, benefit-risk evaluation, pharmacovigilance impact evaluation, post authorisation efficacy studies and pharmacovigilance as an enabler for innovation.
- During 2015, the HPRA transferred the secretariat function for the Benchmarking of European Medicines Agencies (BEMA) to Halmed, the regulatory agency for human medicines in Croatia. The BEMA programme provides assurance to the heads of the EU medicines agency network with respect to the quality of the systems and practices in place in agencies for regulating human and / or veterinary medicines and is a resource for sharing of best practices. As members of the BEMA steering group, the HPRA continued to work with other Member States to prepare for the fourth benchmarking cycle which is due to begin in 2016. Visits will take place over a three-year period to all agencies regulating human and veterinary medicines in the EU and EEA countries.

- HPRA delegates attended three meetings of the European Pharmacopoeia (Ph. Eur.) and participated in a number of the working parties and groups which provide expert advice in respect of the pharmacopoeia.
- The HPRA presented at a meeting of the FOAM (Forum on the Advertising of Medicines) network on advertising. The network is a mechanism whereby those within the EU competent authorities responsible for monitoring advertising of medicines share information on their advertising compliance programmes and related activities.

World Health Organization

The HPRA's Pharmacovigilance Manager continued to represent the World Health Organization (WHO) as a member of the Board of the Uppsala Monitoring Centre (UMC) and WHO Collaborating Centre for International Drug Monitoring during 2015.

The HPRA participated at the annual meeting of national centres participating in the WHO international drug monitoring programme in November and continued to provide details of reports received nationally to the WHO for inclusion on its international database. As outlined in the accompanying graph, the volume of adverse reaction reports from Ireland continued to fall within the top 20 countries participating in the programme with Ireland ranked as the thirteenth highest reporter (population based) during 2015. There are currently 123 countries with full programme membership and 28 countries with associate membership.

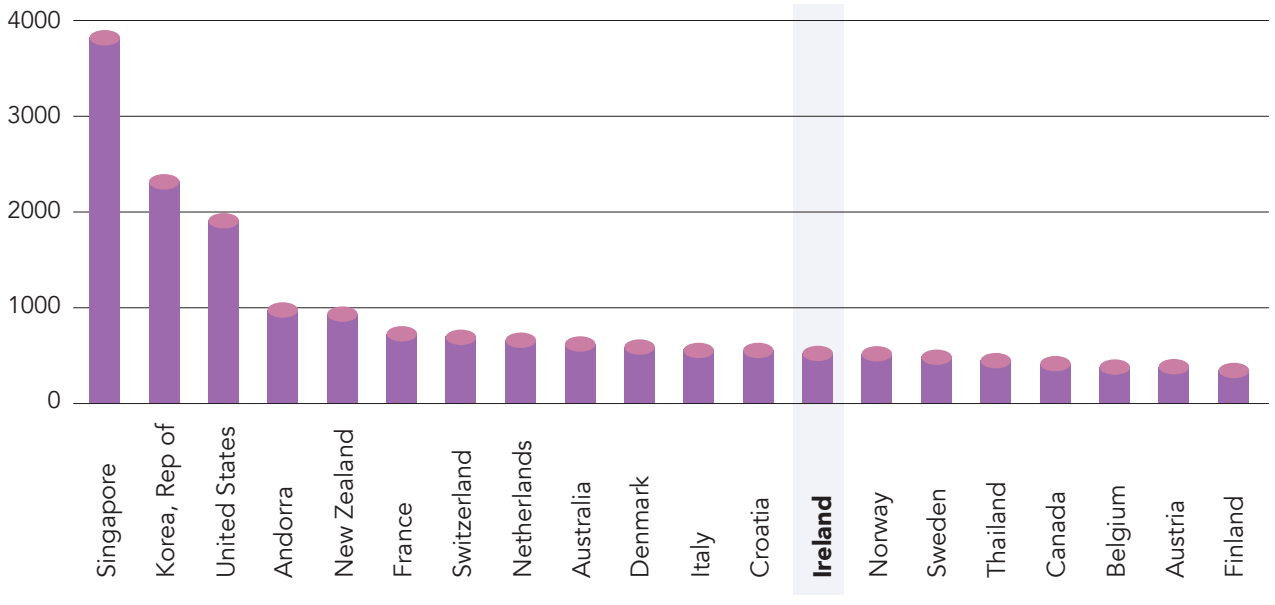
Health Systems Strengthening Programme

The HPRA was part of a successful consortium selected to provide 'Technical Assistance to the Ministry of Health and the Zambia Medicines Regulatory Authority'. This followed a tender process under the EU funded Health Systems Strengthening (HSS) programme. Planning for the delivery of regulatory and capacity building support by the HPRA to the Zambian agency began in 2015 while the project itself is expected to commence in quarter two 2016.

Sub-Committees to the Advisory Committee for Human Medicines

There are a number of sub-committees appointed by the Advisory Committee for Human Medicines. These include the Clinical Trials Sub-Committee which met 12 times in 2015 and the Herbal Medicines Sub-Committee which met once in the same period.

Active ICSRs in the WHO global ICSR database per million inhabitants – 2015



Tissues and Cells

Two Commission Directives were published during 2015. These were:

- Directive (EU) 2015/565, amending Directive 2006/86/EC as regards certain technical requirements for the coding of human tissues and cells;
- Directive 2015/566, implementing Directive 2004/23/EC as regards the procedures for verifying the equivalent standards of quality and safety of imported tissues and cells.

Member States are required to transpose the provisions of these Commission Directives during 2016 and the requirements will apply from 29 April 2017. The HPRA hosted two information sessions to highlight the requirements of these Directives and the presentations and other relevant information were made available online to stakeholders.

Veterinary Medicines

Contributing to the European Regulatory Network

The European regulatory network is the backdrop for reaching a common view on medicines and their regulation. Given that most medicines are supplied to multiple European markets, it is clear that in order for us to maximise our influence, we must have an input in decisions taken at a European level. This we do through our involvement across the EU network which includes active participation at the EMA, where our Veterinary Assessment Manager is the Vice-Chair of the Committee for Medicinal Products for Veterinary Use (CVMP), and the HMA.

Key regulatory issues discussed during 2015 were:

- The new proposal for a regulation on veterinary medicines. The HPRA provided practical support and advice to the Department of Agriculture, Food and the Marine during Council Working Party discussions;
- The European surveillance strategy on pharmacovigilance work-sharing;
- The implementation of the HMA Action Plan on antimicrobial resistance.

Contributing to National Health Initiatives

During 2015, the HPRA participated in a working group of the FSAI tasked with preparing a report on the risk of antibiotic resistance transfer posed by food. The HPRA also participated in two meetings of the National Interdepartmental AMR Consultative Committee.

Throughout the year, support was provided to the Department of Agriculture, Food and the Marine in relation to matters of mutual interest.

Advisory Committee for Veterinary Medicines

The Advisory Committee for Veterinary Medicines is the HPRA's independent expert committee that advises on matters relating to the authorisation of veterinary medicines in Ireland. It met twice during the course of 2015 and considered such matters as:

- Regulatory developments affecting medicines in the European network;
- A report of suspected adverse reactions to veterinary medicines in Ireland for 2014;
- A report on the consumption of veterinary antibiotics in Ireland for 2014;
- Various applications that had been considered by the agency previously but were submitted for peer review by the committee.

2

NEW MEDICAL DEVICES REGULATIONS PROPOSED BY THE EUROPEAN COMMISSION

Medical Devices

Revision of European Medical Devices Legislation

The European Commission's proposals for Regulations on medical devices and *in vitro* diagnostic (IVD) medical devices are intended to develop and reinforce the European legislative framework to ensure a high level of protection for patients and healthcare professionals. At the same time, the proposed changes are focused on ensuring that the regulatory system enables safe innovation of new products and access for patients and healthcare professionals to new therapeutic and diagnostic options. The proposals are subject to the ordinary legislative process which involves examination by both the European Council and the European Parliament.

During 2015, negotiations in respect of the proposals reached a new phase with the adoption of a 'General Approach' on the legislative texts by the European Council. This allowed for the initiation of trialogue with the European Parliament and the EU Commission on the dossiers, which is one of the key elements of the ordinary legislative process.

The two proposed Regulations represent a significant development and improvement in comparison to the existing system which has been in place for over 20 years. However, the negotiations are complex and time-consuming due to the volume and technical intricacy of the legal text. The final compromise text will likely represent a delicate balance of the views of the Member States, the European Parliament and the EU Commission. However, the HPRA considers that the revised legislation is necessary and will represent significant improvement and strengthening of the regulatory system for devices.

During the year, the HPRA provided significant support to Department of Health and the Permanent Representation of Ireland in Brussels for the purposes of negotiation of the legislation at the European Council Working Party and at various expert working groups. This includes advising on the

further development of the legal texts, compromise proposals, assistance with relevant stakeholder consultation and provision of input to the Department as it finalises a national position on the proposals.

The trialogue negotiations will continue during 2016 when it is anticipated that final agreement can be reached under the Dutch Presidency. When the final texts are agreed and the legal texts start to come into effect, the HPRA will conduct an information campaign to provide information, guidance and advice to affected stakeholders on implementation of the legislation.

Ongoing Development and Strengthening of the existing European Regulatory Framework

Along with a number of other European competent authorities and the European Commission, the HPRA has taken a leading role in development and strengthening of the existing regulatory framework for medical devices in advance of the revised legal framework being agreed and implemented. In particular, the HPRA is keen to promote co-ordination and co-operation between authorities to increase safety, effectiveness and reduce duplication.

Oversight and Performance of Notified Bodies for Medical Devices

One of the central components of the European Commission's joint action plan of 2012 was to improve the performance of notified bodies and their oversight by authorities. This was achieved by implementation of an EU wide joint assessment scheme for notified body oversight by authorities which led to the implementation of the 2013 Regulation on notified bodies. The HPRA, having contributed to the development and implementation of this assessment scheme, continues to be part of a small expert group which oversees and co-ordinates its continued implementation. During 2015, the HPRA directly participated as experts in six joint assessments of EU notified bodies. In addition, the Irish notified body was also subject to an EU joint assessment audit during 2015 as part of its application for re-designation as a medical device notified body.

Market Surveillance and Vigilance

Another key element of the joint plan, which was further highlighted by the EU Commission in its 2014 report, was the strengthening of market surveillance activities by national regulatory authorities across Europe. In response, the HPRA has developed its range of market surveillance activities throughout the medical device lifecycle and has a planned continued

development process towards the new legislation. In particular, the HPRA's key emphasis is on proactive surveillance. Areas of proactive market surveillance in 2015 are outlined in Chapter 2 of this report.

The HPRA continues to encourage healthcare professionals and other device users to submit reports of incidents which occurred when using a medical device. In addition, the HPRA has revised our methods for safety reporting to ensure the information is clear and targeted to the correct user group.

As part of the strengthening of medical device regulation, the HPRA has also been focused on improving the functioning of the vigilance system both nationally and at an EU level. This has been in the form of:

- systematic access for notified bodies to reports of adverse events;
- developing an internal system for signal detection and trend analysis;
- encouraging healthcare professionals and empowering patients to report adverse events; and
- enhancing co-ordination in analysing reported incidents in order to pool expertise and expedite necessary corrective actions.

In respect of enhanced co-operation, the HPRA has been participating in the development of a centralised European databases for vigilance. These will also be an area for consideration and further attention in 2016.

During the past year, the HPRA was an active participant in Medical Devices Expert Group (MDEG) vigilance meetings and vigilance teleconferences. The HPRA continued to chair three taskforces which included the vigilance co-ordinating competent authority role and was an active participant in eleven other taskforces relating to specific devices / manufacturers and to the development of guidance such as device specific vigilance guidance.

Contributing to the European and Global Regulatory Network

Competent Authority for Medical Devices

During 2015, the HPRA continued to engage actively and develop its partnerships with other European competent authorities. The HPRA is an elected member of the Competent Authority for Medical Devices (CAMD) Executive Group. The objective of this group is to build mechanisms and structures to enable co-operation between authorities and to identify key work items and priorities for focus at European level. The EU Commission also participates in the group's discussions.

In November 2015, the 37th CAMD meeting was hosted in Dublin by the HPRA on behalf of the Luxembourg Presidency of the European Council. The meeting was attended by over 60 delegates from 25 countries and included representatives from the EU Commission's DG GROW, the Food and Veterinary Office (FVO) and the Joint Research Centre (JRC). The meeting focused on developing the regulatory system further in preparation for the anticipated revision of the medical devices legislation. One of the key focus areas was to agree priorities and work plans for co-funded joint actions in medical device market surveillance under the European Health Programme 2016-2020.

International Medical Device Regulatory Forum

During 2015, the HPRA continued as a member of the European delegation on the Management Committee of the International Medical Device Regulators Forum (IMDRF). This forum aims to develop and promote harmonisation of the regulation of medical devices across the globe. In addition to contributing to the Management Committee, the HPRA continued in the role of secretariat for the IMDRF National Competent Authority Report (NCAR) Exchange mechanism which allows for the exchange of reports and key safety information from each global region. The HPRA also participated in the IMDRF working groups on NCAR and on developing Regulated Product Submission (RPS) standards (which facilitate standard formats for technical documentation for submission to regulatory authorities). As part of this working group the HPRA acted as Chair for the Table of Contents Workstream in 2015 to establish a pilot for regulatory submissions.

In 2015, the HPRA hosted a meeting of the IMDRF Medical Device Single Audit Program (MDSAP) working group in Dublin. The EU is a formal observer to the ongoing MDSAP pilot programme. The programme allows recognised auditing organisations (such as notified bodies) to conduct a single quality system audit of a medical device manufacturer that will satisfy the relevant requirements of the regulatory authorities participating in the programme. The HPRA is also committed to providing experts to conduct MDSAP audits in Europe as part of the pilot programme.

Bilateral Meetings

During 2015, the HPRA held bilateral meetings with the US Food and Drug Administration (FDA), Australia's Therapeutic Goods Administration (TGA), the EU Commission's Joint Research Centre (JRC) and the EU Commission's Food and Veterinary Office. Meetings were also held with other national authorities in Europe including the UK's Medicines and Healthcare products Regulatory Authority (MHRA), the Croatian competent authority (HALMED), the Netherlands healthcare inspectorate (IGZ) and the Netherlands National Institute for Public Health and the Environment (RIVM).

Contributing to National Health Initiatives

As outlined earlier in this report, the HPRA has also been focused on improving the functioning of the vigilance system nationally. Throughout 2015, we worked closely with the HSE to develop a system for the dissemination of medical devices safety information. This also included the identification of a designated person within all HSE and voluntary hospital acute and community settings. Further work will be carried out in these areas during 2016.

Advisory Committee for Medical Devices

The Advisory Committee for Medical Devices met three times in 2015. Regular updates were provided on key medical device issues, regulatory developments, the revision of the medical devices legislation and HPRA activities in regulating medical devices. The term of the current committee concluded at the end of 2015. A new committee was appointed by the Minister for Health to commence in 2016.

Scientific Animal Protection

In relation to the EU network on scientific animal protection, the HPRA contributed to deliberations in respect of a number key topics and played an active role as part of the EU National Committees for the Protection of Animals used for Scientific Purposes.

Nationally, the HPRA published its second annual statistical report on the use of animals for scientific purposes in Ireland. We also provided support to the National Committee for the Protection of Animals used for Scientific Purposes in relation to their role to nurture the creation of a culture of care at the establishments concerned. The committee met twice during 2015.

STAKEHOLDER ENGAGEMENT AND COMMUNICATIONS

The HPRA continues to deliver a comprehensive programme of communications and engagement activities so as to provide all our stakeholders with timely access to relevant safety, licensing and regulatory information. Ensuring effective and timely communications is one of our core strategic goals and will continue to be an area of focus and development over the coming years.

A number of significant communications programmes and initiatives took place during 2015.

Stakeholder Engagement

Meetings with Stakeholders – Human Medicines

During 2015, there were a number of meetings held with industry representative groups including the Association of Pharmaceutical Manufacturers in Ireland (APMI), the Irish Pharmaceutical Healthcare Association (IPHA), the Healthcare Enterprise Alliance (HEA), the Irish Generic Medicines Association (IGMA) and Pharmachemical Ireland. These meetings provide a forum for discussion of items of mutual interest.

There was also one meeting of the Advertising Compliance Technical Group which includes representatives from the HPRA and pharmaceutical industry. Issues of mutual interest were discussed with a goal of promoting good practice and compliance in this area.

Meetings with Stakeholders – Veterinary Medicines

During 2015, the HPRA met with the Department of Agriculture, Food and the Marine in relation to ongoing matters of mutual interest, including the new proposal for the regulation of veterinary medicines in the EU and the shortage of a particular medicinal product. Meetings were also held with a number of stakeholders from the veterinary medicines industry. In addition, an update on the changing regulatory requirements for veterinary medicines was provided at an award ceremony for new graduates of the course for licensed merchants.

Meetings with Stakeholders – Scientific Animal Protection

There was one meeting held in 2015 with the Department of Health in relation to the implementation of Directive 2010/63/EU regarding the protection of animals used for scientific purposes. A large number of presentations on the implementation of the Directive were also delivered to the research community throughout Ireland.

Meetings with Stakeholders – Medical Devices

Regular meetings with key industry stakeholder groups continued during 2015. These meetings provide the HPRA with an opportunity to update stakeholders on regulatory developments at national and European level. They also enable the HPRA to be kept up-to-date on issues affecting the medical devices industry. A key topic for discussion during 2015 was the ongoing revision of the medical devices legislation and the introduction of national fee structures for medical device regulation.

In the past year, meetings were held with the NSAI, the Irish Medical Devices Association (IMDA), the Irish Medical and Surgical Trade Association (IMSTA) and Eucomed (European Medical Technology Industry Association).

As part of the negotiations of the ongoing revision of the medical devices legislation, the HPRA, along with colleagues from the Department of Health, met with Members of the European Parliament to discuss the proposed legislation. This topic was also discussed in a meeting between the HPRA and the Industrial Development Authority (IDA).

In November, the HPRA hosted the 37th meeting of the CAMD in Dublin (see page 61). The agenda incorporated a meeting between the CAMD Executive and representatives from the European industry associations AESGP, COCIR, EDMA and EUCOMED. In addition, during the plenary meeting, a session was held with representatives from the EU Notified Body representative associations.

Also in November, the HPRA, together with the HSE, launched the eAlert IT system and complementary designate person role to facilitate the dissemination of key medical device safety information from the HPRA to the HSE, voluntary hospitals and community settings. This event, which was held at the Royal College of Physicians in Ireland, was attended by a large number of healthcare professionals and included a range of speakers and a panel discussion.

Meetings with Stakeholders – Cosmetic Products

During 2015, meetings were held with the Irish Cosmetics, Detergent & Allied Products Association (ICDA), the Department of Jobs, Enterprise and Innovation (DJEI) and the NSAI.

Presentations to Stakeholders

As in recent years, the HPRA invested significant time in delivering a programme of presentations and talks at a range of external stakeholder events such as meetings, seminars, conferences and training courses. In addition, a programme of presentations was delivered to undergraduate and post graduate students studying courses related to the role of the HPRA.

Such presentations contribute to the HPRA goal of providing stakeholders such as healthcare professionals and regulatory professionals with access to relevant, up-to-date information. The presentations are delivered by HPRA staff from across the organisation and cover all products and functions under our remit. While some are general in nature and primarily focused on explaining the role of the HPRA, others are more specific and deal with specialist areas and / or new regulatory developments. A full list of all presentations delivered during 2015 is provided in Appendix 2.

Events

Information Days and Seminars

HPRA information seminars provide regulatory guidance and updates to a range of stakeholders. As well as presentations from HPRA staff and, where appropriate, external contributors, the events enable all attendees to submit questions, seek clarifications and network with colleagues.

In addition to the meetings outlined earlier in this report, the following events were also held during 2015:

- In January, the HPRA hosted an information seminar on the regulation of herbal medicines. The meeting focused on a number of topics including traditional herbal medicinal products (THMPs) and focused on both pre and post authorisation / registration requirements.
- Three cosmetic information evenings were hosted, free of charge, in Dublin, Cork and Galway during September and October. These events were aimed at small to medium sized cosmetic businesses, both manufacturing and / or distributing cosmetics, and provided guidance on the regulatory compliance required of the industry.
- An animal welfare body training workshop and seminar was held in September. The HPRA organised this event on behalf of the National

Committee for the Protection of Animals used for Scientific Purposes and also presented on relevant topics. This was the first such meeting in Ireland and represented an important networking opportunity for those involved in the sector. It also afforded the Committee an opportunity to establish direct communication links with the establishments concerned.

- A meeting of the International Medical Device Regulators Forum (IMDRF) Medical Device Single Audit Program (MDSAP) working group was hosted by the HPRA in Dublin.
- The HPRA hosted two information sessions to highlight the requirements of two Commission Directives published during 2015 relating to the regulation of human tissues and cells.
- A regulatory information session was hosted in conjunction with TOPRA (The Organisation for Professionals in Regulatory Affairs) in November.

Industry Events

The Professional Beauty Show held in the RDS, Dublin in October, featured an information stand operated by HPRA staff members. Details were provided on the regulatory requirements for the cosmetic and medical device industries to beauty professionals both participating in and attending the event.

6th

YEAR OF HPRA PARTICIPATION AT THE BT YOUNG SCIENTIST AND TECHNOLOGY EXHIBITION

BT Young Scientist and Technology Exhibition 2015

The BT Young Scientist and Technology Exhibition 2015 took place in January in the RDS, Dublin.

Thousands of students as well as teachers, parents and members of the general public from all over Ireland visited the HPRA's exhibition stand in the Industries Hall. This was the sixth year of HPRA participation and our stand again focused on building awareness of the significant role the HPRA plays in protecting public and animal health. In particular, the safe and appropriate use of medicines, medical devices and cosmetic products was highlighted. As in previous years, the stand also focused on the many interesting science related career opportunities that are available in the health products industry.

Publications

Guidance Documents

HPRA guidance documents provide stakeholders, primarily from the industry sectors we regulate, with advice and direction in respect of legislation and regulatory requirements. New and updated HPRA guidance documents are published regularly on our website with alerts issued to website subscribers.

A number of new guidance documents were published during 2015 with a significant number of existing documents also being updated. Among the new documents published during the past year were:

- Guide to Good Manufacturing Practice for cosmetic products;
- Guide to applying for a manufacturer's / importer's authorisation;
- Guide to biosimilars for healthcare professionals and patients.

All of the HPRA guidance documents can be accessed via the publications section of www.hpra.ie.

Newsletters

The HPRA produces three newsletters with a number editions of each published throughout the year.

Medicinal Products Newsletter

This newsletter provides regulatory updates for those working in the pharmaceutical and cosmetics sectors on Irish and European legislation, new / revised HPRA regulatory publications and stakeholder events such as information days.

Three editions of the Medicinal Products Newsletters were published during 2015. Topics covered included:

- Human Medicines
  - Updates to good vigilance practice (GVP) guidelines;
  - Electronic reporting of ICSRs to marketing authorisation holders;
  - Proactive approach to reclassification (switching);
  - New EU Clinical Trials Regulations.
- Veterinary Medicines
  - Using the HPRA as Reference Member State;
  - Changes to requirements for product literature;
  - Certificates of suitability and retest periods;
  - Use of animals for regulatory testing of medicinal products.
- Compliance
  - Reporting the theft or unaccounted loss of controlled drugs and precursor chemicals to the HPRA;
  - New tools for manufacturers to help prevent medicines shortages;
  - Pilot inspection programme for distributors of medical devices;
  - Methylisothiazolinone (MI) in cosmetic products.

The newsletter is published on the HPRA website and is issued to those who subscribe to the HPRA alerts system.

Drug Safety Newsletter

The Drug Safety Newsletter continues to provide important safety information to healthcare professionals in respect of human medicines and incorporates hyperlinks to product information and other relevant documents on the HPRA and EMA websites. Seven issues of the newsletter were published on our website and made available electronically to registered doctors, dentists, nurses and pharmacists during 2015. An overview of the topics covered during the past year is included in Appendix 3.


FEBRUARY 2014

HPRA DRUG SAFETY NEWSLETTER

73RD EDITION

In this Edition

Educational materials-optimising the safe and effective use of medicinal products

Medical Devices Newsletter

This newsletter provides regulatory and safety updates for those working in the medical devices sector and professionals working in the health area who regularly use or purchase medical devices. It provides updates on Irish and European legislation, on safety issues as well as details of HPRA medical devices publications and stakeholder events. There were two editions of this publication issued in 2015 in addition to a feedback survey aimed at reviewing the content of the newsletter to ensure it meets the expectations of our stakeholders.

The following were some of the main topics covered:

- Proposals for new regulation on medical devices and in vitro diagnostic medical devices;
- The Medical Device Single Audit Programme (MDSAP);
- An overview of transcranial Direct Current Stimulation (tDCS);
- Supplier qualification and management;

- European pilot on vigilance reporting;
- Registration and classification;
- Regulatory Science Ireland.


VOL 1 MAY 2015

HPRA MEDICAL DEVICES
NEWSLETTER

ISSUE 42

In this Issue

Letter from the editor

Letter from the editor

HPRA

Scientific Animal Protection – Regulatory Updates

These updates, which were issued on four occasions during the year, are intended to provide the research communities with updates on latest developments, including:

- New and updated HPRA guidance documents, forms and procedures;
- Information on education and training;
- Information on the 3Rs, best practices, compliance with the legislation and other relevant details.

External Articles

In respect of human medicines, there were 22 articles provided for inclusion in MIMS Ireland and two articles were provided for inclusion in the Irish Medicines Formulary. The full list of topics covered in these articles is included in Appendix 3. All articles were also published on the HPRA website. An article was also submitted for inclusion in the Irish PharmaChem Yearbook and Directory. This followed a request from PharmaChemical Ireland to provide information on the issue of falsified medicines and the work being done by the HPRA in this area.

Consistent with our objective to improve stakeholder knowledge of the appropriate use of veterinary medicines, we contributed four articles to the specialist It's Your Field publication. Additionally, an article entitled *Medical device vigilance: A competent authority perspective* was published in the Journal of Medical Device Regulation while the Irish Forum for Global Health published an online article highlighting the HPRA's participation in the BT Young Scientist and Technology Exhibition.

Safety Warning and Notices

Throughout 2015, in addition to the Drug Safety Newsletter, the HPRA continued to publish important safety information and the outcomes of benefit-risk evaluations of human medicines. Following HPRA review and approval, 21 Direct Healthcare Professional Communications were published on the HPRA website and issued to subscribers. The PRAC published monthly agendas, minutes, meeting highlights, notifications of safety reviews and signals throughout the past year and these were also made available via our website.

We also published two advisory notices in respect of veterinary medicines. The first notice related to reported lack of efficacy of a sheep vaccine while the second notice concerned the updating of safety information on specific injectable products.

Separately, a total of 33 HPRA safety notices concerning medical devices were published on the HPRA website and issued to subscribers. These notices were also circulated through the HSE eAlert system. We also published 474 manufacturer field safety notices on our website and a monthly listing was sent to subscribers. In addition, medical device information notices were issued during 2015 on food intolerance testing and on specific medical devices affected by regulatory actions in other global regions.

Reporting Adverse Events – Veterinary Medicines Leaflet

The receipt by the HPRA of reports of suspected adverse events following the use of veterinary medicines is central to the operation of an effective pharmacovigilance system. This leaflet, copies of which were distributed to all registered veterinary practitioners in Ireland, highlights the importance of reporting and explains how the information received by the HPRA is used to monitor the continued safety and efficacy of veterinary medicines. Details on what information should be included in a report are also provided as are

instructions on how to report. Copies of the leaflet can be downloaded from the HPRA website while printed versions can be ordered from leaflets@hpra.ie.

Animal Welfare Body Information Leaflet

This information leaflet, which was distributed to all establishments authorised to use animals for scientific purposes during the year, was developed with the input of the National Committee for the Protection of Animals used for Scientific Purposes. The leaflet is intended to support the work of the Animal Welfare Body in each establishment in promoting the 3R principles and to provide practical information on creating a culture of care. The leaflet can be downloaded from our website while printed versions can be ordered from sap@hpra.ie.

Public Information Campaign

In early 2015, HPRA announced its intention to develop a public information campaign that will communicate important safety messages to those who take, use and / or purchase health products such as medicines and medical devices. It is envisaged that the campaign, which should also contribute to increased awareness of the role of the HPRA, will run over a number of years beginning in 2016. During the past year, the HPRA conducted a procurement process which resulted in the appointment of media buying and creative advertising agencies.

HPRA Website

Our website www.hpra.ie is a key component of the HPRA's communications programme. The site outlines the primary functions and activities of the HPRA and facilitates the dissemination of information to a wide variety of audiences including healthcare and industry professionals as well as patients and other members of the public. As new content is regularly added to the website, we are focused on its continued development and enhancement to ensure it remains an attractive and user-friendly resource.

Developments in respect of the HPRA website during 2015 included the following:

- The launch of a new human medicines information resource featuring educational materials for healthcare professionals and/or patients and care-givers. Educational materials are intended to promote the safe and effective use of individual medicines. The materials provide clear information on specific safety risks and describe concisely what actions are required to prevent and minimise such risks.

- The publication of a dedicated list of vaccines authorised and marketed in Ireland for human use. This information complements the immunisation guidelines issued by the National Immunisation Advisory Committee (Royal College of Physicians of Ireland). Information is provided in respect of the product (and common) name, the authorisation number and the relevant marketing authorisation holder. A link to an online version of the most recently approved patient information leaflet is also provided for each vaccine.

- The implementation of a search engine optimisation (SEO) and pay-per-click (PPC) campaign. SEO is a marketing tool focused on growing visibility in organic (non-paid) search engine results. PPC is a model of internet marketing which is designed to increase visits to a site rather than relying solely on organic visits. As part of the HPRA campaign, both technical and creative elements were applied to improve rankings, increase traffic and expand awareness in search engine results. We also placed a number of adverts to appear on search engine results pages. Overall, the SEO and PPC campaign resulted in increased traffic to the HPRA website and improved rankings for the HPRA in search results. HPRA content is now returned as the number one search result for a number of key regulatory topics.

2015 Statistics

- Almost 206,000 unique visitors accessed the HPRA website during the past twelve months. There were in excess of 536,000 visits in total.
- Of those who accessed the site, 36% were new or first time users.
- Among the most popular sections of the website were the human and veterinary medicines listings, and the medicines regulatory information sections (which include publications and forms).

Media Communications

The HPRA implements a proactive media communications campaign annually so as to communicate important safety messages and build awareness of the role of the HPRA. We prepared 35 press releases and statements which in a number of instances resulted in national and regional media interviews with a HPRA spokesperson.

Among the issues highlighted through press releases and statements during the past year were:

- Advice on seasonal maintenance of automated external defibrillators (AED) including a call for owners to ensure all defibrillators have received import software updates.
- The suspension of medical devices manufactured by Silimed.
- HPRA participation in, and the outcome of, an EMA review of the safety of HPV vaccines.
- The dangers of consuming illegal slimming products containing Dinitrophenol (DNP).
- Advice to consumers on the importance of using, and correctly applying, sunscreen products.
- The dangers of counterfeit cosmetics and how to identify such products.

In addition, we responded to almost 500 queries from national, local and specialist media during the year. Drafting responses to such queries involves subject matter experts from across the organisation.

Research

Third National Consumer Survey

In late 2015, the HPRA commissioned Behaviour and Attitudes to carry out national consumer research to examine how Irish consumers source information about the medicines they take. The research will also examine the use of the internet as a source of medicines information and supply, and will explore the use of long-term and generic medication. The results of the research will be published in the first half of 2016.

Website User Satisfaction Survey

In August, the HPRA carried out an online survey among the users of our new website which by that time had been live for just over 12 months. The goal of the survey was to identify potential areas for improvement as well as any new content or features that users feel should be included on the site. The survey was highlighted via the homepage while a link and request to participate were also sent to key stakeholder groups. Overall, the feedback received was very positive in nature and the specific comments submitted will be used to guide the future development of our online presence.

Public Consultations

Public consultations enable the HPRA to identify the needs and expectations of stakeholders so that we may incorporate their views into the way our services are planned and delivered.

During 2015, the HPRA completed two public consultations. The first was in respect of the regulatory fees proposed for 2016 while the second related to the draft Guide to Biosimilars for Healthcare Professionals and Patients. A consultation on the introduction of a fee based funding model to support the conduct of medical device regulatory activities by the HPRA was also commenced in 2015.

The HPRA also makes submissions to third party consultations where the topic is related to or impacts our regulatory functions and the broader public health agenda. In 2015, we provided comments in respect of 22 public consultations from government departments, including the Department of Health, other national agencies and international bodies such as the European Commission, EMA and World Health Organization.

Freedom of Information

The HPRA is subject to the Freedom of Information Act 2014. The Act asserts the right of members of the public to obtain access to official information to the greatest extent possible consistent with public interest and the right to privacy of individuals. During 2015, the HPRA received 18 Freedom of Information requests none of which related to requests for personal information.

Parliamentary Affairs

Oireachtas Joint Committee on Health and Children

In December 2015, the HPRA was invited to address the Oireachtas Joint Committee on Health and Children. The Committee met to discuss the safety of the HPV vaccine. The Department of Health, the HSE and the National Immunisation Advisory Committee (NIAC) were also in attendance.

Parliamentary Questions

The HPRA received and responded to 125 parliamentary questions. There were also a further 106 requests for information from the Department of Health, other government departments or members of the Oireachtas during the year. Of the total number of queries (231), the largest category related to human medicines (163) and concerned topics such as adverse reactions, the availability or supply of products, clinical trials, exempt medicines, market shortages, reclassification, orphan status and vaccines.

Customer Services

Almost 2,700 queries were received and actioned by the customer services team during 2015. These included queries from industry representatives, healthcare professionals and members of the public. Queries were received primarily via email and by phone.

In addition to the queries managed by customer services staff, a range of stakeholder queries are addressed by specialist staff across the organisation. Many of these queries come from healthcare professionals requesting information about specific medicines. In 2015, 200 queries were also received in respect of the exempt medicines programme while the medical devices team received in excess of 500 regulatory queries.

ORGANISATIONAL MANAGEMENT AND DEVELOPMENT

The HPRA is committed to having the necessary corporate functions, systems and supports in place to deliver on our public health mission. We must ensure that our organisational capabilities continue to expand and evolve in line with regulatory and scientific developments and that we adapt to other changes in our operating environment. We must also apply and maintain the highest possible levels of corporate governance.

Human Resources and Change

The retention, engagement and continuing development of our highly skilled employees, the HPRA's key resource, continued to be the overarching focus of a range of initiatives delivered by the Human Resources and Change department in 2015. While conscious of further advancing the public sector reform agenda, the new organisational competency of innovation and creativity launched as part of the 2015 Performance Development Programme (PDP) process, framed our approach of actively pursuing opportunities for improvement, thinking creatively when generating new solutions and building on existing successes.

Performance Development

The further development and enhancement of our PDP continued in 2015 with the full implementation of a range of tools designed to support employees and people managers in using the programme. Awareness of the development planning guides, forms and additional aids was achieved through a communications programme which highlighted at each stage of the PDP cycle the relevant supports available.

Learning and Development

Our learning and development strategy continued to focus on delivering initiatives to support the retention of staff. A full range of developmental in-house programmes were delivered covering courses such as time management, presentation skills and dignity and respect. On the people management side, the new manager training programme was delivered alongside interview skills training and PDP training. Our learning and development team worked in tandem with IT colleagues to provide training support for the update of the Microsoft Office suite of applications.

The HPRA's accredited Leadership Development Programme (LDP) continues to be an effective development tool for our managers and a second group completed the programme in 2015. The HPRA also continues to support all staff members in meeting various development needs through providing support for third level qualification and technical training.

Externally we continued our collaboration with the EU Network Training Centre, providing input and expertise while also attending a number of fora.

Change Management

A number of projects commenced in 2015 which required change management support. The Human Resources and Change department were involved in the creation of the Quality, Scientific Affairs and Communications directorate which required input into the scoping of the new directorate structure and the development of an internal communications strategy surrounding this change. Support continues to be provided in respect of resourcing the new directorate. Significant input was provided to the ongoing EOLAS workflow system project with the provision of a senior resource from the department to the project to lead in the area of change management supports and impact assessment.

The department also took a leading role in the capacity building project with the Zambian medicines agency (ZAMRA). The main areas of work involved development of the requirements for short term experts to resource the project and communications with HPRA employees about the scope of the project and opportunities for involvement.

The public sector reform agenda continued to have a direct impact on employment terms and conditions during 2015. In this regard, a comprehensive communications programme outlining the detail of the reforms and the associated impact on individual employees was delivered by the Human Resources and Change department which included general and one-to-one advice sessions.

Employee Engagement and Commitment

Building on the success of our wellness and health initiatives in previous years, we further developed our programme to deliver support in five main health areas. These were physical, financial, nutritional, emotional and general health awareness. The programme resulted in the delivery of a range of initiatives during the year, with staff engagement levels for the programme remaining high. In particular, the step challenge, run in conjunction with the Irish Heart Foundation, achieved our highest uptake since its inception in 2010 with 30% of our staff taking part. The HPRA went on to achieve a silver 'Active at Work' award from the Irish Heart Foundation.

Our lunchtime learning programme operated in tandem with the wellness initiatives and focused on providing further support for the creativity and innovation competency which was part of our PDP for 2015. Seminars to unlock and boost personal creativity and for learning practical applications for creativity in a business environment were delivered.

In 2015, we also reintroduced an organisational awareness programme with the purpose of providing employees with an understanding of the activities of each directorate within the HPRA. Each month a directorate is responsible for holding a number of different information sessions to highlight key activities in its area.

Resourcing

We continue to develop and manage our resources in line with public sector policy by focusing where possible on internal skills development and the reallocation of tasks and responsibilities in response to specific challenges. Recruitment of staff in specialist areas was completed in line with Department of Health approvals. One of the most important roles recruited for in 2015 was that of Chief Executive. This process concluded in December with the appointment of Ms. Lorraine Nolan.

The benefits of our new human resource IT system continued to be realised with significant gains in process efficiency and effectiveness with work continuing to further develop the system.

Finally, the development of a human resources and change strategy to align with and support the requirements of the HPRA's new five-year strategic plan began during 2015. Quarter four saw the commencement of research with stakeholders to inform this strategy.

Information Technology and Business Services

The Information Technology and Business Services department is responsible for all aspects of organisational technology, data and telecommunications. The department also manages the business services unit that is responsible for delivering specialist business services to the organisation, including business analysis and project management for both internal and external stakeholders. A core function of the business services unit is the management of the organisational Project Management Office (PMO) that formally manages projects and provides HPRA management with the necessary information to support the planning process while ensuring that organisational initiatives are fully aligned with corporate strategy.

Technology is recognised as a key component in supporting regulatory activities at both national and European levels and during 2015 a number of significant projects and initiatives were progressed.

National Developments

Work commenced on the design and build of the HPRA's new workflow technology solution EOLAS that will provide the organisation with a single workflow and data management system to support its regulatory activities. A planned implementation date of 2016 will coincide with implementation of new EU standards for regulatory data management.

In October of 2015, the HPRA commenced development of the new Emergency Medicines Registration System to support the implementation of legislation (S.I. No.449 of 2015) to widen access to certain prescription-only medicines. This system will provide external organisations with a mechanism to register online for the procurement and storage of emergency medicines under the legalisation.

In keeping with the government strategy for shared service provision, the HPRA also provides hosting services to a number of organisations and works closely with agencies such as the Office of the Revenue Commissioners. The HPRA is also actively engaged at national level through its involvement with the National Health Data Standards Committee and in liaison with other relevant agencies such as the HSE, NSAI, HIQA and eHealth Ireland. During 2015, the HPRA continued to contribute to the development of data set standards for ePrescribing and an electronic medicinal product reference catalogue.

The IT and business services team was also active in the development of processes and technology interfaces to support the exchange of information between stakeholders in areas such as the medical products database for both human and veterinary products, interchangeable medicines for the generic substitution programme and data for clinical and pharmacy systems.

European Initiatives

During the past year, the HPRA continued to play a significant role in the development of European telematics strategies, standards and technologies through its engagement with programmes at the EMA, the European Commission and the HMA forum. The HPRA is represented on the EU telematics management board, the network data board and the eSubmisson group and leads on a number of key initiatives relating to single submission portals and data standards.

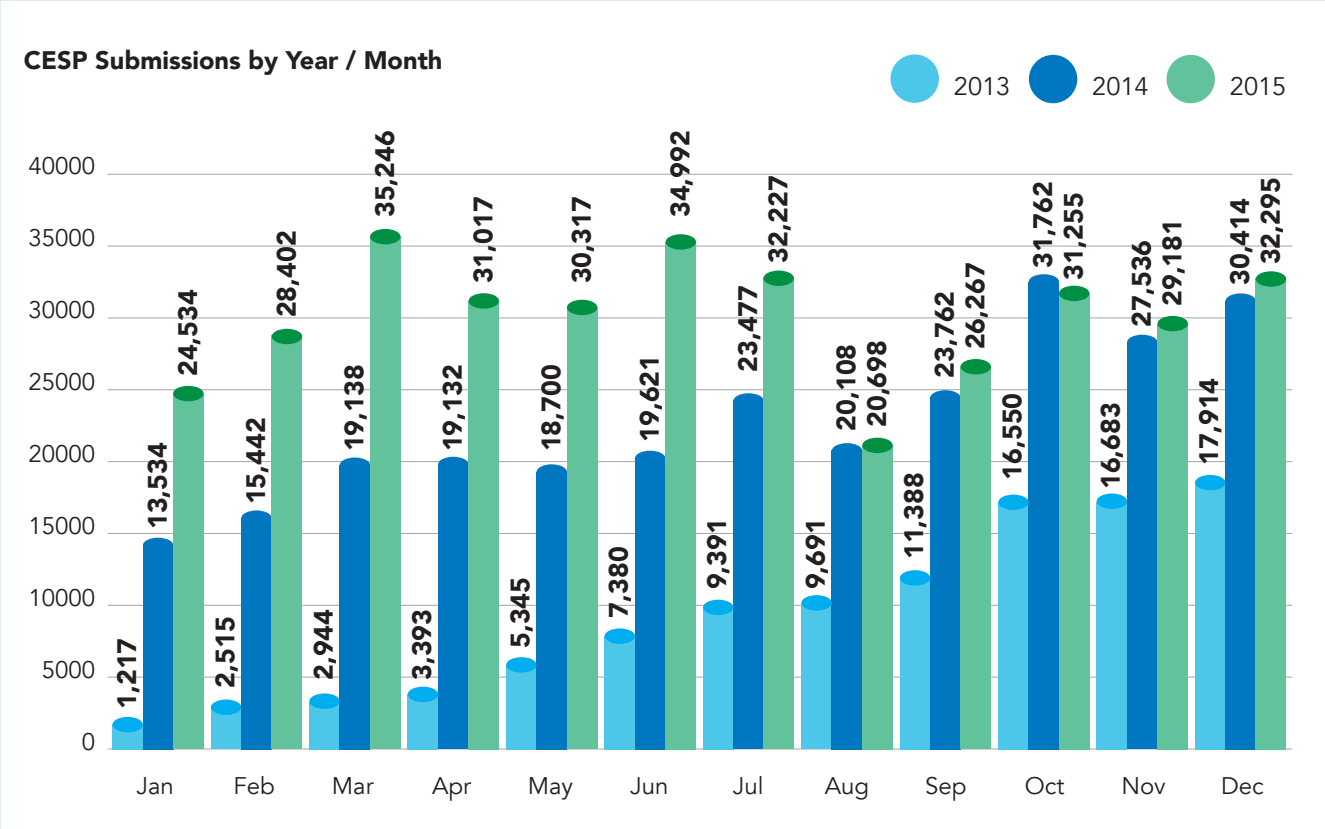
As part of a European consortium, the HPRA is participating within the European Commission's Horizon 2020 research programme on the openMedicine project. We are leading a significant work package within this project which is called Identification of Branded Medicinal Products and this work will continue throughout 2016. The project addresses drug identification and substitution challenges to better enable cross-border healthcare delivery particularly the exchange of ePrescriptions and safe dispensation of prescribed medicinal products. The openMedicine global initiative advances the unique identification of medicinal products and thereby patient safety in cross-border settings.

Common Electronic Submission Portal

A key activity for the HPRA is the development and management of the Common Electronic Submission Portal (CESP) on behalf of the wider EU regulatory community. We provide technical support through the operation of a helpdesk facility and we work with all relevant stakeholders throughout the year to deliver an optimum solution.

In 2015, version 2 of the system was launched providing stakeholders with online tracking of submissions and enhanced reporting capabilities. Participation and activity levels again grew significantly during the year with the portal now handling over 350,000 submissions, compared to 100,000 back in 2013, and supporting over 2,500 pharmaceutical companies and 8,000 users. More than 30 regulatory agencies across Europe are using the system which is available 24 hours a day over a seven day period.

A new version of the system will be designed and built in 2016 to enable the European regulatory network to capture data from online forms based on the new ISO Identification of Medicinal Products (IDMP) data standards.



Corporate Affairs

The corporate affairs team is responsible for the delivery of a number of key service areas to the organisation. These include building and accommodation management as well as the provision of reception, canteen, travel, library and event management services. The department also manages legal matters, international co-operation and Freedom of Information requests. In addition, it provides secretarial support to the Authority and committees and ensures adherence to best practice in the area of corporate governance.

Event Management

The HPRA held six events in 2015 all of which were organised and managed in-house. This approach ensures cost effective delivery of events while also allowing HPRA staff to deal directly with stakeholders. This has resulted in very positive feedback from attendees via event questionnaires. Details of these events are provided on page 67.

Freedom of Information

During 2015, the HPRA received 18 Freedom of Information requests (as per page 73).

Authority and Committees

The corporate services section provides secretarial support to the Authority and committees of the HPRA and ensures adherence to best practice in the area of corporate governance.

- The Authority of the HPRA met 11 times in 2015 and considered a number of strategic matters including corporate policy, planning and finance matters. The latter included monthly management accounts, annual budgets and the financial statements for 2015. The Authority also reviewed update reports from the Statutory Advisory Committees and the Audit Committee. In addition, it reviewed the licences for all medicinal healthcare products as approved by the Management Committee.

  The number of meetings attended by each Authority member during 2015 is as follows:

Authority Member	Number of meetings held during the period the member was on the Authority	Number of meetings attended during the period the member was on the Authority
Mr. Michael D. Hayes (Chair)	11	11
Mr. Pat Brangan	11	11
Mr. Wilfred J. Higgins	11	10
Ms. Ann Horan	11	10
Prof. Mary Horgan	11	5
Dr. Elizabeth Keane	11	10
Mr. Noel O'Donoghue	11	0
Prof. Caitriona O'Driscoll	11	11
Dr. Diarmuid Quinlan	11	7

- The Audit Committee, a subcommittee to the Authority, met four times in 2015. Further details are provided in the HPRA's Financial Statements.
- Also during the year in review, the Advisory Committee for Veterinary Medicines met twice while the Advisory Committee for Medical Devices met three times.
- The Herbal Medicines Sub-Committee, a sub-committee to the Advisory Committee for Human Medicines, met once in 2015. The Clinical Trials Sub-Committee is also a sub-committee to the Advisory Committee for Human Medicines and it met twelve times in the past year.
- The National Committee for the Protection of Animals Used for Scientific Purposes, a statutory committee to provide guidance to the regulator and those working in this area, met twice in 2015.

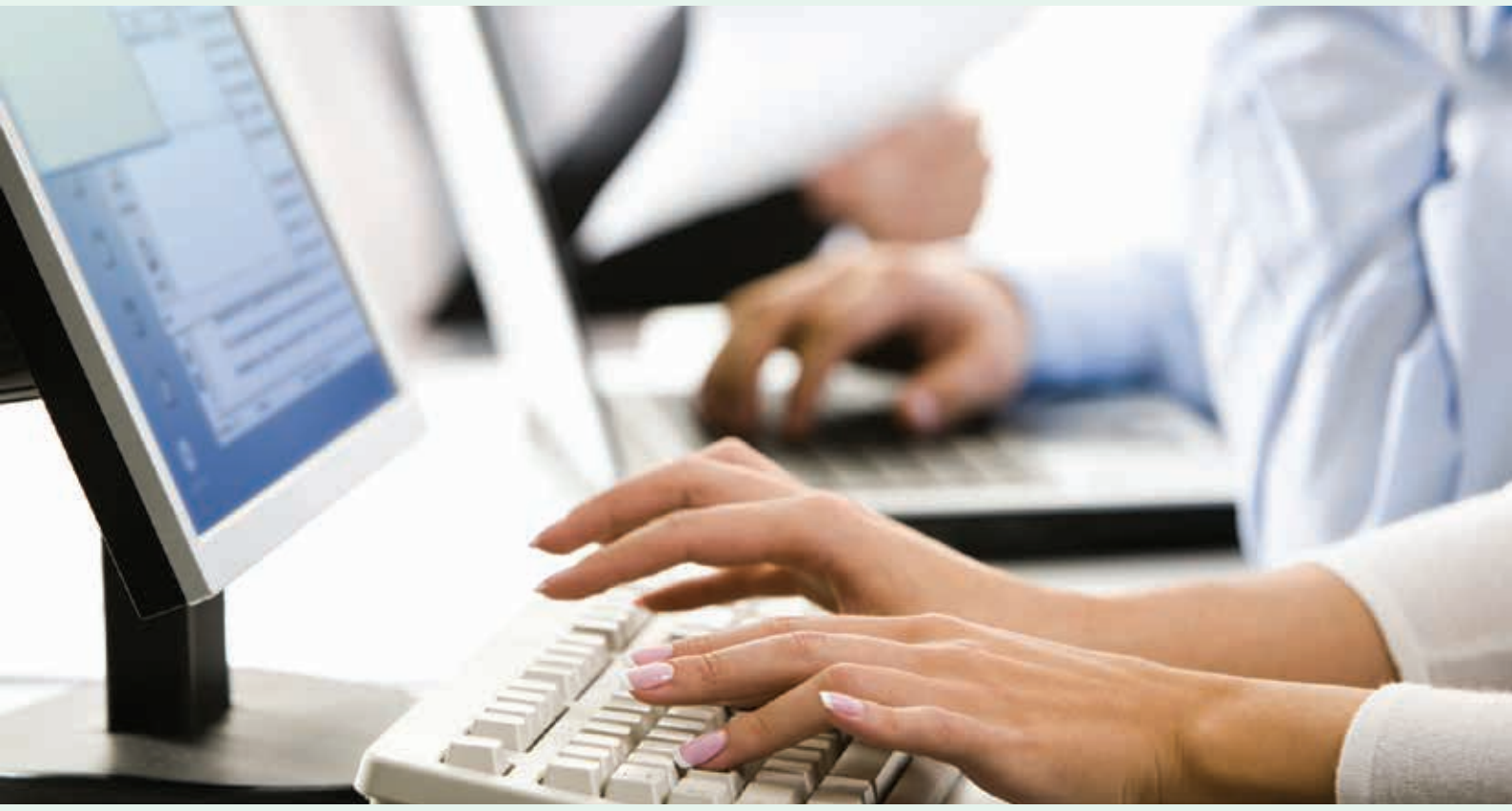
Finance

The HPRA's finance section is responsible for managing and safeguarding the finances of the HPRA. It must ensure that the organisation fulfils its legislative requirements and applies best practice to the governance of its affairs. All procedures are carried out using standard operating procedures under the quality management system.

The 2015 financial statements presented in this report were prepared by the finance section and submitted for audit to the Comptroller and Auditor General. All financial transactions during the period under review are reflected and reported upon in these statements as is our commitment to the highest standards of corporate governance.

Legal

The legal section advised on the implementation of new legislation in addition to other relevant issues. The section dealt with various legal queries from across the organisation and attended and presented at the European meeting of lawyers held under the European Presidency.



Quality Management

During 2015, the HPRA's quality management system continued to be extended with the deployment of policies, guidelines and procedures for clinical field trials. As part of the development of the new workflow system, we also began to develop a new document management policy and procedures.

In September, we reported to the European Commission on internal audits of our pharmacovigilance system, as required under the Pharmacovigilance Directive, 2010/84/EU. A copy of the report was published on our website.

Overview of Energy Usage in 2015

Since 1 January 2011, the HPRA, as a public sector body, has been required to report annually on its energy usage and actions taken to reduce consumption in accordance with the European Union (Energy Efficiency) Regulations 2014 (S.I. No. 426 of 2014).

The HPRA uses electricity for lighting, air conditioning or heating as required and the provision of hot water. Natural gas is used for central heating.

In 2015, the HPRA consumed 1066 MWh of energy consisting of:

- 733 MWh of electricity;
- 333 MWh of fossil fuels;
- 0 MWh of renewable fuels.

Actions Undertaken in 2015

In the past year, the HPRA continued to focus on energy performance by maintaining framework agreements for the supply of both electricity and natural gas. Both of these framework agreements were established by the Office of Government Procurement for the supply of electricity and natural gas to the Irish public sector. The agreements are intended to maximise volume discounts and provide for reductions in administrative and transaction costs for suppliers and public sector purchasers. During 2015, HPRA cost savings were in the region of 2.7% for electricity and 10.7% for gas (compared to the cost of going directly to the market).

Total Energy Savings

The HPRA has been highly focussed on reducing energy usage for the past number of years. This is evidenced by the 2015 Sustainable Energy Authority of Ireland (SEAI) report for the HPRA which confirmed that the organisation has improved its energy usage by 23% since 2009.

Actions Planned for 2016

The HPRA is committed to reducing its energy usage by 33% by 2020 in accordance with S.I. No. 426 of 2014, the National Energy Efficiency Action Plan 2014 and the European Energy Efficiency Directive (2012/27/EU). As a result, we have entered into a partnership agreement with the Office of Public Works (OPW) to roll out the Optimising Power @ Work programme across the organisation. The HPRA has also signed up for the SEAI sponsored Energy Map programme and is seeking a partnership arrangement with the SEAI.

During 2016, the HPRA intends to maintain energy performance by continuing its participation in newly contracted framework agreements for the supply of both electricity and natural gas to the public sector. It is anticipated that both these framework agreements, accessed via the Office of Government Procurement, will deliver savings when compared to the costs of going directly to the market. It is important to note that the Office of Government Procurement contract rates are fixed until early 2017 for electricity and gas.

FINANCIAL STATEMENTS FOR THE YEAR ENDED 31 DECEMBER 2015

Authority Members and Other Information

Authority:

Mr. Michael Hayes	term expired 31/12/2015, Chairman
Mr. Pat Brangan	term expired 31/12/2013, re-appointed 22/05/2014
Mr. Wilfrid Higgins	term expired 31/12/2013, re-appointed 22/05/2014
Ms. Ann Horan	appointed Chairman 01/01/2016
Prof. Mary Horgan *	
Dr. Elizabeth Keane **	term expired 31/12/2013, re-appointed 22/05/2014
Mr. Noel O'Donoghue	term expired 31/12/2015
Prof. Caitriona O'Driscoll	
Dr. Diarmuid Quinlan ***	

The Authority was appointed by the Minister for Health on 18/01/2011.

* Prof. Mary Horgan was appointed on 08/11/2011.
** Dr. Elizabeth Keane was appointed on 24/10/2012.
*** Dr. Diarmuid Quinlan was appointed on 22/05/2014.

Bankers:

Allied Irish Bank
1-3 Lower Baggot Street
Dublin 2

Bank of Ireland Corporate
2 Burlington Plaza
Burlington Road
Dublin 4

Solicitors:

Eugene F. Collins
Temple Chambers
3 Burlington Road
Dublin 4

Head Office:

Kevin O'Malley House
Earlsfort Centre
Earlsfort Terrace
Dublin 2

Auditors:

Comptroller and Auditor General
3A Mayor Street Upper
Dublin 1

Corporate Governance

The Health Products Regulatory Authority (the HPRA) was established under the terms of the Irish Medicines Board Act, 1995 (as amended), and is governed by an Authority which was appointed by the Minister for Health. The Authority of the HPRA (the Authority) consists of a chairman and eight unremunerated non executive members. On 1 July 2014, the organisation changed its name from the Irish Medicines Board, as provided for in Section 36 of the Health (Pricing and Supply of Medical Goods) Act 2013 and SI (205/2014) Health (Pricing and Supply of Medical Goods) Act 2013 (Commencement) order 2014.

The HPRA is committed to the highest standards of Corporate Governance and has implemented the "Code of Practice for the Governance of State Bodies" issued by the Department of Public Expenditure and Reform. This Code of Practice incorporates many of the principles under which the HPRA operates, taking account of the size and legal nature of the organisation.

The HPRA has in place an extensive Code of Conduct and conflicts of interest policy for all staff, committees and Authority members. The HPRA applies the highest standards of disclosure and transparency in respect of interests held by staff, committees and Authority members.

Audit Committee

The HPRA has an audit committee comprising three Authority members, which met on four occasions during 2015. This committee is responsible for reviewing internal control matters, together with any other issues raised by the external auditors, the Authority or management. The external auditor is invited annually to meet with the audit committee to brief them on the outcome of the external audit and the audit committee also meets annually with the internal auditor. During 2015, the internal auditor carried out internal audits on the areas of income and travel/subsistence. They also carried out reviews of the project management office and of the implementation of the new finance system in HPRA. The audit committee has also been involved with the review of the quality systems as described below.

Quality Systems

During 2015, the finance section of the HPRA continued the process of implementing and reviewing standard operating procedures (SOPs) under the quality management system. This process involved a critical review and analysis of internal controls and processes throughout the section with particular emphasis on risk management. This system now underpins the internal control environment and feeds into the internal audit process and ultimately into the audit committee.

Remuneration Policy - Authority Members and Executive Directors

Remuneration and travel expenses paid to Authority members are disclosed in note 17 to the financial statements. The Chairman receives remuneration as directed by the Minister for Health in accordance with the Irish Medicines Board Act, 1995. Other Authority members receive travel expenses in accordance with circulars issued by the Department of Health. The Chief Executive is remunerated in accordance with guidelines issued from Government and other Executive Directors are paid in accordance with Department of Health pay scales. The Chief Executive's remuneration is disclosed in note 18 to the Financial Statements.

Internal Control

The Authority is responsible for the HPRA's systems of internal control. Such systems can only provide reasonable and not absolute assurance against material misstatement or loss. The systems of internal controls in use in the HPRA are described more fully in the Chairman's report on page 88.

Statement on Internal Financial Control

1. I, as Chairman, acknowledge that the Authority is responsible for the body's system of internal financial control.

2. The HPRA system of internal financial control can provide only reasonable and not absolute assurance against material error, misstatement or loss.

3. The Authority confirms that there is an ongoing process for identifying, evaluating and managing the significant risks faced by the HPRA. The HPRA maintains a risk register which is reviewed and updated by management, considered by the audit committee and presented to the Authority.

   Management are responsible for the identification and evaluation of significant risks applicable to their areas of business together with the design and operation of suitable internal controls. These risks are assessed on a continuing basis and may be associated with a variety of internal or external sources including control breakdowns, disruption in information systems, natural catastrophe and regulatory requirements. These risks are recorded in the risk register.

   Management reports fortnightly on operational issues and risks and how they are managed to the Management Committee. The Management Committee's role in this regard is to review on behalf of the Authority the key risks inherent in the affairs of the HPRA and the system of actions necessary to manage such risks and to present their findings on significant matters via the Chief Executive to the Authority.

   The Chief Executive reports to the Authority on behalf of the executive management on significant changes in the work of the HPRA and on the external environment, which affects significant risks. The Deputy Chief Executive provides the Authority with monthly financial information, which includes key performance indicators. Where areas for improvement in the system are identified, the Authority considers the recommendations made by the Management Committee.

   An appropriate control framework is in place with clearly defined matters which are reserved for Authority approval only or, as delegated by the Authority, for appropriate Management Committee approval. The Authority has delegated the day-to-day management of the HPRA and established appropriate limits for expenditure authorisation to the Management Committee. The Chief Executive is responsible for implementation of internal controls, including internal financial control.

   The system of internal financial control is monitored in general by the processes outlined above. In addition, the Audit Committee of the Authority reviews specific areas of internal control. The HPRA has outsourced the internal audit function to an independent professional firm. During 2015 two reviews were conducted. The Audit Committee considers reports from internal audit and recommendations from the Comptroller and Auditor General arising as a result of the external audit.

4. The Authority have carried out a review of the effectiveness of internal financial control, in order to demonstrate compliance with the Code of Practice. This review was carried out at its meeting on 11 May 2016.

Ms. Ann Horan
Chairman to the Authority

15 June 2016

Statement of Authority Members' Responsibilities

The Authority is required by the Irish Medicines Board Act, 1995 to prepare financial statements for each financial year which give a true and fair view of the state of affairs of the HPRA and of its surplus or deficit for that period.

In preparing those statements the Authority is required to:

- select suitable accounting policies and apply them consistently;
- make judgements and estimates that are reasonable and prudent;
- disclose and explain any material departures from applicable accounting standards; and
- prepare the financial statements on a going concern basis unless it is inappropriate to presume that the HPRA will continue in existence.

The Authority is responsible for keeping proper accounting records which disclose with reasonable accuracy at any time the financial position of the HPRA and which enable it to ensure that the financial statements comply with the Irish Medicines Board Act, with accounting standards generally accepted in Ireland and with accounting directions issued by the Minister for Health. It is also responsible for safeguarding the assets of the HPRA and hence for taking reasonable steps for the prevention and detection of fraud and other irregularities.

On behalf of the Authority:

Ms. Ann Horan
Chairman

Mr. Pat Brangan
Authority Member

15 June 2016

Comptroller and Auditor General Report for Presentation to the Houses of the Oireachtas

I have audited the financial statements of the Health Products Regulatory Authority for the year ended 31 December 2015 under the Irish Medicines Board Act, 1995. The financial statements comprise the statement of income and expenditure and retained revenue reserves, the statement of financial position, the statement of cash flows and the related notes. The financial statements have been prepared in the form prescribed under Section 18 of the Act, and in accordance with generally accepted accounting practice as modified by the Minister for Health in relation to accounting for superannuation costs.

Responsibilities of the Board of the Authority

The Board of the Authority is responsible for the preparation of the financial statements, for ensuring that they give a true and fair view and for ensuring the regularity of transactions.

Responsibilities of the Comptroller and Auditor General

My responsibility is to audit the financial statements and report on them in accordance with applicable law.

My audit is conducted by reference to the special considerations which attach to State bodies in relation to their management and operation.

My audit is carried out in accordance with the International Standards on Auditing (UK and Ireland) and in compliance with the Auditing Practices Board's Ethical Standards for Auditors.

Scope of audit of the financial statements

An audit involves obtaining evidence about the amounts and disclosures in the financial statements, sufficient to give reasonable assurance that the financial statements are free from material misstatement, whether caused by fraud or error. This includes an assessment of

- whether the accounting policies are appropriate to the Authority's circumstances, and have been consistently applied and adequately disclosed.
- the reasonableness of significant accounting estimates made in the preparation of the financial statements, and
- the overall presentation of the financial statements.

I also seek to obtain evidence about the regularity of financial transactions in the course of audit.

In addition, I read the Authority's annual report to identify material inconsistencies with the audited financial statements and to identify any information that is apparently materially incorrect based on, or materially inconsistent with, the knowledge acquired by me in the course of performing the audit. If I become aware of any apparent material misstatements or inconsistencies, I consider the implications for my report.

Opinion on the financial statements

In compliance with the directions of the Minister for Health, the Authority accounts for the costs of superannuation entitlements only as they become payable. This basis of accounting does not comply with Financial Reporting Standard 102 which requires such costs to be recognised in the year the entitlements are earned.

In my opinion, except for the accounting treatment of the Authority's superannuation costs and liabilities, the financial statements have been properly prepared in accordance with generally accepted accounting practice in Ireland and give a true and fair view of the state of the Authority's affairs at 31 December 2015 and of its income and expenditure for 2015.

In my opinion, the accounting records of the Authority were sufficient to permit the financial statements to be readily and properly audited. The financial statements are in agreement with the accounting records.

Matters on which I report by exception

I report by exception if I have not received all the information and explanations I required for my audit, or if I find

- any material instance where money has not been applied for the purposes intended or where the transactions did not conform to the authorities governing them, or
- the information given in the Authority's annual report is not consistent with the related financial statements or with the knowledge acquired by me in the course of performing the audit, or
- the statement on internal financial control does not reflect the Authority's compliance with the Code of Practice for the Governance of State Bodies, or
- there are other material matters relating to the manner in which public business has been conducted.

I have nothing to report in regard to those matters upon which reporting is by exception.

Patricia Sheehan

For and on behalf of the

Comptroller and Auditor General

21 June 2016

STATEMENT OF INCOME AND EXPENDITURE AND RETAINED REVENUE RESERVES
For the year ended 31 December 2015

	Note	2015	2014 As restated
		€	€
Fee Income	3	**21,654,894**	21,046,800
Department of Health Funding	3	**3,916,000**	3,916,000
Other Income	4	**585,872**	784,860
		26,156,766	25,747,660
Salaries and Wages	5	**17,926,950**	17,501,062
Other Operating Costs	6	**5,486,959**	4,738,449
Depreciation	2	**1,648,765**	1,310,329
		25,062,674	23,549,840
Surplus for the year before write back of Superannuation contributions		**1,094,092**	2,197,820
Staff Superannuation Contributions		**441,888**	443,890
Surplus for the year		**1,535,980**	2,641,710
Balance brought forward	25	**25,862,197**	23,220,487
Balance carried forward	12	**27,398,177**	25,862,197

All income and the surplus for the year arises from continuing activities.

Chairman

Ms. Ann Horan
15 June 2016

Authority Member

Mr. Pat Brangan

The notes on pages 95 to 105 form part of the financial statements.

STATEMENT OF FINANCIAL POSITION
As at 31 December 2015

	Note	2015 €	2014 €
Fixed Assets			
Property, plant and equipment	2	25,665,558	25,574,039
Current Assets			
Debtors and Prepayments	7	1,191,666	727,029
Inventory of Stationery		2,077	2,259
Cash at Bank and in Hand		475,265	205,531
Short Term Deposits	10	15,991,441	15,649,391
		17,660,449	16,584,210
Creditors - Amounts falling due within one year			
Creditors and Accruals	8	8,787,819	8,362,712
Mortgage	13	793,332	793,332
		9,581,151	9,156,044
Net Current Assets		8,079,298	7,428,166
Creditors - Amounts falling due after more than one year			
Mortgage	13	6,346,679	7,140,008
NET ASSETS		27,398,177	25,862,197
Reserves			
Income and Expenditure Reserve	12	27,398,177	25,862,197
		27,398,177	25,862,197

Chairman

Ms. Ann Horan
15 June 2016

Authority Member

Mr. Pat Brangan

The notes on pages 95 to 105 form part of the financial statements.

STATEMENT OF CASH FLOWS
For the year ended 31 December 2015

	Note	2015 €	2014 €
Cash flows from Operating Activities			
Surplus/(Deficit) for financial year		1,535,980	2,641,710
Depreciation of property, plant and equipment		1,648,765	1,310,329
(Profit)/Loss on Disposal of property, plant and equipment		156	61
(Increase)/Decrease in Debtors		(464,637)	(82,644)
(Increase)/Decrease in Stock		182	148
Increase/(Decrease) in Creditors - amounts falling due within one year		425,107	670,960
Deposit Interest		(79,548)	(131,249)
Bank Interest		243,288	355,712
Cash from Operations		3,309,293	4,765,027
Bank Interest Paid		(243,288)	(355,712)
Net Cash generated from Operating Activities		3,066,005	4,409,315
Cash flows from Investing Activities			
Deposit Interest Received		79,548	131,249
(Increase)/Decrease in Bank Deposits		(2,126,720)	(8,540,234)
Payments to acquire property, plant and equipment		(1,740,789)	(994,135)
Receipts fom sales of property, plant and equipment		352	370
Net cash from Investing Activities		(3,787,609)	(9,402,750)
Cash flows from Financing Activities			
Repayment of Borrowings		(793,332)	(793,332)
Net cash used in Financing Activities		(793,332)	(793,332)
Net increase/(decrease) in Cash and Cash Equivalents		(1,514,936)	(5,786,767)
Cash and Cash Equivalents at beginning of year		3,617,069	9,403,836
Cash and Cash Equivalents at end of year	9	2,102,133	3,617,069

The notes on pages 95 to 105 form part of the financial statements.

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2015

1. Accounting Policies

A. General information

The Health Products Regulatory Authority (HPRA) is a public statutory body established under the Irish Medicines Board Act 1995 (as amended). The principal place of business is at Earlsfort Centre, Earlsfort Terrace, Dublin 2. The Health Products Regulatory Authority is the competent Authority for the regulation of medicines, medical devices and other health products in Ireland.

B. Compliance with FRS 102

The financial statements of the HPRA for the year ended 31 December 2015 have been prepared in accordance with FRS 102, the financial reporting framework applicable in the UK and Ireland, with the exception of superannuation. By direction of the Minister for Health, the provisions of FRS102 in relation to retirement benefits are not being complied with. In all other respects the financial statements comply with FRS102. These are the first set of financial statements prepared in accordance with FRS102. The date of transition to FRS 102 is 1 January 2014. The prior year financial statements were re-stated for material adjustments on adoption of FRS 102. The result of this adoption can be seen in note 25.

C. Basis of preparation

The financial statements have been prepared under the historical cost convention. The following accounting policies have been applied consistently in dealing with items which are considered material in relation to the Health Products Regulatory Authority's financial statements.

D. Critical accounting estimates and judgements

The preparation of the financial statements requires management to make judgements, estimates and assumptions that affect the amounts reported for assets and liabilities as at the balance sheet date and the amounts reported for revenues and expenses during the year. However, the nature of estimation means that actual outcomes could differ from those estimates. The following may involve a higher degree of judgement and complexity:

(a) Provisions

Provisions for legal obligations which it knows to be outstanding at the period-end date. These provisions are generally made based on historical or other pertinent information, adjusted for recent trends where relevant. However, they are estimates of the financial costs of events that may not occur for some years. As a result of this and the level of uncertainty attaching to the final outcomes, the actual outturn may differ significantly from that estimated.

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2015

E. Revenue recognition

Revenue is measured at the fair value of the consideration received.

- In the case of applications for marketing authorisations (new applications, variations to existing authorisations, or transfers) and clinical trial applications, income is recognised on a straight line basis over the specified timeline for the processing of the application by the Authority.
- In the case of wholesale and manufacturing licences and maintenance of marketing authorisations, fees are payable annually and a full year's income is accrued in each financial year.

F. Expenditure recognition

Expenditure is recognised in the financial statements on an accruals basis.

G. Reporting currency and currency translation

The financial statements are prepared in euros. Transactions in currencies other than euro are recorded at the rates ruling at the date of the transactions or at a contracted date. Monetary assets and liabilities are translated into euro at the balance sheet date or at a contracted date. Exchange differences are dealt with in the statement of income and expenditure.

H. Property, plant and equipment

Plant and equipment excluding Premises

Plant and equipment excluding premises are stated at cost less accumulated depreciation. Depreciation is calculated in order to write off the cost of property, plant and equipment to their estimated residual values over their estimated useful lives by equal annual instalments.

The estimated useful lives of property, plant and equipment by reference to which depreciation has been calculated are as follows:

Fixtures and Fittings :	5 years
Computer Equipment :	3 years
Improvements to Premises :	10 years

Premises

The HPRA purchased its premises at Kevin O'Malley House, Earlsfort Centre, Earlsfort Terrace, Dublin 2 on 22 December 2004. The value capitalised was equal to the purchase price plus those costs directly attributable to bringing the asset into use.

No depreciation has been calculated on the value of premises, as the remaining useful economic life is estimated to be greater than 50 years.

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2015

I. Taxation

The HPRA is exempt from liability to Corporation Tax under Section 227 of the Taxes Consolidation Act, 1997.

J. Debtors

Known bad debts are written off and specific provision is made for any amount the collection of which is considered doubtful.

K. Superannuation

The superannuation scheme operated by the HPRA is in accordance with the Local Government (Superannuation Revision) (Consolidation) Scheme, 1986. It is an unfunded statutory scheme and benefits are met from current income as they arise.

The charge to salaries and wages is stated gross of superannuation deductions of €800,889 (2014 - €748,987). The surplus for the year on page 92 is then shown both before and after superannuation deductions less lump sum amounts paid in the year. The income and expenditure reserve on the statement of financial position is split between retained reserves and superannuation reserves in note 12. The balance on the superannuation reserve represents the cumulative superannuation deductions made since 1996.

By direction of the Minister for Health, the provisions of FRS 17 as incorporated into FRS 102 are not being complied with.

L. Provisions

A provision is recognised when the HPRA has a present obligation as a result of a past event, it is probable that this will be settled at a cost to the HPRA and a reliable estimate can be made of the amount of the obligation.

M. Library

No value has been placed on the books, audio-visual resources and electronic databases in the library. Expenditure on these items is written off in the year in which it is incurred.

N. Leases

All leases are treated as operating leases and the rentals thereunder are charged to the Income and Expenditure account on a straight line basis over the lease period.

O. Loans

Loans are recognised initially at the transaction price (present value of cash payable, including transaction costs). Loans are subsequently stated at amortised costs. Interest expense is recognised on the basis of the effective interest method and is included in finance costs.

Loans are classified as current liabilities unless there is a right to defer settlement of the loan for at least 12 months from the reporting date.

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2015

2. Property, plant and equipment

	Fixtures and Fittings €	Computer Equipment €	Leasehold Improvements €	Improvements To Premises €	Premises €	Total €
Cost						
Balance as at 1 January 2015	1,147,971	10,679,242	502,445	4,314,888	23,156,037	39,800,583
Additions for the year	57,005	1,636,454	-	47,330	-	1,740,789
Disposals for the year	(1,346)	(85,403)	-	-	-	(86,749)
As at 31 December 2015	1,203,630	12,230,293	502,445	4,362,218	23,156,037	41,454,623
Depreciation						
Balance as at 1 January 2015	1,022,422	9,722,173	501,193	2,980,756	-	14,226,544
Charge for the year	59,265	1,177,734	1,252	410,514	-	1,648,765
Disposals for the year	(1,346)	(84,898)	-	-	-	(86,244)
As at 31 December 2015	1,080,341	10,815,009	502,445	3,391,270	-	15,789,065
Net Book value at 31 December 2015	123,289	1,415,284	-	970,948	23,156,037	25,665,558
Net Book value at 1 January 2015	125,549	957,069	1,252	1,334,132	23,156,037	25,574,039

3. Income

	2015 €	2014 €
Fee Income		
Clinical Trials	175,148	123,844
Human Medicine - National Fees	6,439,762	6,588,544
Human Medicine - European Fees	6,835,197	6,860,718
Veterinary Medicine - National Fees	1,492,613	1,357,676
Veterinary Medicine - European Fees	1,302,720	1,338,780
Compliance Department	5,067,354	4,294,355
Medical Devices	403,392	374,992
	21,716,186	20,938,909
Movement in deferred revenue	(61,292)	107,891
	21,654,894	21,046,800
Dept Of Health Funding (Vote 38 Subhead E1)	3,916,000	3,916,000
Other Income (Note 4)	585,872	784,860
Total Income	26,156,766	25,747,660

Certain fees, totalling €16,824,480 are required by law to be disposed of in accordance with the directions of the Minister for Public Expenditure and Reform.

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2015

4. Other Income

	2015 €	2014 €
Conference Fee Income	1,850	184,075
Deposit Interest	79,548	131,249
(Loss)/Gain on Disposal of Fixed Assets	(156)	(61)
IT Income	504,630	469,597
	585,872	784,860

5. Salaries and Wages

Salaries and Wages	15,965,979	15,663,696
Pensions	469,680	382,144
Social Welfare Costs	1,491,291	1,455,222
	17,926,950	17,501,062

The average number of staff employed during the year was 298 (2014 - 291).
Payroll numbers at 31 December 2015 can be analysed across the following departments : -

Chief Executive	11	11
Compliance	64	62
Finance, Corporate & International	20	19
Human Products Authorisation & Registration	103	106
Human Products Monitoring	47	44
Human Resources & Change	8	8
IT & Business Services	19	13
Scientific Affairs	1	2
Veterinary Sciences	25	22
Staff	298	287
Pensioners	34	30
	332	317

Pension related deductions for Public Servants of €964,037 were deducted from staff during the year and paid over to the Department of Health.

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2015

While the HPRA does not consider that Circular 13/2014 "Management and Accountability for Grants from Exchequer Funds" applies to HPRA, in the interests of transparency we are disclosing salary breakdowns required under that circular:

Salary Band	2015	2014
€0 to €60,000	197	190
€60,001 to €70,000	48	47
€70,001 to €80,000	14	9
€80,001 to €90,000	20	21
€90,001 to €100,000	9	10
€100,001 to €110,000	6	6
€110,001 to €120,000	2	2
€120,001 to €130,000	1	1
€140,001 to €150,000	1	1
	298	287
Average Salary	€51.4K	€51.9K

Higher salaries replate primarily to scientific and other professional staff e.g. clinicians, pharmacists, veterinarians, lawyers etc. and are in accordance with Department of Health salary scales.

6. Operating Costs

	2015 €	2014 €
Accommodation Costs	1,059,592	1,048,954
Travel, Representation and Training	939,155	730,412
Bank Charges and Interest	246,447	363,697
Legal & Professional Fees	427,161	106,604
Stationery, Publications and Postage	458,007	418,624
Other Operating Costs	2,356,597	2,070,158
	5,486,959	4,738,449

Operating costs of €5,486,959 includes an amount of €4,329 related to staff hospitality.

7. Debtors (all due within one year)

Trade Debtors	1,013,810	303,875
Prepayments	26,339	238,854
Other Debtors	151,517	184,300
	1,191,666	727,029

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2015

8. Creditors (amounts falling due within one year)

	2015 €	2014 As restated €
Trade Creditors	367,776	287,858
Accruals	6,554,867	6,321,754
Deferred Revenue	1,272,212	1,210,920
Revenue Commissioners	592,964	542,180
	8,787,819	8,362,712

9. Cash and Cash Equivalents

	As At 01/01/2015	Cashflow	As At 31/12/2015
Cash at Bank and in Hand	205,531	269,734	475,265
Demand Deposits	3,411,538	(1,784,670)	1,626,868
	3,617,069	(1,514,936)	2,102,133

10. Short Term Deposits

	2015 €	2014 €
Demand Deposits (convertible to cash on demand)	1,626,868	3,411,538
Short Term Deposits (not immediately convertible to cash)	14,364,573	12,237,853
	15,991,441	15,649,391

11. Administration Expenses

Surplus for the year was calculated having charged : -		
Auditor's Remuneration	16,000	17,300

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2015

12. Movement on Income and Expenditure Reserves

	As At 01/01/2015 €	Movement €	As At 31/12/2015 €
Retained Reserves	18,194,845	1,094,092	19,288,937
Staff Superannuation Contributions	7,667,352	441,888	8,109,240
	25,862,197	1,535,980	27,398,177

13. Long Term Liabilities

Mortgage

On 22 December 2004 the HPRA purchased its premises at Kevin O'Malley House, Earlsfort Centre, Earlsfort Terrace, Dublin 2. The purchase was financed by way of a mortgage, secured on the premises of €20,400,000 over 20 years from Bank of Ireland Corporate Lending.

The HPRA is committed to making the following capital repayments on its mortgage :

- within one year	793,332	793,332
- between one and five years	3,173,328	3,173,328
- after five years	3,173,351	3,966,680
	7,140,011	7,933,340

14. Interest Rate Exposure

The HPRA has taken all necessary steps to minimise its interest rate exposure by fixing 2/3s of the borrowings for the mortgage duration. The balance of the borrowings are fully offset by cash reserves. As the mortgage is at a fixed rate, the Authority has no interest rate exposure.

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2015

15. Financial Commitments

Accommodation Costs (Note 6) includes expenditure of €285,984 in relation to operating leases.

On 28 January 2005, the HPRA signed a leasehold interest in respect of the 5th floor, Alexandra House Earlsfort Centre, Dublin 2. At 31 December 2015 this lease had 6 years and four months remaining.

	2015 €	2014 €
The amounts due under this lease are as follows:		
- within one year	285,984	285,984
- between one and five years	1,143,936	1,143,936
- after five years	381,312	667,296
	1,811,232	2,097,216

16. Capital Commitments

Contracted For (Contract Signed)	1,877,410	-
Not Contracted For	405,900	2,510,000
	2,283,310	2,510,000

17. Authority Remuneration

Chairman's Salary	20,520	20,520
Authority Members' Travel Expenses	9,106	5,247
	29,626	25,767

Other than the Chairman, no other Authority member receives a salary.

18. Staff Remuneration

Chief Executive's Total Remuneration		
Basic Salary	145,749	145,985
	145,749	145,985

Mr. Pat O'Mahony served as Chief Executive during the period 1 January to 4 September 2015. He received a salary of €99,535 during this period. Ms. Rita Purcell was appointed acting Chief Executive on 5 September and served in this capacity to 31 December 2015. Her salary for this period was €46,214.

Both Mr. O'Mahony's and Ms. Purcell's pension entitlements do not extend beyond the standard entitlements in the model public sector defined benefit superannuation scheme.

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2015

19. Related Party Transactions

There have been no transactions with related parties which require disclosure under Financial Reporting Standard 102.

20. Prompt Payment of Accounts

The Health Products Regulatory Authority (HPRA) confirms that it is complying with EU law in relation to prompt payments of account.

21. Exchange Rates

The exchange rates used in preparing these financial statements were as follows : -

2015	€1 = STG £0.73693
2014	€1 = STG £0.7825

22. Provisions

The HPRA has been notified of a number of legal proceedings or potential proceedings. The information usually required under by FRS 102 is not disclosed as the HPRA believes that to do so would be prejudicial to the outcome.

23. Going Concern

The HPRA has a reasonable expectation, at the time of appoving the financial statements, that the HPRA has adequate resources to continue its operations. For this reason, the HPRA continues to adopt the going concern basis in preparing the financial statements.

24. Approval of Financial Statements

The financial statements were approved by the Authority of the HPRA on 11 May 2016.

25. Transition to FRS102

	As At 1 Jan 2014 €	As At 31 Dec 2014 €
Reconciliation of Reserves		
Reserves (as previously stated)	24,539,298	27,073,117
Deferred revenue adjustment	(1,318,811)	(1,210,920)
Reserves (as restated)	23,220,487	25,862,197

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2015

Reconciliation of surplus for the year	2014 €
Surplus for the year (as previously stated)	2,533,819
Movement in deferred revenue	107,891
Surplus for the year (as re-stated)	2,641,710

Adjusting items

(a) Deferred revenue

In 2014, the HPRA, in accordance with its then accounting policy, recorded fee income in relation to applications for marketing authorisations on a cash receipts basis. In compliance with FRS102 all such income is now recognised on a straight line basis over the specified timeline for the processing of applications by the Authority. Income received not recognised at year end is recorded as deferred revenue and included in the Statement of Financial Position as a creditor.

The impact of the change is that:

- A liability, in respect of the deferred revenue creditor, is recognised in the amount of €1,318,811 at the transition date and €1,210,920 at 31 December 2014.
- Fee income and thus the Authority's surplus for 2014 has increased by €107,891 to €21,046,800 and €2,641,710 respectively.

APPENDICES

APPENDIX 1
2015 Committee Members

Management Committee

Mr. Pat O'Mahony (resigned September 2015)
Chief Executive

Ms. Rita Purcell
Deputy Chief Executive (Chief Executive Acting - September to December 2015)

Ms. Lorraine Nolan
Director of Human Products Authorisation and Registration
(Appointment as Chief Executive confirmed December 2015)

Dr. Gabriel Beechinor
Director of Veterinary Sciences

Dr. Catríona Fisher (appointed October 2015)
Director of Quality, Scientific Affairs and Communications

Dr. Joan Gilvarry
Director of Human Products Monitoring

Mr. Kevin Horan
Director of Information Technology and Business Services

Mr. John Lynch
Director of Compliance

Dr. Mike Morris (retired December 2015)
Director of Scientific Affairs

Ms. Lynsey Perdisatt
Director Human Resources and Change

Authority

Mr. Michael D Hayes* – Chairman

Mr. Pat Brangan

Mr. Wilfrid J. Higgins

Ms. Ann Horan

Prof. Mary Horgan

Dr. Elizabeth Keane

Mr. Noel O'Donoghue*

Prof. Caitriona O'Driscoll

Dr. Diarmuid Quinlan

*Term expired 31 December 2015

Audit Committee

Ms. Ann Horan - Chairman

Mr. Pat Brangan

Dr. Elizabeth Keane

Advisory Committee for Human Medicines

Prof. Mary Horgan – Chairman

Dr. Paul Browne

Dr. Kevin Connolly

Dr. Desmond Corrigan

Prof. Tom Fahey

Prof. David Kerins

Ms. Marita Kinsella

Prof. Patrick Murray

Dr. Brian O'Connell

Mr. Ronan Quirke

Dr. Patrick A. Sullivan

Prof. Peter Weedle

Advisory Committee for Veterinary Medicines

Mr. Pat Brangan – Chairman

Dr. Ruaidhrí Breathnach

Ms. Eugenie Canavan

Mr. Michael F. Clancy

Dr. Martin Danaher

Dr. Helena Kelly

Mr. Des Leadon

Dr. Nola Leonard

Mr. Ciaran Mellet

Mr. John Moriarty

Mr. John Underhill

Advisory Committee for Medical Devices

Mr. Wilfrid J. Higgins – Chairman

Dr. Gillian Carlos McDowell

Dr. Geoffrey Chadwick

Mr. Darragh Hynes

Dr. Jonathan Lyne

Prof. Fergal O'Brien

Prof. Richard Reilly

Ms. Mary Sharp

Ms. Maebh Smith

Mr. Sean Paul Teeling

Prof. Wil van der Putten

Dr. Vivion Crowley

Clinical Trial Sub-Committee of Advisory Committee for Human Medicines

Dr. Patrick A. Sullivan – Chairman

Dr. Liam Bannan

Dr. Geraldine Boylan

Dr. Paul Browne

Dr. Peter Crean

Dr. Catherine Kelly

Dr. Thomas Peirce

Dr. Bryan Whelan

Dr. Lee Helman (CT Expert)

Dr. Filip Janku (CT Expert)

Advisory Sub-Committee for Herbal Medicines

Dr. Des Corrigan – Chairman

Dr. James Barlow

Dr. Kevin Connolly

Mrs. Ingrid Hook

Ms. Claudine Hughes

Ms. Anna-Maria Keaveney

Dr. Celine Leonard

Dr. Donal O'Mathuna

Dr. Camillus Power

Dr. Helen Sheridan

Ms. Anne Varley (resigned February 2015)

Dr. Emma Wallace

Experts Sub-Committee of the Advisory Committee for Human Medicines

Prof. Mary Horgan – Chairman

Dr. Colin Buckley (resigned January 2015)

Dr. Linda Coate

Dr. Kevin Connolly

Dr. James Colville

Dr. Noreen Dowd

Dr. Stephen Eustace

Dr. Stephen Flint

Dr. Tim Fulcher

Dr. Joseph Galvin

Dr. Patrick Gavin

Dr. Paul Gallagher

Dr. Kevin Kelleher

Dr. Catherine Kelly

Dr. Mary Keogan

Prof. David Kerins

Dr. Mark Ledwidge

Prof. Aidan McCormick (resigned January 2015)

Dr. Frank Murray

Dr. Yvonne O'Meara

Dr. Cormac Owens

Mr. Ashley Poynton

Dr. Brion Sweeney

Dr. Jogin Thakore

Dr. Gerry Wilson

APPENDIX 2
Presentations 2015

Third Level / Professional Development Presentations

Institution	Course	Presentation Title
Athlone IT	Pharmaceutical Sciences	Authorisation of Medicines
Athlone IT	Pharmaceutical Sciences	Pharmacovigilance
Athlone IT	Veterinary Nursing	Regulation of Veterinary Medicines
DIT	Pharmaceutical QA	Quality Risk Management
Dundalk IT	Veterinary Nursing	Regulation of Veterinary Medicines
Griffith College	Pharmaceutical Business Operations / Data Analytics	Good Clinical Practice Inspections
HSE	Registered Nurse Prescribers - CPD Forums	A Series of Presentations on the Role of the HPRA
IT Sligo / NUI Galway (IMDA Skillnet)	MSc in Medical Device Regulatory Affairs	Medical Device Regulation: A Competent Authority Perspective
LAST	Laboratory Animal Science and Training	Directive 2010/63/EU
NUIG	Nurse / Midwife Prescribing	(1) The Role of the HPRA and (2) Pharmacovigilance
PEMBA / University of Auburn	PEMBA Postgraduate Course	Regulating Drugs and Medical Devices in Ireland and Europe
RCSI	Nurse / Midwife Prescribing	(1) The Role of the HPRA and (2) Pharmacovigilance
RCSI	Pharmacy	Quality Defects and Recalls
RCSI	Pharmacy	Regulatory Affairs and Authorities
Sligo IT	Medical Biotechnology and Pharmaceutical Science	Quality Defects / Pharmacovigilance
St. Johns, Cork	Veterinary Nursing	Regulation of Veterinary Medicines
TCD	Immunology	Regulation of Biological Medicinal Products
TCD	Pharmaceutical Medicine	An Overview of Pharmacovigilance
TCD	Pharmaceutical Medicine	Communication of Drug Safety Data
TCD	Pharmaceutical Medicine	Pharmaceutical Medicine Seminar
TCD	Pharmaceutical Medicine	Pharmacovigilance and Risk Management
TCD	Pharmaceutical Medicine	Quality Defects and Recalls
TCD	Pharmaceutical Medicine	The Paediatric Regulation
TCD	Pharmacy	An Overview of Pharmacovigilance
TCD	Pharmacy	Authorisation of Medicines
TCD	Pharmacy	Quality Defects and Recalls

TCD	Pharmacy	Regulation of Biological Medicinal Products
TCD	Pharmacy	The Role of a Pharmacist in the HPRA and Pharmacovigilance
TEARAP	Professional Certificate	Application Process for Authorisations
TOPRA	Introduction to Regulatory Affairs	An Agency Perspective
Trinity College Dublin / BEAI	Continuing Education Series for Clinical Engineers	(1) In Vitro Diagnostics and (2) Medical Device Vigilance
UCC	Medicine and Pharmacy	Notification of Adverse Events
UCC	Pharmacy	Quality Defects and Recalls
UCD	Nurse / Midwife Prescribing	(1) The Role of the HPRA and (2) Pharmacovigilance

Regulatory Presentations

Event / Organiser	Presentation Title
2nd Industry Stakeholder Platform - Operation of EU Pharmacovigilance Legislation	Post-Authorisation Safety Studies – Experience to Date
3rd Industry Stakeholder Platform - Operation of EU Pharmacovigilance Legislation	Referrals – Updates from Regulators
4th Industry Stakeholder Platform - Operation of EU pharmacovigilance legislation	Impact of Pharmacovigilance Systems
5th Industry Stakeholder Platform - Operation of the EU Pharmacovigilance Legislation	Operation of the EU Pharmacovigilance Legislation
Annual OMCL Network Meetings	HMA Drafting Group for Risk-based Approach to Product Testing
Association of Clinical Biochemistry and Laboratory Medicine Conference	Reporting of Issues in Laboratory Medicine
Brazil National Health Surveillance Agency	(1) Regulatory Compliance Inspections and (2) PIC/S
China Food and Drug Administration Visit to Ireland	The Role of the HPRA
CMC Strategy Forum Europe	An Update on Regulatory Expectations for Biosimilars
Cosmetic Compliance Summit	CPSR: Requirements and Challenges
Department of the Environment – Enforcement Forum	HPRA: Enforcement Powers & Role
DIA Annual Meeting	A Series of Presentations on Pharmacovigilance
EPA / Office of Radiological Protection Information Day	Role of the HPRA and the Vigilance Reporting System for Medical Devices
Ethics Committees Meeting (Department of Health)	Clinical Trials Regulations: Interaction between the Competent Authority and Ethics Committees
EUPATI Patient Advocacy Training Event	Pharmacovigilance – Introduction to Signal Management
FakeCare International Conference	Open Source Intelligence
Horse Racing Ireland Committee on Anti-Doping	Veterinary Medicines
HSE / HPRA Launch of eAlert System	Driving Quality Improvement in Medical Device Management through Regulation

HSE Environmental Health Workshop	Social Media and Internet Investigations
IAT Symposium	Directive 2010/63/EU: The Role of the HPRA
Informa Life Sciences	Complying with the Requirements for Medical Device Vigilance
International Society for Pharmaceutical Engineering	Benchmarking for Pharmaceutical Regulators
Irish Association of Chemicals and Ingredients	Active Substance Distribution and Importation
Irish Cosmetics Detergent & Allied Products Association	Compliance with the Cosmetic Regulations
Irish Institute of Pharmacy Seminar	Supporting the Pharmacy Journey: A Healthcare Products Regulatory Perspective
Joint DIA EMA RMP Information Day	Lessons learned from PRAC experience with Risk Management Plans, Reflections from PRAC
Mobile Course on Process Analytical Technology (PAT)	Implementation of a PAT Technology and Thoughts on QbD
Organ Donation and Transplant Ireland	The Role of the HPRA in the Regulation of Blood, Tissues and Organs
PDA	Process Validation: Regulatory Observations
PharmaBioServ Workshop	Quality Risk Management Perspective of Quality Defects
Pharmaceutical Manufacturing Technology Centre Knowledge Day	The Regulatory Framework: The Role of the HPRA and RSI
Pharmaceutical Quality Group	Quality Defect Investigations and Recalls on the Irish Market
PharmaChemical Ireland	Supply Chain Regulation
PharmaChemical Ireland / PDA / ISPE Conference Medicines Regulator	Patient Health and Product Innovation: The Role of the
PharmaChemical Ireland / PDA / ISPE Conference	QRM in the GMP Environment
PIC/S Expert Circle	Computerised Systems and Data Integrity – Inspection Tips
PIC/S Expert Circle	GDP Regulatory Update
POCT Workshop	Vigilance Reporting for Devices in the Point of Care Setting
Process Analytical Technology (PAT) Seminar	PAT: A Regulatory Perspective
QP Forum (TCD)	Electronic Systems: Regulatory Observations
Regulatory Science Ireland	Generating Knowledge from Quality Defect Data
Swissmedic	Development of Veterinary Medicinal Law in the EU
Tissue Establishments / ART Tissue Establishments	(1) Single European Code for Tissues and Cells and (2) Commission Directive 2015/566
TOPRA	Content of the Dossier
TOPRA	Veterinary Regulatory Affairs
Turkish Study Visit to IBTS	EU Blood Legislation: The Role of the HPRA

APPENDIX 3
Human Medicines Safety: Publications and Articles

Drug Safety Newsletters

Edition	Topics Covered
February 66th Edition	- Beta interferons: Risk of thrombotic microangiopathy and nephrotic syndrome - Mycopheolate mofetil (CellCept) and Mycophenolic acid (Myfortic): New warnings about the risks of hypogammaglobulinaemia and bronchiectasis - Eligard (leuprorelin acetate depot injection): Risk of lack of efficacy due to incorrect reconstitution and administration process - Tecfidera (dimethylumarate): Progressive Multifocal Leukoencephalopathy (PML) in a patient with severe and prolonged lymphopenia - New Direct Healthcare Professional Communications published on the HPRA website
April 67th Edition	- Bisphosphonates and denosumab: Minimising the risk of osteonecrosis of the jaw (ONJ) - Risk of severe allergic reactions with ambroxol and bromhexine containing medicines considered small - New restriction for hydroxyzine-containing medicines to further minimise the known risk of QT prolongation - The importance of product information for medicines - New Direct Healthcare Professional Communications (DHPC) published on the HPRA website
June 68th Edition	- Ibuprofen: Review confirms small increased cardiovascular risk with daily doses at or above 2400mg - Codeine: Restricted use in children and adolescents for cough and cold - Adverse reaction reporting - reminder - EU HCP survey - New Direct Healthcare Professional Communications (DHPC) published on the HPRA website
July 69th Edition	- Systemic fusidic acid and interaction with statins: Reminder of risk of rhabdomyolysis - Risk of clinically significant arrhythmias when Harvoni or Daklinza in combination with Sovaldi are given concomitantly with Cordarone X - New Direct Healthcare Professional Communications (DHPC) published on the HPRA website
September 70th Edition	- Proton Pump Inhibitors: Very rare reports of subacute erythematosus (SCLE) - Donepezil: Reports of Rhabdomyolysis. - Adverse Reaction Reporting during 2014 - New Direct Healthcare Professional Communications (DHPC) published on the HPRA website

December 71st Edition	- Reminder: Oral Methotrexate and risk of unintentional overdose due to medication error - Tecfidera (dimethyl fumarate): New measures to minimise the risk of PML - EU review concluded that evidence does not support that HPV vaccines cause CRPS or POTS - New Direct Healthcare Professional Communications (DHPC) published on the HPRA website
December 72nd Edition	- Bisphosphonates: Small risk of osteonecrosis of the external auditory canal - Mycophenolate mofetil (Cellcept) and Mycophenolic acid (Myfortic): Risk of teratogenicity and new pregnancy prevention advice for women and men - The starting dose of thalidomide should be reduced when combined with melphalan in patients over 75 years of age - New Direct Healthcare Professional Communications (DHPC) published on the HPRA website

Articles in External Publications

Month	Publication	Topic
January	MIMS / MIMS Compendium	- Valproate containing medicines: Recommendation to further restrict the use of valproate in women and girls - Recommendation to restrict the combined use of medicines affecting the renin-angiotensin (RAS) system (Circulatory Section of the Compendium) - Transdermal Fentanyl: Reminder about the potential for life-threatening harm from accidental exposure (Pain Section of the Compendium)
February	IMF	- Domperidone-containing medicines: Risk of cardiac adverse reactions and restrictions for use
February	MIMS	- Ivabradine (Procorlan): New contraindication and recommendations to minimise the risk of cardiovascular events and severe bradycardia
March	MIMS / MIMS Cardiac Supplement	- Eligard (leuprorelin acetate depot injection): Risk of lack of efficacy due to incorrect reconstitution and administration process - Ivabradine (Procorlan): New contraindication and recommendations to minimise the risk of cardiovascular events and severe bradycardia
April	MIMS / MIMS Respiratory Supplement	- Beta interferons: Risk of thrombotic microangiopathy and nephrotic syndrome - Risk of severe allergic reactions with ambroxol and bromhexine-containing medicines considered small
May	MIMS / MIMS Oncology Supplement	- Bisphosphonates and denosumab: Minimising the risk of osteonecrosis (ONJ)

June	MIMS	- The Importance of Product Information for Medicines
July	MIMS / MIMS Diabetes Supplement	- Ibuprofen: Review confirms small increased cardiovascular risk with daily doses at or above 2400mg - Adverse Reaction Reporting: Reminder
August	IMF	- Systemic fusidic acid and interaction with statins: Reminder of risk of rhabdomyolysis
August	MIMS	- Systemic fusidic acid and interaction with statins: Reminder of risk of rhabdomyolysis
September	MIMS	- Codeine: Restricted use in children and adolescents for cough and cold
October	MIMS / MIMS MS Supplement	- Proton Pump Inhibitors: Very rare reports of subacute cutaneous lupus erythematosus (SCLE) - Fingolimod (Gilenya): PML in an MS patient without previous treatment with natalizumab or other immunosuppressive medicines
November	MIMS / MIMS Diabetes Supplement	- Donepezil: Reports of Rhabdomyolysis - Risk of diabetic ketoacidosis during treatment with SGLT2 inhibitors
December	MIMS / MIMS Oncology Supplement / MIMS Compendium	- Adverse Reaction Reporting during 2014 - The starting dose of thalidomide should be reduced when combined with mephalan in patients over 75 years - Reminder: Oral methotrexate and risk of unintentional overdose due to medication error

APPENDIX 4
European and National Committee / Working Group Participation

Committee / Working Group	Organisation	Meetings in 2015
Compliance and Enforcement Working Group	Competent Authorities Working Group	3
Committee of Experts Combating Risks of Counterfeit Medicines	Council of Europe	2
European Pharmacopoeia Commission	Council of Europe	3
Pompidou Group – Drug Precursors	Council of Europe	1
P-SC-COS (Committee of Experts on Cosmetics)	Council of Europe	2
Regional Meeting of the Medicrime Convention	Council of Europe	1
Medication Safety Forum	Department of Health	3
Chemicals Interdepartmental / Agency Group	Department of Jobs Enterprise and Innovation	1
Market Surveillance Forum - Cosmetics	Department of Jobs Enterprise and Innovation	4
Official Medicines Control Laboratories - Network Meetings	EDQM	7
Committee for Advanced Therapies	EMA	11
Committee for Medicinal Products for Human Use (CHMP)	EMA	11
Committee for Medicinal Products for Veterinary Use (CVMP)	EMA	11
Committee for Orphan Medicinal Products (COMP)	EMA	11
Committee on Herbal Medicinal Products (HMPC)	EMA	6
Efficacy Working Party - Veterinary	EMA	3
European Surveillance of Veterinary Antimicrobial Consumption	EMA	1
Expert Group on the Application of the 3Rs in Regulatory Testing	EMA	2
GCP Inspectors Working Group	EMA	4
GMDP Inspectors Working Group	EMA	4
Immunological Working Party - Veterinary	EMA	3

Impact of Pharmacovigilance	EMA	1
Paediatric Committee (PDCO)	EMA	12
Pharmacovigilance Inspectors Working Group - Human	EMA	2
Pharmacovigilance Inspectors Working Group - Veterinary	EMA	2
Pharmacovigilance Risk Assessment Committee	EMA	11
Pharmacovigilance Working Party - Veterinary	EMA	6
Quality Defects / Rapid Alerts Meeting	EMA	1
Quality Working Party	EMA	4
Safety Working Party	EMA	4
Scientific Advice Working Party	EMA	11
Project and Maintenance Group 1 (Pharmacovigilance)	EMA and National Competent Authorities	17
Health Advisory Committee	Environmental Protection Agency	3
Notified Body Operations Group	EU Working Group	2
Competent Authorities for Blood	European Commission	2
Competent Authorities for Organs for Human Transplantation	European Commission	2
Competent Authorities for Tissues and Cells	European Commission	2
Cosmetic Borderline Working Group	European Commission	2
Cosmetic Standing Committee and Working Group	European Commission	3
Drug Precursors Working Group	European Commission	2
European Commission Sub-working Group on Cosmetovigilance	European Commission	2
European Surveillance Strategy	European Commission	2
In-Vitro Diagnostic Technical Working Group	European Commission	1
MDEG Working Group on Vigilance	European Commission	2
Medical Device Expert Group	European Commission	
Meeting of Expert Group on Safety Features	European Commission	5
National Contact Points for the Implementation of Directive 2010/63/EU	European Commission	1
PEMSAC (Platform of European Market Surveillance Authorities for Cosmetics) Market Surveillance	European Commission	2
PEMSAC (Platform of European Market Surveillance Authorities for Cosmetics) Analytical Methods	European Commission	2
Project Evaluation Expert Working Group (Directive 2010/63/EU)	European Commission	1
Safe and Timely Access to Medicines (STAMP)	European Commission	1
SCOPE Work Package	European Commission	13

Single European Code Working Group Meeting	European Commission	1
Statistical Reporting Requirements (Directive 2010/63/EU)	European Commission	2
Blood Working Group - Experts Sub-Group on Haemovigilance)	Experts Sub-Group on Haemovigilance	1
Food Fraud Task Force	Food Safety Authority of Ireland	3
Patient Safety Surveillance Advisory Group	HIQA	1
Clinical Trial Facilitation Group (CTFG)	HMA	
Co-ordination Group for Mutual-recognition and Decentralised Procedures (Human) CMD(h)	HMA	10
Co-ordination Group for Mutual-recognition and Decentralised Procedures (Veterinary) CMD(v)	HMA	10
European Medicines Agencies Co-Operation of Legal and Legislative Issues	HMA	2
Homeopathic Medicinal Products Working Group (HMPWG)	HMA	2
Meeting of Heads of Medicines Agencies under EU Presidency	HMA	4
Network Training Centre	HMA	
Pharmacovigilance Procedures Work Sharing Working Party	HMA	7
Telematics Working Groups	HMA	
Working Group of Communications Professionals	HMA	2
Working Group of Enforcement Officers	HMA	5
Working Group of Quality Managers	HMA	2
Operation Pangea	Interpol	4
HPRA – UK Department for Business Innovation & Skills	Ireland/UK Working Group	5
FOAM (Forum on the Advertising of Medicines) Network Meeting	MHRA	1
Meeting of Competent Authorities for Medical Devices under European Presidency	National Competent Authorities	2
Cosmetic Standards Advisory Group	NSAI	2
Permanent Forum on International Pharmaceutical Crime (PFIPC)	PFIPC	1
Committee of Officials	PIC/S	2
Executive Bureau	PIC/S	2
GDP Working Group	PIC/S	2
QRM Expert Circle	PIC/S	1
Point of Care Testing Consultative Group	RCPI	2
HEO Enforcement Forum	Revenue's Customs Service	1
Fakecare	University of Trento, Italy and AEMPS, Spain	2
Fraudulent Medical Products	UNODC	1
Annual National Pharmacovigilance Centres Meeting	WHO	1
Board of the WHO/UMC Collaborating Centre	WHO	3
Member State Mechanism on SSFFC Medical Products	WHO	1

APPENDIX 5
Glossary

AED	Automated External Defibrillator
APMI	Association of Pharmaceutical Manufacturers in Ireland
ASR	Annual Safety Report
ATMP	Advanced Therapy Medicinal Product
BEMA	Benchmarking of European Medicines Agencies
CAMD	Competent Authority for Medical Devices
CAT	Committee for Advanced Therapies
CD	Controlled Drugs
CESP	Common European Submission Portal
CHMP	Committee for Medicinal Products for Human Use
CMC	Central Management Committee
CMD(h)	Co-ordination Group for Mutual Recognition and Decentralised Procedures - Human
CMD(v)	Co-ordination Group for Mutual Recognition and Decentralised Procedures - Veterinary
CMS	Concerned Member State
COMP	Committee for Orphan Medicinal Products
CTFG	Clinical Trials Facilitation Group
CVMP	Committee for Medicinal Products for Veterinary Use
DCP	Decentralised Procedure
DPP	Director of Public Prosecutions
EDQM	European Directorate for Quality of Medicines
EEA	European Economic Area
EMA	European Medicines Agency
EUDAMED	European Database on Medical Devices
FSAI	Food Safety Authority of Ireland
GCP	Good Clinical Practice
GDP	Good Distribution Practice
GMP	Good Manufacturing Practice
GVP	Good Vigilance Practice
HIQA	Health Information and Quality Authority
HMA	Heads of Medicines Agencies
HMPC	Committee on Herbal Medicinal Products
HPSC	Health Protection Surveillance Centre
HSE	Health Service Executive
HTA	Health Technology Assessment
IAHS	Irish Association of Health Stores

IBTS	Irish Blood Transfusion Service
ICH	International Conference of Harmonisation
ICMRA	International Coalition of Medicines Regulatory Authorities
IMDA	Irish Medical Devices Association
IMDRF	International Medical Device Regulators Forum
IMF	Irish Medicines Formulary
IMSTA	Irish Medical and Surgical Trade Association
IPHA	Irish Pharmaceutical Healthcare Association
IVD	*In-Vitro* Diagnostics
MAH	Marketing Authorisation Holder
MEDDEV	Medical Devices Guidance Document from the European Commission
MIMS	Monthly Index of Medical Specialities
MRP	Mutual Recognition Procedure
NBOG	Notified Body Operations Group
NCA	National Consumer Agency
NHO	National Haemovigilance Office
NSAI	National Standards Authority of Ireland
OMCL	Official Medicines Control Laboratories
OTC	Over-the-Counter
PASS	Post Authorisation Safety Studies
PCI	Pharmachemical Ireland
PDCO	Paediatric Committee
PDP	Performance Development Programme
PIC/S	Pharmaceutical Inspection Co-operation Scheme
PIF	Product Information File
PRAC	Pharmacovigilance Risk Assessment Committee
PSUR	Periodic Safety Update Report
PSUSA	EU Single Assessment Procedures
RMP	Risk Management Plan
RMS	Reference Member State
SmPC	Summary of Product Characteristics
THMP	Traditional Herbal Medicinal Product
UMC	Uppsala Monitoring Centre
VHP	Voluntary Harmonisation Procedures
VMD	Veterinary Medicines Directorate
WHO	World Health Organization

An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Kevin O'Malley House
Earlsfort Centre
Earlsfort Terrace
Dublin
D02 XP77
Ireland

Tel: +353 (1) 676 4971
E-mail: info@hpra.ie
www.hpra.ie