ANNUAL REPORT 2014

HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

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Chairman's Statement

It is with great pleasure that I present the annual report for the first time under our new name – the Health Products Regulatory Authority (HPRA). During 2014, we transitioned from being the Irish Medicines Board to the HPRA, our new organisational title which more accurately reflects our broader remit and regulatory functions that have grown significantly since we were first established.

Health products can improve the quality of our lives and indeed can be life-saving. However, there are inherent side effects associated with the use of many of the products we regulate. The role of the HPRA is to apply its expert knowledge using the best available data so as to ensure that members of the public continue to have access to products that work as intended and that are as safe as possible.

The HPRA's five year strategic plan for 2011 to 2015, which the Authority is tasked with overseeing, sets out five high level strategic objectives and a clear roadmap to achieve these goals within that timeframe. Our annual report outlines the extensive work programmes and areas of activity across all our departments under year four of the strategic plan whilst also demonstrating the HPRA's unique and important role in the wider national healthcare arena. This organisations remit is comprehensive, acting as the competent authority for the regulation of human and veterinary medicines, clinical trials, medical devices, blood and blood components, and tissues and cells. It also has a role in regulating the use of human organs intended for transplantation, cosmetic products and the protection of animals used for scientific purposes.

Our primary objective is to safeguard public and animal health by regulating specific health product sectors in line with applicable legislation. For some health products like medicines, we regulate across the entire product lifecycle from clinical trials, through manufacturing, to marketing authorisation, distribution and use by healthcare professionals, patients and animal owners. For others we have no our role in authorising products, our role starts when they first come to market and we then monitor those products and act upon any safety issues that are identified. However, underpinning all our activity regardless of the legislative framework is our core focus on effective regulation. This requires harnessing the best scientific and clinical knowledge available to us through both our specialist staff and experts nationally and through our participation at European committees which inform our decisions and policies.

Our work programme is delivered through our effective divisional structure. Many thousands of applications were assessed and processed for both human and veterinary medicines in 2014. These included new applications, renewals and variations to existing medicines. The licensing of new products in particular is an important regulatory function once a positive assessment of safety, quality and effectiveness can be confirmed.

As in previous year, a key focus of our work in 2014 involved continuously monitoring the safety of health products on the Irish market and, where appropriate, taking action quickly so as to protect patient and / or user safety. A significant part of this action involves the HPRA alerting healthcare professionals and patients to new information as required across an extensive range of health products and cosmetics. In 2014, we received and investigated over 2,800 adverse reaction reports to human medicines, some 300 for veterinary medicines and over 2,100 vigilance reports in relation to medical devices. Each of these reports is individually assessed by the HPRA and shared at EU level to form part of a European wide surveillance programme that utilises cumulatively assessed data to enhance patient safety. The HPRA is extremely grateful to all those healthcare professionals as well as members of the public who contact us with observations or concerns in relation to health products.

During June 2014, the HPRA again participated in Operation Pangea, the INTERPOL coordinated week of action targeting the online sale of counterfeit and illegal medicines. Ireland was one of 110 participating countries and during this week-long initiative we detained, in collaboration with the Revenue's Customs Service and An Garda Síochána, over 100,000 illegal prescription medicines. It was an honour later in 2014 for the HPRA to co-host an international Interpol conference entitled Ten Years of Combating Pharmaceutical Crime: Review and Prospects. Some 200 delegates from 50 countries were in attendance. These initiatives were in addition to the HPRA's ongoing efforts to counter illegal practices linked to the manufacture and supply of medicines and medical devices. We continue to highlight to the general public the serious risks associated with sourcing prescription medicines from unauthorised suppliers such as those found online as there can be no guarantee of the safety or quality of these products.

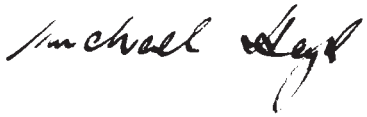
In addition to protecting public health, a robust regulatory system is also important for Ireland as a major international location for the life sciences sector. The pharmaceutical industry alone accounts for over 50% of all exports with nine out of 10 of the largest pharmaceutical companies having operations here. The HPRA's robust regulatory role supports the sectors continued success by ensuring compliance with good manufacturing practices and adherence to legal requirements.

The life sciences sector is also an increasingly globalised, evolving and growing arena. As such, it requires the HPRA to adapt its practices to effectively regulate more innovative and complex products. A key element to our approach to meeting this challenge is to enhance our international co-operation thereby giving us access to the most up-to-date information and best practices that can be use to maximum effect here in the Irish market. This year in review saw the HPRA again participate actively in EU and international activities designed to enhance the safety of health products while also contributing to policies in respect of manufacturing and distribution. The changing regulatory landscape will require us to develop our global links further while simultaneously working to develop the skills base of our staff.

Acknowledgments

On behalf of the Authority, I thank the Minister for Health and the Minister for Agriculture, Food and the Marine as well as their executives and staff for their continued support of the HPRA and its activities. I would also like to thank my fellow Authority members for their time, commitment and invaluable strategic input throughout the past year. In addition, I wish to acknowledge the role played by the members of the various advisory committees and sub-committees of the HPRA. Their active participation and advice is greatly appreciated.

The vast amount of work as detailed further in this report would not have been achievable without the tireless commitment and professionalism of all those who work at the HPRA. While our name has changed, the mission of this unique organisation continues to be the same. I would like to thank the Chief Executive, management and all the staff for their continued dedication to protecting the health and safety of all those who use health products.



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 as of 31 December 2014.

Mr. Michael D. Hayes (Chairman)

Mr. Pat Brangan*

Mr. Wilfred J. Higgins*

Ms. Anne Horan

Professor Mary Horgan

Dr. Elizabeth Keane*

Mr. Noel O'Donoghue

Professor Caitriona O'Driscoll

Dr. Diarmuid Quinlan**

* Reappointed May 2014

** Appointed May 2014

Management Committee

Mr. Pat O'Mahony
Chief Executive

Dr. J.G. Beechinor
Director of
Veterinary Sciences

Dr. Joan Gilvarry
Director of Human
Products Monitoring

Mr. Kevin Horan
Director of ICT and
Business Services

Mr. John Lynch
Director of Compliance

Dr. J.M. Morris
Director of Scientific
Affairs

Dr. Lorraine Nolan
Director of Human
Products Authorisation
and Registration

Ms. Lynsey Perdisatt
Director of Human
Resources and Change

Ms. Rita Purcell
Director of Finance,
Corporate Affairs and
International

Chief Executive's Report

2014 was a very significant year for our organisation as on 1 July the Irish Medicines Board (IMB) became the Health Products Regulatory Authority (HPRA).

Our new name is a reflection of a far broader regulatory remit which has expanded and developed over a number of years since the establishment of the IMB in 1996 and indeed its predecessor, the National Drugs Advisory Board, (NDAB) back in 1966. This is the beginning of an exciting new chapter in the history of our organisation and I am pleased to present our first annual report under the HPRA name and brand.

Strategic Plan 2011 – 2015

The layout of the annual report for 2014 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.

Authorisation, Registration and Licensing Activities

The pre-market authorisation and registration of healthcare products, as well as the licensing of manufacturing, wholesaling and related activities, is one of the HPRA's primary public health functions. We are committed to providing an effective and efficient regulatory framework that is focused on timely availability of appropriate health products. The activities of note during 2014 included the following:

- There were 80 clinical trials for human medicines approved to commence in Ireland compared with 102 the previous year. There were 10 applications for clinical investigations of a medical device, a level of activity broadly similar to the previous 12-month period.
- In the area of human medicines, the HPRA assessed 179 new national applications (including parallel product authorisations), 40 applications via mutual recognition procedures (MRP) and 265 via decentralised procedures (DCP). The total number of new products authorised continues to decrease relative to previous years and this is reflective of a trend throughout Europe which has been attributed to product patent lifecycles.
- Continuing our active contribution to the European human medicines licensing system, we acted as reference (lead) Member State for the assessment of seven MRP and DCP procedures. The HPRA was also allocated as rapporteur or co-rapporteur for eight new marketing authorisation applications by the European Medicines Agency (EMA). Based on 2014 allocations, the HPRA is ranked as fifth in the EU for rapporteurships for centrally authorised human products. We acted as lead in 42 scientific advice procedures for medicines proposed for the treatment of a broad range of conditions.
- We assessed and approved a total 75 applications for new veterinary medicines, a slight reduction when compared to the previous year.
- Over the course of 2014, the HPRA issued 13,205 variations to marketing authorisations for human products authorised through the national or MR procedures. This reduction of 25% in the volume of variations issued is due to the implementation of a new work-sharing procedure for national variations which came into effect in 2013. Of note, at a European level, we acted as rapporteur for eight paediatric Article 45 procedures and 13 procedures relating to Paediatric Investigational Plans (PIPs). The HPRA approved 1,502 variations to veterinary authorisations granted through the national, MR or centralised procedures which continued the upward trend in numbers during recent years.
- There were a total of 361 notifications of medical devices to the medical device register while 26 organisations registered with the HPRA as Irish based manufacturers of medical devices.
- A total of 117 manufacturers' licences were in place at year end for human and veterinary medicines. There were four authorisations for blood establishments and 24 for tissue establishments.

1 July

THE IRISH MEDICINES BOARD BECOMES THE HEALTH PRODUCTS REGULATORY AUTHORITY

Safety and Compliance Monitoring

A core public health function of the HPRA is to monitor the safety and quality of medicines, medical devices and other health products that have been licensed or registered for use in Ireland. This is known as post-market surveillance. Our regulatory decisions are always based on the best available information regarding benefit and risk.

- The operation of a national pharmacovigilance scheme for adverse reactions, or side effects, associated with the use of human medicines is a key element of the HPRA's post-market activities. In the past year, the HPRA received a total of 2,884 valid new adverse reaction reports. This figure is consistent with the reporting rates seen in the previous three years. It is worth noting that nearly 20% of the reports received in 2014 were associated with the use of medicines subject to additional monitoring requirements. These requirements were introduced in the context of the pharmacovigilance legislative revisions in 2012.
- The HPRA continued to contribute to work-sharing for signal detection within the EU during 2014. In the area of human medicines, we acted as lead member state for the detection and management of signals for 58 active substances authorised nationally. We also retained responsibility for assessing any signals arising as a result of signal detection for 21 centrally authorised active substances (or combination of active substances). In addition, the HPRA acted as concerned Member State in 15 EU safety-related referrals.
- Periodic safety update reports (PSURs) are vigilance reports submitted by marketing authorisation holders which are intended to provide an evaluation of the benefit-risk balance of a medicine. For human medicines, the total HPRA output in 2014 was 1,759 PSURs submitted as national, mutual recognition, centralised, EU single-assessment and PSUR work-sharing procedures.
- The HPRA received 300 national reports of suspected adverse events to veterinary medicines in 2014 continuing the upward trend in the number of reports received in recent years. We also completed the evaluation of 852 PSURs for veterinary medicines. While this was a decrease from the 1,072 figure in 2013, our PSUR activity accounts for approximately 30% of the HPRA's overall veterinary medicines workload.
- Post-market surveillance and vigilance are tools used to monitor the safety and quality of medical devices. A total of 2,113 medical device vigilance reports were received and assessed representing a slight decrease on 2013. We commenced 319 market surveillance cases with a significant number of these cases relating to notified body certificate withdrawals.

Another key function of the HPRA is to monitor and inspect industry compliance with legislation, policies and procedures. We are committed to ensuring that all health products manufactured, processed or distributed in Ireland meet essential quality standards.

- During 2014, 260 inspections and audits were performed compared to 313 in 2013 and 315 in 2012. The 2014 figure included 106 Good Manufacturing Practice (GMP) inspections, 76 Good Distribution Practice (GDP) inspections, 12 Good Clinical Practice (GCP) inspections, 20 medical device audits and 23 covering blood, tissues and organs.
- We sent a total of 506 product samples for analytical testing / examination during 2014. This represented a 16% annual increase.
- It may be necessary in certain cases to withdraw, or recall, products from the Irish market in order to protect public health. In 2014, 102 medicine recalls occurred. Of these, 96 related to human medicines while six were veterinary medicines.
- The HPRA initiated ten prosecutions in the District Courts during the course of 2014 as a result of illegal activity involving the manufacture, supply and/or sale of medicines. In total, 3,703 enforcement cases were initiated with 730,056 dosage units being detained.

Legislative and Regulatory Developments

The remit and role of our organisation continues to change and expand due to changes in our operating environment, such as new national and European legislation, and in response to the addition of further competencies.

New Clinical Trials Regulation

New clinical trials legislation (Regulation (EU) No 536/2014) was adopted and published in May 2014. It will come into effect in Europe in mid 2016. The new Regulation is intended to increase the number of clinical trials conducted in Europe and provide for improved transparency. The HPRA contributed significantly to the consultation proposals on the development of the new Regulation. Since its publication, the HPRA has been working to progress the development of systems and procedures to meet the new requirements.

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. There was further significant progress in the development of the list during 2014. By the end of 2014, the list included a total 44 active substances and includes more than 2,500 individual medicines. It is estimated that generic penetration of the first 15 substances published is now at 90% and savings to the state are estimated at €50 million for 2014.

Legal Classification of Medicines

In July, the HPRA published a group of 12 substances which are considered suitable for reclassification. Medicines containing these substances can, in certain circumstances, be reclassified to be made available over the counter in pharmacies and supplied without prescription. The industry was invited to make reclassification applications for these medicines. On foot of this proactive approach, a number of applications are pending and further progress is anticipated during 2015.

Reclassification of NRT to General Sale from Pharmacy Only Status

There was a significant development in 2014 regarding smoking cessation therapies. In July, the HPRA confirmed the authorisation of a nicotine replacement therapy (NRT) product to be sold in general retail and grocery outlets. NRT products were previously only available in pharmacies and the HPRA's decision to switch Nicorette™ NRT from 'pharmacy only status' to 'general sale status', followed an application from the authorisation holder and a detailed assessment of applicable safety and efficacy data.

Responding to Medicine Shortages

We continue to work closely with the Department of Health and the HSE in relation to the management of shortages of medicines within the Irish market place. One mechanism 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'. In the past year, the HPRA issued 129 such approvals.

Veterinary Clinical Field Trials

The role of the HPRA expanded yet further when our organisation became the competent authority for the authorisation of clinical field trials on veterinary medicines on 17 July 2014.

Under legislation, tests and trials on a veterinary medicine for the purpose of generating data to support a marketing authorisation, or for other purposes shall not be conducted without prior licence from the HPRA. A clinical field trial licence application must be submitted and approved in order for work to commence on any clinical field trial. Relevant application forms, guides and fee details are available from our website.

Revision of European Medical Devices Legislation

During 2014, the negotiation of the European Commission's proposed Regulations on medical devices and in-vitro diagnostics continued at the European Council's Working Party on Pharmaceuticals and Medical Devices. The two proposed Regulations represent a significant development and improvement of the existing system. The associated legal text are large and complex and have necessitated detailed review, discussion and negotiation.

The HPRA continues to provide support to the Department of Health for the purposes of the Working Party negotiations and we are also active contributors to a number of relevant expert working groups. It is anticipated that these proposals, which are subject to the ordinary legislative process including examination by both the European Council and the European Parliament, will be finalised by the end of 2015.

European Commission's Joint Plan for Immediate Actions on Medical Devices

In February 2012, the European Commission 'joint plan of immediate actions' was published with the objective of reinforcing the existing regulatory system for medical devices in advance of the proposed revision to the medical devices legislation. The HPRA's approach to medical devices regulation has been closely aligned with the recommendations of the plan in recent years and we remain fully committed to supporting and using the provisions of the joint plan as a basis for development. During 2014, further progress was achieved in respect of the oversight and performance of notified bodies for medical devices and in the area of market surveillance and vigilance.

Participation in the European and International Regulatory Systems

The health products regulated by the HPRA are part of an international industry that is constantly changing and developing. Those products manufactured here are used around the world, while products manufactured elsewhere are used by Irish patients and consumers. The HPRA is therefore committed to playing its part in the global regulatory network and 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 recognise the importance of contributing where possible and appropriate to relevant international organisations.

The following highlights some of main developments and HPRA contributions from 2014.

- The HPRA attended the 8th International Summit of Heads of Medicines Regulatory Agencies. The HPRA continued in the role of Vice-Chair of the International Coalition of Medicines Regulatory Authorities (ICMRA) where discussion continued on the development of terms of reference, rules of procedure and future membership criteria. ICMRA continues to dialogue with existing international regulatory groups and to pursue initiatives with a view to streamlining and enhancing international cooperation.
- The HPRA continued 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.
- The Irish PRAC delegate continued to fulfil the role of Vice-Chair of this important EMA public health committee.

- The HPRA continued its work with relevant stakeholders on the phased implementation of EU pharmacovigilance legislation. We also contributed to the Strengthening Collaborations for Operating Pharmacovigilance in Europe (SCOPE) Joint Action project which aims to support the operation of pharmacovigilance in Europe.
- The Pharmacovigilance and Risk Management Lead was the Regulatory Chair for the ICH Implementation Working Group for the E2C R2 guideline on Periodic Benefit Risk Evaluation Reports which successfully completed its intended deliverables in 2014.
- 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.
- 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 a key focus in 2014 and the HPRA was an active participant in the review of the proposed new framework by both the EMA & HMA.
- A HPRA enforcement officer was elected vice chair of the HMA Working Group of Enforcement Officers (WGEO).
- 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 was elected to the newly formed Executive Group of the Competent Authority for Medical Devices (CAMD).
- The Inspection Manager continued as a member of the Executive Bureau of the Pharmaceutical Inspection Co-operation Scheme (PIC/S) and as chair of its Sub-Committee on Compliance.

Scientific Animal Protection

The HPRA continued to interact with the Department of Health and all relevant stakeholders in relation to the overall implementation of Directive 2010/63/EU on the protection of animals used for scientific purposes. Of particular note in 2014 was the publication by the HPRA of its first annual statistical report on the use of animals for scientific purposes in Ireland. We also provided support during the year to the National Committee for the Protection of Animals used for Scientific Purposes.

Stakeholder Engagement and Communications

The HPRA is committed to expanding and improving our communications activities and to ensuring that all our stakeholders have timely access to relevant safety and regulatory information. As well as our regular meetings and ongoing publication of safety and regulatory updates, newsletters and guidance documents, a number of significant communications programmes and initiatives took place during 2014. A primary focus was the introduction of the Health Products Regulatory Authority name and brand.

The Irish Medicines Board becomes the Health Products Regulatory Authority

Following the decision to adopt the new HPRA name, a new brand identity was developed to help us communicate in a consistent and clear manner with all our stakeholders. The identity consists of a number of core elements, including our logo, fonts and colour palette, that come together to create a strong, credible and unique brand for the HPRA. Our new brand identity reflects what we stand for – protecting and enhancing public and animal health.

Throughout the first six months of 2014, a significant programme of work was undertaken which incorporated a wide-ranging external communications plan to inform stakeholders in addition to a comprehensive staff engagement strategy.

The external plan consisted of a range of activities and projects that were planned to coincide primarily with the 1 July introduction date and included the launch of a new corporate website, a series of 'all-stakeholder' e-mails and the publication of

a new corporate brochure and video. In addition, an information notice was placed in a number of health and related industry publications and series of press releases were issued to national, regional and specialist media. A range of publications including information leaflets, guides, forms and newsletters were also redesigned and there were updates to our corporate stationery and office signage.

On the morning of the launch a stakeholder event was held in the HPRA offices in Dublin 2 with over 60 external attendees representing patient and healthcare professionals, the Department of Health and other government departments and agencies. We were very pleased to welcome RTÉ journalist Mr Tommie Gorman and the then Chief Executive of the IDA, Mr Barry O'Leary, as our guest speakers.

To prepare internally for the change of name and new corporate identity, a brand implementation group was convened with representatives from a range of different organisational functions. This group identified close to 200 individual rebrand tasks that were required to ensure a smooth and efficient introduction of the new name and identity. The vast majority of the tasks were completed in advance of or on the key 1 July date with the remainder planned for completion on a phased basis thereafter.

Finally, an internal communications plan was also implemented to support the introduction of the HPRA name and brand. This was a key element of the communications activity due the associated impact on all departments and sections across the organisation and there is no doubt that the support of all our colleagues was central to what was a hugely successful renaming and rebranding project.

Our New HPRA Website

The development of the new HPRA website which began in 2013 was completed to coincide with the introduction of the HPRA name and brand on 1 July. This was a complementary project as the existing IMB website was due for essential upgrade. In particular, there was a requirement for the introduction of a new content management system to ensure a professional and modern online presence for the HPRA. A primary focus was on ensuring an improved navigation so that all content could be easily found and accessible.

Other enhancements, in addition to the incorporation of the HPRA's new brand identity, are an improved search facility, the ability to access medicines product information directly from the homepage and a more targeted alerting system for subscribers. Based on feedback received from the users of the website, we also introduced redesigned sub homepages for each product area and new sub homepages for our key stakeholder groups: members of the public, industry and healthcare professionals.

Events

In November 2014, the HPRA and An Garda Síochána co-hosted Ten Years of Combating Pharmaceutical Crime: Review and Future Prospects, an INTERPOL conference held in Dublin. This was a major international conference which was attended by senior law enforcement officials from across the world as well as representatives from government, intergovernmental organisations and the pharmaceutical industry. Almost 200 delegates from some 50 countries and 17 international organisations were in attendance. There was significant national and international media interest in the event and the opening address was delivered by Minister of State at the Department of Justice and Equality, Aodhán Ó Ríordáin, TD.

HPRA information days and seminars provide regulatory guidance and updates to a range of stakeholders and include presentations from HPRA staff and, where appropriate, external contributors. These events, which are all organised and managed by an in-house events team, enable all attendees to submit questions, seek clarifications and network

with colleagues. The past 12 months saw a number of information days and seminars being organised focused on topics such as clinical trials, the regulation of medical devices, the regulation of veterinary medicines, and pharmacovigilance. Information days were also held for both manufacturers and distributors of medicines.

In January 2014, we participated at the BT Young Scientist and Technology Exhibition for the fifth time. Thousands of students as well as teachers, parents and members of the general public from all over Ireland visited the HPRA's exhibition stand which focused on the important issue of medicines and medical devices safety.

Publications

The HPRA produces an extensive range of publication each year and 2014 was no different in that respect. In addition to 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. All these documents are available from our website and interested parties can subscribe to our e-mail alerting system to receive notifications when new editions are published.

In November, the HPRA also published a new information leaflet providing guidance to members of the public on the use of self-test products. This leaflet was developed in response to the increasing availability of self-test products for a variety of health conditions and the concerning trends and issues observed by the HPRA when following up on adverse incidents relating to their use. The leaflet can be downloaded from our website while printed versions are also available.

Oireachtas Joint Committee on Health and Children

In June, the Oireachtas Joint Committee on Health and Children met to consider the use and availability of adrenaline auto-injectors. The HPRA was invited to present an update on the authorisation and safety monitoring of these products.

Organisational Management and Development

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

Human Resources and Change

Having the necessary human resources in place and operating to the highest standards of performance, is central to us delivering on our public health mission. There was a particular focus in 2014 on the areas of staff retention and engagement and further advancing the public sector reform agenda. The organisational 'motivation and development' competency, part of the HPRA's Performance Development Programme (PDP), provided the overarching framework for the development of many of our HR 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 2014 with new features piloted across the organisation prior to a planned full implementation in 2015.

Our learning and development strategy continued to focus on staff development as one of our key motivation and retention tools. In support of this, a development planning process was launched while a group of managers commenced our externally accredited Leadership Development Programme (LDP).

The HPRA continues to recognise the importance of supporting employee engagement and commitment. In 2014, we focused on delivering a series of initiatives designed to support employees in meeting the challenges facing them both inside and outside of the workplace. This included financial planning support and the development of a range of staff health and wellness initiatives.

We continue to develop and manage our resources in line with public sector policy. This requires a particular focus on internal skills development and the reallocation of tasks and responsibilities in response to specific challenges. Where appropriate, recruitment of staff in specialist areas was completed in line with Department of Health approvals.

Finally, the remit of the HR department expanded in late 2014 to incorporate the Change Management function. This was preceded by the implementation, testing and piloting of a new human resource IT system during the first six months of the year. The benefits of the system in terms of effectiveness and efficiency have already been realised with users reporting a reduction in time spent administrating routine tasks.

Information Technology and Business Services

Technology is recognised as a key component in supporting regulatory activities at both national and international levels. The HPRA continues to contribute to, and actively lead, a number of key technology projects at a national and European level. 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 grew substantially in 2014, handling over 250,000 submissions on behalf of 32 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 and HIQA on mutually beneficial projects. This includes the provision of technological support to the interchangeable medicines initiative in co-operation with Department of Health and the HSE.

The HPRA is committed to continuous improvement across all areas of our organisation. A key current focus is the development of a new workflow technology solution which will enable the consolidation and replacement of a number of legacy solutions and will provide a new workflow and data management platform for the organisation. The tendering process for the provision of this new system was completed at the end of 2014 and the design and development is scheduled to be carried out in 2015.

Financial Performance

In common with many of its peers internationally, the HPRA is largely self-funded through a regulatory fee system. Fees are approved annually 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 2014, 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 the best possible outcomes for Irish citizens, the HPRA must be ready to respond to both the new challenges and the new opportunities that will no doubt arise during 2015 and beyond.

The overall workload for the organisation will continue to increase and diversify as we respond to the development of new and innovative products and to changes in respect of new European legislation and the addition of further national competencies. The former includes the ongoing development of new legislation in respect of both veterinary medicines and medical devices which are likely to result in significant changes to the regulatory regimes of these products.

As in previous years, we will continue to take a risk-based approach to our regulatory activities. We will adopt changes across the organisation where these are deemed necessary and beneficial, and we will continue to enhance our performance and quality management systems, our IT capabilities and our communications efforts. There will be an ongoing review of our funding provision and we will manage our cost base to ensure optimal use of resources. We expect to see fees introduced for our regulatory role in respect of medical devices.

As regards human resources, we will continue our commitment to applying best practices and to ongoing staff learning and development. This is critical for the HPRA as we must maintain and enhance the skills that are required for our increasingly complex and expanding remit.

Whilst our name has changed, our mission remains the protection and enhancement of public and animal health and this will be at the core of all our work, deliberations and decisions.

Acknowledgements

On behalf of the HPRA management team and staff, I wish to thank the Chairman and all members of the Authority, as well as all the members of the HPRA's various advisory committees, for their valuable contributions throughout 2014. In total, over 100 people give of their time voluntarily to the work of the HPRA through participation on the Authority and these committees. This independent expertise and insight is of huge benefit to our organisation and to the stakeholders we serve.

The commitment and professionalism of the HPRA staff members is critical to the successful delivery of our public health remit. I would like to express my personal appreciation to all colleagues for their valuable contribution to an ever-increasing workload during this past year and I look forward to us all working together to ensure that the HPRA, as the NDAB and the IMB before it, is a professional, expert and progressive public sector organisation.

Finally, 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 their continued support and co-operation during 2014.

Pat O'Mahony
Chief Executive

AUTHORISATION, REGISTRATION AND LICENSING ACTIVITIES

A core public health function of the HPRA is the authorisation and registration of health products. These are the regulatory actions which are carried out before a health product can be marketed and supplied in Ireland. The HPRA is committed to the timely approval of new product applications once we can confirm a positive assessment of their safety, quality and effectiveness.

The HPRA is responsible for the authorisation of medicines and clinical trials and for the registration of certain medical devices. We also licence manufacturers and wholesalers of human medicines, manufacturers of veterinary medicines as well as blood and tissue establishments and organ transplant centres. In addition, we are responsible for issuing export certificates.

The HPRA also provides a classification service to assist stakeholders in clarifying which products should be categorised as human medicines, veterinary medicines, medical devices or cosmetics. 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.

Human Medicines

Borderline Product Classification

The HPRA regularly receives queries in regard to the correct classification of human medicines, veterinary medicines and medical devices.

For products for human use, a classification service is operated for products which are on the borderline between human 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, classification committee.

The Committee, which met 11 times in 2014, consists of appropriately experienced HPRA staff from across the organisation and is chaired by the Director of Scientific Affairs. During the past 12 months, a total of 60 new products were considered consisting of 57 internal applications and three external applications. In addition, there were 20 products revisited from pre-2014.

The Committee has a close working relationship with the Food Safety Authority of Ireland (FSAI) and during the past year there were a number of referrals between both organisations. In total during 2014, the FSAI notified the HPRA of 105 products that it considered relevant to the HPRA's remit and these were reviewed and followed up as appropriate. The committee also engaged in regular dialogue with the Department of Health and with other European regulatory authorities.

Number of Applications	Received	2010	2011	2012	2013	2014
Source	Internal	72	132	127	161	57
	External	33	21	17	7	3
Classification Outcome	Medicinal Product	63	88	91	108	28
	Medical Device	4	9	6	7	
	Food Product	24	36	26	28	8
	Cosmetic Product	6	4	10	19	
	Biocide		2	1	1	
	Pending	7	12	6	1	22
	Other	1	2	4	4	2
	Total	105	153	144	168	60

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 2014, 80 clinical trials were approved to commence in Ireland down from a total of 102 in the previous year. The key areas of interest continue to include oncology and haematology. There were four clinical trials authorised which involved the use of advanced therapy medicinal products (ATMPs).

Voluntary Harmonisation Procedures

The HPRA participated in seven voluntary harmonisation procedures (VHP) during 2014. A 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. In two of these VHPs, the HPRA acted as lead Member State for the assessment.

New Marketing Authorisation Applications

Before a new medicine can be placed on the Irish market, it must be firstly assessed and authorised (licensed) by the HPRA or by the European Commission on the recommendation of the European Medicines Agency (EMA). The assessment involves establishing that a medicine's public 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.

During 2014, the following applications were assessed by HPRA:

- 179 new national applications (including parallel product authorisations);
- 40 applications made under the MRP;
- 265 applications made under DCP.

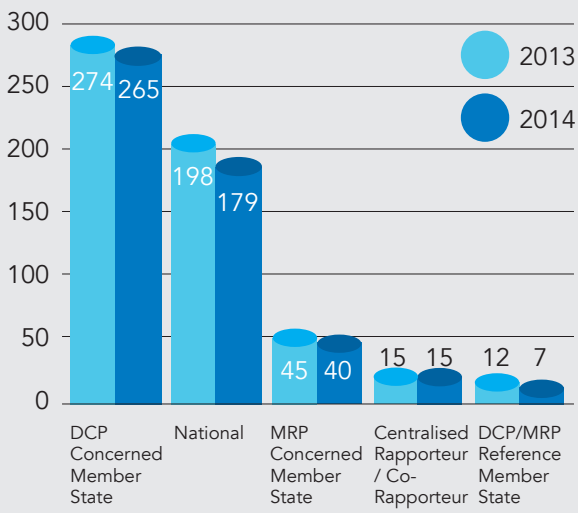
The HPRA acted as reference (lead) Member State for the assessment of seven of the MRP and DCP procedures.

The centralised route is another mechanism whereby products can be authorised in Ireland. In this procedure, the assessment is co-ordinated out by the EMA and 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. The HPRA was allocated as lead assessor (rapporteur) or joint lead assessor (co-rapporteur) for eight new marketing authorisation applications by the Committee for Medicinal Products for Human Use (CHMP) at the EMA in 2014. These included treatments for a range of orphan diseases such as Huntington's Disease and Wilson's Disease as well as treatments for respiratory diseases and will be included in our assessment work during 2015.

Based on 2014 allocations, the HPRA was ranked fifth in the EU for rapporteurships for centrally authorised human products.

The total number of new products authorised in 2014 was 615. This figure also includes 116 products authorised through the centralised route where the HPRA was not rapporteur or co-rapporteur. In overall terms, the number of products authorised continues to decrease relative to previous years and this is reflective of a trend throughout Europe which has been attributed to product patent lifecycles. The total number of new products authorised during 2013 was 752.

New Applications



Products Naming Group

During 2014, a team of human medicine assessors reviewed the existing policy on product names. To facilitate this process, an internal product naming group was established under the chairmanship of the Director of Scientific Affairs. The group advises on product name queries arising from the assessment process. Also in the past year, it revised the HPRA guidance document on names of medicinal products for human use.

Traditional Herbal and Homeopathic Medicinal Products

During 2014, 16 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 35 THMPs were authorised by the end of 2014, relative to 19 at the end of the previous year.

There were 11 homeopathic medicinal products registered during 2014 under the simplified rules scheme, bringing the total number of products registered to 98.

Transfer Applications

The HPRA processed a total 185 human medicine transfer applications in 2014. Of these, 158 related to the transfer of an existing marketing authorisation to a new marketing authorisation holder while, the balance related to a transfer of marketing authorisation holder prior to authorisation.

Variations

After a medicine has been authorised, the terms of the marketing authorisation may need to be changed and the process whereby these 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 13,205 variations to marketing authorisations for products authorised through the national or MR procedures. The number of variations was reduced relative to 2013. This was due to the implementation of a new work-sharing procedure for national variations which came into effect in 2013 and has reduced submission numbers.

Articles 45 and 46 - Variations to Update Product Information

The HPRA acted as rapporteur for eight paediatric Article 45 procedures and 14 procedures relating to Paediatric Investigational Plans (PIPs) during the past 12 months. These are important procedures from a public health viewpoint as they increase the availability of medicinal products specifically indicated for use in children.

Renewals

In 2014, 349 renewals to marketing authorisations for products authorised through the national or MR procedures were processed. In general, the numbers of renewals are decreasing reflecting the lifecycle of the products in question.

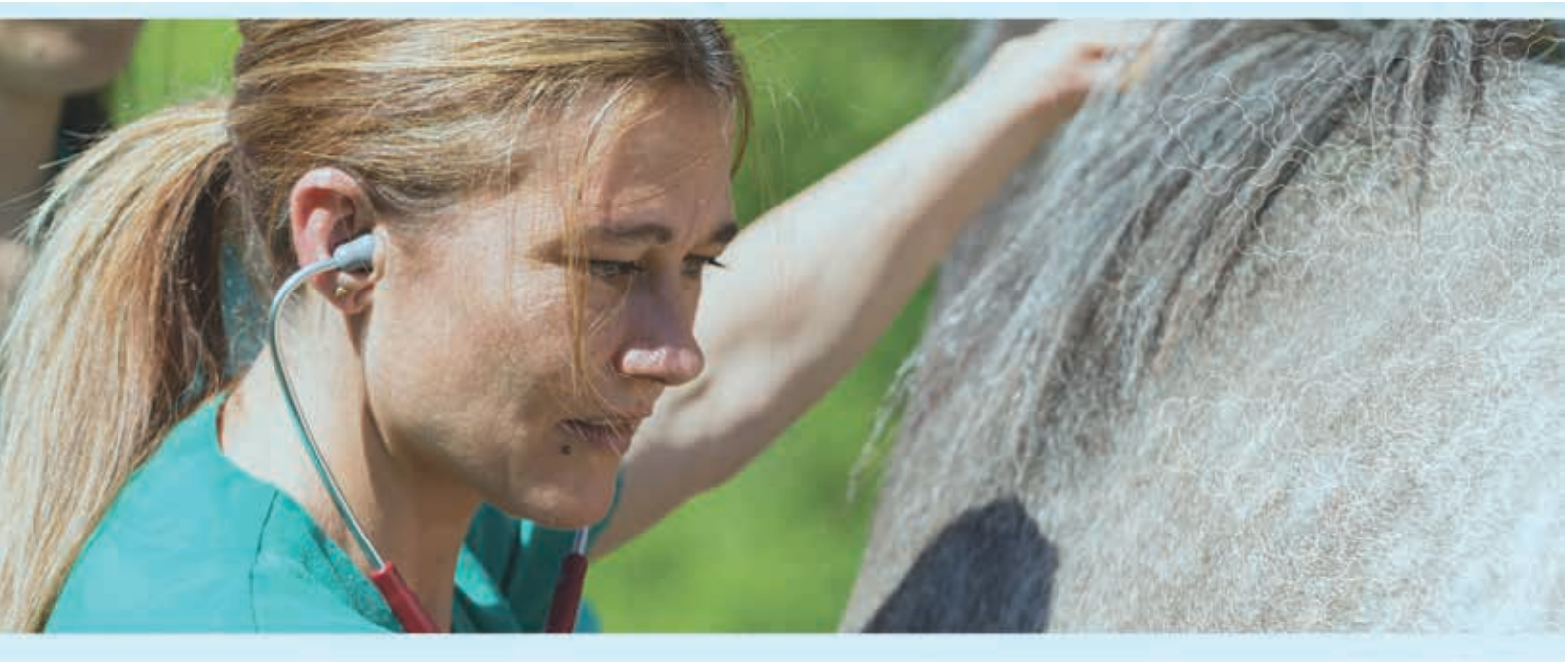
Scientific Advice

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 2014, the HPRA acted as lead in 42 EMA scientific advice procedures for medicines proposed for the treatment of a broad range of conditions. Areas of focus included medicines used in a variety of treatment areas including respiratory disorders, inflammatory diseases, diabetes mellitus and cardiovascular disease.

615

THE TOTAL NUMBER OF NEW PRODUCTS AUTHORISED IN 2014

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.

Product Classification Requests

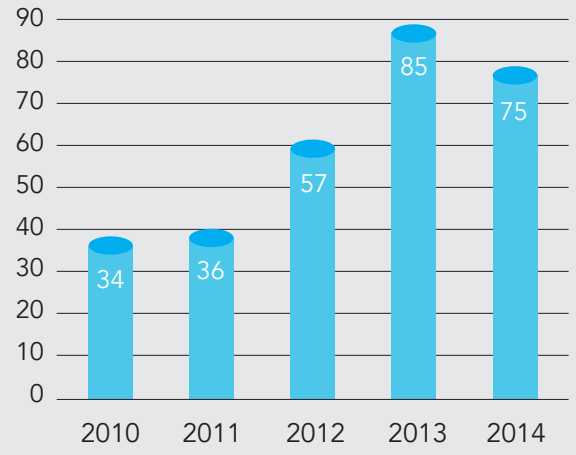
As the competent authority, the HPRA has an important role in deciding which types of products fall within the scope of the veterinary medicines legislation. Products that are regarded as medicinal but which do not have a marketing authorisation are deemed illegal in Ireland and may be seized by the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

During 2014, 49 product classification queries were received in respect of veterinary medicines. A total of 32 queries had been received the previous year.

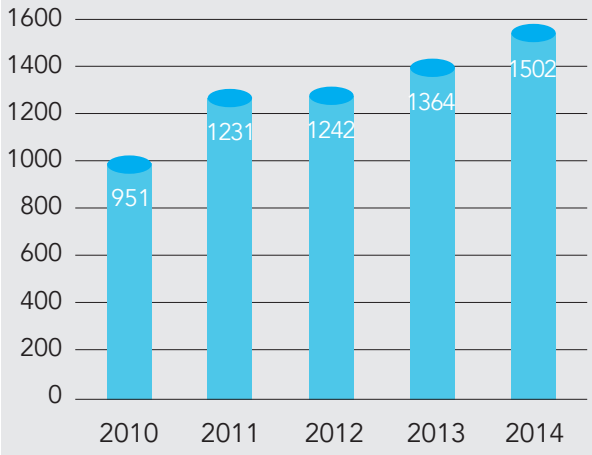
New Applications

Before a new veterinary medicine can be authorised, it must be evaluated to confirm that its animal and public health benefits outweigh its known risks. The HPRA is responsible for authorising the majority of new products coming to the Irish market and is very active at a European level in leading the evaluation of medicines under the so-called decentralised and mutual recognition authorisation procedures. This work continues to be a key focus for the HPRA as, in addition to providing a service to industry, it leads to an increase in the number of available medicines in this country. Additional products coming to the Irish market, relating to innovative or high-tech veterinary medicines, are authorised centrally under the responsibility of the EMA.

New Applications Output



Variations Output



The accompanying graph shows new applications output for 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 a result, variations now represent approximately half of the total number of applications for veterinary medicines processed annually.

The upward trend in variations output is shown in the accompanying graph.

Renewals

New marketing authorisations are valid for five years from the date of first issue, after which time they are usually renewed for an indefinite period. The number of renewals is therefore a reflection of the number of new products brought to the market five years earlier which continue to be marketed nationally. In 2014, 83 renewals of marketing authorisations for veterinary medicines were issued. HPRA activity levels in this area have fallen to around 3% of all case types, which is quite a significant decline since the earlier part of this decade. This reduction reflects a change in the legislative requirements in 2004 which eliminated the need for periodic renewals for all products.

Work-in-Progress Applications

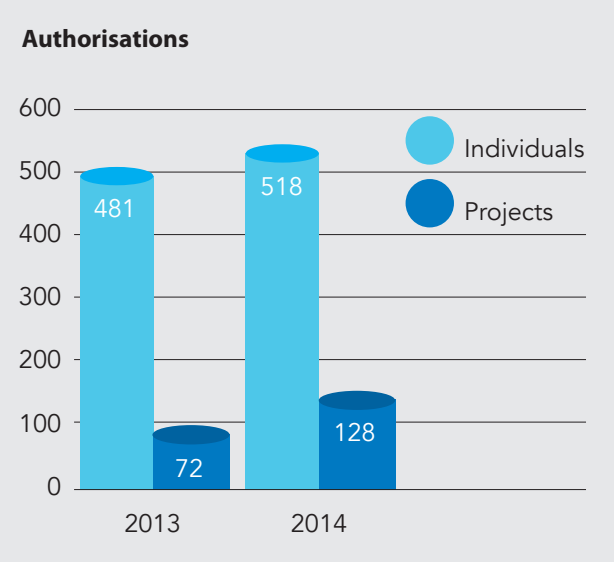
The HPRA actively monitors work-in-progress data as an important indicator of our customer service levels. The overall figure for work-in-progress at the end of the year relevant to veterinary medicines was 656 units (comprising various application types). The overall work-in-progress overdue figure was 65. These 2014 figures are broadly similar to those recorded in the previously 12 month period.

Scientific Animal Protection

The HPRA became the national competent authority responsible for the implementation of Directive 2010/63/EU on the protection of animals used for scientific purposes on 1 January 2013. The accompanying national Regulations are set out in S.I. No. 543 of 2012. This authority was transferred from the Department of Health which regulated this area until 31 December 2012.

The work of the HPRA in this area represents a very important opportunity to improve the welfare of animals used for scientific purposes and to ensure that animals are used only where justified or required. The HPRA's role involves inspection of animals and animal facilities as well as the evaluation of projects and individuals who carry out procedures or conduct euthanasia at the establishments concerned. Inspections, which may be announced or unannounced, follow a risk-based approach.

Significantly during 2014, the HPRA as required under legislation, completed the inspections of all relevant national establishments previously licensed by the Department of Health. There was also an obligation to ensure that all those working in the sector had the required authorisations in place before the end of the year. This resulted in a significant increase in the level of activity as indicated in the following graph:



THE HRPA INSPECTED ALL RELEVANT NATIONAL ESTABLISHMENTS

Medical Devices

Classification Requests

The HPRA received 25 applications for classification of medical devices or products queried as medical devices in 2014. This was a reduction relative to 2013 when 45 applications were received. The queries emanated from other medical device competent authorities in Europe / the European Commission, from medical device manufacturers and from distributors.

The HPRA circulated six enquiries on medical device classification issues 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 medical devices to be conducted in Ireland in 2014. The investigations related to areas such as respiratory, cardiac and software. This level of activity was broadly similar to the previous 12-month period.

Product Registrations

The HPRA received 361 notifications of medical devices to the medical device register. These related 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 2014, 26 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 the same number of registrations as recorded in 2013.

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 and technical aspects of the application and licensing process.

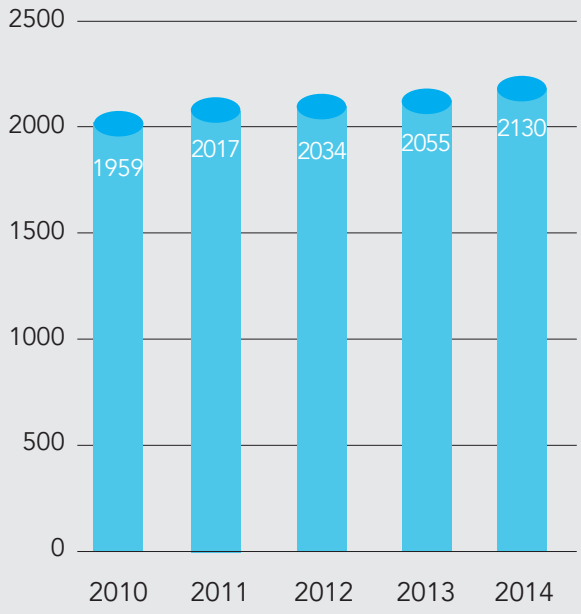
Licensing activity, which consists primarily of export and import licences and letters of no objection, has increased marginally during recent years.

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	2010	2011	2012	2013	2014
Total	48	67	70	27	46

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 guidelines 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 the HPRA. These variations, including updates and amendments, are classified as either administrative or technical.

Total Number of Licences/Authorisations (Sites)	2010	2011	2012	2013	2014
Manufacturers of Medicines for Human Use	86	88	87	89	92
Manufacturers of Veterinary Medicines	27	24	23	24	25
Investigational Medicinal Products for Human Use	51	50	47	49	53
Wholesalers of Medicines for Human use	220	243	258	269	272
Blood Establishments	4	4	3	4	4
Tissue Establishments	16	22	21	23	24
Laboratory Approvals	16	16	17	16	16
Total	420	447	456	474	486

Total number of Variations	2010	2011	2012	2013	2014
Total	645	684	1068	947	815

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 pharmaceutical ingredients are required to register with the HPRA. Brokers of medicines for human use are also required to register.

In 2014, there were 18 registrations relating to active pharmaceutical ingredients consisting of three for manufacturers, five for importers and 10 for distributors. In addition, there were 67 annual updates to existing registrations for active pharmaceuticals ingredients. No applications were received for registration of brokers of medicines for human use.

During 2013, the first year of registration, the HPRA had accepted 95 registrations consisting of 22 manufacturer, 35 importer and 38 distributor registrations. There was also one registration accepted for a broker of medicines in 2013.

Export Certificates

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

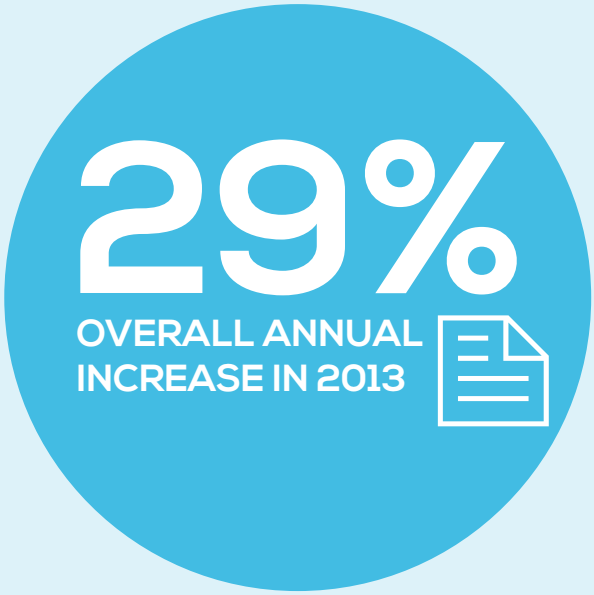
There was an output of 5,219 export certificates as set out below. This represents an overall annual increase of 29% compared with 2013.

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

Product Certification Activity	2010	2011	2012	2013	2014
Certification of Documents	234	239	272	223	231
Certificates of Good Manufacturing Practice for Active Substance and Finished Product Manufacturers	255	272	276	252	255
Certificates for Medicinal Products	1200	1416	1350	1510	2112
Medical Device Free Sale Certificates	2142	1780	1522	1987	2535
Other	28	51	16	50	86
Total	4033	4146	3436	4022	5219

Product Certification Activity	2010	2011	2012	2013	2014
Cosmetics Free Sale Certificates	174*	388	210	242	246

*The HPRA became the competent authority for cosmetics in October 2010



SAFETY AND COMPLIANCE MONITORING

The ongoing monitoring of the safety of medicines, medical devices and other health products that have been authorised, licensed or registered for use in Ireland is a primary function of the HPRA. These activities are often referred to as post-market surveillance.

A range of tools is employed to monitor the safety of health products including the assessment of reports of suspected adverse events / incidents and reactions (also known as side effects), conducting scheduled safety reviews, monitoring field safety corrective actions to medical devices and evaluating new and emerging data from trials and studies. Quality issues concerning how a product is manufactured, packaged, labelled or distributed and stored may also arise at the post-market stage.

In certain cases, where it is established that the risks associated with a particular product outweigh the benefits for those using it, the manufacturer and/or the HPRA may decide that it is necessary to remove or recall that product from the market. We work with all stakeholders impacted to ensure that such recalls are managed 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. In particular, there is a focus on serious and potentially life-threatening risks. If there appears to be a new and serious risk, 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 2014, the HPRA received a total of 2,884 valid new adverse reaction reports associated with the use of human medicines in Ireland. While this represents a slight increase when compared with the 2,835 reports received in 2013, overall reporting rates have remained quite consistent in recent years. In addition, 3,285 follow-up reports were received during the past 12 months.

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.

Nearly 20% of the reports received in 2014 were associated with the use of medicines subject to additional monitoring requirements. 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). The contribution of reporters in highlighting experience with these new medicines, for which limited data may be available, is especially helpful.

Source of Suspected New Adverse Reaction Reports	%
Pharmaceutical company	67
Community Care doctor	7
General Practitioner	4
Hospital Doctor/Specialists	4
Hospital Pharmacist	4
Community Pharmacist	4
Nurse	4
Patient/Consumer	3
Clinical Trial reports	2
Other	1

Reporting rates are also influenced by their ease of recognition and may be stimulated by publicity about a particular medicine or reaction. In addition, reporting rates are also influenced by proactive and repeated requests to healthcare professionals to submit reports on certain medicines as part of ongoing post marketing surveillance, as well as other promotional and data collection activities. All reports received are carefully evaluated and monitored, with reports of experience with use regularly highlighted and reinforced through HPRA communications.

In many instances, reports submitted to the HPRA stem from suspicions raised by 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 60% of the adverse reaction reports received during 2014 (see below table). It is incorrect to interpret the presence or place of a medicine on this list 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 included in Reports	Number of Reports in 2014
Monoclonal Antibodies	624
Vaccines used in the primary immunisation	286
Clozapine	198
Tyrosine Kinase Inhibitors	162
Anticoagulants	156
Fingolimod	128
Human Papilloma Virus (HPV) Vaccine	56
Bortezomib	50
Levodopa/carbidopa	50
Interferons	49

Of the reports received by the HPRA, 168 patients were reported to have died while on treatment. The following table outlines the medicines / class of medicines associated with the highest number of reports.

Suspect Medicine(s)/ Class of Medicines	Number of Reports in 2014
Monoclonal Antibodies	48
Anticoagulants	19
Tyrosine kinase inhibitors	13
Clozapine	13
Antidepressants	11
Ceprotin	7
Mefloquine	4
Colony-stimulating factors	4
Methotrexate	3
Bortezomib	3

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 such as those in place for clozapine.

Online Reporting

The online reporting system, available to healthcare professionals and patients / consumers, continued to be used during 2014 with some 391 reports submitted via our website by year end. While this indicated a decrease compared with usage of the online system in 2013, the volume of reports received directly from patients and consumers increased, with the majority of these reports received by telephone.

Monitoring Compliance with Pharmacovigilance Obligations

Company / sponsor compliance with pharmacovigilance obligations is continuously monitored and the associated inspection programme continued in 2014 (see also Inspections and Audits on page 51).

In May 2014, the HPRA hosted an information session for the Association of Pharmaceutical Manufacturers of Ireland (APMI) which included an overview of the HPRA's pharmacovigilance inspection programme.

Vigilance Assessment and Risk Management

The HPRA proactively participates and leads in risk management planning for medicines in the pre-authorisation phase, throughout product lifecycles, in signal management, as well as benefit-risk evaluations delivered through evaluation of periodic safety update reports and pharmacovigilance referrals. 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 available on the Irish and EU market thus allowing more rapid action when necessary to protect public health. During 2014, 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 58 active substances authorised nationally. The HPRA was also responsible for the management of any signals detected in relation to 21 centrally authorised active substances / combination of active substances for which the HPRA was rapporteur. Labelling changes were also implemented for nationally authorised products during the past year following PRAC recommendations thus ensuring improved medicines information is provided to healthcare professionals and patients.

The HPRA also participated in the Signal Management Review Team at EMA on a regular basis 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 new EU PSUR single assessment (PSUSA) procedure, which allows medicines which are the subject of different marketing authorisations, but containing the same active substance or combination of active substances, to undergo a single periodic assessment at EU level, was fully implemented during 2014. The outcome of these procedures may lead to automatic harmonised regulatory action if considered necessary (such as variation, suspension or revocation). The HPRA also actively participated in the HMA PSUR work-sharing project. National and HMA PSUR work-sharing procedures will now be phased out as a result of full implementation of the PSUSA procedure.

During 2014, the total HPRA output was 1759 PSURs submitted as national, mutual recognition, centralised, EU single-assessment and PSUR work-sharing procedures.

Safety Referrals

For 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, the PRAC makes a recommendation for a harmonised position across the EU which is ultimately implemented nationally by the HPRA.

The past 12 months was a very active period in terms of EU safety-related referrals with the HPRA participating as concerned member state in 15 of these procedures. The implementation of more rigorous timescales for referrals has resulted in more prompt assessments that contribute to safer and more effective use of medicines though labelling changes and, when necessary, restrictions. There has been increased involvement of stakeholders in decision-making during the referrals process at EU level and the HPRA has also engaged directly with healthcare professionals and patient organisations in order to enhance stakeholder involvement in risk communication at national level.

Risk Management Plans and Risk Communications

All new applications for marketing authorisations for human medicines now include a risk management plan (RMP) documenting the proposed risk management system to be implemented once a marketing authorisation is granted. This facilitates the balancing of access to medicines with proactive planning of post authorisation studies and risk minimisation measures. During 2014, the total output was 523 RMPs (new or updated) submitted via national, mutual recognition, decentralised and centralised procedures. The HPRA has consistently demonstrated its commitment to the European pharmacovigilance processes by acting as PRAC rapporteur for 10 new marketing authorisation applications since the establishment of the new processes in July 2012.

As part of its role to promote and support the safe and effective use of medicines, the HPRA reviewed and approved 36 Direct Healthcare Professional Communications (DHPCs) which provided new safety information or risk minimisation advice to prescribers. These were published on the HPRA website. The HPRA also continued to actively review and approve educational materials, required to support the safe and effective use of medicinal products on the Irish market, for distribution to healthcare professionals and/or patients.

Post Authorisation Safety Studies

Post Authorisation Safety Studies (PASS) are non-interventional studies carried out in order to obtain further information on the safety of medicinal products which are already authorised, or to measure the effectiveness of risk minimisation activities that have been introduced. The results of a PASS help to further evaluate the safety and benefit-risk profile of a medicine already in use and may have an impact on the marketing authorisation of the product. During 2014, the HPRA provided assessment input to 131 PASS protocols and reports.

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DIRECT HCP COMMUNICATIONS PROVIDING NEW SAFETY INFORMATION OR RISK MINIMISATION ADVICE

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 2014, 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 2014. The report reflected information received from January to December 2013 and included information on 72 serious adverse reactions and 167 serious adverse events which met the mandatory legislative reporting requirements. While the overall figures for reporting remain consistent, they reflect a decrease in the order of approximately 44% for serious adverse reactions and an increase of 42% for serious adverse events when compared with the previous year's reporting rates. These trends are not unexpected and are consistent with the impact of changes to agreed, EU reporting criteria. The remaining 14 donor reaction reports, while not fulfilling the mandatory reporting requirements, were included on a voluntary basis as requested by the Commission.

The HPRA continued to work closely with the Irish Blood Transfusion Service (IBTS) and the Department of Health to progress with formalising arrangements for haemovigilance activities. 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. The HPRA also completed an audit of the NHO's monitoring system and activities during 2014.

THE HPRA COMPLETED AN AUDIT OF THE NHO'S MONITORING SYSTEM AND ACTIVITIES DURING 2014

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 donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells.

There were a number of tissue and cell vigilance activities progressed during 2014.

The HPRA submitted an annual report on serious adverse reactions and events associated with tissues and cells to the EU Commission during 2014. The report reflected information received in 2013 and consisted of some 47 reports, 42 of which met the legislative reporting requirements, including nine serious adverse reactions and 33 serious adverse events. The overall figures reflect a slight increase over the previous year's reporting rates with increased numbers of adverse reactions and a slight decrease for serious adverse events. The remaining five donor reaction reports, while not fulfilling the mandatory reporting requirements, were included on a voluntary basis as requested by the Commission.

Human Organs for Transplantation

The HPRA and the Health Service Executive (HSE) were appointed as the responsible national competent authorities for the legislation on standards of quality and safety of human organs intended for transplantation in 2012. During 2014, the HPRA continued to liaise closely with the 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 nine reports of serious adverse reactions and events associated with organ donation / transplantation. The majority of these reports involved issues related to retrieval, assessment and equipment which have been followed up with the HSE. In the context of its regulatory role, the HSE acts as the competent authority for clinical and transplant related matters under the framework for quality and safety.

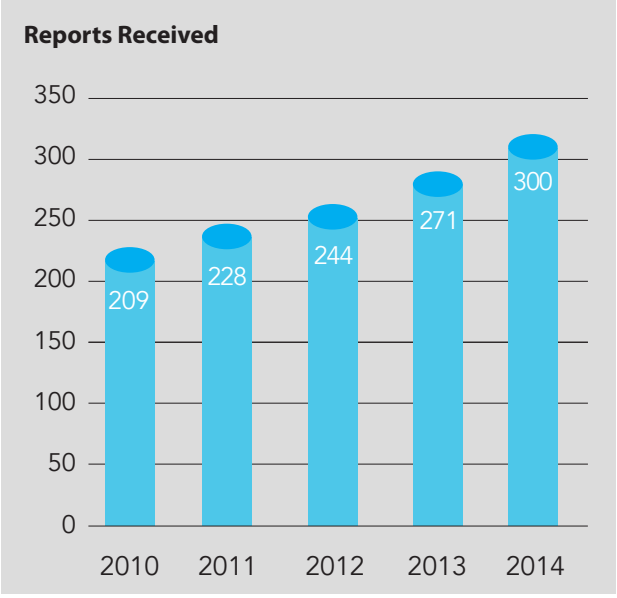
Veterinary Medicines

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 300 national reports of suspected adverse events with veterinary medicines. This continued the upward trend in the number of reports received in recent years.



Periodic Safety Update Reports

Evaluating PSURs on individual products accounts for approximately 30% 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 852 PSURs in 2014 down from a figure of 1,072 in the previous year.

Use of Veterinary Antimicrobials in Ireland

Under a European programme known as the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC), the HPRA collects annual information on the consumption of 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. It also establishes a baseline against which future policy decisions regulating the use of antibiotics can be mapped. The consumption level for 2013 was 100 tonnes. Even if there has been an increase in the overall tonnage used since we started collating the information in 2009, it should be noted that fluctuations of +/- 5% can occur annually due to a variety of factors, such as seasonal disease patterns, end of year sales promotions, animal slaughterings and exports. Moreover, the size of the national livestock herd is expected to have increased during this period.

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
Tonnes sold	88.3	93.9	85.2	97.4	100

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 operates 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-medicinal products and enforcement-related samples.

A total of 506 product samples were sent for analytical testing / examination work during 2014. This was a 16% increase compared with the number tested the previous year. Details are provided in the accompanying tables.

Examination of Packaging and Labelling

The packaging and labelling of 169 medicines and other products available on the Irish market were examined. Over 700 individual checks were carried out on the samples including reviews of the safety information contained in the package leaflets.

Authorised medicines accounted for 86% of the products examined and all of these were examined for signs of counterfeiting and tampering. No issues were identified in this regard. Borderline products accounted for the remaining 14%. In total, 35% of the products examined were parallel imported or parallel distributed products. Braille compliance checks were also carried out on 25% 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)	81
Authorised parallel imported and parallel distributed medicines	65
Borderline medicinal/non-medicinal products (associated with HPRA Classification Committee work)	23
Total	169

Analytical Testing

During the year in review, 337 medicinal and other product samples were sent for analytical testing. These included 250 samples sent to governmental laboratories in Ireland and 85 samples sent to governmental laboratories in other countries as part of European working-sharing arrangements. Two samples were sent to a non-governmental laboratory due to the nature of the testing required.

Product categories selected for analytical testing in 2014	Number of samples analysed
Physico-chemical Analysis / Biological Analysis:	
Nationally authorised medicines for human use	109
Enforcement-related products for human use	89
Non-biological Active / Intermediate pharmaceutical ingredients	32
Centrally authorised medicines for human use	23
MRP/DCP authorised medicines for human use	15
Nationally authorised medicines for veterinary use	13
Borderline medicinal / non-medicinal products for human use	10
Other product categories	16
Microbiological Analysis:	
Nationally authorised medicines for human use	20
Nationally authorised medicines for veterinary use	5
Parallel imported and parallel distributed medicines for human use	3
Borderline medicinal / non-medicinal products for human use	2
Total	337

A breakdown of the types of samples tested is shown in the accompanying table. Approximately 59% were authorised medicines, while 30% related to enforcement and borderline medicines / non-medicines. The remaining 11% were actives and other substances.

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 2014 programme included:

Centrally authorised medicines:

- 24 sampled in Ireland for testing at OMCLs in other Member States and five tested at the HPRA's OMCL (Public Analyst's Laboratory, Galway).
- 18 of the 29 products were sampled as part of an anti-counterfeiting collaboration.

MRP/DCP:

- 15 MRP / DCP medicines sampled in Ireland and analysed at other Member State OMCLs.
- 3 MRP/DCP products analysed at HPRA's OMCL as part of an MRP/DCP project run by the HPRA.

Other products:

- A number were analysed at the HPRA's request at OMCLs in other Member States. For example, 30 products underwent microbiological analysis at the Finnish and Czech OMCLs.
- The HPRA organised the analysis of 14 biological finished product samples and 12 biological active pharmaceutical ingredient / intermediate pharmaceutical ingredients that were obtained from manufacturing facilities in Ireland or from the Irish marketplace. Approximately half of these samples were tested by OMCLs in other countries for the HPRA.

Principal Findings

Analysis	Findings
Laboratory analysis	While the majority of samples tested were compliant with their specifications, 22 out of specification results were obtained. There were also 11 deficiencies identified in the analytical methods and specification documents used by manufacturers of medicines.
Packaging and labelling	In total, 22 non-compliances were identified across samples of a number of human and veterinary authorised medicines. Of these, eight related to parallel imported or parallel distributed products.
Illegal Medicines	Nine samples across seven products were analysed and identified as illegal 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 2014.

Quality Defects and Recalls

The 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. The HPRA also co-ordinates any subsequent recall actions on the Irish market. Reports are received from both the Irish market and through a global network of regulators via a rapid alert system.

Number and Types of Quality Defects

A total of 816 quality defects were reported to, or identified by, the HPRA during the past 12 months representing an increase of 5% on the figure for 2013. Medicines for human use accounted for 777 quality defect reports with 39 reports concerning veterinary medicines.

The following table indicates a levelling off in the number of quality defect investigated by the HPRA over the last five years. The classification of these defects is shown below:

Year	2010	2011	2012	2013	2014
Minor Quality Defects	241	314	236	230	248
Major Quality Defects	332	364	303	300	199
Critical Quality Defects	173	231	189	235	365
Number of Quality Defect Reports Not Justified	5	8	13	9	4
Total Number Quality Defects	751	917	741	774	816

Of the total number of reports received in 2014, falsified medicines was the most common category accounting for 24% of reports. While this represented a significant increase in this area, only six reports were determined to affect Ireland with the majority relating to supply of the implicated products by unauthorised wholesalers in Europe.

Other common categories of defect were:

- Contamination issues - 16%.
- Stability issues - 11%.
- Non-compliance with marketing authorisation - 8%.

Critical quality defects, which are those defects defined as potentially life-threatening or a serious risk to health, accounted for 365 of the total reports received. This was an increase on the 235 such reports received in 2013. Overall, 45 of the 2014 reports were deemed to affect Ireland. These included 10 product contamination issues, 10 lack of sterility issues and six falsified medicine issues. However, in none of the cases was a falsified product identified on the Irish market. The remaining 19 critical reports related to a range of issues including product preparation/ administration, changes in benefit / risk and packaging components.

Sources of Quality Defects

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

Source of Reports	Human Medicines	Veterinary Medicines
Other Competent Authorities (Regulators)	366	12
Companies (Manufacturers, distributors and/or authorisation holders)	329	23
Community Pharmacists	33	
HPRA Staff Members	23	4
Hospital Pharmacists	18	
Patients and/or Members of the Public	5	
Other Health Care Professionals	3	

Recalls of Human and Veterinary Medicinal Products

In order to protect the health and safety of patients, it is deemed necessary in certain cases to withdraw, or recall, products from the Irish market. During the year in review, 102 medicine recalls occurred. Of these, 96 related to human medicines and six to veterinary medicines.

As regards the level of recall, 16% were to patient / user level, 37% to pharmacy / retail level and 47% to wholesale level.

Exempt medicines accounted for 11% of recalls of human medicines while compounded products for human use accounted for 14%. Of the total number of recalls from the Irish market, 24% related to products manufactured at an Irish facility.

The most common causes of human medicine recalls were:

- Contamination issues (25)
- Stability issues (15)
- Non-compliance with GMP (8)
- Non-compliance with marketing authorisation (8)
- Lack of sterility assurance (7)
- Non-compliance with specifications (7)
- Unauthorised products on the Irish market (5)

In respect of veterinary medicines, three recalls related to printed packaging components, one concerned a stability issue and one was due to non-compliance with specifications. There was also one unauthorised veterinary product found on the Irish market.

Retail Sales Monitoring

General Retail Sale Investigations

The sale of consumer health products by retail outlets such as grocery shops, health food shops and, in some instances pharmacies, is monitored by the HPRA using a proactive and reactive, risk based, retail monitoring programme. During 2014, 46 cases, some of which involved multiple products, were investigated. Of these, 29 related to the sale of medicines that did not carry a valid registration number or authorisation number for the Irish market. The remaining 17 pertained to the sale of medicines that had been incorrectly classified as non-medicines by those placing them on the market. A total of 224 products that did not carry a valid registration or authorisation for the Irish market were removed from sale.

Exempt Medicines Programme

In general, 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 regulations do provide for an exemption to this rule. In this case, registered doctors and dentists 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 defined in Irish law as 'exempt medicinal products'.

Under the medicinal products regulations, wholesalers and manufacturers of medicines are obliged to notify certain information to the HPRA 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 2014, 3,235,232 packs of exempt medicines were notified to the HPRA compared to 2,555,351 packs during the previous 12 months. We also answered in the region of 200 queries related to the exempt medicinal products programme.

We continue to work with stakeholders in several areas to identify and develop solutions aimed at limiting the use of exempt medicines in Ireland.

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. Five inspections were carried out 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 our advertising compliance programme.

Human Medicines Advertising Compliance Programme

It is our role at 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.

During 2014, 397 advertisements were reviewed for compliance. While the majority were found to be compliant, non-compliances were identified in respect of 106 advertisements. In one instance, a detail aid was recalled from sales representatives as it included an indication that was not specified in the SmPC.

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

	Total	Advertisements Reviewed	Non-Compliances Identified
Proactive Monitoring: Pre-planned Projects	13	237*	49 individual advertisements were non-compliant.
Proactive Monitoring: Includes Randomly Selected Projects	47	127*	49 individual advertisements were non-compliant.
MAH Inspections Performed	5	Multiple	One critical and seven major deficiencies identified across a number of areas. One major related directly to advertising activities.
Complaints Received	10	16*	Four complaints upheld as being valid. Six advertisements in total were non-compliant. One complaint was carried into 2015.
Queries Received	43	17*	Two 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.

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

We also developed an approach to the surveillance of advertisements in digital media. This involved periodic reviews of social media content. No breaches of the advertising regulations were identified. This work will continue.

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 2014, there was a particular HPRA focus on the review and further development of medical device safety communications.

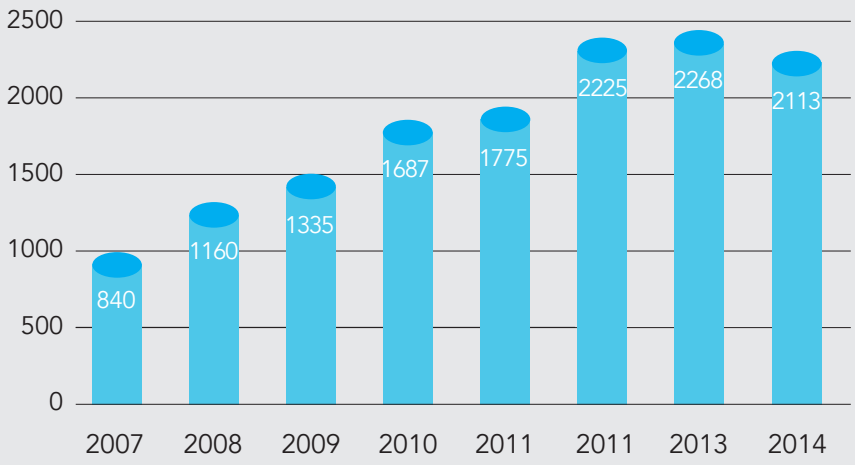
2014 Reports in Summary

A total of 2,113 medical device vigilance reports were received and assessed representing a slight decrease on 2013. Manufacturers accounted for 52% of all vigilance reports received in 2014 while 39% were received from competent authorities. In total, 33% of the reports received were as a result of an incident on the Irish market.

Concerning the regulatory response to the reports received, 63% resulted in an action being taken in Europe. In Ireland, the HPRA published online 548 manufacturer's field safety notices directly affecting the local market which represents a slight increase when compared with 2013. These notices are intended to inform users of safety issues relating to medical devices.

Safety information was also highlighted to the public through HPRA safety notices. There were 47 such notices sent to relevant interest groups and published on the HPRA website. During the year in review, the HPRA issued 104 national competent authority reports.

Number of Vigilance Reports

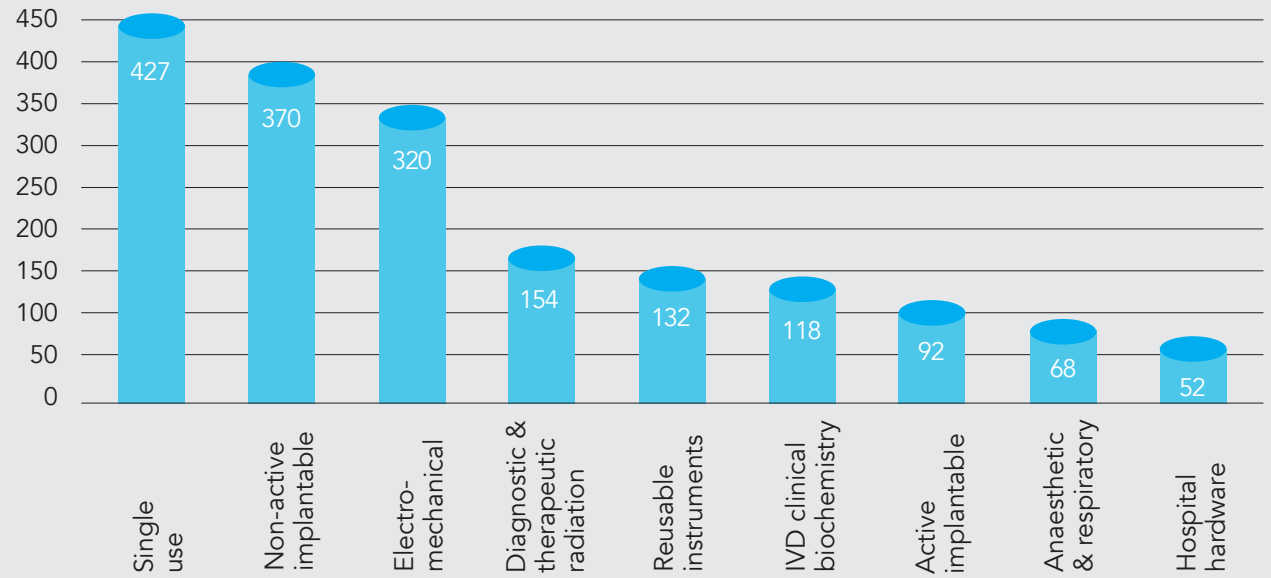


2014 Reports by Product Type

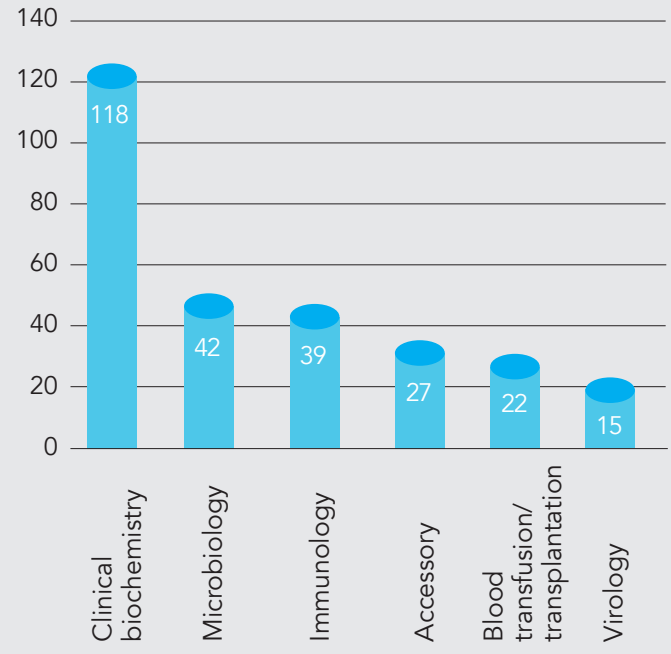
Single use devices, particularly in the areas of infusion, transfusion and dialysis, and orthopaedic implants accounted for a large proportion of vigilance reports received. Reports continue to be received relating to software issues associated with medical devices.

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 - General Medical Devices



Vigilance Reports Received - IVD Family Group



Market Surveillance

Medical device surveillance activities are focused on protecting the health and safety of those who use medical devices by ensuring that all devices on the Irish market comply with the relevant European directives.

Surveillance Cases

In 2014, the HPRA commenced 319 market surveillance cases. A significant number of cases related to notified body certificate withdrawals.

Certificate Withdrawals

The HPRA was notified of 583 notified body certificate withdrawals in 2014. Those with implications for the Irish market and those resulting from reduction or designation of notified bodies were investigated.

Technical File Reviews

In 2014, the HPRA increased its focus on review of technical documentation both in the context of market surveillance activities and notified body oversight. A total of 28 technical file reviews were completed in 2014. The proactive technical file reviews focused on IVD manufacturers in conjunction with audits, technical reviews of client files certified by the NSAI and other technical files requested as part of reactive market surveillance.

Designation and Monitoring of Irish Notified Bodies

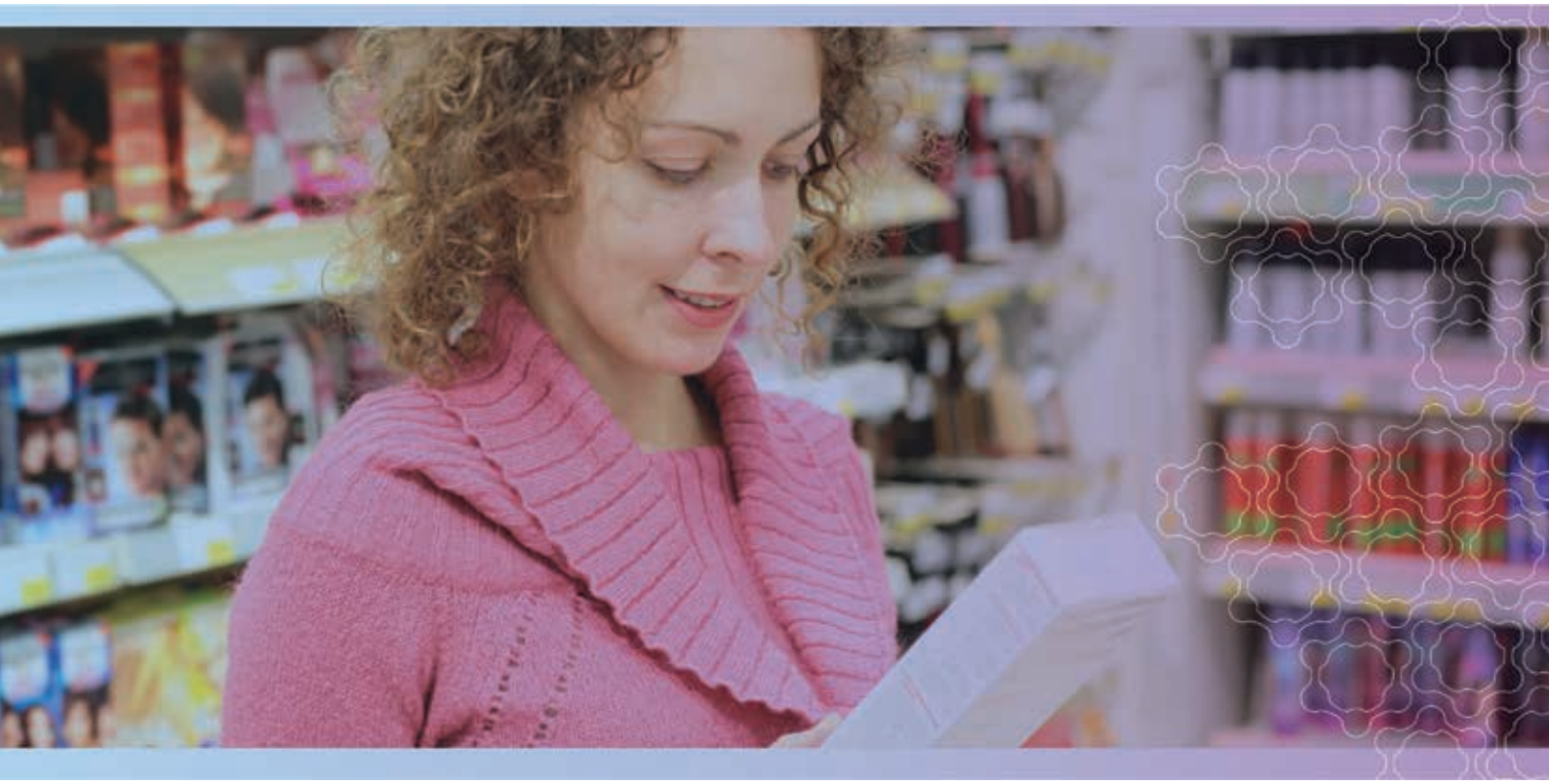
During 2014, the HPRA conducted two surveillance assessments of the National Standards Authority of Ireland (NSAI). One of these surveillance assessments was carried out in its US-based office while the other was carried out in its Dublin headquarters. In addition, two observed audits were conducted by HPRA of NSAI staff auditing medical device manufacturing sites.

The HPRA received 122 certification notifications from the NSAI, including certificate issuance, modification and withdrawal, which were then uploaded as required to the European EUDAMED database.

319

MARKET SURVEILLANCE CASES

Cosmetics



Proactive Market Surveillance

Post market surveillance of cosmetic products includes a national sampling programme and involves close co-operation between the HPRA and the HSE. In this context, the HSE Environmental Health Service and the three Public Analysts' Laboratories based in Cork, Dublin and Galway were involved in the preparation of the market surveillance schedule and the subsequent proactive sampling and analysis of cosmetic products on the Irish market.

There is no pre-market approval of cosmetic products on the European market and, therefore, the safety of cosmetic products is monitored through post-market surveillance, including review of the product information file (PIF). The requirement to have a PIF in place prior to placing a cosmetic product on the market is mandatory and is given legal status by virtue of Article 11 of the Cosmetic Products Regulation (1223/2009). Six product information files were technically reviewed in this regard. Labelling reviews were also carried out as part of the proactive surveillance campaign.

Reactive Market Surveillance

Reactive surveillance includes investigation of quality related complaints (compliance cases) and reports of undesirable effects relating to the use of cosmetics (vigilance cases). During 2014, 116 compliance cases were initiated and these accounted for the vast majority of investigations. There were 21 vigilance cases investigated with one product being withdrawn from the Irish market.

Reactive surveillance of cosmetic products also includes investigation of in-coming RAPEX Alerts (EU safety alerts for cosmetic and other consumer products). The National Consumer Agency (now part of the Competition and Consumer Protection Commission) is the national contact point for Rapex in Ireland. In conjunction with the HSE, the HPRA investigated 101 alerts on the basis of risk and, where appropriate, market action was taken. One of the products was found on the Irish market. In respect of this, a reaction report was submitted to the European Commission outlining the market actions taken.

Inspections and Audits

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

- Regular inspections of manufacturers (human and veterinary) and wholesalers (human) of medicines to check for compliance with EU guidelines on Good Manufacturing Practice (GMP) and Good Distribution Practice (GDP), respectively.
- 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).
- Inspections of manufacturers and distributors of cosmetics on a risk basis.

Overview of the 2014 Inspection Programme

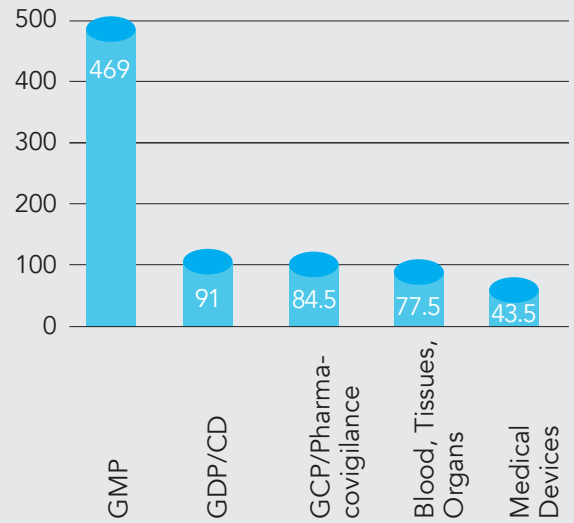
A total of, 260 inspections and audits were performed compared to 313 in 2013 and 315 in 2012. The average number of days required to close-out inspections and audits conducted was 115.

In the past year:

- 106 GMP inspections were carried out at manufacturing sites. These included 22 inspections in non-EEA countries, six of which were carried out at the request of the EMA for centrally authorised products. Of the GMP inspections carried out, 13 were of active substance manufacturers.
- 76 GDP inspections of wholesalers were performed. There were also 17 inspections of sites that handled controlled drugs or scheduled substances (precursors) and one inspection of a registered distributor of active substances.
- 12 GCP inspections were carried out at investigator sites in Ireland.
- Five pharmacovigilance inspections were performed. This included two at the facilities of Irish based marketing authorisation holders and three which related to centrally authorised medicines and were conducted at the request of the EMA.
- 20 medical device audits were performed. These were comprised:
  - Two observed audits of NSAI auditors while they carried out audits at the premises of medical device manufacturers;
  - One joint assessment audit was carried out by the HPRA in conjunction with the competent authority of an EEA country of a medical devices manufacturer in that country;

Performance Results and Statistics	2010	2011	2012	2013	2014
No. of national inspections and audits performed	293	271	289	279	229
No. of foreign inspections and audits performed	30	29	26	34	31
% inspections and audits closed on time (≤ 90 days)	62	66	61	63	59
Average time for close-out (days)	194	79	76	103	115

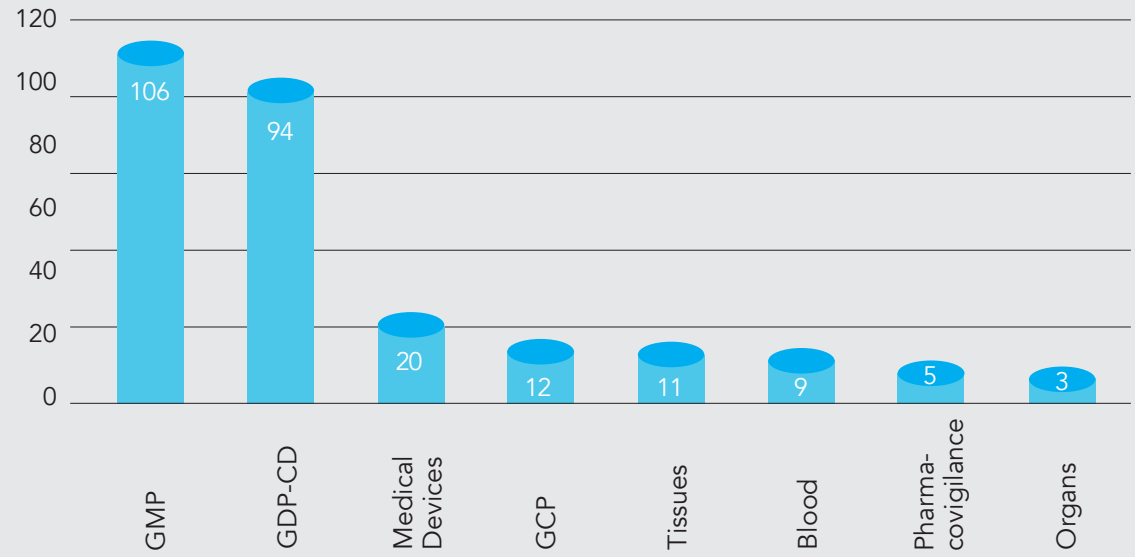
Number of Inspection and Audit Days in 2104



- Two audits of authorised representatives of medical device manufacturers;
- 15 audits at medical device manufacturers' facilities. Of these, two were at manufacturers of custom made medical devices, 12 were at manufacturers of in-vitro diagnostics and the remaining audit was of a general medical devices manufacturer.

- Nine blood establishment inspections were completed. These included seven inspections of facilities maintained by the IBTS and one inspection of the NHO. A total of 11 tissue establishment inspections were carried out.
- Three inspections were carried out to assess applications for authorisation of establishments involved in organ transplantation.

Number of Inspections and Audits in 2014



260
INSPECTIONS AND AUDITS PERFORMED

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

A total of 3,703 enforcement cases were initiated, compared with 3,932 for 2013. There were a total of 730,056 dosage units were detained, down from 919,965 in the previous year.

Sedative products again accounted for over half (56%) of all detentions (51% in 2013). Erectile dysfunction products and weight loss products accounted for 13% (11% in 2013) and 7% (19% in 2013) of detentions, respectively.

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

Inter-Agency Co-operation and Pangea VII

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 and medical devices.

In Ireland, co-operation between the HPRA, the Revenue's Customs Service and An Garda Síochána continued and included Operation Pangea VII. During this operation in May, the inter-agency approach resulted in the detention of 101,182 tablets and capsules, with an estimated value of €297,557. Pangea VII was a global initiative which involved 200 agencies drawn from health product regulatory authorities, police and customs across 110 countries. The operation, which was co-ordinated by INTERPOL, targeted criminal networks behind the sale of falsified and illegal medicines via illicit websites.

In November, the HPRA and An Garda Síochána co-hosted the INTERPOL international conference, *Ten Years of Combating Pharmaceutical Crime: Review and Prospects*.

District Court 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. Ten prosecutions were initiated that included offences in relation to:

- Procurement and importation of medicines without manufacturing authorisations;
- Supply of prescription only medicines without prescriptions;
- Wholesale of medicines without a wholesaler's authorisation;
- Advertising of prescription only and unauthorised medicinal products.

The products in question contained active substances indicated for mood stabilisation, performance enhancement, erectile dysfunction and weight loss.

Nine prosecutions were initiated annually during the three year period from 2011 to 2013.

Expert Statements

The HPRA's Director of Scientific Affairs provides scientific advice to support the work of the enforcement unit. This includes the preparation of expert statements in respect of various products which are the subject of enforcement action. During 2014, 14 such expert statements were prepared including one report requested by the Director of Public Prosecutions (DPP).

Year	2010	2011	2012	2013	2014
Product detained (dosage units)	822,484	762,641	758,276	919,965	730,056
Cases Opened	3,936	4,549	3,911	3,932	3,703
Prosecutions	5	9	11	9	10
Product destroyed	1,400kg	4,519kg	1,065kg	4,194kg	3,440kg
Voluntary Formal Caution (VFC)	19	12	6	27	13

LEGISLATIVE AND REGULATORY DEVELOPMENTS

As the national regulatory authority for health products, the remit and role of our organisation continues to change and expand in line with national and European legislative changes and in response to the addition of further competencies.

This section of the 2014 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

New Clinical Trials Regulation

New clinical trials legislation (Regulation (EU) No 536/2014) was adopted and published in May 2014. It will come into effect in Europe in mid 2016. The new Regulation will create an environment that is favourable for conducting clinical trials in Europe. It allows for a streamlined application procedure via a single entry point, the EU portal and database, for all clinical trials conducted in Europe. There will be a single authorisation procedure for all clinical trials, allowing a faster and thorough assessment of an application by all Member States concerned, to ensure one single assessment outcome and authorisation. The aim is to increase the number of clinical trials conducted in Europe and provide for improved transparency.

The HPRA contributed significantly to the consultation proposals on the development of the new Regulation. Since its publication, the HPRA has been working to progress the development of systems and procedures to meet the new requirements.

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. The Minister for Health requested that the approach to the development of the list be based on the inclusion of priority substances, identified as those which would provide the greatest cost saving to both the state and patients. Initially, 40 priority substances were identified. This was increased by a further eight substances towards the end of 2014.

There was further progress in the development of the list during the past 12 months. By the end of 2014, the list included a total 44 substances corresponding to in excess of 2,500 individual medicines. The list incorporates groups of medicines with products in each group considered appropriate for interchanging.

The work carried out by the HPRA and the HSE in this area has made an important contribution to cost savings at national level. Figures from the Department of Health and HSE indicate that generic penetration of the first 15 substances published is now at 90% and savings to the state are estimated at €50 million for 2014.

Legal Classification of Medicines

Reclassification of the method of sale and supply of medicines was a specific area of focus for the HPRA during 2014. In July, we published a group of 12 substances which are considered suitable for reclassification. These related to over 30 medicines used for treatment of a variety of conditions including migraine, gastro-intestinal disorders and dermatological complaints. Medicines containing these substances can, in certain circumstances, be reclassified to be made available over the counter in pharmacies and supplied without prescription. The industry was invited to make reclassification applications for these medicines. On foot of this proactive approach, a number of applications are pending and it is anticipated that the reclassifications will be completed during 2015. The HPRA is continuing its work in this area.

Reclassification of NRT to General Sale from Pharmacy Only Status

Also in July 2014, the HPRA confirmed the authorisation of a nicotine replacement therapy (NRT) product to be sold in general retail and grocery outlets. NRT products were previously only available in pharmacies and the HPRA's decision to switch Nicorette™ NRT from 'pharmacy only status' to 'general sale status', was the result of an application from the authorisation holder. The HPRA announcement followed a detailed assessment of the safety and efficacy of several NRT products which have been available in non-pharmacy outlets in other EU countries for some time. The availability of NRT on general sale allows these products to become more accessible for people wishing to seek assistance to reduce or quit smoking.

Responding to Medicines Shortages

During 2014, the HPRA continued to collaborate closely with the Department of Health and the HSE in relation to the management of shortages of medicines within the Irish market place. 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 the year the HPRA approved 129 such requests to prevent or alleviate shortages.

New Manufacturing Technologies

The HPRA is committed to supporting the introduction of new technologies to improve efficiency and quality assurance in the manufacture of the products which it regulates. To this end, it has established a multidisciplinary in-house team to assist in the introduction of process analytical technologies (PAT) and quality by design in the manufacture of medicinal products. This group is chaired by the Director of Scientific Affairs.

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. Over the past 2 years of operation, prioritisation has been given to public health and transparency activities thus ensuring:

- more systematic and proactive risk management planning;
- real-time signal management activities;
- EU co-ordination of safety messages;
- more efficient assessment and decision-making processes;
- increased transparency resulting in a strengthening of the link between pharmacovigilance assessments and regulatory action such as labelling changes to optimise the safe and effective use of medicines.

The HPRA was also active in the Strengthening Collaborations for Operating Pharmacovigilance in Europe (SCOPE) Joint Action project which serves to share expertise and best practice and deliver tools and guidance on the operation of pharmacovigilance in Europe. The HPRA is particularly involved in the areas of medicines risk communications and lifecycle management. The latter is focused on risk management planning and benefit-risk evaluation through the product lifecycle.

During 2014, 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.

Contributing to the European and Global Regulatory Network

Europe

Throughout 2014, the HPRA continued to actively participate in the European medicines regulatory systems. HPRA scientific and technical staff contributed 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:

- As part of the HPRA's active contribution to the work of the PRAC, the Irish delegate continued to fulfil the role of Vice-Chair of the committee.
- The Pharmacovigilance and Risk Management Lead acted as Regulatory Chair for the ICH Implementation Working Group for the E2C R2 guideline on Periodic Benefit Risk Evaluation Reports which successfully completed its intended deliverables in 2014. The HPRA also continued its contribution to the development of Good Vigilance Practice Modules.
- The HPRA contributed to a number of EU and International initiatives, including global workshops on accelerated access to innovative medicines for patients in need, Medicines Adaptive Pathways, the Adaptive Licensing Thought Group and joint meetings of EMA and EUnetHTA.
- The HPRA was a contributor to a number of strategies to support stakeholder engagement through participation in routine stakeholder meetings and on specialist topics such as benefit-risk communication and on the use of social media in pharmacovigilance. As part of these efforts, the Pharmacovigilance and Risk Management Lead contributed to a number of publications on topics such as transparency, periodic benefit-risk evaluation reports and the work of the PRAC.
- The HPRA participated in a number of cross committee initiatives including the implementation of the EMA's geriatric strategy, advancing paediatric pharmacovigilance and in the development of regulatory strategies to mitigate the risk of medication errors.
- HPRA delegates attending three meetings of the European Pharmacopoeia (Ph. Eur.) and participated in a number of the working parties and groups which provide expert advice to the Ph. Eur. including Group 13B (herbal medicines) and Group 12 (pharmaceutical dosage forms). The HPRA's Director of Scientific Affairs is Chair of both the Process Analytical Technology (PAT) Working Party and the Homoeopathic Manufacturing Methods (HMM) Working Party each of which met on a number of occasions during 2014.
- The HPRA delegate was elected Vice-Chair of the HMA Working Group of Enforcement Officers (WGEO).
- We continued our active participation in the sampling and analysis programme of the network of Official Control Laboratories (OMCL) (co-ordinated by the EDQM) and in a number of its working.

Pharmaceutical Inspection Co-operation Scheme (PIC/S)

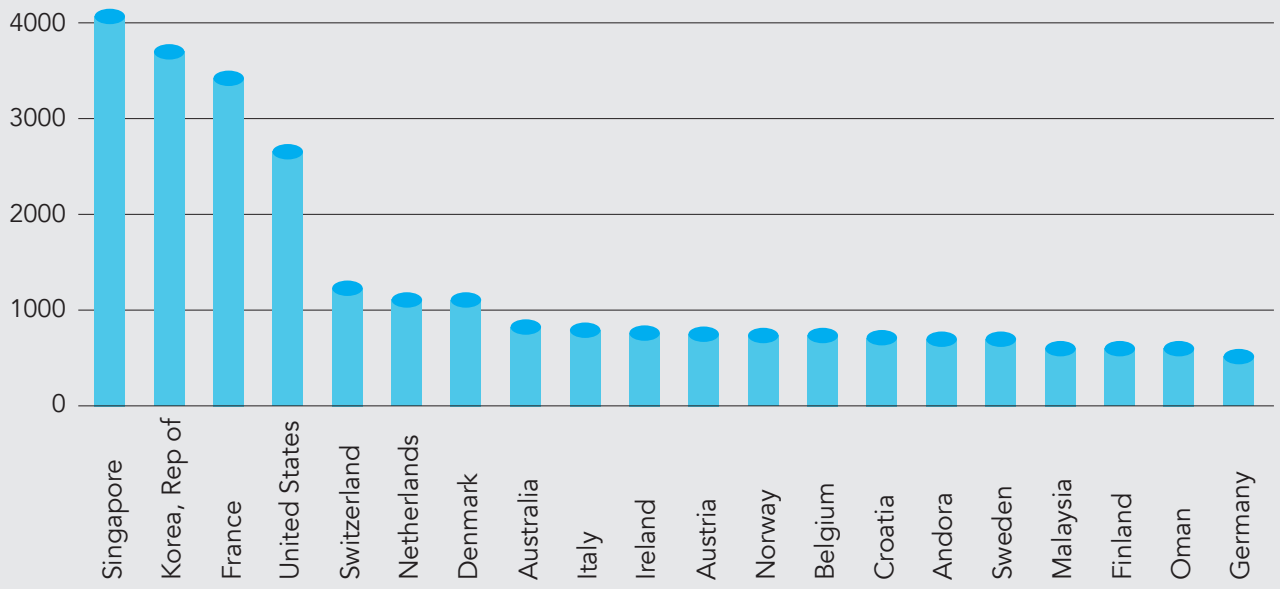
The Inspection Manager continued as a member of the Executive Bureau of the PIC/S and as chair of its Sub-Committee on Compliance. A number of HPRA inspectors were actively involved in organising expert circle activities and in working groups.

International Coalition of Medicines Regulatory Authorities

The HPRA is a member and currently one of the Vice-Chairs of the International Coalition of Medicines Regulatory Authorities (ICMRA). ICMRA is a voluntary, executive level entity of medicines regulatory authorities worldwide providing strategic coordination, advocacy and leadership. It acts as a forum to support international cooperation among medicines regulatory authorities.

During 2014, discussions continued on the development of ICMRA terms of reference, rules of procedure and future membership criteria. ICMRA also continues to dialogue with existing international regulatory groups.

Active ICSRs in the WHO global ICSR database per million inhabitants 2014



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 2014.

The HPRA attended the annual meeting of national centres participating in the WHO international drug monitoring programme in October 2014 and continued to provide details of reports received nationally to the WHO for inclusion on its international database.

The volume of adverse reaction reports from Ireland continued to fall within the top 20 countries participating in the programme (121 full member countries in 2014). As can be seen from the accompanying graph, Ireland ranked as the tenth highest reporter during 2014.

IRELAND WAS THE
10th
HIGHEST NATIONAL REPORTER WITHIN THE WHO INTERNATIONAL DRUG MONITORING PROGRAMME

Advisory Committee for Human Medicines

The Advisory Committee for Human Medicines, which is appointed by the Minister for Health, assists and advises the HPRA Authority in relation to any matters pertaining to the safety, quality or efficacy of medicines for human use. The committee met twice during 2014 and, in addition to considering matters referred to it by the Authority, it also reviewed the authorisations for human medicines, manufacturers and wholesalers as approved by the HPRA's Management Committee.

There are also a number of sub-committees appointed by the Advisory Committee for Human Medicines:

- The Clinical Trials Sub-Committee met 12 times during the year. The Committee considered the suitability of trials submitted for approval under the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004, (S.I. No. 190 of 2004).
- The Herbal Medicines Sub-Committee met once in 2014. The Committee considered a number of matters including the Traditional Herbal Medicinal Products Registration Scheme and updates from the Committee on Herbal Medicinal Products of the EMA.

Veterinary Medicines

Veterinary Clinical Field Trials

The role of the HPRA expanded further when our organisation became the competent authority for the authorisation of clinical field trials on veterinary medicines on 17 July 2014.

The HPRA understands a 'clinical trial' to mean a study which aims to examine, under field conditions, the safety or efficacy (or both) of a veterinary medicinal product under normal conditions of animal husbandry or as part of normal veterinary practice for the purpose of obtaining a marketing authorisation or a change thereof.

Under legislation, tests and trials on a veterinary medicine for the purpose of generating data to support a marketing authorisation, or for other purposes, shall not be conducted without prior licence from the HPRA. A clinical field trial licence application must be submitted and approved in order for work to commence on any clinical field trial. The HPRA is obliged to consult with the Department of Agriculture, Food and the Marine prior to granting a licence for a clinical field trial.

Relevant application forms, guides and fee details were developed and published by the HPRA during the second half of the year and are available from our website.

Contributing to the European Regulatory Network

The European regulatory network for veterinary medicines has gained increased importance in recent decades. This is due to the fact that decisions on individual medicines that are on the market in several Member States, as well as policies, guidelines and initiatives which affect the systems and standards under which products are evaluated, are harmonised at an EU level. Given that most medicines are supplied to multiple European markets, it is obvious that in order for us to maximise our influence, we must have an input to 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 at the HMA.

Key regulatory issues discussed during 2014 were:

- The revision of the legal framework for veterinary medicines;
- The European surveillance strategy on pharmacovigilance work-sharing;
- The implementation of the HMA Action Plan on antimicrobial resistance.

We also contributed to EU discussions regarding restrictions on the use of barium selenate in injectable veterinary medicines.

JULY2014

HPRA BECOMES THE COMPETENT AUTHORITY FOR VETERINARY CLINICAL FIELD TRIALS

Contributing to National Health Initiatives

During 2014, the HPRA participated in a working group of the Food Safety Authority of Ireland (FSAI) tasked with preparing a report on the risk of antibiotic resistance transfer posed by food.

We also provided support 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 2014 and considered such matters as:

- The content and implications of the proposal for a new Regulation for veterinary medicines in the EU;
- Regulatory developments affecting medicines in the European network;
- A report of suspected adverse reactions to veterinary medicines in Ireland for 2013;
- A report on the consumption of veterinary antibiotics in Ireland for 2013;
- Various applications that had been considered by the HPRA previously but were submitted for peer review by the committee.

Advanced Therapies

An advanced therapy medicinal product (ATMP) is a biological medicinal product which is a gene therapy medicinal product, a somatic cell therapy medicinal product or a tissue engineered product. This definition is set out in Directive 2001/83/EC, as amended, to reflect new innovative therapeutic products. Given their innovative nature, applications for marketing authorisations for advanced therapy products proceed through the centralised procedure in accordance with Regulation 726/2004/EC.

We continued to actively participate in the EMA's Committee for Advanced Therapies (CAT). The HPRA's internal group on biological products and ATMPs also continued to meet regularly as a forum for information exchange and for discussion of areas of regulatory interest as relevant to ATMPs, blood, tissue and biological products.

Controlled Substances

Controlled Drugs

There were two main amendments to the controlled drug legislative framework. In the first instance, the combination of the Misuse of Drugs (Designation) (Amendment) Order 2014 (S.I. No. 324 of 2014) and the Misuse of Drugs (Amendments) Regulations 2014 (S.I. No. 323 of 2014) facilitated the legal introduction into the Irish market of authorised medicinal products containing a liquid extract of cannabis. Any such products must have a specified composition and presentation in order to permit prescription, supply and possession for the treatment of patients. In addition, S.I. No. 323 of 2014 removed the handwriting requirements in relation to certain details on prescriptions for controlled drugs that had been specified in the Schedule to the Misuse of Drugs (Supervision of Prescription and Supply of Methadone) Regulations 1998.

The second major amendment was the Misuse of Drugs (Amendment) (No. 2) Regulations 2014 (S.I. 583 of 2014). This added certain substances to Schedule 1 of the Misuse of Drugs Regulations (1988), as amended, and increased the extent of the controls applicable to 4-Hydroxybutanoic acid by changing its listing from Schedule 3 to Schedule 2.

Precursor Chemicals

There were two additions to the EU Voluntary Monitoring List of non-scheduled substances. These substances were chlorephedrine and chlorpseudoephedrine. The activity of trade in these substances will be monitored over time with the future potential for these substances to be included within the scheduled substances (precursor chemicals) legislative framework.

Medical Devices

Revision of European Medical Devices Legislation

During 2014, the negotiation of the European Commission's proposed Regulations on medical devices and in-vitro diagnostics (IVDs) continued at the European Council's Working Party on Pharmaceuticals and Medical Devices.

The proposals are intended to develop and reinforce the European legislative framework for medical devices and IVD medical devices 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 and access for patients and healthcare professionals to new therapeutic and diagnostic alternatives. The two proposed Regulations represent a significant development and improvement in comparison to the existing system but, as the associated legal text is lengthy and complex, it necessitates detailed review, discussion and negotiation.

The HPRA has provided significant support to the negotiation of the legislation at the Working Party and at various expert working groups. The HPRA anticipates, that these proposals, which are subject to the ordinary legislative process including examination by both the European Council and the European Parliament, will be finalised by the end of 2015. The HPRA will continue to provide support to the Department of Health for the purposes of the Working Party negotiations. This will include advising on the further development of the legal texts, assistance with relevant stakeholder consultation and provision of input to the Department as it finalises a national position on the proposals.

Ongoing Development and Strengthening of the existing European Regulatory Framework

Along with other European competent authorities and the European Commission, the HPRA has been dedicated to strengthening and developing the existing regulatory framework for medical devices in advance of the revised legal framework being agreed and coming into place.

Since 2012, the HPRA has been using the European Commission's Joint Plan for Immediate Actions as a roadmap for this development. This valuable plan outlined key actions for Member States and the Commission in the areas of notified body oversight, market surveillance, coordination and communication within the regulatory network, and transparency.

During 2014, the European Commission published its report on the implementation of the joint plan across Europe and identified those areas of ongoing focus. The HPRA remains fully committed to supporting and using the joint plan as a basis for development.

Oversight and Performance of Notified Bodies for Medical Devices

One of the central components of these joint actions is the implementation of the 2013 legislation that provides for joint assessment of notified bodies for medical devices by the relevant national authority and expert European assessors. The HPRA, having contributed to the development and implementation of this assessment scheme, is now part of a small expert group which oversees and co-ordinates its continued implementation. During 2014, the HPRA directly participated as experts in three joint assessments of EU notified bodies.

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.

During the past year, the HPRA was an active participant in Medical Devices Expert Group (MDEG) vigilance meetings and vigilance teleconferences. The HPRA is chair of three taskforces including the vigilance co-ordinating competent authority role and is an active participant in eight other taskforces relating to specific devices or manufacturers.

In response to the joint plan, the HPRA has also reviewed its existing market surveillance activities and has placed increased emphasis on proactive surveillance activities throughout the lifecycle of a medical device. Communication, and in particular reporting of medical device safety issues from users, is a continued focus for the HPRA. We continue to encourage users at national level to submit reports and have revised our methods for safety reporting to ensure the information is clear and targeted to the correct user group.

Contributing to the European and Global Regulatory Network

International Medical Device Regulatory Forum

During 2014, 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 issues across the globe and, in particular, in the member regions including Australia, Brazil, Canada, China, the EU, Japan, the Russian Federation and the US. In addition to contributing to the Management Committee, the HPRA assumed 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).

Competent Authority for Medical Devices

During 2014, the HPRA continued to engage actively and develop its partnerships with other European competent authorities. A key milestone in this work was achieved during 2014 with the formation of the Competent Authority for Medical Devices (CAMD) Executive Group the objective of which is to build mechanisms and structures to enable cooperation between authorities and to identify key work items and priorities for focus at European level. The HPRA was elected to this Executive Group along with colleagues from Austria, Belgium, France, Germany, the Netherlands and the UK (Chair).

Bilateral Meetings

During 2014, the HPRA hosted bilateral meetings with the US Food and Drug Administration (FDA), the EU Commission's Joint Research Centre (JRC), the UK's Medicines and Healthcare products Regulatory Authority (MHRA), the Croatian Ministry of Health and the Saudi FDA.

Advisory Committee for Medical Devices

The Advisory Committee for Medical Devices met three times in 2014. 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 Committee also invited a number of external stakeholders, such as academic researchers, to make presentations to the Committee in respect of their activities.

Blood, Tissues and Cells, and Organs

We worked with Organ Donation and Transplant Ireland (ODTI) and the transplant centres on development of a Framework for the Quality and Safety of Human Organs intended for transplantation. The final text was published by ODTI, which is part of the HSE.

We participated in European Commission Competent Authority meetings in these three areas. The primary purpose of these is to build and harmonise the regulatory systems and to identify emerging issues.

We contributed to Council of Europe / EDQM work on Guidelines, including that of the drafting group for the Guide to the Quality and Safety of Tissues and Cells for Human Application.

Scientific Animal Protection

The HPRA became the competent authority responsible for the implementation of Directive 2010/63/EU on the protection of animals used for scientific purposes on 1 January 2013. This authority was transferred from the Department of Health which regulated this area until 31 December 2012.

During 2014, there continued to be significant engagement with stakeholders within the research sector in order to highlight the requirements of the legislation. As part of this process, we published a number of further guidance documents in respect of authorisation procedures and policies and there continued to be a specific focus on the implementation of the 3R principles (reduction, refinement and replacement of animal testing). The HPRA also published its first annual statistical report on the use of animals for scientific purposes in Ireland. The report, which examined data for 2013, is a requirement under Article 54(2) of the Directive. The Department of Health published all previous reports in this area prior to the HPRA becoming the competent authority.

The HPRA continued to interact with the Department of Health in relation to the overall implementation of the legislation and its potential impact on animal research in this country. Engagement also continued in respect of the development of an associated fee model for the regulation of this area. We provided support to the National Committee for the Protection of Animals used for Scientific Purposes in relation to its role in nurturing a culture of care at the establishments concerned.

In relation to the EU network on scientific animal protection, the HPRA was involved in key topics such as the creation of an EU statistical database on the use of animals and played an active role as part of the EU National Committees for the Protection of Animals used for Scientific Purposes.

STAKEHOLDER ENGAGEMENT AND COMMUNICATIONS

The HPRA is committed to delivering a comprehensive programme of communications activities so as to ensure that all our stakeholders have timely access to relevant safety, licensing and regulatory information. This commitment 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 2014 with a key focus being the introduction of the Health Products Regulatory Authority name and brand.

The Irish Medicines Board becomes the Health Products Regulatory Authority

The Irish Medicines Board (IMB) changed its name to the Health Products Regulatory Authority (HPRA) on 1 July 2014.

Over the course of our 18 years as the IMB our regulatory remit expanded to include other health products as well as a number of health related functions. Consequently, the IMB name and brand identity did not accurately reflect the nature and character of the organisation and our identity has not evolved in step with our size and expanding new areas of responsibility.

The HPRA name now clearly reflects the wider scope of our work, functions and responsibilities across the health products sector. At the same time, it is intended to build on the IMB's established reputation as a professional, progressive and science driven public sector organisation.

The introduction of the HPRA name was provided for in the Health (Pricing and Supply of Medical Goods) Act 2013.

HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Our New Brand Identity

The HPRA's brand identity was developed following careful consideration to help us communicate in a consistent and clear manner with all our stakeholders. The identity consists of a number of core elements that come together to create a strong, credible and unique brand for the HPRA.

Our logo, consisting of the acronym HPRA and the 'molecule' symbol, has been crafted to reflect the foundation on which our brand identity system is built. The letters HPRA use a strong, balanced and modern font which projects a sense of authority and clarity. The 'molecule' design reflects the evidence and science that support all our actions and decisions.

The connected circular molecule also stands for the way we work collaboratively with stakeholders including healthcare professionals, the research community and our colleagues in other health and regulatory agencies in Ireland and abroad. It stands too for the wider community, the public and patients who are at the heart of what we do.

The colour palette combines the strong graphite colour of the letters with a blend of blues and greens. Blue signifies health, trust and authority while green symbolises safety, natural and national.

Finally, our corporate fonts have been chosen for their clarity and legibility.

To support the introduction of the new identity and logo, a HPRA brand guidelines document was published and shared with all staff. These guidelines provide clear direction on the application of the new brand across all platforms and publications and will help to ensure that all our materials display a coherent and recognisable design. The document includes guidance on the design of external publications, the use of the brand on digital platforms and the adoption of a new typeface and templates for internally produced documents, presentations and e-mail.

Preparing for the Introduction of our New Name and Brand

The introduction of a new name and brand is a major project for any organisation and demands significant planning and preparation. In addition to a wide-ranging external communications plan to inform stakeholders, a comprehensive internal strategy is also required.

The external communications plan consisted of a range of activities and projects that were planned to coincide primarily with the 1 July introduction date and included:

- The launch of a new corporate website – www.hpra.ie;
- A series of 'all-stakeholder' e-mails which were sent to close to 5,000 key contacts identified by employees from across the organisation;
- The publication of a new corporate brochure and video outlining the reasons behind the name change and introducing the new brand identity;
- A stakeholder launch event on the morning of 1 July which was held in the HPRA offices in Dublin 2. Over 60 external attendees representing patient and healthcare professionals, the Department of Health and other government departments and agencies were present. Guest speakers included RTÉ journalist Mr Tommie Gorman and the then Chief Executive of the IDA, Mr Barry O'Leary;
- The placement of an information notice in a series of health and related industry publications. The first notices started to appear in early July with the initiative repeated in the autumn;
- The redesign and publication of all HPRA external guides and application forms for industry and other interested parties;
- The redesign and publication of 12 HPRA leaflets primarily intended for patients and members of the public;
- The dissemination of a number of press releases to national, regional and specialist media. A number of related articles were also published across various publications;
- The introduction a new external e-mail address across the organisation incorporating '@hpra.ie';
- The redesign and print of all corporate stationery;
- The installation of new external and reception signage in the HPRA offices.

To prepare internally for the change of name and new corporate identity, a brand implementation group was convened with representatives from a range of different organisational functions including IT, HR, finance, corporate services, quality management, business processing and communications.

Together, this group identified close to 200 individual rebrand tasks that were required to ensure a smooth and efficient introduction of the new name and identity. The vast majority of these tasks were successfully completed in advance of or on the key 1 July date with the remainder planned for completion on a phased basis thereafter.

The following is just a small sample of the rebrand tasks involved:

- The rebrand of all internal IT platforms and systems;
- The design and print of newly branded staff ID cards;
- The introduction of a new corporate font for all word processor documents, presentations and e-mails;
- The introduction of newly branded document templates such as for meeting minutes and agendas;
- The rebrand of all finance documents and the internal financial IT system;
- The redesign of all regulatory certificates issued by the HPRA.

Finally, an internal communications plan was also implemented to support the introduction of the HPRA name and brand. Given the extent of the rebrand project, which impacted all departments and sections across the organisation, it was essential that staff were kept up-to-date and informed of progress and planned activities. Among the internal communications activities completed were regular e-mails including a brand newsletter, presentations, competitions and a number of staff events. A commemorative notebook to mark the introduction of the new name was also distributed to all staff members on the morning of 1 July.

Our New HPRA Website

Development of the new HPRA website began in 2013 and was completed to coincide with the introduction of the HPRA name and brand on 1 July. This project incorporated a total redesign of the organisation's online offering including a review of the user experience and all content. In particular, the focus was on ensuring an improved navigation thus allowing for easier access to content of interest. In addition, a new and modern look and feel for the site featuring the HPRA's new brand identity was required. Other enhancements include:

- a more comprehensive and accurate search facility;
- the ability to search the medicines product information section directly from the homepage. This is an important enhancement as this feature is by far the most used by visitors to the site;
- an improved and more targeted alerting system for subscribers;
- the inclusion of new sub homepages for each product divided clearly into 'safety and quality' and 'regulatory information' sections;
- the inclusion of new sub homepages for key stakeholder groups: members of the public, industry and healthcare professionals;
- the inclusion of a 'latest news' section for each product area and stakeholder group;
- the inclusion of quick links on the homepage which are based on the most popular visitor topics.

As with all websites however, we are conscious of the need to continuously improve the user experience and we are committed to the further enhancement of www.hpra.ie, including the launch of a mobile friendly responsive version of the site during the first half of 2015.

Visitor Statistics

During the six month period from July to December 2014, almost 126,000 unique visitors accessed the new HPRA website. There were in excess of 250,000 visits in total. Of those who accessed the site, 38% were new or first time users. Among the most popular sections of the website were the human and veterinary medicines listings and the interchangeable medicines listing.

Stakeholder Engagement

Meetings with Stakeholders – Human Medicines

A number of meetings were held with industry representative groups including the Association of Pharmaceutical Manufacturers in Ireland (APMI), the Irish Pharmaceutical Healthcare Association (IPHA), the Irish Health Trade Association (IHTA), Pharmachemical Ireland and the Pharmaceutical Distributors Federation. These meetings provide a forum for discussion of items of mutual interest. Among the main topics of discussion were timelines and deliverables, interchangeable medicines, the regulation of biosimilar medicines, increasing the number of applications for herbal medicines registrations and issues relating to the distribution of medicines.

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.

Regular meetings took place with the Pharmaceutical Society of Ireland and the Irish Pharmacy Union.

Meetings with Stakeholders – Veterinary Medicines

During 2014, we 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 transfer of the competent authority function for the authorisation of veterinary clinical trials to the HPRA. Meetings were also held with a number of stakeholders from the veterinary medicines industry and from the general agricultural and veterinary sectors.

Meetings with Stakeholders – Scientific Animal Protection

A number of meetings were held with the Department of Health in relation to the implementation of Directive 2010/63/EU regarding the protection of animals used for scientific purposes. We also held a number of meetings with individual establishments and interested parties, including the Irish Laboratory Animal Science Association and the Irish University Association, in relation to the protection of animals used in research nationally. 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 2014. These included meetings with the National Standards Authority of Ireland (NSAI), the Irish Medical Devices Association (IMDA) and the Irish Medical and Surgical Trade Association (IMSTA). 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 2014 was the European Commission's joint plan for immediate actions and the ongoing revision of the medical devices legislation.

Meetings with Stakeholders – Blood, Tissues and Cells, and Organs

A number of meetings were held with key stakeholders. These included the Department of Health on all of these areas, National Haemovigilance Office of the IBTS (blood) and Organ Donation and Transplant Ireland (organs).

Meetings with Stakeholders – Cosmetics

Regular meetings took place with the HSE (Environmental Health Service and Public Analyst Laboratories) in relation to the monitoring, sampling and analysis of cosmetics and implementation of the EU regulation and national legislation. We also participated in the Market Surveillance Forum hosted by the Department of Jobs, Enterprise and Innovation. We met with the Irish Cosmetics and Detergents Association which represents the industry.

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 were general in nature and primarily focused on explaining the role of the HPRA, others were more specific and dealt with specialist areas and/or new regulatory developments. A full list of all presentations delivered during 2014 is provided in Appendix 2.

Events

Ten Years of Combating Pharmaceutical Crime – Global Conference

In November 2014, the HPRA joined An Garda Síochána as co-hosts of *Ten Years of Combating Pharmaceutical Crime: Review and Future Prospects,* a global INTERPOL conference held in Dublin.

This major conference was attended by senior law enforcement officials from across the world as well as representatives from government, intergovernmental organisations and the pharmaceutical industry. The event reviewed experiences to date, lessons learned, opportunities and constraints of international action against pharmaceutical crime. It also focused on identifying and recommending ways forward for strengthening international collaboration.

The two-day (19 and 20 November) event attracted close to 200 participants from some 50 countries and 17 international organisations. There was significant national and international media interest in the conference resulting in extensive coverage which included a number of interviews with the HPRA Director of Compliance. The opening address was delivered by Minister of State at the Department of Justice and Equality, Aodhán Ó Ríordáin, TD.

Information Days and Seminars

HPRA information days and 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 attendees to submit questions, seek clarifications and network with colleagues. The following events were held during 2014:

- In January, we hosted an information seminar on the regulation of clinical trials for investigators and academic sponsors. The purpose of this event was to further enable and support clinical research in Ireland. The seminar included discussion on a range of topics including safety reporting, clinical trial applications and good clinical practice (GCP) requirements.
- In May 2014, we hosted an information session for the Association of Pharmaceutical Manufacturers of Ireland (APMI). This session included overviews of the HPRA pharmacovigilance inspection programme, the monitoring of pharmacovigilance compliance and an interactive discussion with attendees.
- An information event for parallel product authorisation holders (PPAs) was held in June. The agenda focussed on promotion of regulatory compliance in this area and discussion topics included requirements for regulatory submissions, quality defect investigations and recall requirements.
- On 23 October, we hosted an information day for the medical devices industry. This event was attended by over 250 delegates and included participation from a number of regulatory and industry partners including the European Commission, the UK's MHRA and the European Medical Device Association. The meeting was also addressed by Ms. Mairead McGuinness MEP. A range of topics were discussed with a particular focus on the development of the European regulatory systems for medical devices and the on-going revision of the legislation governing medical devices.
- A wholesale distribution information day was held on 11 November and was aimed primarily at distributors of medicines. Among the topics discussed on the day were good distribution practices (GDP), including the Commission guidelines on GDP, the protection of the supply chain and the impact of medicine recalls on distributors.

- On 12 November, we hosted an information day focused on good manufacturing practices (GMP) which was attended by manufacturers of medicines and active substances. As well as general GMP updates, the topics for discussion also included quality defect and product recalls, the Directive on falsified medicines, sterile manufacturing and market compliance.
- A pharmacovigilance information day was held on 21 November 2014 and was attended by over 250 participants from industry as well as healthcare professionals and patient organisation representatives. The aim of the event was to provide updates on implementation of the revised legislative provisions and to discuss their impact for stakeholders.
- Also in November, the HPRA hosted a Topra networking meeting. This was an evening event focussing on a number of topics of regulatory interest including the new clinical trial regulation and HPRA's role in the regulation of medical devices.
- On 2 December, an information day was held for marketing and manufacturing authorisation holders of veterinary medicines as well as other stakeholders with an interest in this area. The event was focused primarily on the proposed new EU legislative framework while an overview of recent changes to national legislation on clinical field trials was also provided. As well as presentations from HPRA staff, there were also contributions from representatives of the Department of Agriculture, Food and the Marine, and from the animal health industry.

BT Young Scientist and Technology Exhibition 2014

In January 2014, 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. This was the fifth year of HPRA participation at this high profile event which was held in Dublin's RDS.

Our stand focused on building awareness of the significant role the HPRA plays in protecting public and animal health. In particular, the important issue of medicines and medical devices safety 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 guidance documents are published regularly on our website with alerts issued to website subscribers.

A number of new guidance documents were published during 2014 with a significant number of existing documents also being updated. In addition, a consultation process was commenced in respect of a number of proposed new guides.

Among the new documents published during the past year were:

- Guide to the Notification System for Exempt Medicinal Products;
- Guide for Manufacturers and Sponsors on Clinical Investigations carried out in Ireland;
- Guide to Refusals and Appeals under Scientific Animal Protection Legislation;
- Guide to Transfers of Project Authorisations under Scientific Animal Protection Legislation;
- Guide to Managing Changes to Registration for Active Substance Manufacturers, Importers and Distributors;
- Clinical Field Trial Licence Applications under Animal Remedies Legislation.

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

Newsletters

The HPRA publishes three newsletters with a number of editions of each being published throughout the year. Each newsletter was redesigned during 2014 to reflect the new HPRA name and brand.

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 2014. Topics covered included:

- Regulation of clinical trials on veterinary medicines in Ireland;
- Publication of public assessment reports for veterinary medicines on the HPRA website;
- Proactive approach to reclassification (switching);
- New EU clinical trials Regulation;
- New tools for manufacturers to help prevent medicines shortages;
- Amendment to the Misuse of Drugs Regulations;
- Report on veterinary antimicrobial consumption in 2012 and update on collection of the 2013 data;
- Update on certificates of free sale for cosmetic products.

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

Drug Safety Newsletter

January 2014 marked the first fully electronic distribution of the HPRA Drug Safety Newsletter. Healthcare professionals are invited to register with the HPRA to receive alerts when new editions of the DSN are published while we also work closely with relevant healthcare professional organisations to facilitate distribution of the newsletter via their networks. The electronic version of the newsletter is in PDF format, thus allowing the reader to save the publication to their own systems and to print specific pages. The online version also contains hyperlinks to product information and other relevant documents on the HPRA and EMA websites.

Seven editions of the newsletter were published on our website and made available electronically to registered doctors, dentists, nurses and pharmacists during 2014. An overview of the topics covered is included in Appendix 3.

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 three editions of this newsletter published in 2014. The following are some of the main topics covered:

- Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) – Opinion update;
- HPRA post market surveillance audit plan for 2014;
- Voluntary joint assessments update;
- 3D printing: Potential in implants and surgery;
- IMDRF unique device identification (UDI) implementation for medical devices and IVDs;
- Bringing medical device software development standards into a single model;
- HPRA overview of software as a medical device;
- Proposals for new regulation on medical devices and in vitro diagnostic medical devices.

External Articles

Human Medicines

There were 16 articles published in MIMS Ireland by the HPRA. A further two articles were published in the Irish Medicines Formulary. The full list of topics covered in these articles in included in Appendix 3. All articles were also published on the HPRA website.

Veterinary Medicines

Consistent with our objective to improve stakeholder knowledge on the use of veterinary medicines, we contributed several articles to the relevant publications. This included an article on pharmacovigilance in the December edition of the Veterinary Ireland Journal and four articles in the specialist It's Your Field publication.

Medical Devices

An article providing an overview of the medical devices vigilance system and an outline of the HPRA role in managing reports of suspected adverse incidents was published in the spring edition of the BEAI Spectrum publication.

Safety Warning and Notices

Throughout 2014, the HPRA published various warning statements and notices on safety issues or benefit-risk evaluations of human medicines. There were 36 Direct Healthcare Professional Communications concerning human medicines published on the HPRA website and issued to subscribers. The PRAC published monthly agendas, minutes, meeting highlights, notifications of safety reviews and signals throughout 2014 and these were also made available via the HPRA website.

Separately, 47 medical devices safety notices were sent to the relevant stakeholder groups and published online. Following feedback via a communications survey, the design of these notices was updated so as to highlight key content and enhance the structure and layout. More than 500 manufacturers field safety notices concerning medical devices on the Irish market were also published on the HPRA website. In addition, we published three generic safety notices with advice in relation to MRI safety, potential microbial contamination when using heater cooler units and finally to raise awareness of some of the common problems that have been identified with the use of insulin infusion pumps.

Self-Test Products Consumer Information Leaflet

In November, we published *Self-Test Products*, an information leaflet to assist those patients and members of the public who use self-tests for a medical purpose. This publication was developed in response to the increasing availability of self-test products for a variety of health conditions and the concerning trends and issues observed by the HPRA when following up on adverse incidents relating to their use. Such products can be used to diagnose a variety of conditions or to monitor a particular treatment, including pregnancy tests and test kits for measuring blood sugar. The HPRA leaflet includes advice for people who are thinking about buying a self-test and highlights the potential risks associated with self-testing. The leaflet can be downloaded from our website while printed versions can be ordered from lealfets@hpra.ie.

Media Communications

Throughout 2014, we continued our media communications programme to proactively communicate important safety messages and to build awareness of the role of the HPRA. We prepared 34 press releases and statements which in a number of instances resulted in national and regional media interviews with a HPRA spokesperson. During the second half of the year, there was a particular focus on highlighting the introduction of the new HPRA name and explaining the rationale for this change.

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

- Nicotine replacement therapy (NRT) medicines approved for sale in retail outlets;
- Publication of list of active substances suitable for reclassification (switching);
- Largest ever Interpol operation targeting online counterfeit and illegal medicines (Operation Pangea VII);
- Advice on seasonal maintenance of automated external defibrillators (AED).

The HPRA also published a number of press releases to highlight successful prosecutions related to the illegal supply of unauthorised medicines.

In addition, we responded to approximately 400 queries from national, local and specialist media during the year. Drafting responses to such queries involves subject matter experts from across the organisation.

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 2014, the HPRA completed a public consultation in respect of regulatory fees proposed for 2015 and also commenced a consultation on a draft version of the Guide for Retail Sale of Herbal Medicinal Products.

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 2014, we provided comments in respect of eight public consultations from the Department of Health, The Medical Council, the Pharmaceutical Society of Ireland and CORU.

Freedom of Information

The HPRA is subject to the Freedom of Information Acts 1997 and 2003. The Acts assert 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 2014, we received 17 Freedom of Information requests none of which related to requests for personal information.

Parliamentary Affairs

Oireachtas Joint Committee on Health and Children

In June 2014, the HPRA was invited to address the Oireachtas Joint Committee on Health and Children. The issue being considered by the Committee was the use and availability of adrenaline auto-injectors and the HPRA presented an update on the authorisation and safety monitoring of these products.

Parliamentary Questions

The HPRA received and responded to 54 parliamentary questions. There were also 109 additional requests from the Department of Health, other government departments or members of the Oireachtas during the year. Of the total number of queries (163), the three largest categories related to human medicines (88), staff, finance and payroll (20) and corporate (16). The human medicines queries concerned topics such as adverse reactions, the availability or supply of products, market shortages, enforcement, clinical trials, orphan status, herbals, vaccines, licensing or importation.

Customer Services

Close to 3,000 queries were received and dealt with by the customer services team. 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.

For example, 200 queries were received relating to the exempt medicines programme while there were 418 pre-market and surveillance queries relating to medical devices.

ORGANISATIONAL MANAGEMENT AND DEVELOPMENT

It is essential that the HPRA have the necessary corporate functions, systems and supports in place to deliver on our public health mission. We must be flexible and proactive as an organisation to respond to regulatory and other external developments, and to adopt necessary changes in how we deliver our services. We must also ensure that the highest levels of corporate governance are developed and maintained.

Human Resources and Change

The HPRA's people management practices and policies are central to the achievement of our strategic goals. Throughout 2014, the human resources department continued to focus on the areas of staff retention and engagement whilst at the same time further advancing the public sector reform agenda. The organisational 'motivation and development competency', rolled out as part of the Performance Development Programme (PDP), provided the overarching framework for the development of many of our HR initiatives during the past year. The focus of this competency is to actively promote a continuous learning environment where individuals are encouraged to take on new responsibilities, challenges and to continually learn to support their own development.

Performance Development

PDP continues to be one of our core platforms to support high performance, superior service delivery and the development of our staff. In line with our ethos of continuous improvement and in response to employee feedback from 2013, the programme was enhanced during 2014. A variety of support tools were designed and published to a dedicated page on the HPRA intranet. The amendments were initially piloted across the organisation prior to a planned full implementation in 2015.

Learning and Development

Our learning and development strategy continued to focus on staff development as one of our key motivation and retention tools.

In support of this, a development planning process was launched. The implementation of the process was supported through;

- The design and publishing of a development planning guide, job aid and individual development plan form within the PDP;
- The design and delivery of a workshop to support managers in partnering with staff in the development process.

The HPRA's accredited Leadership Development Programme (LDP) continues to be an effective development tool for our managers and a second group commenced the programme in 2014. 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 there is a focus on expand our knowledge and we collaborate as part of the EU Network Training Centre (EU NTC). We actively participated in the creation of the EU NTC vision, strategy, guiding principles and assessment of the current state of training and development activities across the network of regulators.

Change Management

The remit of the HR department expanded in late 2014 to incorporate the change management function. This requires HR to be responsible for the effective management of change projects that provide for the availability, effective use and engagement of human resources within the HPRA so as to contribute to the delivery of the HPRA's strategic plan.

Employee Engagement and Commitment

The HPRA continues to place a high degree of emphasis on activities that will support employee engagement and commitment. In 2014, we focused on delivering a series of initiatives designed to support employees in meeting the challenges facing them both inside and outside of the workplace. Some examples include:

- Financial planning support, delivered via a seminar, and the opportunity to avail of one-to-one financial wellbeing sessions;
- The development of a range of staff health and wellness initiatives including the provision of flu vaccines and the establishment of a smoking cessation initiative. We also continue to provide all staff with access to the Employee Assistance Programme (EAP);
- An emotional wellbeing week that focused on areas such as meditation, mindfulness and a healthy lifestyle.

In addition to the above, we continued with our lunchtime learning initiatives which are highly popular with staff. Topics ranged from growing your own vegetables through to parenting and work, and mind mapping for life.

Often an indicator of levels of commitment and organisational health, we continue to record absence rates well within national averages with an overall 2.4% rate recorded for 2014.

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.

As planned, a significant focus of human resources activity during the first six months of 2014 was the implementation, testing and piloting of a new human resource IT system selected via a public procurement process in 2013. All members of the human resources team were heavily engaged in providing training and on-going support to users post go-live. The benefits of the system in terms of effectiveness and efficiency have already been realised with users reporting a reduction in time spent administrating routine tasks.

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 2014 a number of significant projects and initiatives were progressed.

National Developments

A tender process was undertaken for the design and implementation of HPRA's new workflow technology solution which is to be known as EOLAS. This 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 organisation. The tendering and evaluation process was completed at the end of 2014 and the design and development of the system is scheduled to be carried out in 2015. A planned implementation date of 2016 will coincide with implementation of new EU standards for regulatory data management.

In July of 2014, to coincide with the launch of the HPRA name, we launched a new website that provides stakeholders with improved access to information and enhanced product search capabilities online. Additional updates to the site and the information it provides are planned for 2015.

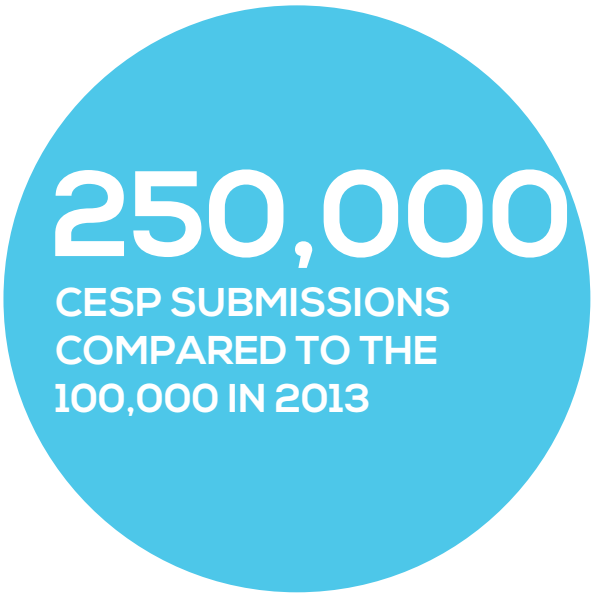
In keeping with the government strategy for shared service provision, the HPRA also provides hosting services to a number of organisations, and works closely with agencies such as the Office of the Revenue Commissioners. The HPRA is also actively engaged at national level through its involvement with the National Health Data Standards Committee and in liaison with other relevant agencies, such as the HSE, NSAI and HIQA. During 2014, the HPRA contributed to the development of a National Medicinal Product and the ePrescribing data set standards developed by HIQA.

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 2015. 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.

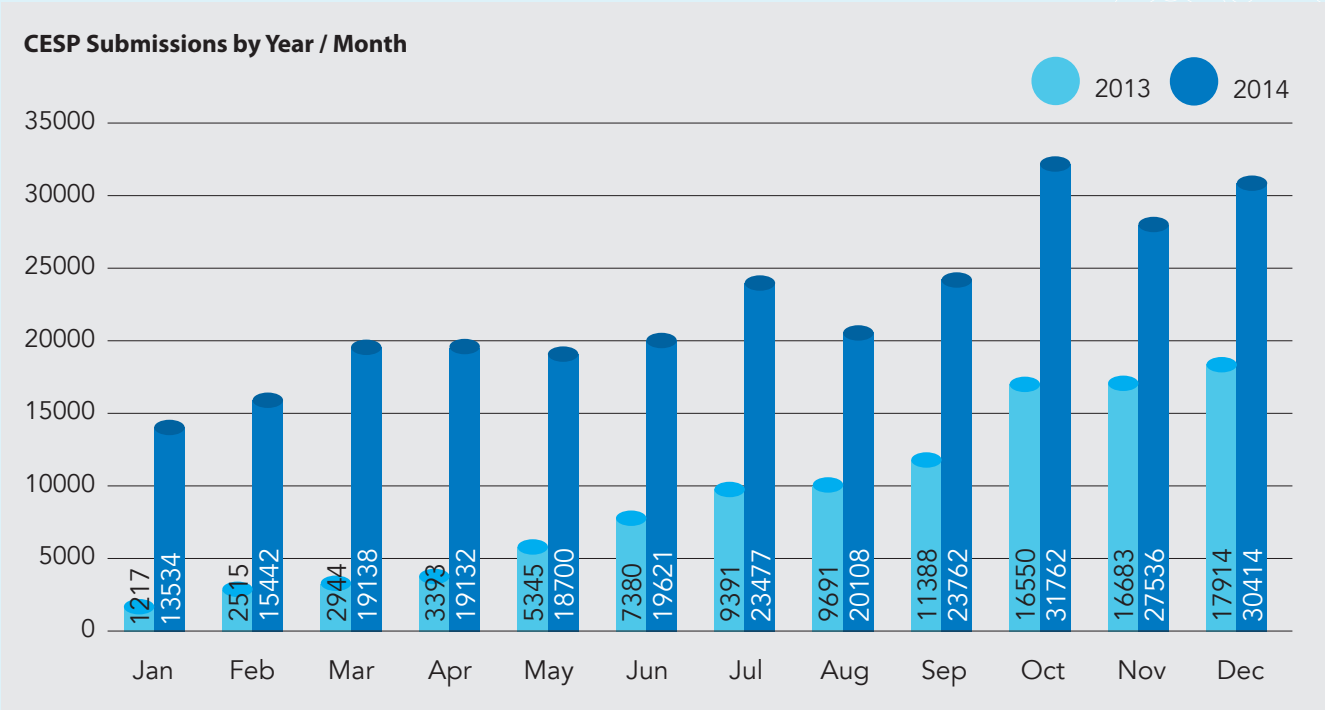


Common Electronic Submission Portal

A key activity for the IMB 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 2014, the CESP participation and activity levels grew significantly handling over 250,000 submissions compared to the 100,000 in 2013 and the portal now supports over 2,000 pharmaceutical companies and 6,000 users. The number of regulatory agencies using the system has also increased to over 32 across Europe and the system is now available 24 hours a day over a 7 day period.

In 2015, the system will be further developed to provide online tracking capabilities and reporting for stakeholders.



Chief Executive's Office

The Chief Executive's Office is responsible for communication, strategy and planning, quality management and a number of information functions for external stakeholders. It also provides the secretariat for the benchmarking programme across EU medicines agencies.

BEMA

The Benchmarking of European Medicines Agencies (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 medicines and is a resource for sharing of best practices. The HPRA's chief executive is co-chair of the BEMA steering group. The HPRA provides the secretariat for the group and is responsible for visit logistics. During 2014, we continued to lead the steering group as assessment visits were finished in this benchmarking cycle and the group began to review the outcomes.

Quality Management

During 2014, the HPRA's quality management system continued to be extended with the deployment of procedures for functions and legislative requirements introduced in recent years. These included new and amended processes under the falsified medicines Directive, 2011/62/EU, our functions for scientific animal protection according to the European Union (Protection of Animals Used for Scientific Purposes) Regulations 2012, additional legislative requirements for pharmacovigilance systems (Directive 2010/84/EU) and the establishment and maintenance of lists of interchangeable medicines under the Health (Pricing and Supply of Medical Goods) Act 2013.

Corporate Affairs

The HPRA's corporate affairs department 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 nine events in 2014 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.

A number of these events were information days which typically provide regulatory guidance and updates to interested parties. The 2014 information days focused on a range of topics including:

- Medical Devices
- GMP
- GDP
- Pharmacovigilance
- Clinical Trials
- Veterinary Sciences
- Regulatory Science.

Freedom of Information

During 2014, the HPRA received 17 Freedom of Information requests (as outlined on page 76).

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.

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)	6	6
Mr. Pat Brangan	4	3
Mr. Wilfred J. Higgins	4	2
Ms. Ann Horan	6	6
Prof. Mary Horgan	6	5
Dr. Elizabeth Keane	4	4
Mr. Noel O'Donoghue	6	3
Prof. Caitriona O'Driscoll	6	6
Dr. Diarmuid Quinlan	4	3

- The Authority of the HPRA met six times in 2014 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 2013. 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 2014 is as follows:

- The Audit Committee, a subcommittee to the Authority, met four times in 2014. Further details are provided in the HPRA's Financial Statements for 2014;

- Also during the year in review, the Advisory Committee for Human Medicines met twice, the Advisory Committee for Veterinary Medicines met twice and the Advisory Committee for Medical Devices met twice;

- The Herbal Medicines Sub-Committee, a sub-committee to the Advisory Committee for Human Medicines, met once in 2014. 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 2014.

Finance

It is the role of the finance section to manage and safeguard the finances of the HPRA. It must ensure that the HPRA 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 2014 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 oversaw the implementation of new legislation and advised on 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.

Overview of Energy Usage in 2014

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 S.I. 542 of 2009. These regulations transpose the Energy End Use Efficiency and Energy Services Directive (Directive 2006/32/EC) into Irish law.

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 2014, the HPRA consumed 953 MWh of energy consisting of:

- 775 MWh of electricity;
- 178 MWh of fossil fuels;
- 0 MWh of renewable fuels

Actions Undertaken in 2014

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 (formerly the National Procurement Service) 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 2014, cost savings in respect of electricity was 5.3% while cost savings in respect of gas was 5% (compared to the cost of going directly to the market).

Total Energy Savings

The HPRA building, Kevin O'Malley House, was extended upward by two floors during the course of 2012 and 2013. Therefore, 2014 was the first full year of occupancy of the two additional floors and this resulted in an increase of 14% in total energy usage for the building.

Since 2009, the HPRA has been highly focussed on reducing energy usage. This is evidenced by the 2013 Sustainable Energy Authority of Ireland (SEAI) report for the HPRA which confirmed that the organisation has improved its energy usage by 23.3% since 2009.

Actions Planned for 2015

In 2015, 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, which will again be 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

Board Members and Other Information

Board :

Mr. Michael Hayes	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	
Prof. Mary Horgan *	
Dr. Elizabeth Keane **	term expired 31/12/2013 re-appointed 22/05/2014
Mr. Noel O'Donoghue	
Prof. Caitriona O'Driscoll	
Dr. Diarmuid Quinlan ***	

The Board 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
Dublin Castle
Dublin 2

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 a Board which was appointed by the Minister for Health. The Board of the HPRA (the Board) 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 Department of Finance "Code of Practice for the Governance of State Bodies". This Code of Practice, which was issued to the HPRA in January 2002, incorporates many of the principles under which the HPRA operates, taking account of the size and legal nature of the organisation.

An updated Code of Practice was published by the Minister for Finance in June 2009, to take account of administrative and legislative developments in the corporate governance framework since 2001. The HPRA has carried out a detailed review of this updated Code, to ensure that its provisions are still reflected in the principles under which the HPRA operates.

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

Audit Committee

The HPRA has an audit committee comprising three Board members, which met on 4 occasions during 2014. This committee is responsible for reviewing internal control matters, together with any other issues raised by the external auditors, the Board 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 2014 the internal auditor carried out internal audits and reported to the audit committee on the areas of salaries/payroll and bank/finance. The audit committee has also been involved with the review of the quality systems as described below.

Quality Systems

During 2014, 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 - Board Members and Executive Directors

Remuneration and travel expenses paid to Board 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 Board 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.

Remuneration Committee

The HPRA has established a remuneration committee as a sub-committee of the Board to review the remuneration of the Chief Executive, in accordance with guidelines issued by the Department of Finance and the Department of Health. The Chief Executive's remuneration is disclosed in note 18 to the Financial Statements.

Internal Control

The Board 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 93.

Statement on Internal Financial Control

1. I, as Chairman, acknowledge that the Board 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 Board 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 Board.

   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 Board 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 Board.

   The Chief Executive reports to the Board 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 Director of Finance, Corporate and International provides the Board with monthly financial information, which includes key performance indicators. Where areas for improvement in the system are identified, the Board considers the recommendations made by the Management Committee.

   An appropriate control framework is in place with clearly defined matters which are reserved for Board approval only or, as delegated by the Board, for appropriate Management Committee approval. The Board 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 Board reviews specific areas of internal control. The HPRA has outsourced the internal audit function to an independent professional firm. During 2014 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 Board 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 20 May 2015.

Mr. Michael Hayes

Chairman to the Board

Date: 16 June 2015

Statement of Board Members' Responsibilities

The Board 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.

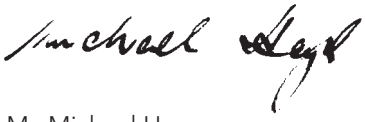
In preparing those statements the Board is required to:

- 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 Board 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 and with accounting standards generally accepted in Ireland. 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 Board

Chairman



Mr. Michael Hayes
16 June 2015

Board Member

Ms. Ann Horan

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 2014 under the Irish Medicines Board Act, 1995. The financial statements, which have been prepared under the accounting policies set out therein, comprise the accounting policies, the statement of income and expenditure, the balance sheet, the cash flow statement 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 in Ireland as modified by the directions of 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 of the state of the Authority's affairs and of its income and expenditure, 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 annual report to identify material inconsistencies with the audited financial statements. 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 17 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 2014 and of its income and expenditure for 2014.

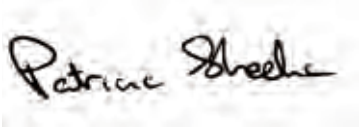
In my opinion, proper books of account have been kept by the Authority. The financial statements are in agreement with the books of account.

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
- my audit noted 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
- 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
- I find 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

25 June 2015

Accounting Policies

Historical Cost Convention

The financial statements are prepared in accordance with generally accepted accounting practice under the historical cost convention and comply with the financial reporting standards issued by the Financial Reporting Council, with the exception of superannuation - see note below.

Income Recognition

Income is recognised in the financial statements on the following basis:

- In the case of applications for marketing authorisations (new applications, variations to existing authorisations, or transfers) and clinical trial applications, income is recognised in the financial statements when a valid application form is received.
- 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.

Expenditure Recognition

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

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 income and expenditure account.

Tangible Assets

Tangible Assets excluding Premises

Tangible assets excluding premises are stated at cost less accumulated depreciation. Depreciation is calculated in order to write off the cost of tangible assets to their estimated residual values over their estimated useful lives by equal annual instalments.

The estimated useful lives of tangible assets 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.

Taxation

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

Debtors

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

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 €748,987 (2013 - €800,739). The surplus for the year on page 100 is then shown both before and after superannuation deductions less lump sum amounts paid in the year. The income and expenditure reserve on the balance sheet is split between retained reserves and superannuation reserves in note 11. 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 are not being complied with.

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.

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.

Leases

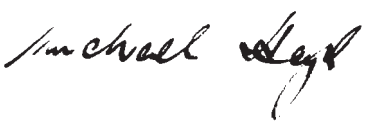
All leases are treated as operating leases and the rentals thereunder are charged to the Income and Expenditure account on a straight line basis over the lease period.

STATEMENT OF INCOME AND EXPENDITURE
for the year ended 31 December 2014

	Note	2014 €	2013 €
Fee Income	2	20,938,909	20,225,400
Other Income	3	4,700,860	4,430,585
		25,639,769	24,655,985
Salaries and Wages	4	17,501,062	17,765,250
Other Operating Costs	5	4,738,449	4,823,934
Depreciation	1	1,310,329	1,150,820
		23,549,840	23,740,004
Surplus for the year before write back of Superannuation contributions		2,089,929	915,981
Staff Superannuation Contributions		443,890	749,418
Surplus for the year		2,533,819	1,665,399
Balance brought forward		24,539,298	22,873,899
Balance carried forward		27,073,117	24,539,298

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

Chairman



Mr. Michael Hayes
16 June 2015

Board Member

Ms. Ann Horan

The accounting policies on pages 98 to 99 and the notes on pages 103 to109 form part of the financial statements.

BALANCE SHEET
for the year ended 31 December 2014

	Note	2014 €	2013 €
Tangible Assets	1	25,574,039	25,890,663
Current Assets			
Debtors and Prepayments	6	727,029	644,387
Stock of Stationery		2,259	2,407
Cash at Bank and in Hand	12	205,531	160,832
Short Term Deposits		15,649,391	12,940,623
		16,584,210	13,748,249
Creditors - Amounts falling due within one year			
Creditors and Accruals	7	7,151,792	6,372,942
Mortgage	13	793,332	793,332
		7,945,124	7,166,274
Net Current Assets		8,639,086	6,581,975
Long Term Liabilities			
Mortgage	13	7,140,008	7,933,340
TOTAL NET ASSETS		27,073,117	24,539,298
Financed by			
Income and Expenditure Reserve	11	27,073,117	24,539,298
		27,073,117	24,539,298

Chairman

Mr. Michael Hayes
16 June 2015

Board Member

Ms. Ann Horan

The accounting policies on pages 98 to 99 and the notes on pages 103 to109 form part of the financial statements.

CASH FLOW STATEMENT
For the year ended 31 December 2014

	Note	2014 €	2013 €
Reconciliation of surplus to net cash inflow from operating activities			
Surplus for Year		2,533,819	1,665,399
Depreciation Charge		1,310,329	1,150,820
(Increase)/Decrease in Debtors		(6,127)	228,197
Decrease in Stocks		148	296
Increase/(Decrease) in Creditors - amounts falling due within one year		777,470	(1,035,225)
Deposit Interest		(131,249)	(183,195)
Bank Interest and Charges		355,712	393,502
Loss/(Gain) on Disposal of Fixed Assets		61	(1,290)
Net Cash Inflow from Operating Activities		4,840,163	2,218,504
Cash Flow Statement			
Net Cash Inflow from Operating Activities		4,840,163	2,218,504
Return on Investments and Servicing of Finance	8	(299,599)	(133,976)
Capital Expenditure	8	(993,765)	(3,877,741)
Management of Liquid Resources	8	(2,708,768)	2,560,202
Financing	8	(793,332)	(793,332)
Increase/(Decrease) in Cash		44,699	(26,343)
Reconciliation of net cash flow to movement in net debt			
Increase/(Decrease) In Cash		44,699	(26,343)
Increase/(Decrease) In Short Term Deposits		2,708,768	(2,560,202)
Decrease In Long Term Finance		793,332	793,332
Change In Net Funds/(Debt)		3,546,799	(1,793,213)
Net Funds at start of year		4,374,783	6,167,996
Net Funds at end of year	9	7,921,582	4,374,783

The accounting policies on pages 98 to 99 and the notes on pages 103 to109 form part of the financial statements.

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2014

1. Tangible Assets

	Fixtures and Fittings	Computer Equipment	Leasehold Improvements	Improvements To Premises	Premises	Total
	€	€	€	€	€	€
Cost						
Balance as at 1 January 2014	1,134,883	9,849,076	502,445	4,314,888	23,156,037	38,957,329
Additions for the year	16,683	977,452	-	-	-	994,135
Disposals for the year	(3,595)	(147,286)	-	-	-	(150,881)
As at 31 December 2014	1,147,971	10,679,242	502,445	4,314,888	23,156,037	39,800,583
Depreciation						
Balance as at 1 January 2014	969,013	9,097,438	450,948	2,549,267	-	13,066,666
Charge for the year	57,004	771,591	50,245	431,489	-	1,310,329
Disposals for the year	(3,595)	(146,856)	-	-	-	(150,451)
As at 31 December 2014	1,022,422	9,722,173	501,193	2,980,756	-	14,226,544
Net Book value at 31 December 2014	125,549	957,069	1,252	1,334,132	23,156,037	25,574,039
Net Book value at 1 January 2014	165,870	751,638	51,497	1,765,621	23,156,037	25,890,663

2. Income

	2014 €	2013 €
Fee Income		
Clinical Trials	123,844	152,714
Human Medicine - National Fees	6,588,544	6,597,201
Human Medicine - European Fees	6,860,718	5,809,092
Veterinary Medicine - National Fees	1,357,676	1,226,329
Veterinary Medicine - European Fees	1,338,780	1,682,126
Compliance Department	4,294,355	4,406,871
Medical Devices	374,992	351,067
	20,938,909	20,225,400
Other Income (Note 3)	4,700,860	4,430,585
Total Income	25,639,769	24,655,985

Certain fees, totalling €16,815,145 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 2014

3. Other Income

	2014 €	2013 €
Dept Of Health Funding (Vote 38 Subhead E1)	3,916,000	3 ,937,000
Conference Fee Income	184,075	6 ,100
Deposit Interest	131,249	183,195
(Loss)/Gain on Disposal of Fixed Assets	(61)	1 ,290
IT Income	469,597	303,000
	4,700,860	4,430,585

4. Salaries and Wages

Salaries and Wages	15,663,696	15,948,022
Pensions	382,144	359,984
Social Welfare Costs	1,455,222	1,457,244
	17,501,062	17,765,250

The average number of staff employed during the year was 291 (2013 - 292).
Payroll numbers at 31 December 2014 can be analysed across the following departments : -

Chief Executive	11	10
Compliance	62	62
Finance, Corporate & International	19	19
Human Products Authorisation & Registration	106	103
Human Products Monitoring	44	46
Human Resources & Change	8	9
IT & Business Services	13	14
Scientific Affairs	2	2
Veterinary Sciences	22	25
Staff	287	290
Pensioners	30	25
	317	315

Pension related deductions for Public Servants of €942,745 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 2014

5. Operating Costs

	2014 €	2013 €
Accommodation Costs	1,048,954	1,281,687
Travel, Representation and Training	730,412	920,613
Bank Charges and Interest	363,697	398,152
Legal & Professional Fees	106,604	124,286
Stationery, Publications and Postage	418,624	409,221
Other Operating Costs	2,070,158	1,689,975
	4,738,449	4,823,934

Operating costs of €4,738,449 includes an amount of €7,894 related to staff hospitality.

6. Debtors (all due within one year)

Trade Debtors	303,875	336,335
Prepayments	238,854	186,716
Other Debtors	184,300	121,336
	727,029	644,387

7. Creditors (amounts falling due within one year)

Trade Creditors	287,858	268,817
Accruals	6,321,754	5,563,837
Revenue Commissioners	542,180	540,288
	7,151,792	6,372,942

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2014

8. Gross Cash Flows

	2014 €	2013 €
Returns on Investment and Servicing of Finance:		
Deposit Interest	54,732	259,169
Bank Interest and Charges	(354,331)	(393,145)
	(299,599)	(133,976)
Capital Expenditure		
Payments to acquire Tangible Fixed Assets	(994,135)	(3,879,031)
Receipts from sales of Tangible Fixed Assets	370	1,290
	(993,765)	(3,877,741)
Management of Liquid Resources		
(Increase)/Decrease in Short Term Deposits	(2,708,768)	2,560,202
	(2,708,768)	2,560,202
Financing		
(Decrease) in Long Term Finance	(793,332)	(793,332)
	(793,332)	(793,332)

9. Analysis of Changes in Net Funds/(Debt)

	As At 01/01/2014	Cashflow	As At 31/12/2014
Cash at Bank and in Hand	160,832	44,699	205,531
Short Term Deposits	12,940,623	2,708,768	15,649,391
Debt Due Within One Year	(793,332)	0	(793,332)
Debt Due After One Year	(7,933,340)	793,332	(7,140,008)
	4,374,783	3,546,799	7,921,582

10. Administration Expenses

	2014	2013
Surplus for the year was calculated having charged : -		
Auditor's Remuneration	17,300	17,390

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2014

11. Movement on Income and Expenditure Reserves

	As At 01/01/2014 €	Movement €	As At 31/12/2014 €
Retained Reserves	17,315,836	2,089,929	19,405,765
Staff Superannuation Contributions	7,223,462	443,890	7,667,352
	24,539,298	2,533,819	27,073,117

12. Cash and Bank Balances

	2014	2013
Current Account Balances	204,441	160,302
Cash on Hand	1,090	530
	205,531	160,832

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	3,966,680	4,760,012
	7,933,340	8,726,672

14. Interest Rate Exposure

The HPRA have 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. For 2015 it is estimated that the net borrowings for which an interest rate exposure may arise is €0.

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2014

15. Financial Commitments

	2014 €	2013 €
Operating Leases		
Amounts payable during the next twelve months in respect of leases which expire		
- within one year (in respect of Ormonde House)	-	-
- within one year (in respect of Longphort House)	-	-
- after five years (in respect of Alexandra House)	285,984	285,984
	285,984	285,984

Included in Accommodation Costs (Note 5) is expenditure of €285,984 under 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 2014 this lease had 7 years and four months remaining.

16. Capital Commitments

Contracted For (Contract Signed)	-	440,000
Not Contracted For	2,510,000	2,600,000
	2,510,000	3,040,000

17. Board Remuneration

Chairman's Salary	20,520	20,520
Board Members' Travel Expenses	5,247	6,710
	25,767	27,230

18. Staff Remuneration

Chief Executive's Total Remuneration		
Basic Salary	145,985	151,186
	145,985	151,186

The Chief Executive'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 2014

19. Related Party Transactions

There have been no transactions with related parties which require disclosure under Financial Reporting Standard 8.

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 : -

2014	€1 = STG £0.7825
2013	€1 = STG £0.8348

22. Provisions

The HPRA has been notified of a number of legal proceedings or potential proceedings. The information usually required by FRS 12 Provisions, contingent liabilities and contingent assets 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 board of the HPRA on 20 May 2015.

APPENDICES

APPENDIX 1
Committee Members

Management Committee

Mr. Pat O'Mahony
Chief Executive

Dr. Gabriel Beechinor
Director of Veterinary Sciences

Dr. Joan Gilvarry
Director of Human Products Monitoring

Mr. Kevin Horan
Director of Information Technology
and Business Services (appointed July 2014)

Ms. Frances Lynch
Director of Human Resources (resigned October 2014)

Mr. John Lynch
Director of Compliance

Ms. Suzanne McDonald
Director of Information Technology and Change
Management (resigned July 2014)

Dr. Mike Morris
Director of Scientific Affairs

Dr. Lorraine Nolan
Director of Human Products Authorisation
and Registration

Ms. Lynsey Perdisatt
Director Human Resources and Change
(appointed October 2014)

Ms. Rita Purcell
Director of Finance and Corporate Affairs

Board

Mr. Michael D Hayes – Chairman

Mr. Pat Brangan (reappointed May 2014)

Mr. Wilfrid J. Higgins (reappointed May 2014)

Ms. Ann Horan

Prof. Mary Horgan

Dr. Elizabeth Keane (reappointed May 2014)

Mr. Noel O'Donoghue

Prof. Caitriona O'Driscoll

Dr. Diarmuid Quinlan (appointed May 2014)

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. Ruaidhri Breathnach

Ms. Eugenie Canavan

Mr. Michael F. Clancy

Dr. Martin Danaher

Dr. Rodhri Evans (resigned July 2014)

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
Dr. Emma Wallace

Experts Sub-Committee of the Advisory Committee for Human Medicines

Prof. Mary Horgan – Chairman
Dr. Colin Buckley
Dr. Owen Carey (resigned January 2014)
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. Lorraine Kyne (resigned May 2014)
Dr. Mark Ledwidge
Prof. Aidan McCormick
Dr. Frank Murray
Dr. Yvonne O'Meara
Dr. Cormac Owens (appointed May 2014)
Mr. Ashley Poynton
Dr. Brion Sweeney
Dr. Jogin Thakore
Dr. Gerry Wilson (appointed May 2014)

APPENDIX 2
Presentations 2014

Third Level Presentations

Institution	Course	Presentation Title
Letterkenny IT	Veterinary Nursing	Regulation of Veterinary Medicines
PIER / UCC	Pharmacy	Vigilance Assessment and Career Paths
RCSI	Industrial Pharmaceutical Science and Overview of the CT Directive	Clinical Trials: Investigational Medicinal Product Dossier
RCSI	Nurse/Midwife Prescribing	Pharmacovigilance
RCSI	Nurse/Midwife Prescribing	Role of the HPRA
RCSI	Pharmacy	Advanced Therapy Medicinal Products
RCSI	Pharmacy	Regulation of New and Generic Medicines
RCSI	Pharmacy	Regulatory Affairs and Authorities
RCSI	Pharmacy	The Regulation of Biotechnology
Sligo IT	Medical Biotechnology and Pharmaceutical Science	HPRA Inspections / Pharmacovigilance
St. Johns, Cork	Veterinary Nursing	Regulation of Veterinary Medicines
TCD	Bioprocess Engineering	Biopharmaceuticals – Introduction to EU Regulation
TCD	Pharmaceutical Manufacturing	Role of the Pharmacopoeia in the Regulation of Medicines
TCD	Pharmaceutical Medicine	Clinical Trials for Biologics and Advanced Therapies (2 presentations)
TCD	Pharmaceutical Medicine	Communication of Drug Safety Data
TCD	Pharmaceutical Medicine	Implementation of the EU Pharmacovigilance Legislation
TCD	Pharmaceutical Medicine	Medicines Regulation: International Quality Standards and Pharmacopoeias
TCD	Pharmaceutical Medicine	Pharmacovigilance Risk Assessment Committee (PRAC)
TCD	Pharmaceutical Medicine	Quality Issues relating to Clinical Trials for Biologicals and ATMPs
TCD	Pharmaceutical Medicine	Regulation of Traditional Herbal Products (2 presentations)
TCD	Pharmacy	Overview of Pharmacovigilance Role and Career Paths
UCC	Pharmacy	Notification of Adverse Events
UCD	Biopharmaceutical Engineering	Biopharmaceuticals – Introduction to EU Regulation
UCD	Nurse/Midwife Prescribing	Pharmacovigilance (2 presentations)
UCD	Nurse/Midwife Prescribing	Role of the HPRA (2 presentations)
UCD	Veterinary Medicine	Regulation of Veterinary Medicines

Regulatory and Training Presentations

Event/Organiser	Presentation Title
Association of Irish Racecourse Veterinary Surgeons	New EU proposed Legislation on Regulation and Use of Veterinary Medicines
Association of Occupational Therapists of Ireland	The Role and Functions of the HPRA / Management of Suspected Medical Device Adverse Incidents
CMG Conference	Medication Errors – The Regulatory Role
DIA EuroMeeting	Periodic Benefit Risk Evaluation Reporting
Drug Safety Research Unit EU Conference	Measuring the Effectiveness of Risk Minimisation
EDQM	Committee of the Supply Classification of Medicines
EMA Pharmacovigilance Stakeholder Information Day	Update on Post Authorisation Safety Studies
Enterprise Ireland / Health Research Board (NCRF Panel Briefing)	About the HPRA
Informa Conference	Module 3: Drug device Combinations
Informa Conference	Commission Regulation 712/2012 – An Update
Informa Conference	Examining Opportunities for Harmonisation under Commission Regulation 712/2012
Irish Cosmetics and Detergents Association	Cosmetic Products Regulation
Irish External Quality Assessment Scheme	Overview of the Medical Device Vigilance System
Irish Medical Devices Association	Selling Medical Devices in Ireland
Joint CP - Ph. Eur. Seminar	Specific Monographs in European Pharmacopoeia (Ph. Eur.)
Joint CP - Ph. Eur. Seminar	Quality Control and Product Registration in the EU
Management Forum: Pharmaceutical Packaging, Labelling and Artwork	A Regulatory Perspective
Laboratory Animal Science and Training (LAST)	Directive 2010/63/EU (2 presentations)
Medicines Adaptive Pathways Workshop	An Agency Perspective
MedTec Ireland	Overview of the Medical Devices Vigilance System
NMBI Medicines Management Workshop	The Role and Functions of the HPRA / Reporting of Suspected Adverse Reactions
PDA Conference	GDP Guidance
PDA Conference	BEMA – Benchmarking for Pharmaceutical Regulators
PDA Seminar	The Supply Chain – A GDP Regulatory Perspective
PharmaChemical Ireland CMC Regulatory Affairs Training	Common Deficiencies in CMC Part of Application

Regulatory and Training Presentations continued

Event/Organiser	Presentation Title
PharmaChemical Ireland CMC Regulatory Affairs Training	Module 3: Drug Product
PharmaChemical Ireland CMC Regulatory Affairs Training	Common Issues with Variations
PIC/S Expert Circle Meeting on GDP	Computerised Systems Validation
Q1 Medical Devices Conference	Post Market Trends
Seminar on Strategies and Product Development of Veterinary Medicines	View of Regulatory Authority on Quality Aspects for Pharmaceuticals
Stem Cells and Tissue Engineering Conference	The Regulatory Environment of ATMPS
Teagasc	Implementation of Directive 2010/63/EU
Topra Annual Meeting	Pharmacovigilance – A view from PRAC and a National Competent Authority

APPENDIX 3
Human Medicines Safety: Publications and Articles

Drug Safety Newsletters

Edition	Topics Covered
February 59th Edition	- Combined Hormonal Contraceptives: Update on risk of VTE
April 60th Edition	- Strontium ranelate: New restricted indication and monitoring recommendations due to concerns regarding cardiovascular safety - Hydroxyethylstarch (HES) Infusion Solutions: EU review confirms products should not to be used in patients with sepsis or burn injuries or in critically ill patients - Cetuximab: Update on revised recommendations for use and risk of infusion-related reactions - IMB Pharmacovigilance Information day
May 61st Edition	- Domperidone-containing medicines: Risk of cardiac adverse reactions and restrictions for use - Recommendations to restrict the combined use of medicines affecting the renin-angiotensin (RAS) system - Ferumoxytol: Reminder regarding the risk of serious hypersensitivity reactions
June 62nd Edition	- Ivabradine: Reminder of conditions for use to avoid potentially dangerous bradycardia - HIQA: New Guidance for HCPs aimed at reducing medication errors - IMB Name Change
September 63rd Edition	- Transdermal fentanyl: Reminder about the potential for life-threatening harm from accidental exposure - Denosumab: Updated information to minimise the risk of osteonecrosis of the jaw and hypocalcaemia - Ferumoxytol: New important advice to mitigate the risk of serious hypersensitivity reactions - Beta Interferons: Risk of thrombotic microangiopathy and nephrotic syndrome - Adverse Reaction Reporting during 2013
November 64th Edition	- Oral Anticoagulants: Update on National Monitoring Experience - Chlorhexidine cutaneous solutions: Chemical injury including burns when used in skin disinfection in premature infants - Reminder regarding arrangements for DSN distribution - Adverse Reaction Reporting-Reminder
December 65th Edition	- Valproate-containing medicines: Recommendation to further restrict use in women andgirls - Ivabradine: New contraindication and recommendations to minimise the risk of cardiovascular adverse events - Agomelatine: Reminder of the importance of hepatic monitoring to reduce the risk of serious hepatic adverse reactions - Testosterone: EU review does not confirm increased risk of cardiovascular events

HPRA Articles in External Publications

Month	Publication	Topic
January	MIMS	Agomelatine: New contraindication and a reminder of the importance of liver function monitoring
February	MIMS	Combined Hormonal Contraceptives: Update on risk of venous thromboembolism
February	IMF	Domperidone-containing medicines: Risk of cardiac adverse reactions and restrictions for use
March	MIMS	Trazodone: Reminder of the risk of postural hypotension and somnolence in the elderly
March	MIMS Supplement (Cardiology)	Ondansetron: Updated information on posology to mitigate dose-dependent risk of QT interval prolongation
April	MIMS	Strontium Ranelate: New restricted indication and monitoring recommendations due to concerns regarding cardiovascular safety
May	MIMS	Metoclopramide-containing medicines: Update on outcome of review and revised recommendations for use
May	MIMS Supplement (Oncology)	Cetuximab: Update on revised recommendations for use and risk of infusion related reactions
June	MIMS	Medicines subject to additional monitoring requirements: Update
July	MIMS	Domperidone-containing medicines: Risk of cardiac adverse reactions and restrictions for use
August	MIMS	Recommendation to restrict the combined use of medicines affecting the renin-angiotensin (RAS) system
August	IMF	Recommendation to restrict the combined use of medicines affecting the renin-angiotensin (RAS) system
September	MIMS	New important advice to mitigate the risk of serious hypersensitivity reactions with Ferumoxytol
October	MIMS	Denosumab: Updated information to minimise the risk of osteonecrosis of the jaw and hypocalcaemia
November	MIMS	Transdermal Fentanyl: Reminder about the potential for life-threatening harm from accidental exposure
November	MIMS Supplement (Diabetes)	Adverse Reaction Reporting during 2013
December	MIMS	Agomelatine: Reminder of the importance of liver function monitoring to reduce the risk of serious hepatic adverse reactions
December	MIMS Compendium	Oral Anticoagulants: Update on National Monitoring Experience

APPENDIX 4 European and National Committee / Working Group Participation

Third Level Presentations

Committee/Working Group	Organisation	Meetings in 2014
Compliance and Enforcement Working Party (COEN)	Competent Authorities Working Group	3
In-Vitro Diagnostic Technical Working Group	Competent Authorities Working Group	2
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
Medication Safety Forum	Department of Health	2
Market Surveillance Forum	Department of Jobs Enterprise and Innovation	4
Official Medicines Control Laboratories network	EDQM	6
Tissues and Cells Guide / ART Drafting Group	EDQM	1
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	EMA	3
ESVAC	EMA	1
GCP Inspectors Working Group	EMA	4
GMDP Inspectors Working Group	EMA	4
Immunological Working Party	EMA	3
Paediatric Committee (PDCO)	EMA	12
Pharmacovigilance Inspectors Working Group - Human	EMA	4

Committee/Working Group	Organisation	Meetings in 2014
Pharmacovigilance Inspectors Working Group - Veterinary	EMA	4
Pharmacovigilance Risk Assessment Committee	EMA	13
Quality Working Party	EMA	4
Safety Working Party	EMA	4
Scientific Advice Working Party	EMA	11
Heads of Medicines Agencies meetings – Human	EU Presidency	4
Heads of Medicines Agencies meetings – Veterinary	EU Presidency	4
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
MDEG Working Group on Vigilance	European Commission	2
Medical Device Expert Group	European Commission	3
National Contact Points for Directive 2010/63/EU	European Commission	2
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
SCOPE Launch and Work Package Meetings	European Commission	3
Working Group of the Implementation of the Single European Code (SEC) for Tissues and Cells	European Commission	2
Working Group on Import of Human Tissues and Cells	European Commission	2
Medicines Reconciliation Advisory Group	HIQA	3
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
EU PSUR Work-Sharing Working Party	HMA	11
HMA ICT Working Groups	HMA	

Committee/Working Group	Organisation	Meetings in 2014
Homeopathic Medicinal Products Working Group (HMPWG)	HMA	2
Working Group of Communications Professionals	HMA	2
Working Group of Enforcement Officers	HMA	2
Working Group of Quality Managers	HMA	2
HPRA – UK Department for Business Innovation & Skills	Ireland/UK Working Group	5
HSE/National Organ Donation and Transplant Office (ODTI)	HSE / ODTI / HPRA	5
Cosmetic Standards Advisory Group	NSAI	2
Permanent Forum on International Pharmaceutical Crime (PFIPC)	PFIPC	1
PIC/S GDP Working Group	PIC/S	5
National Immunisation Advisory Committee	RCPI	6
Anti-doping Committee of the Sports Council	Sports Council	3
Board of the WHO/UMC Collaborating Centre	WHO	3

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
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

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