ANNUAL REPORT 2016

HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Contents

2016 Statistics at a Glance

637

THE TOTAL NUMBER OF NEW HUMAN MEDICINES AUTHORISED

108

CLINICAL TRIALS OF HUMAN MEDICINES WERE APPROVED TO COMMENCE IN IRELAND

15,548

VARIATIONS TO MARKETING AUTHORISATIONS ISSUED – 14,207 FOR HUMAN MEDICINES AND 1,341 FOR VETERINARY MEDICINES

51

THE NUMBER OF EMA SCIENTIFIC ADVICE PROCEDURES WHERE THE HPRA ACTED AS LEAD

126

NEW MARKETING AUTHORISATION APPLICATIONS FOR VETERINARY MEDICINES RECEIVED

10

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

127

MANUFACTURING LICENCES IN PLACE AT YEAR END – 103 FOR HUMAN MEDICINES AND 24 FOR VETERINARY MEDICINES

3,551

EXPORT CERTIFICATES ISSUED – 1,429 CERTIFICATES FOR MEDICINES AND 2,122 FREE SALE CERTIFICATES FOR MEDICAL DEVICES

31

EU PSUR SINGLE ASSESSMENT PROCEDURES FOR HUMAN MEDICINES LED BY THE HPRA

3,264

SUSPECTED ADVERSE REACTION REPORTS FOR HUMAN MEDICINES RECEIVED

337

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

2,216

MEDICAL DEVICE VIGILANCE REPORTS RECEIVED AND ASSESSED

209

MEDICINE RECALLS CONSISTING OF 201 HUMAN MEDICINES AND 8 VETERINARY MEDICINES

94

GMP INSPECTIONS CONDUCTED AT MANUFACTURING SITES FOR HUMAN AND VETERINARY MEDICINES AND ACTIVE SUBSTANCES

471

COSMETIC PRODUCTS SENT FOR LABORATORY TESTING

4,054

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

335

MARKET SURVEILLANCE CASES INVESTIGATED IN RESPECT OF MEDICAL DEVICES

1st

EVER HPRA PUBLIC INFORMATION CAMPAIGN PROMOTING THE SAFE USE OF MEDICINES

Chairperson's Statement

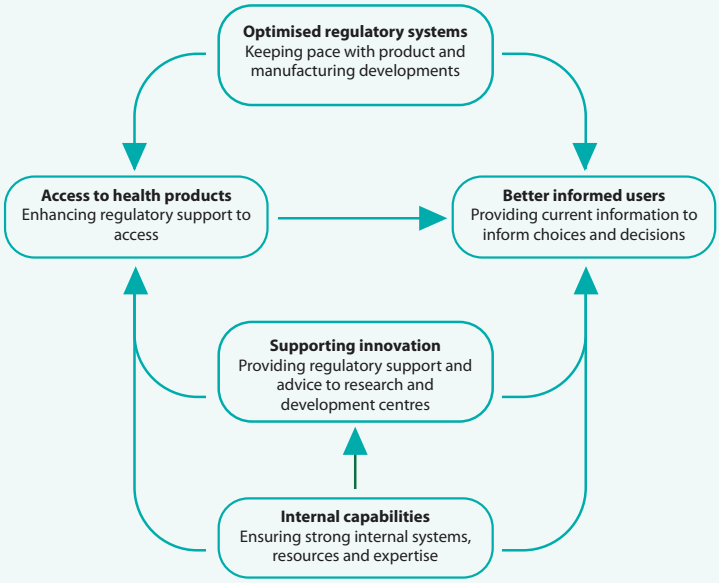
It was a great honour to be appointed Chairperson of the HPRA and I now have the pleasure of presenting the 2016 Annual Report.

2016 was the 50th anniversary of the establishment of the National Drugs Advisory Board (NDAB), a key milestone in our organisation's history. The NDAB developed over the years to become the Irish Medicines Board and eventually the HPRA. In the intervening period, the role of this organisation has grown from a purely advisory capacity to the Minister for Health for medicines, through to the competent authority it is today overseeing the regulation of a range of health products on the Irish market. Over time, it has secured a reputation nationally and internationally for the excellence of its regulatory model and approach.

The year in review is particularly significant in that it witnessed the start of the HPRA's new Strategic Plan 2016-2020. This follows the successful completion and delivery of our last strategy from 2011-2015 which elevated the organisation's work platforms to new levels of output and engagement. The new strategy builds on this success, setting out a robust roadmap to focus the organisation's activities into the future. It was developed after lengthy and detailed consultation with staff and a range of external stakeholders, including, importantly those who use health products, and is in line with Department of Health priorities. The Strategic Plan was approved by the Authority at its meeting in December 2015.

Our role is to continually protect and enhance public and animal health. In short, we seek to ensure that the health products we regulate are effective and that they are as safe as possible for those that rely on the benefits they can give. Ours is a broad and extensive remit as we act as the competent authority for the regulation of human and veterinary medicines, medical devices, blood products, tissues and cells, organs for transplantation and controlled drugs. We are also responsible for the regulation of cosmetic products and for the protection of animals used for scientific purposes. The Strategic Plan 2016-2020, which reflects the key issues and work areas highlighted during the consultative process, will enable us to continue to deliver on our consumer protection role whilst also shaping our organisation to evolve as dynamically as the industries and sectors that we regulate. It sets out five core strategic goals (as outlined below) which are supported by 17 high level actions.

HPRA Strategic Goals 2016-2020



These goals and defined actions will underpin our workload for the next four years. As this timeframe is long, we must also be ready to adapt to significant changes in our operating environment and be flexible in terms of renewing our strategic priorities. However, we have already completed the first year of an exciting journey and 2016 saw the delivery of some key highlights and firsts for our organisation.

We undertook our first ever public information advertising campaign across a range of media channels, including social media. The focus of our campaign was to encourage people taking medicines themselves or caring for others to *Take 3 Minutes* to read the information on the label and leaflet that accompanies their medicine. It was devised in light of consumer research we commissioned which showed that a quarter of Irish adults do not read the directions for use that comes with the medicines that they take. We will relaunch the campaign at various stages during 2017 to continue to remind people of the vital importance of taking care when taking medicines.

We had another first with the launch of our Innovation Office which we established to provide regulatory advice and assistance to those entrepreneurs, academics and small innovative companies developing novel health products or technologies. The Innovation Office focuses on directly assisting them in their understanding and compliance with EU and national regulations at the development stage of their innovations. Our dedicated in-house service is managed by a team of experienced regulatory and scientific experts who can help with queries relating to initial research and design, formulation, testing, clinical studies and the manufacture of new products or technologies. Ultimately, our goal is to facilitate the delivery of innovative products and technologies to the market and, by so doing, ensure patients have timely access to the most effective and safe health products possible.

Brexit was a major event in 2016. Following the news of the UK's referendum decision to exit the EU in June, the HPRA reviewed the potential impact this could have on the various aspects of our regulatory work and we commenced engagement with our European colleagues.The focus of our Brexit planning is clear and that is to ensure that patients continue to have access to necessary and appropriate health products both during and post the exit process. This will be an important part of our work in the coming years and will necessitate close continued collaboration with our partners nationally, with the European Medicines Agency and with our colleagues in the other European competent authorities for medicines, medical devices and other health products.

Acknowledgments

On behalf of the Authority, I extend our gratitude to the Minister for Health, the Minister for Agriculture, Food and the Marine, their advisors and the staff of their departments for their continued support of the HPRA and its activities.

I would like to thank the Chief Executive, management and all the staff and acknowledge everything that has been achieved in 2016. The significant workload and results are clear for everyone to see in the following pages of this report. As an organisation we are fortunate to have such a dedicated and professional workforce who are so clearly committed to delivering on the HPRA's mission to protect and enhance public and animal health.

On a personal note, I would like to thank the members of the Authority for their support and guidance and for making my role as Chairperson so much easier. My thanks also to the Chairs and members of the HPRA advisory committees and sub-committees. The deliberations and recommendations of all the independent experts who serve on the Authority and its supporting committees is of immense value to our organisation. Together with the management and staff of the HPRA, we are all fully committed and focused on the common goal of protecting the health and safety of all those who use health products.

Finally, I wish to acknowledge the diligent work of my predecessor Michael Hayes and commend him on overseeing such effective Authority structures and practices. My thanks to Michael for his commitment and contribution to the HPRA.

Ann Horan

Chairperson

Authority Members

The Authority of the HPRA is appointed by the Minister for Health in accordance with the powers conferred by subsection 2 of section 7 of the Irish Medicines Board Act, 1995. There were nine Authority members up to 31 December 2016.

Ms. Ann Horan
(Chairperson)

Mr. Pat Brangan

Mr. Wilfred J. Higgins

Mr. David Holohan

Prof. Mary Horgan

Mr. Brian Jones

Dr. Elizabeth Keane

Prof. Caitriona O'Driscoll

Dr. Diarmuid Quinlan

Management Committee

Ms. Lorraine Nolan
Chief Executive

Ms. Rita Purcell
Deputy
Chief Executive

Dr. J.G. Beechinor
Director of
Veterinary Sciences

Dr. Jayne Crowe
Director of Human
Products Authorisation
and Registration

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

Dr. Joan Gilvarry
Director of Human
Products Monitoring

Mr. Kevin Horan
Director of ICT and
Business Services

Mr. John Lynch
Director of Compliance

Ms. Lynsey Perdisatt
Director of Human
Resources and Change

Chief Executive's Report

2016 was my first year as Chief Executive of the HPRA, a role that I commenced at the beginning of January. I am very proud of what has been another year of high performance for the HPRA which demonstrates again our absolute commitment to the protection and enhancement of public and animal health.

At the start of the year, the organisation launched its Strategic Plan 2016-2020 which outlines our goals, objectives and high-level strategic actions for this period. The plan was prepared in consultation with staff and a range of external stakeholders including those who use health products, and in line with Department of Health priorities.

The strategic goals are:

1. Optimised regulatory systems;
2. Better informed users;
3. Access to health products;
4. Supporting innovation;
5. Internal capabilities.

The actions and activities identified in our strategic plan provide a clear roadmap for the future focus and development of the HPRA. It involved an extensive analysis and consultation process through which we gained an important insight into how our environment will evolve over the coming years. We are committed to acting upon this to ensure continued regulatory excellence.

However, it must be acknowledged that the year passed has presented unanticipated developments, which may have an impact on our priorities. The most notable being the outcome of the United Kingdom's European Union membership referendum, which has potential consequences for our role in the regulation of medicines, medical devices and cosmetics. These also extend to the continuity of the European networks within which we operate for these products. One direct consequence of the UK's decision to leave the EU is that the European Medicines Agency (EMA) will have to move from London. During 2016, a key focus for the HPRA has been supporting the Irish Government in its bid to relocate this Agency, with its crucial role in the authorisation and monitoring of medicines, to Dublin. As an organisation, we can be confident in our demonstrated ability to adapt and evolve to changing needs and we will embrace and overcome the challenges that lie ahead to ensure the continued protection of public and animal health.

The regulatory role of the HPRA continues to evolve and grow in line with new national and European legislation, and in response to other changes and developments in our operating environment. I would like to take this opportunity to highlight a number of specific initiatives where we have made significant progress this year and where our work will enhance the support we are providing to our valued stakeholders.

New Developments for Patients and Animal Health

2016 saw our organisation make significant advancements in our approach to supporting innovation. Key to this was the establishment of the HPRA Innovation Office. The office provides regulatory support and advice to individuals, academics, small and medium enterprises, pharmaceutical and medical device companies, and other groups in the development of a novel concept, idea or approach into a prototype, product or technology. The aim is to provide real and practical benefits for patients, health providers and the life sciences sector spanning from early stage development to post-authorisation research and monitoring.

The HPRA holds at its core protection of the health of those who use and benefit from the products we regulate. Patient engagement is therefore of immense importance to the HPRA and an area in which we continue to expand our focus. An example of this was our commitment in 2016 to support the Irish Platform for Patient Organisations, Science and Industry (IPPOSI) in their initiative to develop a national expert patient training programme. Graduates of the programme will bring invaluable patient expertise and insight throughout the entire medicines development process.

Another important development, which will directly benefit Irish patients, is our commitment to taking on a new and expanded role in the co-ordination and management of medicines shortages in order to ensure, insofar as possible, uninterrupted supplies of medicines. Collaboration with those already involved in the management of shortages at a national level as well as interaction with our European counterparts will be key to the success of this initiative.

The last year saw a number of significant legislative developments in the finalisation of new medical device legislation, which will provide a new framework in Europe focused on better public health protection through enhanced requirements for the safety and performance of devices. We also continued our work on the implementation of the new Clinical Trials Regulation, which aims to enhance the number of clinical trials conducted in Europe for the direct benefit of patients.

Network Participation

During the year, we continued with our absolute commitment to the European regulatory networks. Of particular significance, was the unanimous election of our colleague Dr David Murphy as Chair of the EMA Committee for Medicinal Products for Veterinary Use (CVMP) in June.

Our network participation goes beyond involvement at a European level; we continue to be strong participants within the International Collation of Medicines Regulatory Agencies and the International Medical Device Regulators Forum. The HPRA continues to play leadership roles in both of these forums through our membership of their executive committees. This work plays a vital role in bringing about greater harmonisation and convergence of regulatory approaches at a global level to the benefit of regulators and our stakeholders.

Parliamentary Affairs

The HPRA engaged significantly with elected representatives and government officials throughout 2016. We responded to 53 parliamentary questions during the year while a further 116 requests for information were received from the Department of Health, other Government departments and members of the Oireachtas.

In November 2016, the Minster for Health requested the HPRA to provide scientific advice in respect of the potential medical use of cannabis. The HPRA convened an expert working group to assist with its review of this matter. 'Cannabis for Medical Use - A Scientific Review', which outlines the key findings and conclusions of the working group, was published by the Minister in February 2017. We also addressed the Oireachtas Joint Committee on Health on 24 November of 2016 on this matter.

Stakeholder Engagement and Communications

As an organisation, we value the importance of engagement with healthcare professionals, patients, industry and other key stakeholders. We have strived to achieve this through active communication and events throughout the year. One of the highlights included our information day for medical devices while we also hosted a range of seminars and training events.

I am particularly proud of the work our communications team completed in 2016 which brought about new mechanisms to facilitate this engagement through social media and our first ever national public information campaign, entitled 'Take 3 Minutes'. The focus of these initiates was to develop a greater public awareness of the HPRA and our role.

Organisational Management

In this year, we have also enhanced our focus on the development of internal capabilities including the progression of a major infrastructure project through the development of a new consolidated workflow system. Other key initiatives include the launch of our first HR strategy focused on many key talent management objectives, and the development of systems to enhance our knowledge management capabilities.

The HPRA is largely self-funded by a system of fees which are approved annually by the Minister for Health, following a public consultation. This approach is in line with the typical funding model of health products regulation worldwide. We are committed to the highest standards of independence and governance so as to ensure quality of service combined with value for money and we continued in 2016 to successfully manage the affairs of the HPRA in line with our statutory obligation that income at least meets costs.

The Future

2016 was also a significant milestone for the HPRA in that we celebrated the 50th anniversary of the establishment of our organisation. We have had an incredible journey over that timeframe bringing us to the point today where we now regulate nine distinct classes of health products. As a health product regulator we have one of the widest remits of any agency operating in this area on a global basis. We are also well placed to continue on our development trajectory. Our investment in innovation, stakeholder engagement and building internal capabilities position us well as we continue on our journey to meet the challenges of being a regulator of the future.

Acknowledgments

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 during 2016.

On behalf of the Management Committee and all our colleagues, I want to thank sincerely the members of the Authority and advisory committees for their contribution and huge commitment to the HPRA. Their expertise and advice is of immense value to our organisation.

My particular gratitude to the Authority Chairperson, Ann Horan, and the Authority members for their support and dedication to our organisation throughout the year.

Finally, I wish to express my thanks and appreciation to all colleagues within the HPRA, for their passion and achievements during 2016 and their commitment and professionalism everyday throughout the year. I look forward to working with you all, as well as our Chairperson and our Authority and committee members, in continuing to focus all our efforts on the protection and enhancement of public and animal health.

Lorraine Nolan

Chief Executive

Human Medicines

It is the role of the HPRA to ensure that medicines are as safe as possible and do what they are intended to do. We grant licences for medicines subject to a review of their safety, quality and effectiveness and continuously monitor their use once they become available on the Irish market. We also approve and monitor clinical trials, inspect and license manufacturing sites and wholesalers, and investigate activities associated with the illegal supply, manufacture, wholesale or advertising of medicines.

Authorisation and Registration

Scientific Advice

Scientific advice is a pre-authorisation activity which assists product and technology innovation and development.

European Scientific Advice

The European Medicines Agency (EMA) operates a scientific advice system for innovative medicinal products (medicines) which may ultimately be the subject of applications under the centralised authorisation system. During 2016, the HPRA acted as lead in 51 EMA scientific advice procedures for medicines proposed for the treatment of a broad range of conditions. Areas of focus included medicines to treat respiratory disorders, auto immune inflammatory diseases, cancers and blood disorders, monoclonal antibodies and biosimilar medicines.

National Scientific Advice

A new national scientific and regulatory advice procedure was established by the HPRA in July 2016. Advice is issued to applicants to assist in the development of new or existing human medicines for commercial and non-commercial entities. Advice can be sought from the HPRA on preclinical, quality and specific clinical areas as well as regulatory issues. A guideline, template request form and fee structure were developed and published on the HPRA website. By the end of 2016, we had received 13 enquiries under this procedure. We issued national scientific advice in respect of four applications while in nine cases scientific advice was not required.

Borderline Product Classification

For products for human use, a classification service is operated for products which are on the borderline between medicines and other products such as food supplements, cosmetics and medical devices. Requests for classification, whether external or internal, are presented to an internal, multidisciplinary classification committee. This committee met six times in 2016 considering a total of 49 new products and revisiting five products from pre-2016.

The committee has a close working relationship with the Food Safety Authority of Ireland (FSAI). During the course of 2016, the FSAI notified the HPRA of 185 products which had been brought to its attention and which it considered to fall more appropriately under the HPRA's remit. Where this turned out to be the case, these products were followed up by the HPRA.

Clinical Trials

The role of the HPRA is to assess applications from sponsors to conduct clinical trials in Ireland. Sponsors include pharmaceutical companies and academic 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 subjects.

In 2016, 108 clinical trials were approved to commence in Ireland. The same number of trials was approved in the previous year.

Voluntary Harmonisation Procedures

A voluntary harmonisation procedures (VHP) is a co-ordinated work-sharing assessment procedure for multinational clinical trials. This procedure was established by the national competent authorities for clinical trials across the European Union. The VHP is similar to the approval process for clinical trials under planned new legislation, which is expected to come into force in 2019. For this reason, it is popular with sponsors wishing to gain experience and the HPRA continues to actively participate in this procedure.

The HPRA participated in 22 VHPs for clinical trials during 2016, compared with 15 during the previous year. The HPRA acted as lead Member State for the assessment of eight of these VHPs in 2016.

Medicinal Product Authorisations

New Marketing Authorisation Applications

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

There are a number of routes through which a medicine 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 medicine. The DCP route differs from the MRP in that the medicine has not previously been authorised within the EU.

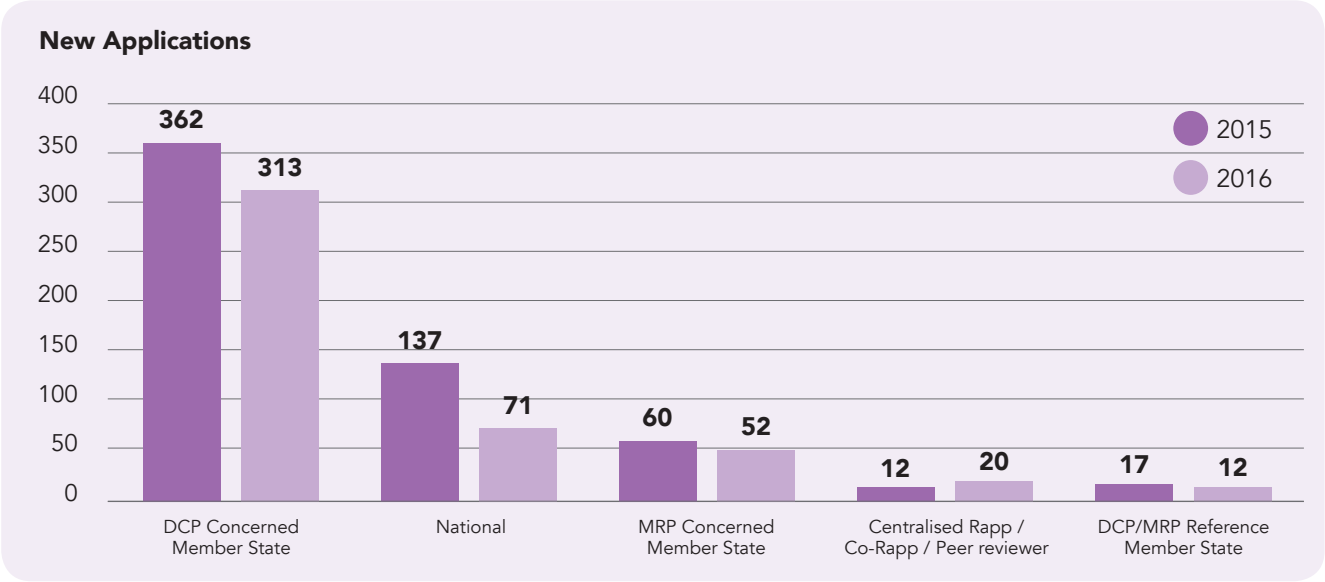
The following applications were assessed by the HPRA during 2016:

- 71 new national applications;
- 55 applications made under the MRP;
- 322 applications made under DCP.

The HPRA acted as reference (lead) Member State for the assessment of three of the MRPs and nine of the DCPs.

The centralised route is another mechanism whereby medicines can be authorised in Ireland. In this procedure, the assessment is carried out by Member States appointed as lead assessor (rapporteur), joint lead assessor (co-rapporteur) and peer reviewer, with input also from all other Member States. A centralised procedure is coordinated by the EMA with authorisation granted by the European Commission. The centralised route involves the submission of a single application to the EMA, and the authorisation once granted is valid in all Member States. In 2016, the HPRA was allocated five rapporteurships, nine co-rapporteurships and six procedures as peer reviewer by the Committee for Medicinal Products for Human Use (CHMP) at the EMA. These included treatments for respiratory, musculoskeletal, dermatological, gynaecological and orphan diseases. A number of these applications were for biological medicines.

The total number of new medicines authorised in 2016 was 637. This figure includes 169 medicines authorised through the centralised route where the HPRA was neither rapporteur nor co-rapporteur. In overall terms, the number of medicines authorised decreased relative to 2015 when the total number of new medicines authorised was 806.



Parallel Product Authorisations

A parallel imported medicine is a product which is equivalent to one already authorised on the Irish market and imported from an EU Member State or from a European Economic Area (EEA) country, by someone other than the importer appointed by the marketing authorisation holder of the product on the Irish market. A total of 57 parallel product applications were authorised by the HPRA in 2016.

Traditional Herbal and Homeopathic Medicinal Products

During 2016, nine 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 medicines. 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 49 THMPs are now authorised for sale in Ireland.

One homeopathic medicine was granted a marketing authorisation during 2016. There were no homeopathic medicines authorised under the simplified rules scheme. As a result, the total number of these medicines registered at year end was 99.

Transfer Applications

The HPRA processed a total 209 human medicine transfer applications in 2016. Of these, 187 related to the transfer of an existing marketing authorisation to a new marketing authorisation holder while the balance related to a transfer of a marketing authorisation holder prior to authorisation.

Variations

After a medicine has been authorised, the terms of its marketing authorisation may need to be changed and the process whereby such changes are implemented is known as a 'variation'. Examples of variations include the addition of a new indication, a new potential side effect, or updates to the company's manufacturing or contact details. In the past year, the HPRA issued 14,207 variations to marketing authorisations for medicines authorised through the national or MR procedures. The figure compared with a total of 15,691 variations during the previous year. The HPRA also issued 576 work-sharing variations in 2016 through national procedures. For 28 of these procedures, the HPRA acted as lead Member State.

Articles 45 and 46 - Variations to Update Product Information

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

Renewals

A total of 351 renewals to marketing authorisations for medicines authorised through national (33) and MR/DC (318) procedures were assessed during 2016. While the number of renewals can vary from year to year, in general the trend is downwards, reflecting the reduced number of medicine authorisation applications.

Interchangeable Medicines

Following commencement of the Health (Pricing and Supply of Medical Goods) Act in June 2013, the HPRA was tasked by the Minister for Health 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 Health Service Executive (HSE). By the end of 2016, the list included a total of 51 active substances.

Legal Classification of Medicines

Medicines are classified, in law, as prescription or non-prescription. Since 2014, the HPRA has taken a proactive approach to the reclassification of the legal status of medicines, with the aim of increasing the number of medicines available without prescription, where it is safe to do so. The HPRA has identified medicines which we consider could be safely made available without a prescription in pharmacies, or made more widely available in general retail outlets such as supermarkets, and has invited the industry to make applications to have these medicines reclassified. A number of reclassification applications were completed in 2016 and further progress is anticipated during 2017.

Authorisation / Licensing of Sites and Facilities

The authorisation / licensing of manufacturers and wholesalers of human medicines 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 and Quality) during which adherence to relevant European guidance is evaluated.

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

Number of Licences/ Authorisations (Sites)	2012	2013	2014	2015	2016
Manufacturers of medicines for human use	87	89	92	95	103
Investigational medicinal products for human use	47	49	53	52	55
Wholesalers of medicines for human use	258	269	272	287	318

Additionally, there were 11 contract laboratory approvals in place at year end, an increase of one compared with 2015.

Variations to Authorisations / Licences

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

In respect of human medicines, there were 565 variations associated with manufacturers, 248 associated with wholesalers and 230 related to investigational products. There was also one variation to a laboratory approval.

Registrations for Active Pharmaceuticals Ingredients and Brokers of Medicinal Products

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

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

Number of Registrations for Active Pharmaceuticals Ingredients	2013	2014	2015	2016
Manufacturers	22	22	22	21
Importers	35	37	37	41
Distributors	38	36	37	49

Brokers of medicines for human use are also required to register with us. During 2016, three new broker registrations were issued, meaning that there was a total of five registrations in place at year end.

Annual Updates and Variations to Registrations

There were 26 annual updates to registrations processed across the three categories of manufacturers, importers and distributors. This was in addition to five variations.

Export Certificates

Export certificates are required by health authorities in many so-called third country markets as an indication that a product registered, authorised and / or manufactured in the country of origin is of appropriate quality. The inspection and authorisation / registration programmes that we operate form the basis on which certificates are issued.

During 2016, there were 1,274 certificates issued in respect of human medicines which was down from a figure of 1,646 in the previous year.

Exempt Medicines Programme

Where no equivalent product is authorised or available, a registered medical practitioner is permitted to prescribe unauthorised medicines for individual patients under her / his direct responsibility in order to fulfil the special needs of those patients. Such products are referred to in Irish law as 'exempt medicinal products'. Wholesalers and manufacturers are obliged to notify certain information to our database in relation to any exempt medicinal products that they source. This information facilitates, when required, the effective recall of any defective exempt medicine from the Irish market.

In 2016, 1,827,047 packs of exempt medicines were notified to us compared to 1,639,312 packs during 2015. In addition, we responded to approximately 200 queries related to the programme.

The HPRA continued to work with key stakeholders to encourage the submission of applications for marketing authorisations for high volume and other important exempt medicines supplied to the Irish market.

Safety and Quality

Pharmacovigilance

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

During 2016, the HPRA received a total of 3,264 reports of new adverse reaction reports occurring in Ireland associated with the use of human medicines. This represents a 15% increase in overall reporting rates compared with 2015.

In addition, 3,242 follow-up reports were also received during the past 12 months with any duplicate case reports reconciled with previously submitted cases and invalid / nullified reports managed appropriately.

Source of Suspected New Adverse Reaction Reports	%
Pharmaceutical Company	69
Patient / Consumer	10
Community Pharmacist	4
General Practitioner	3
Nurse	3
Community Care Doctor	3
Hospital Pharmacist	3
Hospital Doctor / Specialist	2
Healthcare Professional - Other	2
Clinical Trial Reports	1

As in previous years, the majority of adverse reaction reports were notified to the HPRA by pharmaceutical companies in the context of their regulatory reporting obligations. It is important to note that these reports will have initially been received by the companies from healthcare professionals, patients or consumers.

Medicines subject to additional monitoring accounted for 29% of the reports submitted during 2016. Such medicines are identifiable by a black inverted triangle which is included on the accompanying package leaflet (PL) and the summary of product characteristics (SmPC).

The medicines most frequently included in reports to the HPRA accounted for some 76% of the adverse reaction reports received during 2016 (see table). It is important to note that the place of a medicine on this list cannot be taken as an indicator of safety or risk. The number of reports received cannot be used as a basis for determining the incidence of a reaction as neither the total number of reactions occurring, nor the number of patients using a medicine, is known.

Suspect Medicine(s) / Class of Medicines	Number of Reports*
Antineoplastics, including immunomodulating medicines, monoclonal antibodies and endocrine medicines	589
Immunosuppressants	500
Psycholeptics	287
Vaccines	285
Respiratory medicines	181
Anti-infective medicines, including antibacterials, antimycotics and antivirals	179
Antithrombotics	137
Cardiovascular medicines, including antihypertensives and lipid lowering agents	117
Analgesics and anti-inflammatory medicines	107
Medicines for the treatment of bone disease	91

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

Of the new adverse reaction reports received by the HPRA in 2016, 161 patients were reported to have died while on treatment. The accompanying table outlines the medicines / class of medicines associated with the highest number of reports.

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

Suspect Medicine(s) / Class of Medicines	Number of Reports*
Antineoplastics, including immunomodulating medicines and monoclonal antibodies	45
Antithrombotics	29
Psycholeptics	27
Immunosuppressants	14
Anti-infective medicines, including antibacterials, antimycotics and antivirals	12
Analgesics and anti-inflammatory medicines	11
Cardiovascular medicines, including anti-arrhythmics and antihypertensives	9
Systemic hormones, including steroids	7
Antidepressants	6
Medicines for the treatment of bone disease	4

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

Online and Electronic Reporting

The online reporting system, available to healthcare professionals and patients / consumers, accounted for 44% of reports received throughout the year.

Monitoring Compliance with Pharmacovigilance Obligations

Company/sponsor compliance with pharmacovigilance obligations continued to be monitored throughout 2016, with follow up and feedback provided as appropriate. See Inspections and Audits on page 22 for details of the associated inspection programme.

Vigilance Assessment and Risk Management

The HPRA plays a key role in monitoring the safety of medicines available on the Irish market. In co-operation with our EU counterparts, we regularly assess signals and emerging safety issues, and carry out routine and urgent benefit-risk evaluations. We also proactively participate in evaluating and approving risk management plans for medicines so that appropriate studies are carried out to gain more knowledge about their safety and efficacy. In addition, we serve as a key source of advice and information on the safe and effective use of medicines.

The HPRA is represented at a European level on the Pharmacovigilance Risk Assessment Committee (PRAC) and works continuously with the EMA and other Member States within the EU to ensure robust and timely decision-making on safety-related issues.

Signal Management Activities

Signal detection and management activities are focused on the real-time detection of new or changing safety issues relating to medicines ensuring availability of the most up-to-date information on benefits and risks. These activities allow for more rapid action when necessary to protect public health. Throughout 2016, the HPRA continued its participation in the work-sharing initiative for signal detection within the EU acting as lead Member State for the monitoring of 54 nationally-authorised active substances. Serving as PRAC rapporteur, the HPRA was also responsible for the further management of any signals detected in relation to 40 centrally authorised medicines (containing 27 active substances / combination of active substances). Labelling changes were also implemented for nationally authorised medicines during the past year following PRAC recommendations thus ensuring improved and up-to-date medicines information was provided to healthcare professionals and patients. We continued our participation during 2016 in the Signal Management Review Team at the EMA which focuses on improving tools, methods and processes for signal detection as well as developing methodological guidance.

Periodic Safety Update Reports

Periodic safety update reports (PSURs) are pharmacovigilance documents submitted by marketing authorisation holders at defined time points following the authorisation of medicines. PSURs are intended to provide a continuous cumulative update and analysis on the benefit-risk profile of a medicine throughout its lifecycle. The outcome of these procedures may lead to automatic harmonised regulatory action if considered necessary such as a variation, suspension or revocation. During the year in review, the HPRA continued its active contribution to the EU PSUR single assessment (PSUSA) procedure, contributing to the evaluation of 1,059 PSURs and leading the single EU assessment for 31 of these procedures. We consistently rank in the top 10 for appointments as lead Member State for PSUSA evaluation for nationally authorised medicines at EU level.

Additionally in 2016, the HPRA worked with the EMA and other Member States to ensure the successful delivery of a centralised European repository for PSURs and their assessment reports as well as to ensure successful integration into our national business processes. Under EU pharmacovigilance legislation, there was a legal requirement for the EMA to set up the repository so as to enhance access to data and information, thereby supporting benefit-risk assessments of medicines. Use of the repository became mandatory in June 2016.

Safety Referrals

Safety referrals are used to resolve issues around the safety or benefit-risk balance of a medicine or class of medicines. The EMA conducts a scientific assessment of a particular medicine or class of medicines through the PRAC on behalf of the EU. The PRAC, on which all Member States are represented, makes a recommendation for a harmonised position across the EU which is ultimately implemented nationally by the HPRA. The HPRA participated as Concerned Member State in eight newly initiated safety referrals in 2016 and a further six safety referrals which reached a conclusion during the year. The HPRA ensures that the final outcomes of referrals are implemented nationally and communicated to stakeholders.

Risk Management Plans and Post-Authorisation Safety Studies

All new applications for marketing authorisations now include a risk management plan (RMP) documenting the proposed risk management system to be implemented once a marketing authorisation is granted. During 2016, the HPRA contributed to the review of 305 RMPs (newly approved or updated) submitted via national, mutual recognition, decentralised and centralised procedures. We ranked 12th amongst the EU member states for PRAC rapporteurship / co-rapporteurship appointments for RMP evaluations relating to initial marketing authorisation applications. These medicines include treatments for orphan diseases including cystic fibrosis as well as other innovative products.

The HPRA also provided assessment input to 331 post authorisation safety study (PASS) procedures (protocols, reports and other post authorisation safety-related measures). A PASS is used to further evaluate the safety and benefit-risk profile of a medicine in the post-authorisation phase, or to measure the effectiveness of risk minimisation activities that have been introduced.

Sampling and Analysis Programme

The HPRA's risk based sampling and analysis programme is part of our monitoring of the quality and safety of medicines on the Irish market or which are manufactured in Ireland for export. It involves the analytical testing of products and / or examination of their packaging and labelling. It applies to medicines, active substances, borderline medicines / non-medicines and enforcement-related samples. A total of 404 samples were taken for analytical testing and / or examination in 2016.

Examination of Packaging and Labelling

The packaging and labelling of 132 medicines and other products available on the Irish market were examined. This included checks on the safety information contained in package leaflets. All were examined for signs of falsification and tampering but none was found.

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)	97
Authorised parallel imported and parallel distributed medicines	27
Borderline products (medicines / food supplements)	5
Product supplied via the exempt medicines route	2
Products for export	1
Total	132

Analytical Testing

A key element of our sampling and analysis programme is the analytical testing of medicines. While the majority of testing is carried out by governmental laboratories in Ireland, a number of samples are also sent to governmental laboratories in other countries as part of European working-sharing arrangements. In total, 255 medicines and other product samples for human use were sent for analytical testing during the past year. Approximately 44% were authorised medicines, 39% related to enforcement cases while 17% were active substances and intermediate materials. A breakdown of the types of products tested is outlined in the accompanying table.

Product categories selected for analytical testing in 2016	Number of samples analysed
Physico-chemical Analysis / Biological Analysis:	
Enforcement-related products	104
Nationally authorised medicines	42
MRP/DCP authorised medicines	28
Biological/biotechnological products	23
Compounded products	18
Parallel imported medicines	12
Products supplied via the exempt medicinal products route	9
Centrally authorised medicines for human use	7
Other products (manufactured for export)	6
Active substances / intermediate pharmaceutical ingredients	5
Borderline medicinal / non-medicinal products	1
Total	255

255

medicines and other product samples sent for analytical testing

Participation in EU Co-ordinated Market Surveillance Activities

We are an active participant in EU in the Official Medicines Control Laboratory (OMCL) network which is co-ordinated by the European Directorate for the Quality of Medicines and Healthcare (EDQM). Work completed during 2016 included:

- Centrally authorised medicines: Samples of four human medicines were sent for testing at OMCLs in other member states. Samples of five human medicines were received for testing at the HPRA's OMCL (the Public Analyst's Laboratory in Galway).
- MRP/DCP medicines: Two MRP / DCP medicines for human use were sampled in Ireland and tested at other member state OMCLs.
- Other products: A number of other products were tested for the HPRA by OMCLs in other member states.

Principal Findings

Laboratory Analysis

While the majority of the samples tested were compliant with their specifications, a number of out-of-specification results were also obtained. The most frequent of these was appearance not being in accordance with the specification. Eight deficiencies were also identified in the analytical methods and/or specification documents used by the manufacturers. Appropriate follow-up actions were taken in each case.

Packaging and Labelling

A total of 28 non-compliances were identified. These included:

- braille-related issues;
- product packaging and labelling that did not comply with the marketing authorisation;
- key safety information that had not been updated after a variation.

Again, appropriate follow-up actions were taken in each case.

Acknowledgements

The HPRA would like to thank the staff of the Public Analyst's Laboratory in Galway, and the staff of the State Laboratory in Celbridge, Co. Kildare, for their invaluable contributions to the 2016 sampling and analysis programme.

Quality Defects and Recalls

The quality defect and recall programme investigates, on a risk basis, reports of suspected quality defects in medicines and in their related active substances. It also co-ordinates recalls from the Irish market.

Quality Defects

Quality defects pertaining to 835 medicines for human use were reported or identified. The risk classifications that were assigned, along with the corresponding figures for the previous year, are outlined in the accompanying table.

Year	2015	2016
Critical quality defects	213	119
Major quality defects	218	331
Minor quality defects	301	382
Number of reports not justified	5	3
Total Number Quality Defects	737	835

Stability, defects relating to CMC / artwork and non-compliance with specification were the three largest defect categories. In addition, 22 reports relating to falsified medicines detected in other countries were considered, primarily because the genuine medicines were manufactured in Ireland. In none of these cases was the falsified product detected on the Irish market nor was the genuine manufacturer found to have had any part in their manufacture.

In respect of the sources of quality defect reports, pharmaceutical companies and other competent authorities again accounted for the majority of reports received.

Source of Reports	Human Medicines
Companies (manufacturers, distributors and/or authorisation holders)	596
Other competent authorities	171
Community pharmacists	43
HPRA staff members	42
Other health care professionals	42
Hospital pharmacists	18
Patients and/or other members of the public	3
Competitor companies	1

Recalls of Human Medicines

In certain cases, in order to protect public or animal health, it is deemed necessary to withdraw, or recall, medicines from the Irish market. During the year in review, 201 medicine recalls occurred which representing an 83% increase when compared to 2015. This increase is due mainly to a significant rise in the number of medicines that were recalled due to distribution issues. Overall, the most common causes of recalls during 2016 recalls were:

Source of Reports	Human Medicines
Erroneous distribution	99
Cold-chain	34
Stability	14
Lack of sterility assurance	9
SPC/printed artwork component	9
CMC/Artwork variation	8
Non-compliance with GMP	7
Product preparation/administration	7
Non-compliance with specifications	6

Retail Sales Monitoring

General Retail Sale Monitoring

The sale of consumer healthcare products by retail outlets such as grocery shops, health food shops and, where necessary, pharmacies, is monitored by the HPRA using a proactive and reactive, risk based, retail monitoring programme. During 2016, 53 cases, some of which involved multiple products, were investigated. Of these, 22 related to the sale of medicines that did not carry a valid registration number or authorisation number for the Irish market. An additional 31 cases related to the sale of medicines that had been incorrectly classified as non-medicines by those placing them on the market while one case related to the sale of a pharmacy-only medicine by a non-pharmacy retailer. A total of 218 products that did not carry a valid registration or authorisation for the Irish market were removed from sale.

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. Four inspections were carried out, and a number of non-compliances, including 15 major deficiencies, were identified. These were followed up and we monitored the implementation of corrective actions at the companies concerned. This inspection activity is linked to the HPRA's advertising compliance programme with three of the major deficiencies identified directly related to advertising activities.

Advertising Compliance Programme

It is the role of the HPRA to monitor and review advertising and promotion activities by the industry for compliance with the requirements of the Medicinal Products (Control of Advertising) Regulations, 2007. Some 213* advertisements were reviewed during 2016. Non-compliances, including both major and minor issues, were identified in respect of 112 of these. The major issues included misleading advertisements and advertisements that were not in line with the approved product information. Five advertisements were recalled.

The key data relating to the five main components of the programme are shown in the accompanying table.

	Total	Advertisements Reviewed	Non-Compliances Identified
Proactive Monitoring: Pre-planned Projects	14	144	72 individual advertisements were non-compliant.
Proactive Monitoring: Includes Randomly Selected Projects	21	33	11 individual advertisements were non-compliant.
MAH Inspections Performed	4	Multiple	Three major deficiencies related directly to advertising activities.
Complaints Received	12	18	17 advertisements in total were non-compliant. 11 of the complaints were upheld as being valid.
Queries Received	29	18	12 advertisements were non-compliant.

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

Inspections and Audits

As part of our regulatory role, the HPRA is focused on ensuring industry compliance with relevant standards and legislation. During 2016, we carried out an extensive programme of work which incorporated a range of inspections and audits in respect of human medicines.

Good Clinical Practice (GCP) Inspections

The purpose of these inspections is to:

- verify compliance with the approved protocols during the conduct of clinical trials;
- ensure that the rights and safety of trial participants are protected;
- ensure the integrity of the data reported from the clinical trials that are intended to support marketing authorisation applications and post-authorisation studies.

Compliance with GCP and applicable regulations is also verified.

During the year in review, nine GCP inspections were carried out. In connection with the review of applications for centralised marketing authorisations, we undertook two GCP inspections at the request of the EMA. The first of these inspections was at an investigator site in South Korea while the second was at a sponsor site in the US. There were seven routine GCP inspections at investigator sites in Ireland.

Pharmacovigilance Inspections

Pharmacovigilance inspections are performed to ensure that marketing authorisation holders comply with pharmacovigilance regulatory obligations and to facilitate compliance.

Two inspections of pharmacovigilance systems were performed in 2016. One of these was of a marketing authorisation holder that had not previously undergone a pharmacovigilance inspection. The other was performed as part of the EMA's programme of inspections related to centrally authorised medicines.

Good Manufacturing Practice (GMP) Inspections

GMP inspections are performed to ensure that holders of manufacturing and importation authorisations comply with GMP guidelines and national regulatory obligations, and to facilitate compliance.

A total of 81 GMP inspections were conducted at manufacturing sites that produce human medicines or active substances in 2016. These included eight inspections that were conducted in countries outside of the European Economic Area (EEA) incorporating seven which were carried out at the request of the EMA, relating to centrally-authorised medicines, and one which was of an active substance manufacturer. Ten sites in Ireland that manufactured active substances were also inspected.

Health Products Distribution Inspections

The HPRA carried out 129 inspections of wholesalers and distributors of medicines to check for compliance with EU guidelines on Good Distribution Practice (GDP). We also carried out two inspections of registered distributors of active substances.

Enforcement

Illegal activity involving the manufacture, supply and sale of medicines can potentially have consequences for public health. It is the role of the HPRA to investigate potential breaches of human medicines legislation and, where necessary, we will take the appropriate corrective action, up to and including legal proceedings.

Enforcement Cases and Detained Medicines

During 2016, 4,054 enforcement cases were initiated, compared to 3,677 in the previous year. There were a total of 673,906 dosage units detained, down from 1.1 million units in 2015. While the year-on-year decrease in products detained can be partly attributed to the ongoing inter-agency approach, both nationally and internationally, to combating the illegal supply of sedative products onto the Irish market, these products still accounted for 40% of all detentions. Anabolic steroids and erectile dysfunction medicines accounted for 16% and 14% of detentions, respectively.

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

Year	2012	2013	2014	2015	2016
Product detained (dosage units)	758,276	919,965	730,056	1,136,494	673,906
Cases Opened	3,911	3,932	3,703	3,677	4,054
Prosecutions	11	9	10	5	6
Voluntary Formal Caution (VFC)	6	27	13	14	13

Inter-Agency Co-operation

The HPRA continues to liaise and work closely with other enforcement agencies both nationally and internationally, in preventing, detecting and combating the unauthorised supply of medicines. The co-ordinated approach by the HPRA with the Revenue's Customs Service and An Garda Síochána was clearly evident during Operation Pangea IX. This operation, which is co-ordinated globally by INTERPOL, targets the criminal networks behind the sale of falsified and illegal medicines via illicit websites. The inter-agency approach employed nationally during this operation resulted in 60,000 tablets and capsules worth over €350,000 being detained. Of note, anabolic steroids accounted for over 50% of the products detained in Ireland.

The HPRA also actively co-operates with Sport Ireland in combating the use of doping substances and with the Department of Agriculture, Food and the Marine, the Pharmaceutical Society of Ireland (PSI), the FSAI and the HSE to address specific offending behaviours on the market.

Prosecutions

The HPRA is also responsible for prosecuting cases where it considers that there is a significant risk to public health. In 2016, six prosecution cases were initiated while there were also 13 voluntary formal cautions issued. The prosecutions related to the supply of products including slimming medicines, anabolic steroids, and erectile dysfunction medicines. We also support prosecutions brought by the Director of Public Prosecutions in relation to the illegal supply of medicines.

Legislation and Regulation

New Clinical Trials Regulation

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

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

Falsified Medicines

On 9 February 2016, the European Commission published Commission Delegated Regulation (EU) No. 2016/161. This Regulation supplements Directive 2001/83/EC of the European Parliament and of the Council by laying down detailed rules for safety features that will appear on the packaging of medicines for human use. The purpose of the Delegated Regulation is to detail the characteristics of the obligatory safety features for medicines introduced by the Falsified Medicines Directive, 2011/62/EU, the intent of which is to prevent the entry of falsified medicines into the legal supply chain in the EU.

The safety feature will consist of two elements placed on the packaging of a medicine:

- a unique identifier; and
- a device allowing the verification of whether the packaging of the medicine has been tampered with (anti-tampering device).

The unique identifier can be scanned to authenticate a pack at various points in the supply chain but particularly at the point of dispensing.

Supra-national and national repository systems will be established across the EU and will retain records of operations in relation to the unique identifier. This system, which is intended to enable the investigation of suspected falsified medicines, will be set up and managed by a non-profit legal entity established in the EU by manufacturers and marketing authorisation holders for medicines bearing the safety features. The HPRA has liaised closely with the Irish Medicines Verification Organisation (IMVO), the entity which has been established in Ireland. The competent authorities of the individual EU Member States will have access to the repository system located within their territory for certain purposes including supervision and monitoring.

The Delegated Regulation will apply in Ireland, and the majority of EU member states, as of 9 February 2019.

Stakeholders and Partners

Contributing to the European and Global Regulatory Network

Europe

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

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

Pharmacovigilance

During 2016, the HPRA continued to contribute actively to the work of the PRAC, with the Irish PRAC Member continuing to serve as Vice-Chairperson of the Committee.

The HPRA continued its work with stakeholders to support the implementation of the pharmacovigilance legislation. We contributed to the Pharmacovigilance Business Team of the EMA / Member State governance structure for pharmacovigilance. The Pharmacovigilance and Risk Management Lead contributed to the project oversight governance through membership of the Project Coordination Group and the European Risk Management Strategy Facilitation Group.

The Pharmacovigilance and Risk Management Lead contributed to a number of initiatives exploring development of the regulatory environment, strategies to facilitate access to innovative medicines for patients in need and benefit-risk management through the product lifecycle. The Pharmacovigilance and Risk Management Lead also contributed to a number of strategies to support stakeholder engagement through participation in routine stakeholder meetings and on specialist topics such as risk management planning, benefit-risk evaluation, pharmacovigilance impact evaluation, post-authorisation efficacy studies and pharmacovigilance as an enabler for innovation.

SCOPE

The Strengthening Collaboration for Operating Pharmacovigilance in Europe (SCOPE) Joint Action was created to support operations of pharmacovigilance in Europe following new requirements introduced by the European pharmacovigilance legislation that came into effect in June 2012. During 2016, the HPRA contributed to two main areas:

- The HPRA is the topic lead in respect of carrying out an impact assessment of risk communications under work package 6 (WP6). This incorporates the collection of information on risk communications practices in the EU network to better understand the communication channels and tools used. During 2016, we contributed to and participated in the delivery of a two-day risk communication workshop which shared relevant research results and facilitated discussions with experts from patient and healthcare professional organisations, and from academia. The workshop focused on how EU national agencies can optimise their communications on the risks associated with medicines.
- They also contributed as a partner under work package 8 (WP8) relating to lifecycle pharmacovigilance. Finalised recommendations, guidance and training for regulators was delivered in 2016 to support EU pharmacovigilance work.

Biosimilars

The HPRA contributed to a number of initiatives in 2016 in respect of biosimilar medicines. This included chairing the EMA drafting group on quality requirements for biosimilar heparins. In addition, the HPRA participated as a member of the organising committee for EMA assessor training on biosimilars and as a member of the EMA drafting group for a pilot study on extended scientific advice for biosimilars.

GMP Inspections

We participated in audit teams as part of the Joint Audit Programme (JAP) of GMP inspectorates of competent authorities. This also included the allied Joint Reassessment Programme (JRP) of the Pharmaceutical Inspection Co-operation Scheme (PIC/S).

Telematics

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. We continued to be represented on the EU telematics management board, the network data board and the e-submissions group and led on a number of key initiatives relating to single submission portals and data standards. The HPRA also participated in meetings to assist in the definition of the ICT requirements to support the implementation of the new European clinical trials legislation.

The HPRA business services team is participating, as part of a European consortium, in the European Commission's Horizon 2020 research programme on the openMedicine project. During 2016, an annual technical review was carried out by the Commission in respect of this project. The HPRA presented the core work package relating to the Identification of Branded Medicinal Products and was commended on the deliverable by the Commission review team. The project continued throughout 2016, with the HPRA participating in a number of other associated work packages and representing the project at meetings with the FDA and other relevant events.

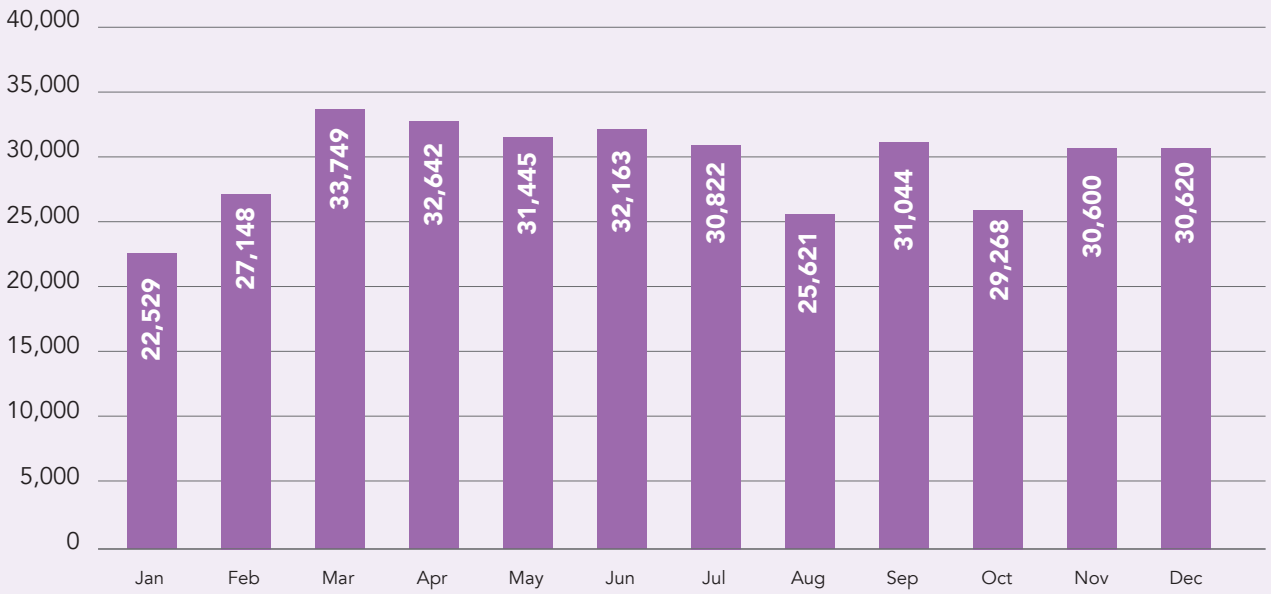
As part of our continued co-operation with other regulatory agencies in Europe, we are assisting the Malta Medicines Authority in the development of a new regulatory management system for product authorisation. The first phase of this project is due for completion in 2017.

Common Electronic Submission Portal

A key activity for the HPRA is the ongoing 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. Currently, there are 39 regulatory agencies across Europe using the system which is available to accept submissions 24 hours a day.

Participation and activity levels increased again during 2016 with the portal now handling more than 390,000 submissions, compared with 100,000 back in 2013, and supporting over 4,000 organisations with 14,000 users. Of the total number of applications submissions received, over 90% related to human medicines.

CESP Submissions by Month - Human Medicines



To assist in the end user training, we developed a training pack of videos and other materials that can be accessed online and provided online training to 560 participants throughout the year. During 2016, we also commenced the development of version three of the system with an additional goal to provide the European regulatory network with data from online forms based on the new ISO Identification of Medicinal Products (IDMP) data standards. The first phase of the project is due for delivery in 2017.

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 2016.

The HPRA participated at the annual meeting of national centres participating in the WHO international drug monitoring programme in November 2016 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 (currently 125 countries with full membership and 28 countries with associate membership) with Ireland ranked as the eleventh highest reporter (population based) during 2016.

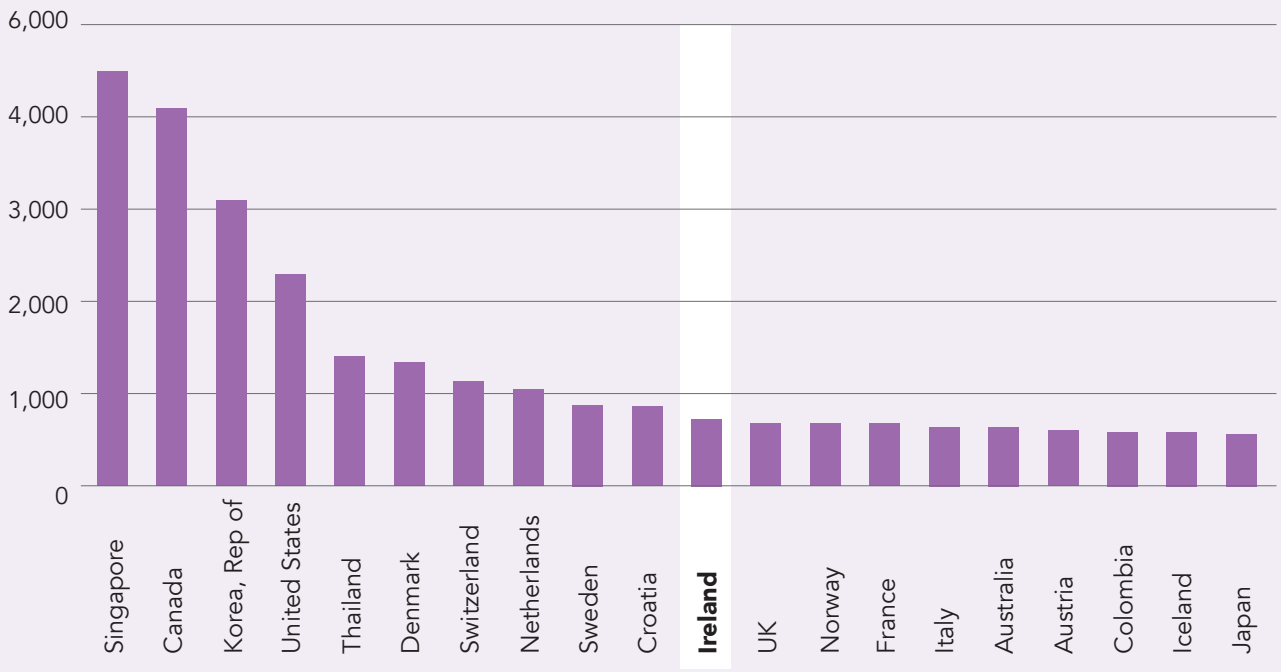
International Coalition of Medicines Regulatory Authorities

During 2016, the interim phase (2014-2016) for the International Coalition of Medicines Regulatory Authorities (ICMRA) ended. As the authority leading the Governance working group, the HPRA led the development of a new structural model for the coalition and the writing of a new Terms of Reference to allow for expansion of the ICMRA membership. The agreed new structure saw a changeover from the previous management committee structure and chair (Canada) and vice chairs (HPRA and Japan) to a newly elected Executive Committee led by the UK as chair and Australia and Mexico as vice chairs along with the preceding chair and vice chairs, including the HPRA. In line with the new Terms of Reference, ICMRA became open for applications for new Associate Members and the HPRA took on the role of coordinating applications to assist with the work of the ICMRA secretariat. We also led on a pharmacovigilance project during 2016, which was successfully completed before the end of the year, and we participated in the supply-chain integrity drafting group.

Health Systems Strengthening Programme

The HPRA was part of a successful consortium selected to provide 'Technical Assistance to the Ministry of Health and the Zambia Medicines Regulatory Authority (ZAMRA)'. This followed a tender process under the EU funded Health Systems Strengthening (HSS)

Active ICSRs in the WHO global ICSR database per million inhabitants – 2016



programme. Planning for the delivery of regulatory and capacity building support by the HPRA to ZAMRA began in 2015 while the project itself commenced in quarter two 2016. This included the provision of short term experts in the areas of clinical assessment and risk management in addition to facilitating a week long study visit from a ZAMRA delegation to the HPRA.

Contributing to National Health Initiatives

Responding to Medicines Shortages

The HPRA works closely with all relevant stakeholders to limit the impact of human medicines shortages on the Irish market. One of the mechanisms used by the HPRA to aid continuity of supply to the market place in the event of a shortage includes the granting of a temporary authorisation for a batch of a medicine known as a 'batch specific request'. Such applications may be appropriate when a medicine in full compliance with its registered marketing authorisation dossier is temporarily unavailable or where action is proposed to bring a batch into compliance with the registered details. During 2016, the HPRA reviewed 126 batch specific requests to facilitate continuity of supply of specific medicines in Ireland and prioritised other applications where expedited review was required to avoid shortages. We continued to follow up on instances of shortage of a particular medicine and worked with marketing authorisation holders, including suppliers of alternative products, in efforts to mitigate and alleviate the effects.

Emergency Medicines

Legislation (S.I. No. 449/2015) has been introduced to allow for trained non-medical persons to administer specific prescription-only medicines to a person, without a prescription, for the purpose of saving their life or reducing severe distress in an emergency situation.

During quarter one of 2016, the HPRA launched the new Emergency Medicines Registration System to support the implementation of this legislation. This online system, which was developed in collaboration with the Pre-Hospital Emergency Care Council (PHECC) and the Pharmaceutical Society of Ireland (PSI), enables organisations to notify the HPRA of their intention to procure or purchase a specified medicinal product from a pharmacy or other supplier for supply and administration in an emergency situation.

Information Technology

Throughout 2016, the HPRA's IT and business services team continued to enhance the 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 medicines, interchangeable medicines for the generic substitution programme and data for clinical and pharmacy systems. In keeping with the government strategy for shared service provision, we also provided hosting services to a number of organisations and worked closely with other agencies on technology related initiatives. In addition, we continued in 2016 to contribute to the development of data set standards for ePrescribing and an electronic medicinal product reference catalogue.

Meetings with Stakeholders

During 2016, there were a number of meetings held with industry representative groups including the Irish Pharmaceutical Healthcare Association (IPHA), BioPharmaChem Ireland (BPCI), the Healthcare Enterprise Alliance (HEA), the Irish Generic Medicines Association (IGMA), the Irish Association of Health Stores (IAHS) and the Irish Health Trade Association (IHTA). Such meetings provide a forum for discussion of items of mutual interest.

Meetings were also held with the PSI, the Irish Pharmacy Union (IPU) and the Irish Food Allergy Network (IFAN) to discuss issues of medicine availability and patient safety.

In addition, as part of our compliance work programme, there was extensive engagement with industry stakeholders. This included a large number of meetings with existing and prospective manufacturers and marketing authorisation holders, and with individual entities wholesaling or intending to wholesale medicines.

Presentations

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 postgraduate students studying courses related to the role of the HPRA.

Such presentations contribute to the HPRA goal of providing stakeholders such as healthcare professionals and regulatory professionals with access to relevant,

up-to-date information. The presentations are delivered by HPRA staff from across the organisation and cover all products and functions under our remit. While some are general in nature and primarily focused on explaining the role of the HPRA, others are more specific and deal with specialist areas and / or new regulatory developments. A full list of all presentations delivered during 2016 relevant to human medicines is provided in Appendix 2.

Regulatory Information Seminars and Training

HPRA information seminars and training events provide regulatory guidance and updates to a range of stakeholders. The HPRA also partners with other regulatory organisations to co-host relevant events.

EU Directive 2011/62/EU on falsified medicines introduces the requirement for safety features, including a unique identifier, to be added to the outer packaging of specified medicines for human use. In May, we hosted four workshops for stakeholders regarding the implications of this incoming requirement for marketing authorisation holders, manufacturers and wholesalers of human medicines. The workshops were hosted in Athlone, Cork and Dublin (2).

In September 2016, the HPRA hosted a training workshop in collaboration with the EU Network Training Centre. Approximately 50 people attended this event which was focused on benefit-risk training for clinical and safety assessors. The EU Network Training Centre is a joint HMA and EMA initiative set up to increase harmonisation of training within the EU regulatory network.

Advanced Quality Risk Management (QRM) training was hosted in the offices of the EMA in September. This training was organised jointly by the HPRA and the Pharmaceutical Inspection Co-operation Scheme (PIC/S).

In October, the HPRA hosted an informal meeting of the Committee for Advanced Therapies (CAT). The meeting was held on behalf of the Slovakian State Institute for Drug Control.

We also provided training in 2016 to industry in relation to aspects of controlled drug licensing.

Publications and Information

As part of our on-going commitment to ensuring stakeholders have access to information to support the safe use of human medicines, the HPRA continued during 2016 to publish newsletters, articles and important safety updates. We also published updated information and guidance for those working in the pharmaceutical sector.

Drug Safety Newsletter

The Drug Safety Newsletter continues to provide important safety information to healthcare professionals in respect of human medicines and incorporates hyperlinks to product information and other relevant

documents on the HPRA and EMA websites. Six issues of the newsletter were published and distributed to registered healthcare professionals, all of which are accessible from the HPRA website. A full index of topics covered during the past year is included in Appendix 3.

Risk Communications

The HPRA continued to publish educational materials and tools for healthcare professionals and patients which have been developed by marketing authorisation holders (MAHs) as additional risk minimisation measures for their medicines. Such materials are approved by the HPRA at national level and published on our website. Risk minimisation tools for more than 420 individual medicinal products are currently available on www.hpra.ie. During 2016, 77 suites of educational materials were approved by the HPRA in addition to 27 direct healthcare professional communications (DHPCs). The PRAC published monthly agendas, minutes, meeting highlights, notifications of safety reviews and signals throughout the past year and these were also made available via our website.

External Articles

There were 21 articles provided for inclusion in the MIMs (Ireland) publication and two articles provided for inclusion in the Irish Medicines Formulary. The full list of topics covered in these articles is included in Appendix 3. All articles were also published on the HPRA website.

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. One new publication in respect of human medicines, the Guide for National Scientific and Regulatory Advice, was published during 2016. A number of existing documents were also updated during the past year. These updated versions include tracked changes so that readers can easily access the revised content. All of the HPRA guidance documents can be accessed via the publications section of www.hpra.ie.

Medicinal Products Newsletter

This newsletter provides regulatory updates for those working in the pharmaceutical sector 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 2016. Topics covered that were relevant to human medicines included:

- The Medicinal Products (Prescription and Control of Supply) (Amendment) (No.2) Regulations 2015
- Change to requirements regarding applications for certificates of pharmaceutical product and certificates of free sale for medicines
- European Commission delegated Regulation for safety features on medicinal products for human use
- Revision to Annex 16 of the EU GMP guide: Certification by a qualified person and batch release
- Pseudoephedrine – Implementation of risk minimisation measures
- Good practice guide on medication errors
- Parallel importation – Update to variation categories
- Introduction of a regulatory contact point for marketing authorisation holders
- Sale or supply of traditional herbal medicinal products (THMPs) that have been granted their certificate of traditional use registration

Oireachtas Joint Committee on Health

In November, the HPRA was invited to address the Oireachtas Joint Committee on Health. The Committee met to discuss issues related to the potential use and possible legalisation of cannabis for medical use. Earlier that month, the Minster for Health requested the HPRA to provide scientific advice in respect of this matter. We outlined to the Committee our plans to convene an expert working group to assist with our review and committed to the publication of our deliberations by the end of January 2017.

Veterinary Medicines

It is the role of the HPRA to ensure that veterinary medicines are as safe as possible and do what they are intended to do. We grant licences for medicines subject to a review of their safety, quality and effectiveness and continuously monitor their use in animals once they become available on the Irish market. We also authorise clinical field trials in addition to inspecting and licensing manufacturing sites.

Authorisation and Registration

Scientific Advice

At a European level, the EMA co-ordinates the provision of scientific advice to companies on the appropriate tests and studies in the development of a veterinary medicine. This is designed to facilitate the development and availability of high-quality, effective and acceptably safe medicines. During 2016, the HPRA acted as co-ordinator for two requests under the EMA scientific advice procedure.

Product Classification Requests

As the competent authority, we have an important role in deciding which types of products fall within the scope of the veterinary medicines legislation. During 2016, 16 product classification queries were received, down from the 21 queries received in the previous year.

Clinical Field Trials

Tests and trials on a veterinary medicine for the purpose of generating data to support a marketing authorisation, or for other purposes, require a licence from the HPRA. We received one application for a new clinical field trial in 2016 as well as two variation requests for existing trials.

Medicinal Product Authorisations

New Marketing Authorisation Applications

As with human medicines (see page 12), there are a number of routes through which a veterinary medicine can be authorised by the HPRA. These include the national procedure, the mutual recognition procedure (MRP) and the decentralised procedure (DCP).

The following applications were received by the HPRA during 2016:

- 8 new national applications;
- 62 applications made under the DCP;
- 26 applications made under MRP.

We acted as reference (lead) Member State for the assessment of four of the MRPs and six of the DCPs.

The MRP may be used after completion of a first MRP or a DCP for the recognition of a marketing authorisation by other Member States for the same veterinary medicinal product. This is referred to as a Repeat Use Procedure. We received four applications under this procedure in 2016.

The centralised route is another mechanism whereby veterinary medicines can be authorised in Ireland. The centralised route involves the submission of a single application to the EMA and the authorisation, once granted, is valid in all Member States. In 2016, the HPRA was allocated five rapporteurships and six co-rapporteurships for veterinary medicines. An additional 14 new medicine applications were received through the centralised route where we were neither the rapporteur nor co-rapporteur.

We were also allocated the assessment of one maximum residue limit (MRL) application in 2016. Before a veterinary medicine intended for food-producing animals is authorised in the EU, the EMA evaluates the safety of its pharmacologically active substances and their residues and recommends MRLs.

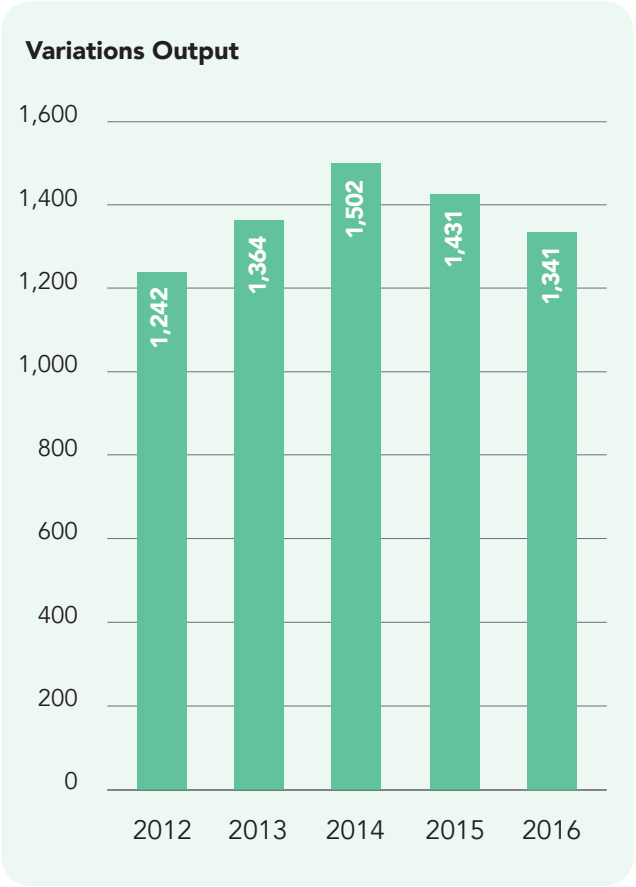
Transfer Applications

A marketing authorisation for a veterinary medicine may be transferred from the existing marketing authorisation holder to another using a transfer procedure. We processed a total 99 veterinary medicine transfer applications in 2016.

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 significant numbers of variations in recent years as shown in the accompanying graph.



In 2016, we issued 1,341 variations to marketing authorisations for medicines authorised through the national (416), MR (768) and centralised (157) procedures.

Renewals

Marketing authorisations are valid for five years from the date of first issue. For the authorisation to remain valid, it must be renewed at the end of this five-year period. A total of 100 renewals to marketing authorisations were assessed during 2016. Of these, 95 related to medicines authorised through the MRP with the HPRA acting as reference Member State in respect of 23 of these applications. There were two renewals for medicines authorised through national procedures and three for centrally authorised medicines.

Authorisation / Licensing of Sites and Facilities

The authorisation / licensing of manufacturers of veterinary medicines 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 and Quality) during which adherence to relevant European guidance is evaluated.

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

Number of Licences/ Authorisations (Sites)	2012	2013	2014	2015	2016
Manufacturers of veterinary medicines	23	24	25	25	24

Additionally, there were five contract laboratory approvals in place at year end, the same number as in 2015.

Variations to Authorisations / Licences

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

In respect of veterinary medicines, there were 57 variations assessed during 2016.

Export Certificates

Export certificates are required by health authorities in many so-called third country markets as an indication that a product registered, authorised and / or manufactured in the country of origin is of appropriate quality.

There was a total of 155 certificates issued in respect of veterinary medicines in 2016 which was an increase on the figure of 99 in the previous year.

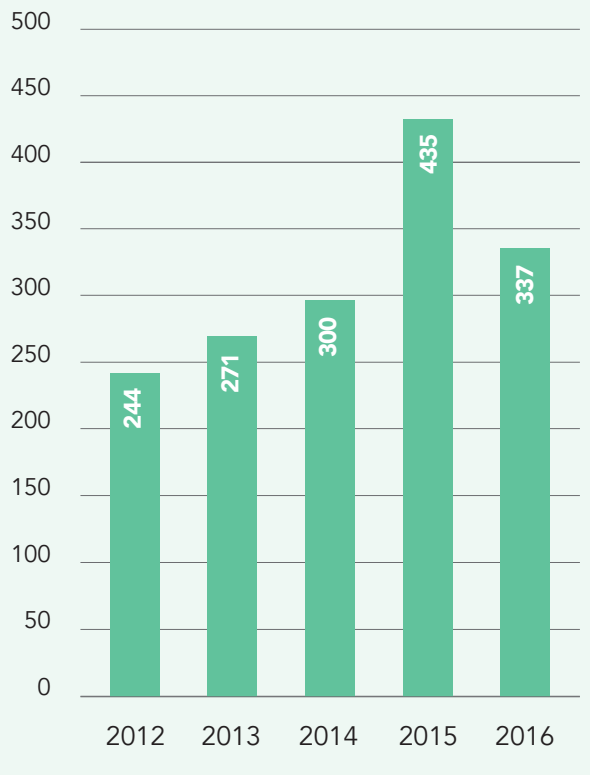
Safety and Quality

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 medicine. 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 medicines concerned. These reports may be submitted either directly to the HPRA or to the companies' marketing the medicines. The companies, in turn, must relay the data to the HPRA.

Reports Received



Over the course of 2016, we received 337 national reports of suspected adverse events to veterinary medicines with the vast majority of reports again received from pharmaceutical companies. While this represents a 23% reduction compared with 2015, the long-term trend in the number of reports being received on an annual basis is generally upwards.

Monitoring Compliance with Pharmacovigilance Obligations

Company / sponsor compliance with pharmacovigilance obligations is monitored by the HPRA. Additional details of the associated inspection programme are included under Inspections and Audits on page 34.

Periodic Safety Update Reports

Evaluating periodic safety update reports (PSURs) on individual medicines accounts for a significant proportion of the HPRA's overall veterinary medicines workload 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.

Type of PSUR	Number of PSURs
National	116
Mutual Recognition	562
Centralised	61
Work-sharing as Reference Member State	1
Work-sharing as Concerned Member State	234
Total	974

We completed the evaluation of 974 PSURs in 2016 which was a decrease on the figure of 1,205 in the previous 12-month period.

Use of Veterinary Antimicrobials in Ireland

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

Consumption of Antibiotics	2009	2010	2011	2012	2013	2014	2015
Tonnes sold	88.3	93.9	85.3	97.4	100.2	90.6	96.7

We continue 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.

Sampling and Analysis Programme

The HPRA's risk based sampling and analysis programme is part of our monitoring of the quality and safety of medicines on the Irish market or which are manufactured in Ireland for export. A key component of the programme is the analytical testing of products.

Analytical Testing

In total, 16 veterinary medicines and other product samples were sent for analytical testing during the past year. Of these, five were centrally authorised medicines while two were MRP / DCP medicines. Of the remaining tests, seven related to other medicines (manufactured for export), one was of an active substance and one was of a biological / biotechnological medicine.

Participation in EU Co-ordinated Market Surveillance Activities

We are an active participant in the EU in the Official Medicines Control Laboratory (OMCL) network which is co-ordinated by the European Directorate for the Quality of Medicines and Healthcare (EDQM). Work completed during 2016 included:

- Centrally authorised medicines: One veterinary medicine sample was sent for testing at an OMCL in another member state. Samples of four veterinary medicines were received for testing at the HPRA's OMCL (the Public Analyst's Laboratory in Galway).
- MRP/DCP medicines: Two MRP / DCP medicines for veterinary use were sampled in Ireland and tested at other member state OMCLs.
- Other products: A number of other products were tested for the HPRA by OMCLs in other member states.

Quality Defects and Recalls

The quality defect and recall programme investigates, on a risk basis, reports of suspected quality defects in veterinary medicines, and in their related active substances. It also co-ordinates recalls from the Irish market.

Quality Defects

A total of 41 quality defects relating to veterinary medicines were reported or identified. The risk classifications that were assigned, along with the corresponding figures for the previous year, are outlined in the accompanying table.

Year	2015	2016
Critical quality defects	1	7
Major quality defects	8	12
Minor quality defects	25	22
Number of reports not justified	1	0
Total number quality defects	35	41

Of the 41 reports received, 26 were determined to affect Ireland in that the defective batch or batches were either on the Irish market and / or were manufactured in Ireland. On investigation, it was determined that none of the defects, classified as critical, affected medicines on the market here. Product stability and defects related to CMC / artwork were the two most significant defect categories.

As regards the sources of the quality defects reports, 24 came from industry, 16 from other competent authorities and one from a HPRA staff member.

Recalls of Veterinary Medicines

In certain cases, in order to protect animal and / or public health, it is deemed necessary to withdraw, or recall, a veterinary medicine from the Irish market. In 2016, eight recalls of medicines occurred compared to three in 2015. Of these, seven were recalled due to stability issues while one was due to a lack of therapeutic efficacy.

Inspections and Audits

As part of our regulatory role, the HPRA is focused on ensuring industry compliance with relevant standards and legislation. During 2016, our work programme incorporated a number inspections related to veterinary medicines.

Pharmacovigilance Inspections

Pharmacovigilance inspections are performed to ensure that marketing authorisation holders comply with pharmacovigilance regulatory obligations and to facilitate compliance.

One re-inspection of the pharmacovigilance systems of a marketing authorisation holder was performed in 2016.

Good Manufacturing Practice (GMP) Inspections

GMP inspections are performed to ensure that holders of manufacturing and importation authorisations comply with GMP guidelines and national regulatory obligations, and to facilitate compliance.

During the year in review, 13 GMP inspections were conducted at sites in Ireland that are involved in manufacturing or testing veterinary medicines, of which 10 were routine re-inspections and three were non-routine. These included one GMP inspection in a country outside the EEA.

Legislation and Regulation

New Veterinary Medicines Regulation

New legislation which is intended to enhance the legal framework for the authorisation of veterinary medicines in the European Union was proposed by the European Commission in 2014. The draft framework is aimed at improving the health and wellbeing of animals by stimulating the development and availability of veterinary medicines. The proposal also focuses on the growing concerns over antimicrobial resistance.

During 2016, the HPRA continued to provide input into the ongoing discussions of the Council Working Group in Brussels in respect of the new legislation through the provision of comments to the Department of Agriculture, Food and the Marine on the impact of the proposals on the regulatory procedures. The Department participates at European Council meetings.

Stakeholders and Partners

Contributing to the European Regulatory Network

The European Regulatory Network is the backdrop for reaching a common view on medicines and their regulation. Given that most medicines are supplied to multiple European markets, it is clear that in order for us to maximise our influence, the HPRA must have an input in decisions taken at a European level. This we do through our involvement across the EU network which includes active participation at the EMA and the HMA.

Of particular note during 2016, was the election of Dr David Murphy as Chair of the EMA's Committee for Medicinal Products for Veterinary Use (CVMP). Dr Murphy was the Veterinary Assessment Manager at the HPRA and served as the Irish member of the CVMP for a number of years. The CVMP is responsible for preparing European Medicines Agency opinions on all questions concerning veterinary medicines. In particular, it plays a vital role in the marketing authorisation procedures of the European Union working to ensure that veterinary medicines that reach the marketplace have a positive benefit-risk balance in favour of the animal population they are intended for. The members of the CVMP, who are nominated by the European Union Member States in consultation with the EMA's Management Board, are chosen on the strength of their qualifications and expertise with regard to the evaluation of medicines.

Also in 2016:

- The HPRA became a member of the steering group on veterinary vaccines shortages;
- We became a member of the CMDv taskforce on variations.
- The HPRA delegate was elected Vice-Chair of the EMA's Quality Working Party (QWP) while the co-opted CVMP member from Ireland was re-elected to serve for a further term as a CVMP member.
- We contributed to the acceptance testing of a newly created pharmacovigilance training module.

Common Electronic Submission Portal

As outlined earlier in this report, a key activity for the HPRA is the ongoing development and management of the Common Electronic Submission Portal (CESP) on behalf of the wider EU regulatory community.

During 2016, more than 33,000 applications in respect of veterinary medicines were submitted through the portal.

Contributing to National Health Initiatives

Availability of Veterinary Medicines

Availability of veterinary medicines continues to be an issue for many veterinary practitioners tasked with treating many different species and conditions. Problems of non-availability can arise from a number of issues and different solutions are needed depending on the issues involved.

During 2016, in order to better understand the current situation, the HPRA carried out a survey amongst drug companies and their consultants in respect of the drivers and constraints to availability of veterinary medicinal products nationally. In addition, we carried out a survey in respect of clinical field trials conducted in Ireland. Finally, we also authorised a veterinary medicine from the so-called AR16 list. Under the AR16 licensing procedure, a needed product can be imported from another country under licence from the Department of Agriculture, Food and the Marine where there is no suitable medicine authorised in Ireland.

Antimicrobial Resistance

Containment of the development of antimicrobial resistance (AMR) is essential for public and animal health. AMR is a complex issue and a co-ordinated approach from all stakeholders in the human health, animal health and agriculture sectors is required to address this issue.

The primary responsibility of the HPRA is to ensure that only those medicines that meet the EU standards of quality, safety and efficacy are authorised, and that the benefit / risk assessment of the medicines remains positive throughout their life cycle. Through our diverse regulatory activities, we collaborate with and support the many stakeholders involved in managing AMR, with the common goal of enabling and promoting prudent and responsible use of antimicrobials.

In January 2016, at the request of the Authority of the HPRA, we produced a report on antimicrobial resistance which was published online and shared with relevant stakeholders. The report references existing European and global reports on AMR in bacteria and considers their implications for the HPRA in relation to our role as the national regulator of human and veterinary medicines.

We also participated in two meetings of the National Interdepartmental AMR Consultative Committee and contributed, in collaboration with the Department of Agriculture, Food and the Marine, to a WHO survey on AMR.

Meetings with Stakeholders

We met with the Department of Agriculture, Food and the Marine in relation to ongoing matters of mutual interest, including medicine shortages and the new proposal for the regulation of veterinary medicines.

Presentations

As in recent years, we delivered a programme of presentations to veterinarian students and veterinary nursing students on the role of the HPRA and the promotion of veterinary pharmacovigilance. A full list of all presentations delivered during 2016 is provided in Appendix 2.

Publications

As part of its on-going commitment to ensuring stakeholders have access to informative and up-to-date information relevant to the regulation of veterinary medicines, the HPRA continued during 2016 to publish newsletters, articles and important safety updates.

Medicinal Products Newsletter

This newsletter provides regulatory updates for those working in the pharmaceutical sector 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 2016. Topics covered that were relevant to veterinary medicines included:

- Mock up submissions to the HPRA
- Active substance supply
- Future strategy for the regulation of PBT substances
- QP declaration for intermediate sites
- Update on legislative proposal for new EU Regulation
- Update to the product literature standard
- Use of animal test methods for regulatory testing of human and veterinary medicines

External Articles

Consistent with our objective to improve stakeholder knowledge on the use of veterinary medicines, we contributed four articles to the specialist, 'It's Your Field' publication. The topics covered were:

- Substantiating the efficacy of a medicine
- Availability of veterinary medicines
- Conduct of studies in animals
- Residue benchmarks for veterinary antibiotics in milk

Risk Communications

Notices relating to the safety of veterinary medicines are published by the HPRA and classified under several priority related categories. The issues covered by these notices will range from quality defect information and medicines safety information through to updated information on the appropriate usage of medicines.

During 2016, we published two safety advisory notices on the HPRA website. The first notice, published in June, related to serious adverse events involving recumbency and death in cattle (dairy cows) following use of Velactis in Europe. The second notice, which was published in December, concerned the safety of injectable gentamicin for horses.

Medical Devices

As the competent authority, the HPRA monitors the safety of medical devices available in Ireland. Our aim is to make sure that these products perform as intended and do not compromise the health and safety of the patient or the person using them.

The HPRA also assesses applications for clinical investigations, operates relevant registration systems, inspects manufacturing sites and monitors the performance of notified bodies designated to approve medical devices for the European market.

Authorisation and Registration

Product Classification Requests

The HPRA received 40 applications for classification of medical devices or other products queried as medical devices in 2016. The queries emanated from other medical device competent authorities in Europe (60%), from medical device manufacturers (20%), notified bodies (5%), and users (5%) of medical devices. The remainder (10%) resulted from the HPRA's proactive market surveillance activities.

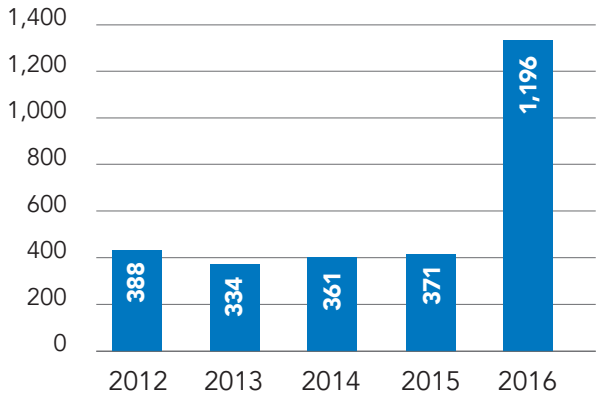
Clinical Investigation Applications

We received 10 applications for clinical investigations of a medical device, including three amendments to ongoing investigations, to be conducted in Ireland in 2016. These clinical investigations were received from a range of established manufacturers and device innovators. They included medical device software, closure devices, cardiac devices and novel devices for the management of complications linked to diabetes. This level of activity was broadly similar to the previous 12-month period. During the past year, the HPRA also received five applications to use medical devices in Ireland on compassionate grounds.

Product Registrations

We received 1,196 notifications of medical devices to the medical device register in 2016 representing a three-fold annual increase in device registrations when compared with the period 2012 to 2015. These registrations apply to self-declared class I, *in-vitro* diagnostic and custom made medical devices and to system and procedure packs. Registration of these devices is required in the Member State in which the manufacturer or their authorised representative is based.

Device Registrations



Organisation Registrations

During 2016, 30 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.

Export Certificates

The HPRA issued 2,122 certificates of free sale in 2016 for medical devices manufactured by or on behalf of organisations based in Ireland. These certificates are required for registration / market access purposes to certain non-European countries. This is a reduction on the 2,601 certificates issued during the previous year.

Safety and Quality

Market Surveillance

Medical device surveillance activities are focused on protecting the health and safety of those who use medical devices by seeking to ensure that medical devices available in Ireland and Europe are safe and perform as intended. This role includes continuous surveillance of the market to monitor the regulatory compliance of medical devices after they are placed on the market. The focus is on ensuring that issues detected are appropriately addressed and that there is follow up on any issues or learnings relevant to the pre-market aspects of the device, such as technical standards, design and conformity assessment, to minimise the possibility of recurrence.

Surveillance Cases

Since the European Commission's joint plan for immediate actions came into effect in 2012, the HPRA has almost doubled the number of cases it assesses on an annual basis, with particular focus placed on proactive rather than reactive surveillance activities.

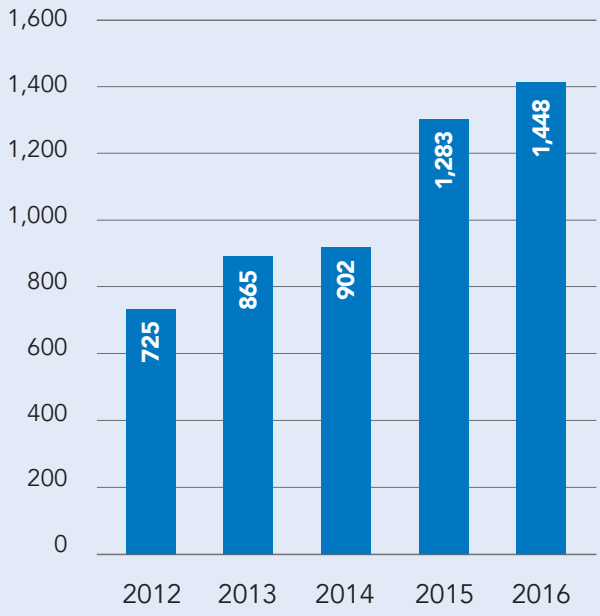
During 2016, the HPRA continued to develop its lifecycle approach to market surveillance and investigated 335 market surveillance cases. In addition, we experienced further increases in the number of notifications of certificate withdrawals or suspensions, and of notifications from other Member States via the European Compliance and Enforcement (COEN) network.

Other market surveillance activities conducted in 2016 included:

- Proactive review of cardiac valve implants;
- Proactive review of certain urogynaecological devices;
- Assessment of a variety of medical device counterfeit issues;
- Assessment of medical device software products;
- *In-vitro* diagnostic medical device issues.

The HPRA also initiated plans for a sampling and analysis programme for a specific type of medical device as part of our proactive surveillance activities.

Market Surveillance Cases - Adjusted*



The accompanying graph shows the annual number of market surveillance cases since 2012. From the start of 2014, the HPRA changed the way we define market surveillance cases and so the figures in the graph have been adjusted* by applying the pre-2014 definition to allow for comparison with 2012 and 2013 figures. The increasing work load in respect of surveillance cases during the past five years is clearly shown in the upward trend.

Joint Action on Market Surveillance of Medical Devices (JAMS) Project

During 2016, the HPRA contributed to the development of an EU-wide joint action project on medical device market surveillance. The project is part of the EU Commission's Health Programme 2014-2020 and is being led by the UK's MHRA, the Dutch IGZ and the HPRA. The HPRA is participating in all elements of the project and is leading a work package on clinical resource and development. We are also a contributing partner to a work package to establish co-ordination and best practice for market surveillance audits of manufacturers by regulatory authorities. This project will run between 2017 and 2019.

COEN Joint Action Project on Reusable Instruments

The COEN Joint Action (JA) 2014 project aims to improve the transparency regarding compliance of medical devices designed to be re-used such as specified surgical instruments. As part of the project, technical information for over 30 reusable devices was requested from seven manufacturers in Ireland for review against an agreed European checklist.

Certificate Notifications

Certificate notifications from Member State authorities relate to certificate refusals, withdrawals and suspensions by notified bodies. While the upward trend in the number of notifications received continued, the 2016 total of 1,062 certificate notifications represented only a small increase compared to 2015. This levelling off in numbers may be a consequence of the joint assessment process for notified bodies which has increased the consistency and performance of these organisations across the EU. The HPRA investigated certificate notifications with implications for the Irish market, those arising from identified safety concerns and major non-compliances, and those arising from a reduction in the designation scope or de-designation of notified bodies.

Technical File Reviews

The HPRA continued its increased focus on review of technical documentation both in the context of market surveillance activities and notified body oversight. A total of 21 detailed technical file reviews were completed in 2016.

Clinical Evaluation Reviews

During 2016, the HPRA increased its activities further in the assessment of clinical data presented by manufacturers to support the safety and performance of their devices. A total of 30 clinical evaluation reviews were conducted. This work was carried out as part of proactive market surveillance activities including in some cases as part of broad reviews of specific product ranges. Clinical evaluations were also triggered as a result of a number of specific device issues.

Designation and Monitoring of Irish Notified Bodies

During 2016, the HPRA conducted its ongoing surveillance activities of the National Standards Authority of Ireland (NSAI) as a notified body for medical devices in Ireland. In addition to the annual surveillance assessment (see also Inspections and Audits on page 41), a number of observed audits of NSAI auditors were conducted as they undertook assessments of quality systems at manufacturing sites.

We also provided technical, clinical and quality system experts to support six joint assessments of medical device notified bodies in other European countries during 2016. We have contributed expert assessors to more EU joint assessments than any other European authority since the scheme was introduced in 2013.

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 2016, we continued to focus our work on the area of user reporting and dissemination of HPRA medical device safety communications.

2016 Reports in Summary

A total of 2,216 medical device vigilance reports were received and assessed representing a slight increase on 2015. Manufacturers accounted for 56% of all vigilance reports received in 2016 while 37% were received from other competent authorities. Of the incidents reported, 38% were as a result of an incident on the Irish market. Of the Irish incidents, 23% were related to an ongoing field safety corrective action.

Concerning the regulatory response to the reports received, 59% resulted in an action being taken in Europe. In Ireland, there were 147 product removals conducted in Ireland during 2016.

The HPRA also issued 98 national competent authority reports during the past year.

2016 Reports by Product Type

Surgical devices, orthopaedic devices and infusion devices accounted for 42% of the total vigilance reports. Reports continue to be received relating to diagnostic imaging and radiotherapy devices. We also continue to receive reports relating to revision procedures associated with the ASR Articular Surface Replacement and ASR XL Acetabular system manufactured by DePuy.

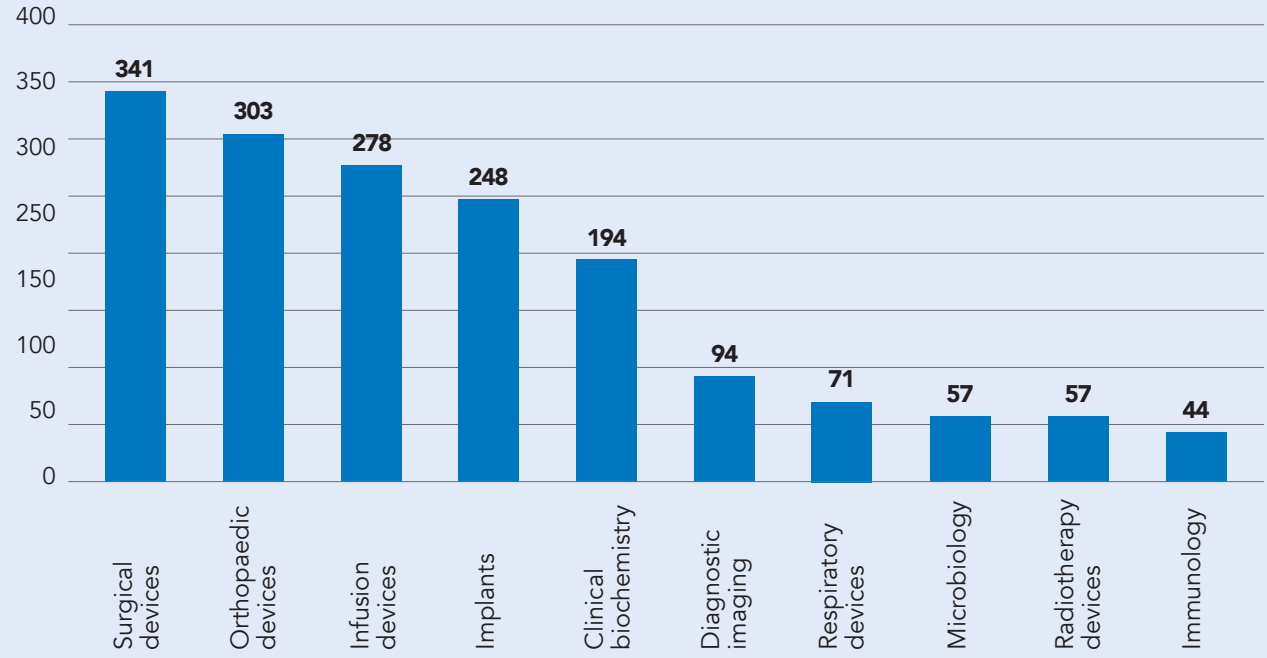
In addition, 411 were received in respect of *in-vitro* diagnostic (IVD) devices, the majority of which related to clinical biochemistry. Field safety corrective actions relating to clinical biochemistry reagents and analysers continued to have a high impact on the number of IVD vigilance cases.

Enhancing the Vigilance System

As part of our focus on strengthening the existing regulation of medical devices, the HPRA continued in 2016 to focus on improving the functioning of the vigilance system both nationally and at an EU level. This included the provision of systematic access for notified bodies to reports of adverse events as well as encouraging healthcare professionals and empowering patients to report adverse events. There was also enhanced co-ordination in analysing reported incidents in order to pool expertise and expedite necessary corrective actions.

As regards the dissemination of safety information, the HPRA delivered a number of workshops throughout the year in conjunction with the HSE. The workshops were focused on promoting user reporting, highlighting the role of the vigilance liaison officer and raising awareness of HPRA safety communications. We also circulated a step-by-step guide on adverse incident reporting to 121 healthcare centres and developed a user engagement page on the HPRA website.

Vigilance Reports Received - Top 10 Product Types



The HPRA continues to develop enhanced systems for the analysis of vigilance data and is an active participant in efforts to promote co-ordination at a European level.

Inspections and Audits

As part of our regulatory role, we are focused on ensuring industry compliance with relevant standards and legislation. In respect of medical devices, this includes proactive audits of manufacturers of Class I devices and 'for cause' audits as required, for example, as part of the follow-up to a defect. We also carry out regular audits of the NSAI, the notified body for medical devices that is designated by the HPRA.

Medical Device Audits

During 2016, 16 audits were performed at both medical device manufacturers and authorised representative facilities, of which:

- two were for cause audits, one of which was in the US;
- eight were reactive audits based on vigilance / market compliance issues;
- four were audits based on proactive market surveillance projects;
- two were of authorised representatives of medical device manufacturers.

Notified Body Assessment

We conducted a full redesignation assessment of the Irish notified body, the NSAI. This assessment was also performed as part of the joint assessment program with the European Commission's Directorate on Health and Food Audits and Analysis and national experts. An observed assessment of an NSAI auditor at a class III implantable medical device manufacturer based in the US was also conducted.

Legislation and Regulation

New Medical Devices Legislation

In June 2016, a political agreement was reached between the European Council, European Parliament and the European Commission on the new Regulations on medical devices and *in-vitro* diagnostic devices. This agreement followed four years of intense negotiation and development of these complex regulatory proposals involving close to 100 meetings of the European Council's Working Party on Pharmaceuticals and Medical Devices. Throughout the negotiation, the HPRA provided regulatory and technical support to the Department of Health for the purposes of representing the national position at the European Council Working Party and in other fora.

The new legislation has been formally adopted and was published in the Official Journal of the European Union during Q2 2017. The Regulations replace the existing Directives. Some elements will become legally binding from the end of 2017 while the remainder will be applicable from 2020 for medical devices and 2022 for *in-vitro* diagnostic devices.

During 2016, the HPRA commenced detailed planning for implementation of the new legislation at organisational and national level. The EU Competent Authorities for Medical Devices (CAMD) network has, at the request of the HPRA, established a taskforce to discuss and co-ordinate implementation of the new legislation. This will help prioritise and coordinate work at a European level while facilitating effective implementation, a consistent approach and understanding of the requirements across Europe, and clear communication and guidance from EU regulators.

A critical component of the HPRA's implementation plan will be to provide affected stakeholders with guidance and communications relevant to the new requirements. This commenced in November 2016 when we hosted our medical device information day in Dublin.

Ongoing Development of the Existing Regulatory Framework

Throughout 2016, the HPRA continued its commitment and leadership in the development of the EU regulatory system for medical devices to strengthen and improve co-ordination and co-operation between medical device authorities, the European Commission and relevant stakeholders.

Central to this improved co-ordination is the work of the Competent Authorities for Medical Devices (CAMD)

network. The HPRA was re-elected to the Executive Group of the CAMD in 2016. We also continued to provide support across all of the different working groups of the European Commission. See Contributing to the European and Global Regulatory Network below for further details.

National Fees for Medical Devices

In 2016, the HPRA finalised a proposal to the Department of Health to introduce a national fee model to cover the cost of all of the HPRA's medical device regulatory activities so as to enable the HPRA to become self-funding in this area. The new EU legislation on medical devices makes specific provision for Member States to levy fees to cover the costs of their regulatory activities. The HPRA has engaged over the last number of years with relevant stakeholders and, in particular, the medical device industry on the introduction of fees and conducted a public consultation in mid-2015 on a proposed model. Following on from this, the model was further clarified to address concerns raised during the consultation process. The fee model was finalised by the Department at the end of 2016 to come into effect from 1 January 2017. The HPRA has committed to complete an annual review of this fee model.

Stakeholders and Partners

Contributing to the European and Global Regulatory Network

Europe

During 2016, the HPRA continued its commitment and leadership in the development of the EU regulatory system for medical devices to strengthen and improve coordination and cooperation between medical device authorities, the European Commission and relevant stakeholders. As the regulatory system for devices is decentralised and mutually reliant, it is essential that there is consistency and cooperation across the European regulatory network.

- Central to this improved coordination EU regulatory system for medical devices is the revamp of the Competent Authorities for Medical Devices (CAMD) network. This network promotes partnership and allows for close cooperation between all of the regulatory authorities responsible for medical devices across Europe and the European Commission. It has driven opportunities for joint working on medical devices issues between authorities, most notably through formal joint actions on medical device market surveillance issues which fall under the EU health programme 2014-2020. During 2016, the HPRA was re-elected to the Executive Group of the CAMD (along with Austria, France, Germany, Sweden, Switzerland and the UK).
- The HPRA continued to provide support across all of the different working groups of the European Commission. During 2016, the HPRA was nominated as the co-chair of the Clinical Investigation and Evaluation Working Group (CIEWG). This adds to our existing co-chair roles at the Compliance and Enforcement Working Group (COEN) and the Notified Body Operations Group (NBOG). During 2016, the HPRA were also key contributors to the establishment, development and delivery of to two training workshops hosted by the European Commission.
- The HPRA participated in meetings to assist in the definition of the ICT requirements to support the implementation of the new European medical devices legislation.

International Medical Device Regulators Forum

Over the past number of years, the HPRA has also been contributing to the development of regulatory systems for medical devices at international level with a view to promoting harmonisation of international regulatory systems and consistency and co-operation between device regulatory authorities across the globe.

In 2016, the HPRA continued its membership of the Management Committee of the International Medical Device Regulators Forum (IMDRF) as part of the European delegation (along with France, Germany and the EU Commission).

During this calendar year, the Management Committee considered a number of ongoing work items including adverse event nomenclature systems, competence and training requirements for pre-market reviewers, NCAR exchange, and registries for medical devices. Regulated product submissions and the requirements for clinical evaluation of software as a medical device were also discussed.

In March, the Management Committee agreed to initiate a new work item: Improving the quality of international medical device standards for regulatory use. This item will be led by Europe. The Committee also approved a number of final documents and launched public consultations on a range of others.

In addition, the HPRA continued its role as the international secretariat for the IMDRF's NCAR Exchange programme. This scheme allows for the exchange of information between international regulatory authorities on identified or emerging safety issues relating to medical devices. During 2016, 18 reports were exchanged between authorities via this system.

Medical Device Single Audit Programme

The goal of the Medical Device Single Audit Programme (MDSAP) scheme is to allow for mutual recognition of quality system assessments of manufacturers by appointed auditing organisations (many of which are EU notified bodies). This scheme helps to promote consistency, efficiency and trust across regulatory systems.

The HPRA continued its contribution to the MDSAP pilot scheme in 2016 while also continuing to encourage the EU's full participation in the scheme once the pilot comes to an end. The HPRA acted as observers for Europe on MDSAP audits and assessment activities. In addition, the HPRA were active participants in MDSAP assessments on a bilateral basis with the MDSAP consortium (Australia, Brazil, Canada, Japan, US). By September 2016, the scheme had 126 manufacturing sites participating in MDSAP assessments.

China Food and Drug Administration

During 2016, the HPRA hosted a high-level delegation from the China Food and Drug Administration (CFDA) to discuss medical device regulation in Ireland and bilateral relationships. Arising from this meeting, the HPRA has held a number of meetings with CFDA officials on medical device issues and we were invited by the CFDA to participate in their annual national conference on medical devices, the China International Medical Device Regulatory Forum. We updated this conference on the regulation of medical devices in Europe and anticipated changes in legislation.

Medical Devices Information Day

In November 2016, the HPRA hosted an information day for medical device manufacturers based in Ireland. The day provided the HPRA with an opportunity to provide an overview of the anticipated requirements in the new EU Regulations and to highlight the expected implications that these will have for manufacturers.

The day was attended by over 200 people and was officially opened by the Minister of State for Health Promotion, Marcella Corcoran Kennedy, TD, who spoke about the importance of medical devices and the Regulations for Ireland. The meeting also was addressed by MEP Mairead McGuinness, Vice-President of the European Parliament, who played a leading role in the discussions of these Regulations at the Parliament. The HPRA provided an overview of the implications of the new regulations and specific technical topics. Invited speakers from the medical device industry, from the UK's MHRA and from the German Ministry for Health, also addressed the audience on the implications of the new legislation for industry, the requirements around unique device identification (UDI) and the European database.

Pictured at the Medical Devices Information Day (l-r): Mairead McGuinness MEP, Vice President of the European Parliament; Marcella Corcoran Kennedy, TD, Minister of State for Health Promotion; and Lorraine Nolan, Chief Executive, HPRA.

Meetings with Stakeholders

During 2016, the HPRA continued its regular liaison meetings with the Irish Medtech Association (formerly the Irish Medical Device Association). Specific meetings were also arranged during the year to discuss the medical device regulations and the introduction of national fees. The HPRA also participated in a number of conferences and events arranged by the Irish Medtech Association including its biannual Global Access Conference, the CEO Forum, a conference on additive manufacturing and a clinical research event hosted in RCSI during European Medtech week.

The HPRA also continued its engagement with the Irish Medical and Surgical Trade Association in 2016 including specific meetings on the introduction of national fees and briefings on the new Regulations and on the HPRA's pilot inspection programme for medical device distributors.

Presentations

The HPRA continues to deliver 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 is delivered to undergraduate and post graduate students studying courses related to the role of the HPRA. A full list of all presentations related to the regulation of medical devices that were delivered during 2016 is provided in Appendix 2.

Publications and Information

Safety Notices

The HPRA continues to disseminate safety information by issuing medical device safety notices and by publishing manufacturers' field safety notices (FSNs). In 2016, 46 safety notices concerning medical devices were published on the HPRA website and issued to subscribers. This represented an increase of 39% on the previous year. Safety notices are also circulated through the HSE eAlert system. In addition, we published 476 manufacturers FSNs on our website in 2016 with a monthly listing sent to subscribers. A total of 33 targeted healthcare professional communications to raise awareness of certain field safety corrective actions were also issued.

Medical Devices Newsletter

This newsletter provides regulatory and safety updates for those working in the medical devices sector and professionals working in the health area who regularly use or purchase medical devices. It provides updates on Irish and European legislation, on safety issues as well as details of HPRA medical devices publications and stakeholder events.

There were two editions of this publication issued in 2016. The following were some of the main topics covered:

- Clinical investigations
- Mobile apps – are they medical devices?
- Automated external defibrillators – managing your device
- The gift of sound: Clinical benefits of cochlear implants
- Cochlear implant research in the Trinity Centre for Bioengineering
- Proposals for new Regulations on medical devices and *in-vitro* diagnostics.

Blood, Tissues and Organs

The HPRA is responsible for monitoring the safety and quality of blood and blood components, tissues and cells, and organs intended for transplantation. We were designated as the Competent Authority responsible for the regulation of blood legislation in 2005, for tissues and cells legislation in 2006 and joint Competent Authority, with the HSE, for organs legislation in 2012.

Authorisation and Registration

Authorisation / Approvals of Establishments

The authorisation of blood establishments, tissue establishments and organ procurement organisations / transplantation centres permits those facilities to carry out specified activities. Authorisation by the HPRA is subject to the review of supporting documentation and inspections during which adherence to relevant European guidance is evaluated (see also under Safety and Quality).

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

Number of Authorisations	2012	2013	2014	2015	2016
Blood establishments	3	4	4	3	3
Tissue establishments	21	23	24	24	25
Organ procurement/ transplantation	0	0	0	4	4

Variations to Authorisations

We regularly process applications from authorisation holders to vary the information on which the authorisation is based. During 2016, we issued 18 variations in respect of tissue establishments, six in respect of blood establishments and six that related to organ procurement organisations / transplantation centres.

Safety and Quality

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 / reactions in donors or recipients and the epidemiological follow-up of donors.

Following collaboration with the National Haemovigilance Office (NHO), we submitted an annual report of serious adverse reactions and events to the EU Commission during 2016. The report reflected information received by the NHO in 2015 and included information on 64 serious adverse reactions and 167 serious adverse events which met the mandatory legislative reporting requirements.

We continued to work with the Irish Blood Transfusion Service (IBTS) and the Department of Health with the aim of formalising arrangements for haemovigilance activities and to provide for the development of an online reporting system, to facilitate simultaneous submission of mandatory reports to both the NHO

and HPRA. Pending finalisation of these formalised arrangements, and access to an online reporting system, the interim arrangements, first agreed for reporting to the HPRA in 2008, continued to operate throughout the past year. These arrangements have facilitated consistency and timeliness in reporting allowing appropriate regulatory oversight.

Tissue and Cell Vigilance

The tissues and cells legislation focuses on standards of quality and safety for donations, procurement, testing, processing, preservation, storage and distribution of human tissues and cells.

We submitted an annual report on serious adverse reactions and events associated with tissues and cells to the EU Commission during 2016. The report reflected information received in 2015 and consisted of some 55 reports, 42 of which met the legislative reporting requirements, including two serious adverse reactions and 32 serious adverse events.

Human Organs for Transplantation

We continued to liaise with the HSE lead and colleagues from Organ Donation and Transplant Ireland in relation to serious adverse reaction and event reporting, in accordance with the legislative provisions in place. During 2016, the HPRA received six reports of serious adverse reactions and events associated with organ donation / transplantation.

Inspections of Establishments

As part of our regulatory role, the HPRA inspects relevant establishments, organisations and centres to monitor compliance with applicable EU guidelines on the quality and safety of blood, blood products, tissues and cells, and human organs intended for transplantation.

Our inspection programme in 2016 consisted of:

- Fifteen tissue establishment inspections of which eight were non-routine;
- Seven routine inspections of blood establishments; and
- Four non-routine inspections of organ procurement organisations / transplantation centres.

Legislation and Regulation

Tissues and Cells: New Commission Directives

Two Commission Directives were published during 2015. These were:

- Directive (EU) 2015/565, amending Directive 2006/86/EC: The purpose of this Directive is to improve the traceability of human tissues and cells from procurement to human application or disposal. It obliges tissue establishments to affix a single European code (SEC) on tissues and cells distributed for clinical application in the EU;
- Directive 2015/566, implementing Directive 2004/23/EC: The purpose of this Directive is to ensure that tissues and cells imported into the EU from third countries meet quality and safety standards equivalent to those tissues and cells procured, processed and distributed in the EU.

The HPRA continued to prepare for the implementation of the new Directives which are due to come into force throughout the EU on or before 29 April 2017.

Stakeholders and Partners

Contributing to the European Regulatory Network

VISTART

The key goal of the EU co-funded Joint Action on Vigilance and Inspection for the Safety of Transfusion, Assisted Reproduction and Transplantation (VISTART) is to promote and facilitate the harmonisation of inspection, authorisation and vigilance systems in the EU for blood, tissues and cells used in transfusion, transplantation and assisted reproductive technology (ART). It is a crucial step towards increasing both collaboration among EU member states and mutual confidence in their respective systems, thus ensuring an equivalent level of quality and safety for substances of human origin (SoHO).

VISTART is co-ordinated by the Italian National Blood Centre and the Italian National Transplant Centre. The HPRA is participating in five of the work packages and is leading one of these, which is a voluntary programme of inter-member state inspection system auditing.

Meetings with Stakeholders

We continued our regular interaction with the NHO during 2016, including discussion of issues of mutual interest and concern at bilateral quarterly meetings.

Information Seminars and Training

Training and updates on the coding and import Directives for human tissue and cells were provided to tissue establishments and the presentations provided were also published on our website.

Presentations

We invest significant time at the HPRA in delivering a programme of presentations and talks at a range of external stakeholder events such as meetings, seminars, conferences and training courses. 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. Details of presentations delivered during 2016 relevant to blood, tissues and organs are provided in Appendix 2.

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. In January 2016, we published a new guide entitled Serious Adverse Reaction / Event Reporting for Human Organs Intended for Transplantation. All of the HPRA guidance documents can be accessed via the publications section of www.hpra.ie.

Cosmetics

The role of the HPRA is to regulate the manufacture, sale and supply of cosmetic products in Ireland. We identify and address cosmetic product quality and safety issues, in conjunction with the HSE, so that a cosmetic product will not compromise the health and safety of the consumer or the person applying the product.

Authorisation and Registration

Free Sale Certificates

Cosmetic companies exporting to third countries may require a certificate of free sale as part as their export dossier. A certificate issued by the HPRA indicates that the product intended to be imported is compliant with EU regulations.

During 2016, there were 369 certificates issued in respect of cosmetic products representing an increase of over 70% compared with the previous year.

Safety and Quality

Market Compliance of Cosmetics

Proactive Market Surveillance

Post-market surveillance of cosmetic products includes a national sampling and analysis programme and involves close co-operation between the HPRA and the HSE's Environmental Health Service and Public Analyst Laboratories in Galway, Cork and Dublin.

During the past year, 471 cosmetic products were sent for laboratory testing with 54 (11%) found to be non-compliant. The largest areas of non-compliance included microbial contamination of talcum powders and face paints, heavy metals in make-up and children's products, phenol in henna products and the presence of kojic acid not declared on the labelling of some skincare creams.

Reactive Market Surveillance

Reactive surveillance includes investigation of quality-related complaints (compliance cases), reports of adverse events relating to the use of cosmetics (vigilance cases) and RAPEX serious risk alerts. There were 163 compliance cases opened of which 150 involved cosmetic products that were deemed to be non-compliant with EU regulations. The majority of non-compliances were in the areas of labelling, the presence of prohibited substances, contamination (mainly microbiological or heavy metals) and unsupported efficacy claims. There were five withdrawals from the Irish market as a result of non-compliances due to issues such as microbiological contamination, counterfeiting and labelling issues.

During the year, 13 vigilance cases (undesirable effect reports) were investigated. These related to hair products, creams, lotions, make-up products and others. A total of 110 RAPEX serious risk alerts were received from other European member states regarding non-compliant cosmetic products. Five of these products were found on the Irish market and removed from sale.

Reactive Market Surveillance	2014	2015	2016
Compliance cases opened	105	107	163
Compliance cases closed	109	99	171
Vigilance cases opened	21	11	13
Vigilance cases closed	14	20	14
RAPEX alerts received	100	56	110
Recalls/withdrawals from the Irish market	1	4	5

Stakeholders and Partners

Regulatory Information Seminars and Training

We provided training and support for HSE environmental health officers (EHOs) and Public Analyst's Laboratories in the monitoring of retailers of cosmetic products. The training and support included hosting the National Cosmetics Surveillance Forum and Open Cases meeting as well as presenting at two training days for EHOs.

The first of these was for training of the newly appointed steering committee of the Environmental Health Service on the cosmetic regulations, focusing on the compliance notice process.

The second training day was open to the wider group of EHOs and focused on the cosmetic regulations and market surveillance of retailers.

We also hosted an information stand at the Professional Beauty Show held in the RDS, Dublin in October. We provided information on the regulatory requirements for cosmetics to beauty professionals both participating in and attending the event.

Publications and Information

Guidance Documents

We developed a Guide to Essential Oils in Cosmetics on behalf of the Council of Europe.

Presentations

Presentations enable the HPRA to provide cosmetic stakeholders with relevant, up-to-date regulatory information. We presented at two cosmetic products conferences in 2016. A full list of all presentations delivered by the HPRA during the year is provided in Appendix 2.

471

cosmetic products sent for laboratory testing

Controlled Substances

Authorisation and Registration

Processing of Applications for Licences and Registrations

Controlled Drugs

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

Licensing activity consists primarily of export and import licences, and letters of no objection. Data for the past five years are outlined in the accompanying table.

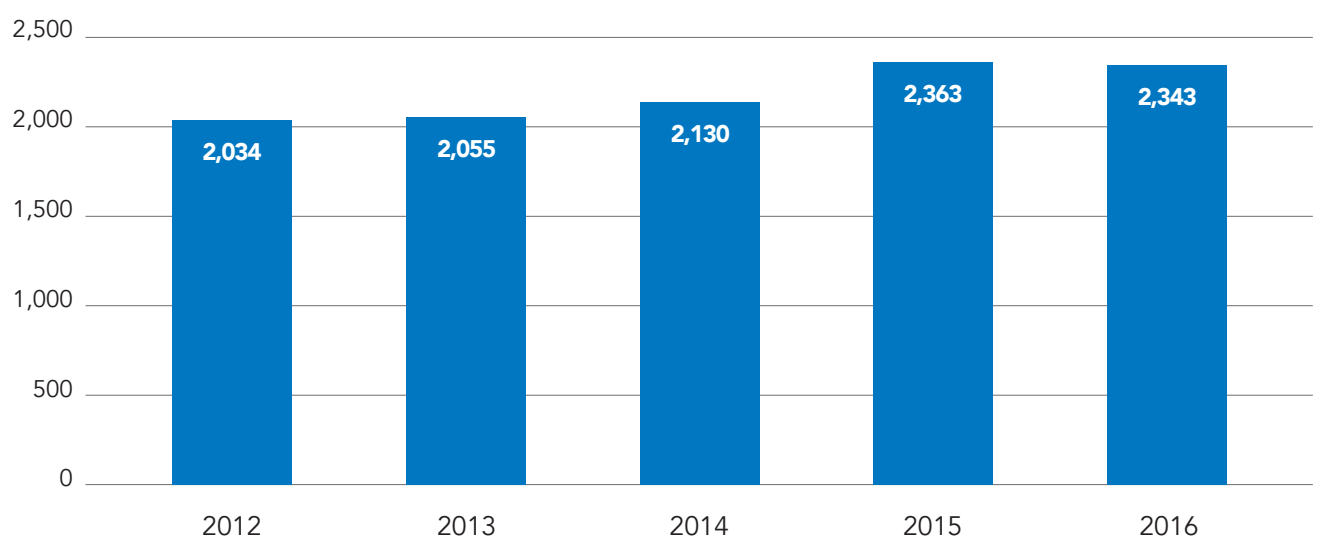
Precursor Chemicals

Precursor chemicals are substances which are used in a wide variety of industrial processes and consumer products, such as medicines, flavourings and fragrances but additionally have the potential to be diverted for use in the chemical synthesis of illicit substances.

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

Precursor Chemicals Licensing Activity	2012	2013	2014	2015	2016
Total	70	27	46	32	16

Controlled Drugs Licensing Activity



Legislative Developments

Misuse of Drugs

The Misuse of Drugs (Amendment) Act 2016 was passed by the Oireachtas in July. The primary purpose of the Act is to protect public health by bringing certain substances which are open to misuse and known to be traded on the illicit market, under the scope of the Misuse of Drugs legislation, thereby aiding the law enforcement activities of An Garda Síochána and Revenue's Customs Service. The Act will come into operation on foot of commencement orders and will enable the Minister for Health to introduce new regulations.

Stakeholders and Partners

Contributing to the European Regulatory Network

We were involved in the development of a European Guidance for Operators that is aimed at stakeholders involved in the distribution of precursor chemicals.

2,343

The number of controlled drug licences processed in 2016

Scientific Animal Protection

The HPRA is the competent authority in Ireland responsible for the implementation of EU legislation (Directive 2010/63/EU) for the protection of animals used for scientific purposes. We are committed to ensuring that the care and use of animals for scientific purposes is in line with the 3Rs principles (replacement, reduction and refinement).

Authorisation and Registration

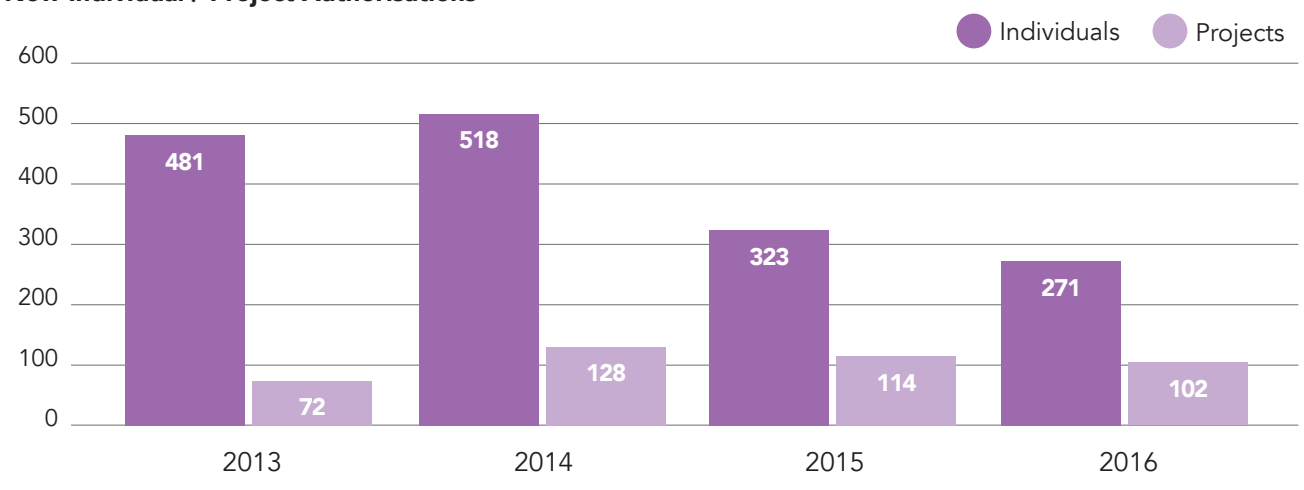
Authorisations of Establishments, Projects and Individuals

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

During the past year, the total number of new individual and project authorisations granted decreased somewhat when compared to 2015. Please note that the higher level of individual authorisations during the previous two-year period was due to the legal requirement for existing establishment personnel to apply for individual authorisations before the end of 2014. Hence, there were a large number of applications for individual authorisations, which are valid for five years, in that period. It is likely that the application numbers for 2016 and 2015 mainly reflect new individuals joining the sector.

We also processed 277 amendments to existing authorisations throughout the year. The majority of these amendment applications (170) were for project authorisations, which, depending on the nature of the amendment requested, may involve significant assessor input. The remaining amendment applications

New Individual / Project Authorisations



were for individual authorisations (97) and breeder / supplier / user establishment authorisations (10). There were 16 renewal applications processed. Two of these were to renew breeder / supplier / user establishment authorisations while 14 were to renew project authorisations.

National Statistical Report

In July, the HPRA published its third annual statistical report on the use of animals for scientific purposes in Ireland. We are required to collect and make publicly available, on an annual basis, statistical information on the use of animals in procedures, including information on the actual severity of the procedures.

Safety and Quality

Inspection Programme

The second key component of our work involves the inspection of animal facilities to monitor animal welfare standards and compliance with legislation. Our inspections, an increasing percentage of which have been unannounced, follow a risk-based approach with a focus on the welfare of animals used for scientific purposes. Inspections also allow us to verify compliance with the scientific animal protection legislation.

During 2016, there were a total of 33 inspections performed, 48% of which were unannounced. This compares with 2015 when 28% of the 29 completed inspections were performed on an unannounced basis.

Stakeholders and Partners

Contributing to the European Regulatory Network

In relation to the EU network on scientific animal protection, the HPRA contributed to deliberations in respect of a number key topics and played an active role as part of the European Commission's National Contact Point Network for the implementation of scientific animal protection legislation.

Contributing to the National Initiatives

We provided support to the National Committee for the Protection of Animals used for Scientific Purposes in relation to their role to nurture the creation of a culture of care at the establishments concerned. The committee met on two occasions during 2016.

We continued to liaise with Science Foundation Ireland and the Health Research Board to explore ways of raising awareness of the 3Rs amongst the research community in Ireland. One significant development was the agreement among our three agencies to host a conference focused on promoting awareness of the 3Rs amongst the research community in Ireland during May 2017. Planning for the event, which was co-ordinated by the HPRA, commenced during the latter part of the year.

Presentations

We delivered six Laboratory Animal Science and Training (LAST) lectures in relation to EU legislation and the role of the HPRA. We also delivered a similar lecture to the Association for Veterinary Teaching and Research Work in UCD.

Publications

Regulatory Updates

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

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

33

The number of inspections of establishments completed in 2016

Organisation-Wide Initiatives and Development

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

Organisation-Wide Programmes

Scientific Affairs

Innovation Office

As part of our strategic goal to support innovation, the HPRA's Innovation Office was launched in 2016. The main function of the office is to provide regulatory support and advice to individuals or groups who are developing innovative health products or technologies. Queries can relate to any area within the HPRA's remit and can be submitted at any stage of development.

Although the Innovation Office was launched in late 2016, by the end of the year nine queries had already been received. The queries related to novel medical devices and medicinal products, and to innovative manufacturing and testing technologies. Responses to all queries were issued within the standard 20 day timeframe.

Horizon Scanning

The HPRA has identified the need to perform horizon scanning to ensure that we are in a position to effectively and appropriately regulate innovative products and technologies that are currently under development and thereby support the advancement of novel approaches within the life sciences sector.

To this end, we established an internal horizon scanning group to proactively identify such innovations and help to ensure that the HPRA is prepared for future developments within our remit. As part of its work, the group will consider whether changes to regulatory tools or approaches and / or the development of additional knowledge and expertise within the HPRA is required. This group held its first meeting in 2016 and will continue its work in 2017.

Communications

Communications Strategy 2016 – 2020

At the beginning of the year, the Authority of the HPRA approved the Communications Strategy 2016 – 2020. The communication activities identified in the strategy are intended to support the successful delivery of our new strategic plan and, in particular, the goal to ensure that users of health products are as well informed as possible. Open and proactive communications will also be critical to maintaining public trust and confidence in the regulatory system.

This strategy document sets out the HPRA's approach to communications over the five year period and outlines our core communications objectives, the key

target audiences we need to reach and the various channels and platforms we will employ to reach them. A particular focus in the coming years will be to increase public awareness of the HPRA and our role. There is also an emphasis on developing our consumer communications and patient engagement initiatives.

Public Information Campaign

As part of our commitment to increasing consumer communications, we launched our first ever national public information campaign in September to raise awareness of the safe and effective use of medicines. Entitled 'For the full benefit, take three minutes', the campaign was officially launched by Minister for Health, Simon Harris TD, and ran over six weeks across national and regional radio as well as digital and print media. The focus of the adverts was to advise members of the public that to get the most benefit from their medicine, they should take the time to always read the information printed on the packaging and / or the product leaflet. This information includes essential details such as the correct dose, instructions for use and potential side effects.

The campaign was developed in response to our ongoing research programme which shows a worrying downward trend in the number of consumers not reading product information both for over-the-counter and prescription only medicines. Data published by the HPRA in 2016 showed that one in four (26%) adults admit that they never read the product information for an over-the-counter medicine with one in five (21%) never reading the information for a prescription only medicine. The corresponding figures from the same survey conducted in 2010 were 14% and 12% respectively.

The campaign will be repeated on a number occasions during 2017.

Market Research

During 2016, we published results and findings from a series of national consumer surveys. Our research programme assists us in better understanding the general public's views, opinions and behaviours in respect of the range of health products that we regulate.

Where necessary and appropriate, we will respond to specific findings by changing current HPRA practices or by developing new initiatives and campaigns focused on consumers. An example of this was the development of our public information campaign to address the fact that fewer Irish adults are reading the product information that comes with a medicine. This finding was highlighted in the results of a survey to examine how Irish consumers source information about health in general and, more specifically, the medicines that they take. The results of this research, which also examined the use of the internet as a source of medicines information and supply, were published in May.

Additional research published during 2016 included:

- Human medicines: Further research examining the extent to which members of the public read specific sections of the product information leaflet such as the directions for use and the potential side effects.
- Veterinary medicines: The levels and nature of pet ownership in Ireland as well as the extent to which owners purchase medicines for their animals. This research also focused on the percentage of pet owners reading the printed information supplied with veterinary medicines.
- Sunscreens: The extent to which consumers understand the terminology and symbols printed on the labelling of sunscreens such as UVA and UVB, the two harmful rays from the sun, and the sun protection factor (SPF). This research also asked consumers to rank in order of importance the issues they take into consideration when choosing to purchase a specific sunscreen product.

Summary results from all the research published by the HPRA during 2016 is available from our website.

Media Communications

Throughout the year, we continued our media communications programme to proactively communicate important safety messages and to build awareness of the role of the HPRA. We issued 23 press releases and statements concerning safety and regulatory issues to ensure consumers, healthcare professionals and other stakeholders received timely and accurate information and advice. In a number of instances, these communications resulted in national and regional media interviews with a HPRA spokesperson.

Among the issues highlighted via press releases during the past year were:

- HPRA launches strategic plan for 2016 to 2020
- New campaign urges people to Take 3 Minutes to get full benefit of medicines
- HPRA consumer research reveals fewer Irish adults reading important product information
- Almost 750 potentially life-saving defibrillators require urgent updates
- Global operation targeting falsified medicines – Over 60,000 units of illegal prescription medicines detained in Ireland
- Majority of pet owners take great care when giving medicines to their pets
- Sunscreens - the burning questions: HPRA national survey findings on consumer understanding of sunscreens

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

In addition, we responded to more than 440 initial and follow-up queries from national, local and specialist media during the year. Drafting responses to such queries involves subject matter experts from across the organisation.

Awards for Excellence in Public Relations

In July, the HPRA was confirmed as one of the winners of the Awards for Excellence in Public Relations 2016. Along with our public relations advisor, Weber Shandwick, we received the Best Healthcare Campaign award for our work in promoting the safe use of cosmetic products. These annual awards are considered a benchmark for excellence in public relations and showcase the very real value of proactive and planned media engagement.

The HPRA campaign, which was developed by a cross-functional team and phased throughout the second half of 2015, was based around the seasonal use of a number of specific cosmetic products. In addition to highlighting important consumer safety advice, the campaign also served to build awareness of our regulatory role in respect of cosmetic products.

Online and Digital Communications

Website

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

Developments in respect of the HPRA website during 2016 included the following:

- Implementation of a pay-per-click (PPC) campaign. PPC is an internet advertising model used to direct traffic to a website rather than relying solely on organic visits.
- Development of new pages and content to support the launch of our public information campaign.
- Increased new outgoing MRP/DCP web content for relevant veterinary stakeholders.
- Launch of a new section promoting the HPRA's Innovation Office and incorporating an online query form.
- Design and publication of a series of infographics and other images to highlight and simplify the presentation of key safety and regulatory information.

We continuously monitor and analyse key statistics in respect of the website including overall visitor numbers and the most widely viewed pages. Among the key findings from 2016 were:

- Almost 284,000 unique visitors accessed our website during the past twelve months representing a 38% increase compared to 2015. There were in excess of 682,000 visits in total in 2016.
- Of those who accessed the site, 40% were new or first time users.
- As in previous years, the most popular sections of the website were the human and veterinary medicines listings, and the medicines regulatory information sections (which include publications and forms).

Twitter

In November, we launched our @TheHPRA Twitter account. Social media is a key tool in supporting our communications activities and also serves to direct additional traffic to the HPRA website.

Our Twitter content incorporates tweets in respect of all products and areas that we regulate. There is a particular focus on urgent safety updates and recall notices, especially where these contain safety advice for patients and members of the public, HPRA events and consultations, publications and media / news announcements.

We also retweet content from other public sector bodies and organisations if we feel it will be of interest to our followers. We are committed especially to prompting important public health initiatives and messages.

A HPRA Twitter policy was published to coincide with the launch of @TheHPRA and this document explains to users how we manage our Twitter presence and how we engage with followers.

Publications

Innovation Office Leaflet

In addition to the product specific publications highlighted earlier in this report, we also designed and published an information leaflet entitled Supporting Innovation through Regulation and Science. The leaflet, which highlights the activities of the HPRA's Innovation Office, is in a question and answer format and outlines the nature of the innovation support we can provide in addition to the process our stakeholders can use for submitting queries.

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 2016, we completed our annual consultation in respect of the regulatory fees proposed for the coming year. We also published the outcome of the consultation (which commenced in 2015) on the introduction of a fee based funding model to support the conduct of medical device regulatory activities by the HPRA.

We also make submissions to third party consultations where the topic is related to or impacts our regulatory functions and the broader public health agenda. In 2016, we provided comments in respect of 15 public consultations from the Department of Health, the Department of Jobs, Enterprise and Innovation, the European Commission, the Royal College of Physicians of Ireland and from a number of other national agencies.

Event Management

Information and Training Events

HPRA information days, seminars and training workshops provide regulatory guidance and updates to a range of stakeholders. We held nine events in 2016 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.

As well as presentations from our staff and, where appropriate, external contributors, the events enable all attendees to submit questions, seek clarifications and network with colleagues. While additional details concerning a number of these events are provided in earlier sections of this report, the following is a summary of the HPRA organised information sessions and meetings held during 2016:

- Four workshops focused on the requirement for manufacturers / MAHs to add safety features to the outer packaging of specified medicines for human uses were hosted in Athlone, Cork and Dublin during May.
- A training workshop for clinical / safety assessors was organised in September in collaboration with the EU Network Training Centre (EU NTC).
- Advanced Quality Risk Management (QRM) training, which was hosted in the offices of the EMA in September, was organised jointly by the HPRA and the Pharmaceutical Inspection Co-operation Scheme (PIC/S).
- The HPRA hosted an informal meeting of the Committee for Advanced Therapies (CAT) in October on behalf of the Slovakian regulatory authority.
- In November, the HPRA hosted an information day for the medical devices industry to provide an overview of the anticipated requirements for manufacturers under the new EU Regulations. This seminar, which included a number of external guest speakers, was attended by approximately 250 delegates.
- A meeting was held in November under the Joint Action on Market Surveillance of Medical Devices (JAMS).

BT Young Scientist and Technology Exhibition 2016

Thousands of students as well as teachers, parents and members of the general public from all over Ireland again visited the HPRA's exhibition stand at the annual BT Young Scientist and Technology Exhibition. The exhibition took place in mid-January in the RDS, Dublin.

Our stand highlighted the importance of the safe and appropriate use of medicines, medical devices and cosmetic products. We also sponsored and presented a special award focused on health product safety.

Customer Services

Almost 3,000 queries were received and actioned by the customer services team during 2016. These included queries from industry representatives, healthcare professionals and members of the public. A large proportion of the queries received related to compliance issues, product variations and the product information for medicines. 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.

Information and Transparency

Freedom of Information

The HPRA is subject to the Freedom of Information Act 2014. The Act asserts the right of members of the public to obtain access to official information to the greatest extent possible consistent with public interest and the right to privacy of individuals. During 2016, the HPRA received 26 Freedom of Information requests. Of these, three were requests for personal information. The HPRA has a policy of posting a disclosure summary of non-personal FOI requests on our website for reference purposes. The 2016 summary can be viewed on www.hpra.ie.

Protected Disclosures

During 2016, there were concerns raised by external persons in relation to organisations regulated by the HPRA. These concerns were handled under the HPRA's process for protected disclosures. All eight were investigated, of which three are still ongoing and five have concluded. Any matter arising from the investigations was addressed, and the outcomes were communicated to the discloser where known.

During the same period, no disclosures under the Protected Disclosures Act were received from HPRA staff members.

Parliamentary Questions and Requests for Information

The HPRA received and responded to 53 parliamentary questions. There were also a further 116 requests for information received from the Department of Health, other government departments or members of the Oireachtas during the year. Of the total number of queries (169), the largest category related to human medicines (111) and concerned topics such as adverse reactions, the availability or supply of medicines, reclassification / switching, clinical trials and counterfeit products.

Data Protection

The HPRA is subject to the Data Protection Acts 1988 and 2003. The Acts gives individuals the right to obtain a copy, clearly explained, of any personal information relating to them kept on computer or in a structured manual filing system or intended for such a system by any entity or organisation. During 2016, we received one data access request.

Complaints

No complaints regarding the standard of service provided by the HPRA were received during the year.

Authority and Committees

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

- The Authority of the HPRA met seven times in 2016 and considered a number of strategic matters including corporate policy, planning and finance matters. The latter included monthly management accounts, annual budgets and the financial statements for 2015. The Authority also reviewed update reports from the Statutory Advisory Committees and the Audit Committee. In addition, it reviewed the licences for all medicinal healthcare products as approved by the Management Committee.

The number of meetings attended by each Authority member during 2016 was as follows:

Authority Member	Number of meetings held during the period the member was on the Authority	Number of meetings attended during the period the member was on the Authority
Ms. Ann Horan (Chairperson)	7	7
Mr. Pat Brangan	7	7
Mr. Wilf Higgins	7	6
Mr. David Holohan	6	6
Prof. Mary Horgan	7	5
Mr. Brian Jones	6	5
Prof. Elizabeth Keane	7	7
Prof. Caitriona O'Driscoll	7	7
Dr. Diarmuid Quinlan	7	5

- The Audit Committee, a subcommittee to the Authority, met four times in 2016. Further details are provided in the HPRA's Financial Statements.
- The Advisory Committee for Veterinary Medicines met twice as did the Advisory Committee for Medical Devices.
- The Herbal Medicines Sub-Committee, a sub-committee to the Advisory Committee for Human Medicines, met once. The Clinical Trials Sub-Committee is also a sub-committee to the Advisory Committee for Human Medicines and it met 12 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 2016.

Decisions of the Authority

The terms of reference of the Authority, which are published on the HPRA website, include an overview of how the Authority operates, an overview of all decisions taken by the Authority and those devolved to the Management Committee.

The following decisions are reserved functions of the Authority:

- The Authority takes decisions relating to very significant and serious public and/or animal health matters except in circumstances where a meeting of the Authority cannot be convened, in which case the Management Committee takes the decision and informs the Chairperson at the earliest opportunity and the Authority as soon as is practical.
- The Authority refuses applications, or suspends, revokes or terminates authorisations as set out in legislation except in circumstances where:
  a) the urgency is such that a meeting of the Authority cannot be convened, or
  b) the application or authorisation is subject to a binding European decision, or
  c) the application or authorisation is for a clinical trial or clinical investigation;

  in which case the Management Committee takes the decision and informs the Authority.
- Through its Audit Committee, the Authority approves the internal financial controls and the financial audit function and satisfies itself that the financial controls and systems of risk management are robust and defensible. The Authority appoints the internal financial auditor.
- The Authority approves the investment policy, major investments, capital projects and the terms of major contracts.
- Significant acquisitions and the disposal or retirement of assets above a threshold set by the Authority are subject to Authority approval.
- The Authority approves treasury policy and risk management policies.
- The Authority approves corporate plans as required.
- The Authority approves the annual budget, monitors expenditure and supervises the preparation and submission of the annual statutory accounts.
- The Authority makes an annual report on the activities of the HPRA, including a financial statement, to the Minister for Health. This report is then published.
- The Authority selects and appoints the Chief Executive, with the consent of the Minister for Health. The terms of office and the remuneration of the Chief Executive are determined by the Minister for Health, after consultation with the Authority and with the consent of the Minister for Finance. The Authority, through its Performance Review Committee, conducts a process of annual performance appraisal of the Chief Executive. Succession planning for the role of Chief Executive is also undertaken by the Authority.

Organisational Management and Development

Human Resources and Change

In line with the HPRA's strategic focus on the development of internal capabilities, the launch of the Human Resources and Change Strategy 2016-2020 was a significant deliverable in 2016. Using a framework of six core themes, the strategy identifies and delivers key supports required by the organisation to achieve its goals over this five year period. Under each theme, an action plan for 2016 highlighted the main priorities for the year.

As part of the development and launch of the strategy, a branding exercise was completed to create an internal human resources and change logo. An organisational communications programme, which included an online introductory video, was also implemented.

Retention and Engagement

The ability to retain and engage highly skilled staff in light of improvements in the economy and ongoing developments in the sectors we regulate continues to present a challenge for the HPRA. As part of our ongoing initiatives to foster high levels of engagement, and therefore ensure the retention of our staff, we continued throughout 2016 to deliver our core range of programmes such as our;

- Health and wellbeing and lunchtime learning programmes which are focused on five main areas; physical, financial, nutritional, emotional, and general health and wellbeing. We continue to carry out research into how to further develop and enhance these offerings using survey feedback. The receipt of a Silver Active@Work Award was a key achievement in 2016 and recognition of our work in this area in recent years;
- Suite of management development supports and initiatives including; new manager training, coaching and mentoring, developing others training, and performance development programme (PDP) training for managers.

With a view to extending our retention and engagement programme, among the research activities conducted in 2016 for future initiatives were;

- Completion of a number of employee surveys, workshops and focus groups to gain insight into areas such as flexible working patterns and management competency frameworks;
- Commencement of research into the development of a tailored management development programme to further support and promote management and leadership skills;
- Continuation of research into the optimum approach to establish engagement levels.

Organisation Design

To support our focus on cross-department engagement and knowledge sharing, we continued to successfully deliver our organisational awareness programme during 2016. There was a total attendance of 333 staff across 16 separate events. Externally, we continued to support knowledge sharing and cross-fertilisation of skills by keeping up-to-date with the ongoing work of the EU Network Training Centre.

Career Development

Succession planning was an area of major focus in 2016. A comprehensive review of succession planning frameworks resulted in agreement to take a risk-based approach to this key component of career development. The required tools to complete the planning process were developed for implementation in 2017.

With a view to establishing specific roles that employees can develop into over time, on the basis of the acquisition of related skills and experience, an initial step in 2016 was the commencement of a research project to determine the value and feasibility of introducing a formal graduate recruitment programme in the HPRA.

Change Management

The Human Resources and Change department continued to provide change management support to two significant organisation-wide projects:

- Health Systems Strengthening Programme: The HPRA is providing technical assistance to the Zambia Medicines Regulatory Authority (ZAMRA) under the EU funded Health Systems Strengthening (HSS) programme. The change management team maintained a lead role in planning for the delivery of regulatory and capacity building support to ZAMRA during 2016. The main areas of work involved supporting the identification and provision of short term experts in addition to facilitating a week-long study visit from a Zambian delegation to the HPRA in November.
- EOLAS: As well the provision of ongoing support as project lead in the area of change management, leadership and development support, the department was also allocated to assist with the development of training that is required for the introduction of phase one.

The public sector reform agenda continues to have a direct impact on employment terms and conditions. In this regard, a comprehensive communications programme outlining the associated impact on individual employees was delivered during 2016.

Talent Management

The HPRA takes an integrated approach to correctly identifying our resource requirements. Our focus is on recruiting the right people with the right skills at the right time while also ensuring we develop our talent to maximise effectiveness. This was an area of significant activity during 2016 with a particular focus on:

- Working with the organisation to maintain resource requirements through internal redeployment, training development and recruitment activities as required, while operating within public sector employment control frameworks;
- The delivery of the leadership and development programme of activities to support staff in their roles. This included the provision of internal training such as personal effectiveness, time management and telephone techniques, facilitating expert witness training in-house and providing access to a range of activities externally;
- The completion of research to identify the optimum approach to, and key requirements for, a technology-based learning system.

HR and Change

In the development of its strategy for 2016-2020, the Human Resources and Change department continued to focus on how we can add value, operating as internal experts to the business. Helpful in this regard was the identification of our vision 'to enhance organisational performance by developing and delivering innovative solutions' and our mission 'to work in partnership with the organisation delivering a range of supports and services that maximise positive outcomes for all in the HPRA'.

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 2016 a number of significant projects and initiatives were progressed.

Extensive work continued on the development of the HPRA's new workflow technology solution, EOLAS, which will provide the organisation with a single workflow and data management system to support its regulatory activities. The phased development of the system will coincide with the implementation of new EU standards for regulatory data management and will commence with the implementation of the system in the Veterinary Sciences department in 2017.

There was also significant work carried out on the internal information technology infrastructure, making it more reliable and robust to support the requirements of the organisation. These improvements included our backup and recovery capabilities, system security and disaster recovery.

In addition, as outlined earlier in this report, the HPRA contributed IT support in connection with a range of national and European initiatives and platforms. Nationally, this included the launch of the new Emergency Medicines Registration System,

the provision of hosting services to a number of organisations and contributing to the development of data set standards for ePrescribing and an electronic medicinal product reference catalogue. We also continued to support the exchange of information between stakeholders in areas such as the medical products database for both human and veterinary products, interchangeable medicines and data for clinical and pharmacy systems.

At a European level, the HPRA again played a significant role in the development of European telematics strategies, standards and technologies. We were members of the EU telematics management board, the network data board and the e-submissions group and led on a number of key initiatives relating to single submission portals and data standards. The HPRA also participated, as part of a European consortium, in the European Commission's Horizon 2020 research programme on the openMedicine project. We continued the development and management of the Common Electronic Submission Portal (CESP) on behalf of the wider EU regulatory community in addition to assisting the medicines authority in Malta with the development of a new regulatory management system for product authorisation.

Quality Management

During 2016, the HPRA's quality management system continued to be extended with the deployment of policies and procedures for cosmetics regulation, retail sales compliance and 'risk-based' approaches to regulatory activities.

As part of the development of EOLAS, the new workflow and case management system, we continued working on a new management policy and procedures document. In addition, we completed the document tagging structure and began preparing some standard document templates for use in the new system.

Finance

The HPRA's finance section is responsible for managing and safeguarding the finances of the HPRA. It must ensure that the organisation fulfils its legislative requirements and applies best practice to the governance of its affairs. All procedures are carried out using standard operating procedures under the quality management system. The 2016 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.

During 2016, as part of an on-going programme to integrate and streamline HPRA internal corporate processes, we implemented a new IT system for financial management and control.

Legal

Throughout 2016, the legal section advised on the implementation of new legislation in addition to other relevant issues. The section dealt with various legal queries from across the organisation. It also attended and presented at the European meeting of lawyers held under the European Presidency.

Overview of Energy Usage in 2016

Since 1 January 2011, the HPRA, as a public sector body, is required to report annually on its energy usage and actions taken to reduce consumption in accordance with the European Union (Energy Efficiency) Regulations 2014 (S.I. No. 426 of 2014). As an organisation, we use electricity for lighting, air conditioning or heating as required and the provision of hot water. Natural gas is used for central heating.

In 2016, the HPRA consumed 1040 MWh of energy consisting of:

- 708 MWh of electricity;
- 332 MWh of fossil fuels;
- 0 MWh of renewable fuels.

Actions Undertaken in 2016

In the past year, we continued to focus on energy performance by maintaining framework agreements for the supply of both electricity and natural gas. Both of these framework agreements were established by the Office of Government Procurement for the supply of electricity and natural gas to the Irish public sector. The agreements are intended to maximise volume discounts and provide for reductions in administrative and transaction costs for suppliers and public sector purchasers. During 2016, HPRA cost savings were in the region of 2.7% for electricity and 5% for gas (compared to the cost of going directly to the market).

Also in 2016, we formed a partnership with the Office of Public Works (OPW) in relation to the Optimising Power @ Work initiative to effect energy savings through staff engagement. We also partnered with the

Sustainable Energy Authority of Ireland (SEAI) to focus on energy saving through the Energy Map programme. As part of these initiatives, the HPRA has set up an in-house Energy Efficiency Project Team, sponsored by the Deputy Chief Executive, to maintain focus on energy reduction.

Total Energy Savings

The HPRA has been highly focussed on reducing energy usage for the past number of years. This is evidenced by the 2016 SEAI report for the HPRA which confirmed that as an organisation we have improved our energy usage by 27.1% since 2009. As a result of our partnership with the OPW Optimising Power @ Work initiative, which was launched in the HPRA in October 2016, we had reduced energy usage by up to a further 2.7% by the end of 2016 progressing the organisation ever nearer to the 2020 public sector 33% energy reduction target.

Actions Planned For 2017

We are committed to reducing our energy usage by 33% by 2020 in accordance with S.I. No. 426 of 2014, the National Energy Efficiency Action Plan 2014 and the European Energy Efficiency Directive (2012/27/EU). As a result, we will maintain our focus in 2017 on our partnership agreements with the OPW and the SEAI. We also intend to maintain energy performance by continuing our participation in newly contracted framework agreements for the supply of both electricity and natural gas to the public sector. It is anticipated that both these framework agreements, accessed via the Office of Government Procurement, will deliver savings when compared to the costs of going directly to the market. It is important to note that the Office of Government Procurement contract rates are fixed until early 2019 for electricity and gas.

Financial Statements for the Year Ended 31 December 2016

Authority Members and Other Information

Authority:
Ms. Ann Horan, Chairman
Mr. Pat Brangan
Mr. Wilfrid Higgins
Mr. David Holohan
Prof. Mary Horgan
Mr. Brian Jones
Dr. Elizabeth Keane
Prof. Caitriona O'Driscoll
Dr. Diarmuid Quinlan

All Authority members are appointed by the Minister for Health.

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

Eversheds
1 Earlsfort Centre
Earlsfort Terrace
Dublin 2

Head Office:
Kevin O'Malley House
Earlsfort Centre
Earlsfort Terrace
Dublin 2

Auditors:
Comptroller and Auditor General
3A Mayor Street Upper
Dublin 1

Corporate Governance

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

The HPRA is committed to the highest standards of Corporate Governance and has implemented the "2009 Code of Practice for the Governance of State Bodies" issued by the Department of Public Expenditure and Reform. This Code of Practice incorporates many of the principles under which the HPRA operates, taking account of the size and legal nature of the organisation.

For the year ended 31 December 2016, the HPRA was in compliance with the 2009 Code of Practice. A revised Code of Practice was issued in August 2016 and applies to all financial reporting periods beginning on or after 1 September 2016. The HPRA will comply with the revised Code in respect of its 2017 financial statements.

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

Audit and Risk Committee

The HPRA has an audit and risk committee comprising three Authority members, which met on four occasions during 2016. This committee is responsible for reviewing internal control matters, together with any other issues raised by the external auditors, the Authority or management. The external auditor is invited annually to meet with the audit and risk committee to brief them on the outcome of the external audit, and the audit and risk committee also meets annually with the internal auditor. During 2016, the internal auditor carried out internal audits on the areas of fixed assets and budgeting. The audit and risk committee has also been involved with the review of the quality systems as described below.

Quality Systems

During 2016, 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 and risk committee.

Remuneration Policy - Authority Members and Executive Directors

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

Internal Control

The Authority is responsible for the HPRA's systems of internal control. Such systems can only provide reasonable and not absolute assurance against material misstatement or loss. The systems of internal controls in use in the HPRA are described more fully in the Chairman's report on page 66.

Statement on Internal Financial Control

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

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

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

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

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

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

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

   The system of internal financial control is monitored in general by the processes outlined above. In addition, the Audit and Risk Committee of the Authority reviews specific areas of internal control. The HPRA has outsourced the internal audit function to an independent professional firm. During 2016 two reviews were conducted. The Audit and Risk Committee considers reports from internal audit and recommendations from the Comptroller and Auditor General arising as a result of the external audit.

4. The Authority have carried out a review of the effectiveness of internal financial control, in order to demonstrate compliance with the 2009 Code of Practice. This review was carried out at its meeting on 15 March 2017.

Ms. Ann Horan
Chairman to the Authority

Date: 16 June 2017

Statement of Authority Members' Responsibilities

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

In preparing those statements the Authority is required to:

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

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

On behalf of the Authority:

Ms. Ann Horan
Chairman

Date: 16 June 2017

Mr. David Holohan
Authority Member

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 2016 under the Irish Medicines Board Act, 1995. The financial statements comprise the statement of income and expenditure and retained revenue reserves, the statement of financial position, the statement of cash flows and the related notes. The financial statements have been prepared in the form prescribed under Section 18 of the Act, and in accordance with generally accepted accounting practice as modified by the Minister for Health in relation to accounting for superannuation costs.

Responsibilities of the Board of the Authority

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

Responsibilities of the Comptroller and Auditor General

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

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

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

Scope of audit of the financial statements

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

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

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

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

Opinion on the financial statements

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

In my opinion, except for the accounting treatment of the Authority's superannuation costs and liabilities, the financial statements, have been properly prepared in accordance with generally accepted accounting practice in Ireland and give a true and fair view of the state of the Authority's affairs at 31 December 2016 and of its income and expenditure for 2016.

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

Matters on which I report by exception

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

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

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

Patricia Sheehan
For and on behalf of the
Comptroller and Auditor General

29 June 2017

STATEMENT OF INCOME AND EXPENDITURE AND RETAINED REVENUE RESERVES
For the year ended 31 December 2016

	Note	2016 €	2015 €
Fee Income	3	**21,461,418**	21,654,894
Department of Health Funding	3	**3,916,000**	3,916,000
Other Income	4	**1,090,096**	585,872
		26,467,514	26,156,766
Salaries and Wages	5, 24	**18,684,512**	18,285,952
Other Operating Costs	6	**5,138,378**	5,486,959
Depreciation	2	**2,099,770**	1,648,765
		25,922,660	25,421,676
Surplus for the year before write back of Superannuation contributions		**544,854**	735,090
Staff Superannuation Contributions	24	**746,723**	800,890
Surplus for the year		**1,291,577**	1,535,980
Balance brought forward		**27,398,177**	25,862,197
Balance carried forward	12	**28,689,754**	27,398,177

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

Ms. Ann Horan
Chairman

Mr. David Holohan
Authority Member

Date: 16 June 2017

The notes on pages 73 to 82 form part of the financial statements.

STATEMENT OF FINANCIAL POSITION
As at 31 December 2016

	Note	2016	2015 as restated
		€	€
Fixed Assets			
Property, plant and equipment	2	26,039,261	25,665,558
Current Assets			
Debtors and Prepayments	7	1,129,190	1,191,666
Inventory of Stationery		5,029	2,077
Cash at Bank and in Hand		1,989,592	475,265
Short Term Deposits	10	14,308,652	15,991,441
		17,432,463	17,660,449
Creditors - Amounts falling due within one year			
Creditors and Accruals	8	8,435,294	8,787,819
Mortgage	13	793,332	793,332
		9,228,626	9,581,151
Net Current Assets		8,203,837	8,079,298
Creditors - Amounts falling due after more than one year			
Mortgage	13	5,553,344	6,346,679
NET ASSETS		28,689,754	27,398,177
Reserves			
Income and Expenditure Reserve	12	28,689,754	27,398,177
		28,689,754	27,398,177

Ms. Ann Horan
Chairman

Mr. David Holohan
Authority Member

Date: 16 June 2017

The notes on pages 73 to 82 form part of the financial statements.

STATEMENT OF CASH FLOWS
For the year ended 31 December 2016

	Note	2016 €	2015 €
Cash flows from Operating Activities			
Surplus/(Deficit) for financial year		1,291,577	1,535,980
Depreciation of property, plant and equipment		2,099,770	1,648,765
(Profit)/Loss on Disposal of property, plant and equipment		(20)	156
(Increase)/Decrease in Debtors		62,476	(464,637)
(Increase)/Decrease in Stock		(2,952)	182
Increase/(Decrease) in Creditors - amounts falling due within one year		(352,528)	425,107
Deposit Interest		(35,829)	(79,548)
Bank Interest		222,798	243,288
Cash from Operations		3,285,292	3,309,293
Bank Interest Paid		(222,798)	(243,288)
Net Cash generated from Operating Activities		3,062,494	3,066,005
Cash flows from Investing Activities			
Deposit Interest Received		35,829	79,548
(Increase)/Decrease in Bank Deposits		2,058,857	(2,126,720)
Payments to acquire property, plant and equipment		(2,473,473)	(1,740,789)
Receipts fom sales of property, plant and equipment		20	352
Net cash from Investing Activities		(378,767)	(3,787,609)
Cash flows from Financing Activities			
Repayment of Borrowings		(793,332)	(793,332)
Net cash used in Financing Activities		(793,332)	(793,332)
Net increase/(decrease) in Cash and Cash Equivalents		1,890,395	(1,514,936)
Cash and Cash Equivalents at beginning of year		2,102,133	3,617,069
Cash and Cash Equivalents at end of year	9	3,992,528	2,102,133

The notes on pages 73 to 82 form part of the financial statements.

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2016

1. Accounting Policies

A. General information

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

B. Compliance with FRS 102

The financial statements of the HPRA for the year ended 31 December 2016 have been prepared in accordance with FRS 102, the financial reporting framework applicable in the UK and Ireland, with the exception of superannuation. By direction of the Minister for Health, the provisions of FRS 102 in relation to retirement benefits are not being complied with. In all other respects the financial statements comply with FRS 102. The date of transition to FRS 102 is 1 January 2014.

C. Basis of preparation

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

D. Critical accounting estimates and judgements

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

(a) Provisions

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

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2016

E. Revenue recognition

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

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

F. Expenditure recognition

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

G. Reporting currency and currency translation

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

H. Property, plant and equipment

Plant and equipment excluding Premises

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

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

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

Premises

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

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

I. Taxation

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

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2016

J. Debtors

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

K. Superannuation

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

The charge to salaries and wages is stated gross of superannuation deductions of €746,723 (2015 - €800,890). The surplus for the year on page 70 is then shown both before and after superannuation deductions. The income and expenditure reserve on the statement of financial position is split between retained reserves and superannuation reserves in note 12. The balance on the superannuation reserve represents the cumulative superannuation deductions made since 1996.

By direction of the Minister for Health, the provisions of FRS 102 Section 28 Retirement Benefits are not being complied with.

L. Provisions

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

M. Library

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

N. Leases

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

O. Loans

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

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

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2016

2. Property, plant and equipment

	Fixtures and Fittings	Computer Equipment	Leasehold Improvements	Improvements To Premises	Premises	Total
	€	€	€	€	€	€
Cost						
Balance as at 1 January 2016	1,203,630	12,230,293	502,445	4,362,218	23,156,037	41,454,623
Additions for the year	16,247	2,455,246	-	1,980	-	2,473,473
Disposals for the year	(14,284)	(95,231)	-	-	-	(109,515)
As at 31 December 2016	1,205,593	14,590,308	502,445	4,364,198	23,156,037	43,818,581
Depreciation						
Balance as at 1 January 2016	1,080,341	10,815,009	502,445	3,391,270	-	15,789,065
Charge for the year	52,949	1,688,829	-	357,992	-	2,099,770
Disposals for the year	(14,284)	(95,231)	-	-	-	(109,515)
As at 31 December 2016	1,119,006	12,408,607	502,445	3,749,262	-	17,779,320
Net Book value at 31 December 2016	86,587	2,181,701	-	614,936	23,156,037	26,039,261
Net Book value at 1 January 2016	123,289	1,415,284	-	970,948	23,156,037	25,665,558

3. Income

	2016	2015
	€	€
Fee Income		
Clinical Trials	181,082	175,148
Human Medicine - National Fees	6,324,512	6,439,762
Human Medicine - European Fees	6,853,136	6,835,197
Veterinary Medicine - National Fees	1,650,596	1,492,613
Veterinary Medicine - European Fees	1,288,314	1,302,720
Compliance Department	4,593,694	5,067,354
Medical Devices	400,817	403,392
	21,292,151	21,716,186
Movement in deferred revenue	169,267	(61,292)
	21,461,418	21,654,894
Dept Of Health Funding (Vote 38 Subhead E1)	3,916,000	3,916,000
Other Income (Note 4)	1,090,096	585,872
Total Income	26,467,514	26,156,766

Certain fees received by the Authority under the Irish Medicines Board Act 1995 (as amended), totalling €16,382,593 in 2016, shall be paid into or disposed of for the benefit of the Exchequer in such manner as the Minister for Public Expenditure and Reform directs.

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2016

4. Other Income

	2016	2015
	€	€
Conference Fee Income	134,355	1,850
Deposit Interest	35,829	79,548
(Loss)/Gain on Disposal of Fixed Assets	20	(156)
IT Income	876,283	504,630
Zambia Project Income	43,609	-
	1,090,096	585,872

5. Salaries and Wages

	Note	2016	2015 as restated
		€	€
Salaries and Wages		16,353,458	15,965,979
Pensions	24	739,910	828,682
Social Welfare Costs		1,591,144	1,491,291
		18,684,512	18,285,952

The average number of staff employed during the year was 312 (2015 - 298).
Payroll numbers at 31 December 2016 can be analysed across the following departments : -

Chief Executive	2	11
Compliance	67	64
Finance, Corporate & International	21	20
Human Products Authorisation & Registration	111	103
Human Products Monitoring	48	47
Human Resources & Change	7	8
IT & Business Services	21	19
Quality, Scientific Affairs & Communications	11	1
Veterinary Sciences	29	25
Staff	317	298
Pensioners	34	34
	351	332

Pension related deductions for Public Servants of €809,795 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 2016

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

Salary Band	2016
€0 to €60,000	214
€60,001 to €70,000	50
€70,001 to €80,000	9
€80,001 to €90,000	26
€90,001 to €100,000	9
€100,001 to €110,000	5
€110,001 to €120,000	2
€120,001 to €130,000	1
€140,001 to €150,000	1
	317
Average Salary	€51.7K

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

6. Operating Costs

	2016 €	2015 €
Accommodation Costs	1,186,524	1,059,592
Travel, Representation and Training	859,595	939,155
Bank Charges and Interest	229,547	246,447
Legal & Professional Fees	257,284	427,161
Stationery, Publications, Postage and Communications	698,613	458,007
Other Operating Costs	1,906,815	2,356,597
	5,138,378	5,486,959

Operating costs of €5,138,378 includes an amount of €13,899 related to staff hospitality.

7. Debtors (all due within one year)

Trade Debtors	917,685	1,013,810
Prepayments	181,669	26,339
Other Debtors	29,836	151,517
	1,129,190	1,191,666

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2016

8. Creditors (amounts falling due within one year)

	2016 €	2015 €
Trade Creditors	191,082	367,776
Accruals	6,508,352	6,554,867
Deferred Revenue	1,102,945	1,272,212
Revenue Commissioners	632,915	592,964
	8,435,294	8,787,819

9. Cash and Cash Equivalents

	As At 01/01/2016	Cashflow	As At 31/12/2016
Cash at Bank and in Hand	475,265	1,514,327	1,989,592
Demand Deposits	1,626,868	376,068	2,002,936
	2,102,133	1,890,395	3,992,528

10. Short Term Deposits

	2016 €	2015 €
Demand Deposits (convertible to cash on demand)	2,002,936	1,626,868
Short Term Deposits (not immediately convertible to cash)	12,305,716	14,364,573
	14,308,652	15,991,441

11. Administration Expenses

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

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2016

12. Movement on Income and Expenditure Reserves

	As At 01/01/2016 €	Movement €	As At 31/12/2016 €
Retained Reserves	19,288,937	544,854	19,833,791
Staff Superannuation Contributions	8,109,240	746,723	8,855,963
	27,398,177	1,291,577	28,689,754

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	2,380,016	3,173,351
	6,346,676	7,140,011

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. As the mortgage is at a fixed rate, the Authority has no interest rate exposure.

NOTES TO THE FINANCIAL STATEMENTS
For the year ended 31 December 2016

15. Financial Commitments

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

On 28 January 2005 the HPRA signed a leasehold interest in respect of the 5th floor, Alexandra House Earlsfort Centre, Dublin 2. At 31 December 2016 this lease had 5 years and four months remaining.

	2016 €	2015 €
The amounts due under this lease are as follows:		
- within one year	285,984	285,984
- between one and five years	1,143,936	1,143,936
- after five years	95,328	381,312
	1,525,248	1,811,232

16. Capital Commitments

Contracted For (Contract Signed)	2,094,971	1,877,410
Not Contracted For	-	405,900
	2,094,971	2,283,310

17. Authority Remuneration

Chairman's Salary	11,970	20,520
Authority Members' Travel Expenses	8,284	9,106
	20,254	29,626

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

18. Staff Remuneration

Chief Executive's Total Remuneration		
Basic Salary	143,413	145,749
	143,413	145,749

Mr. Pat O'Mahony served as Chief Executive during the period 1 January to 4 September 2015. He received a salary of €99,535 during this period.
Ms. Rita Purcell was appointed acting Chief Executive on 5 September 2015 and served in this capacity to 31 December 2015. Her salary for this period was €46,214.
Ms. Lorraine Nolan was appointed Chief Executive on 1 January 2016.
Mr. O'Mahony's, Ms. Purcell's and Ms. Nolan'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 2016

19. Related Party Transactions

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

20. Prompt Payment of Accounts

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

21. Exchange Rates

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

2016	€1 = STG £0.85637
2015	€1 = STG £0.73693

22. Provisions

The HPRA has been notified of a number of legal proceedings or potential proceedings. The Authority has provided in full for its 'best estimate' of the expenditure it is likely to incur in relation to those cases. The Authority is availing of the reduced disclosures allowed by FRS 102 in instances where full disclosure might prejudice seriously its position in a dispute with other parties on the subject matter of the provision.

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. Prior Year Adjustment

In 2016, the Authority accounted for lump sum pension payments in Salaries and Wages. Staff Superannuation Contributions report gross contributions received. In 2015, the Authority had accounted for such lump sums by netting the payments of €359,002 against superannuation contributions.
The effects of this change in accounting treatment is to increase the 2015 Pension Costs by €359,002 and to increase the 2015 Staff Superannuation Contributions by €359,002. There is no overall effect on the 2015 surplus.

25. Approval of Financial Statements

The financial statements were approved by the Authority of the HPRA on 1 June 2017.

Appendix 1
2016 Committee Members

Management Committee

Dr. Lorraine Nolan
Chief Executive

Ms. Rita Purcell
Deputy Chief Executive

Dr. Gabriel Beechinor
Director of Veterinary Sciences

Dr. Jayne Crowe
Director of Human Products Authorisation and Registration

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

Dr. Joan Gilvarry
Director of Human Products Monitoring

Mr. Kevin Horan
Director of Information Technology and Business Services

Mr. John Lynch
Director of Compliance

Ms. Lynsey Perdisatt
Director Human Resources and Change

Authority

Ms. Ann Horan – Chairperson
Mr. Patrick Brangan
Mr. Wilfrid Higgins
Mr. David Holohan
Prof. Mary Horgan
Mr. Brian Jones
Prof. Elizabeth Keane
Prof. Caitriona O'Driscoll
Dr. Diarmuid Quinlan

Audit Committee

Mr. Patrick Brangan – Chair
Mr. David Holohan
Prof. Elizabeth Keane

Advisory Committee for Human Medicines

Prof. Mary Horgan – Chair
Dr. Kevin Connolly
Prof. Desmond Corrigan
Ms. Maria Egan
Prof. Tom Fahey
Prof. David Kerins
Ms. Fionnuala King
Prof. Patrick Murray
Dr. Fionnuala Ní Ainle
Dr. Brian O'Connell
Mr. Ronan Quirke
Dr. Patrick Sullivan

Advisory Committee for Veterinary Medicines

Mr. Patrick Brangan – Chair
Dr. Ruadhrí Breathnach
Ms. Eugenie Canavan
Dr. Martin Danaher
Dr. Helena Kelly
Dr. Nola Leonard
Dr. Bryan Markey
Dr. Ciaran Mellet
Dr. Warren Schofield
Dr. Robert Shiel
Dr. Christina Tlustos

Advisory Committee for Medical Devices

Mr. Wilfrid Higgins – Chair
Prof. David Barton
Dr. Vivion Crowley
Mr. Ger Flynn
Dr. Fergal McCaffrey
Ms. Margaret O'Donnell
Prof. Martin O'Donnell
Prof. Richard Reilly
Prof. Mary Sharp
Mr. Sean-Paul Teeling
Prof. Sean Tierney

Clinical Trial Sub-Committee of Advisory Committee for Human Medicines

Dr. Patrick Sullivan – Chair
Dr. Liam Bannan
Dr. Geraldine Boylan
Dr. Paul Browne
Dr. Peter Crean
Prof. Lee Helman (CT Expert)
Dr. Filip Janku (CT Expert)
Dr. Catherine Kelly
Dr. Patrick Morris
Dr. Thomas Peirce
Dr. Bryan Whelan
Dr. Jennifer Westrup

Advisory Sub-Committee for Herbal Medicines

Prof. Des Corrigan – Chair
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
Dr. Emma Wallace

Experts Sub-Committee of the Advisory Committee for Human Medicines

Prof. Mary Horgan – Chair
Dr. Linda Coate
Dr. Kevin Connolly
Dr. James Colville
Dr. Noreen Dowd
Dr. Stephen Eustace
Dr. Stephen Flint
Dr. Tim Fulcher
Dr. Joseph Galvin
Dr. Patrick Gavin
Dr. Paul Gallagher
Dr. Kevin Kelleher
Dr. Catherine Kelly
Dr. Mary Keogan
Prof. David Kerins
Dr. Mark Ledwidge
Dr. Frank Murray
Dr. Yvonne O'Meara
Dr. Cormac Owens
Mr. Ashley Poynton
Dr. Brion Sweeney (resigned March 2016)
Dr. Jogin Thakore
Dr. Gerry Wilson

Appendix 2
Presentations 2016

Third Level / Professional Development Presentations and Training

Institution	Course	Presentation Title
Athlone IT	Veterinary Nursing	Regulation of Veterinary Medicines
BioPharmaChem Ireland	CMC Regulatory Affairs Training	Common Errors in Variations
BioPharmaChem Ireland	CMC Regulatory Affairs Training	Common Deficiencies in CMC Part of Application
BioPharmaChem Ireland	CMC Regulatory Affairs Training	Introduction to Regulatory Affairs – Module 3 of the CTD
CMG	Reducing Medication Errors In Healthcare Services	Medication Errors – The Regulatory Role
DIT	Pharmaceutical Quality Assurance	The GMP Inspection Process
DIT	Medical Device Decontamination	Medical Device Legislation And Vigilance
Dundalk IT	Veterinary Nursing	Regulation of Veterinary Medicines
EU Network Training Centre	Clinical Trials – General Regulation	Safety Issues and Regulatory Action
EU Network Training Centre	Clinical Trials Safety	Safety Reporting Routes
EU Network Training Centre	Clinical Trials Safety	Reference Safety Information
EU Network Training Centre	Clinical Trials Safety	DSUR Assessments
EU Network Training Centre	Clinical Trials - Clinical Assessment	Introducing the Part I AR Template
Hospital Pharmacists Association of Ireland	Intern Study Day	The Role of the HPRA's Health Product Distribution Section
Irish Association of Physicists in Medicine	Radiation Safety Course: Dental Radiology Equipment	CE Marking
LAST	Laboratory Animal Science and Training (multiple courses)	Implementation of Scientific Animal Protection Legislation
Letterkenny IT	Veterinary Nursing	Regulation of Veterinary Medicines
Medicademy	Regulatory Affairs – Module 10	Biosimilars – Quality, non-clinical and clinical requirements
Medicademy	Regulatory Affairs – Module 14	Detail and Critical Summaries
Medicademy	Regulatory Affairs – Module 14	Special Cases: Cascade, MUMS, GMOs etc.
PIC/S Expert Circle on Quality Risk Management	Advanced Quality Risk Management Training	Use of QRM to support a PAT Change Control

PIC/S Expert Circle on Quality Risk Management	Advanced Quality Risk Management Training	Risk-based Classification of GMP Deficiencies
PIC/S Expert Circle on Quality Risk Management	Advanced Quality Risk Management Training	Formal vs. Informal Quality Risk Management
PIC/S Expert Circle on Quality Risk Management	Advanced Quality Risk Management Training	Risk-based GMP Inspection Planning
PLS Pharma	Responsible Person Forum	Responsible Person – A Regulators Perspective
QQI	Retail, Sale and Supply of Animal Remedies	Presentation to Graduates
RCSI	Pharmacy	Quality Defect Investigations and Product Recalls
RCSI	Pharmacy	Regulation of Biological Medicinal Products
RCSI	Nurse / Midwife Prescribing	(1) The Role of the HPRA and (2) Pharmacovigilance
RCSI	Pharmacy	Regulatory Affairs and Regulatory Authorities
Sligo IT	Medical Biotechnology and Pharmaceutical Science	Quality Defects / Pharmacovigilance
St. Johns, Cork	Veterinary Nursing	Regulation of Veterinary Medicines
TCD	Centre for Health Sciences: Regulatory Affairs Workshop	Medical Devices Legislation
TCD	QP Forum	HPRA - Overview of Strategy 2016-2020
TCD	Pharmaceutical Medicine	Quality Aspects in the Regulation of Biologicals and ATMPs
TCD	Pharmaceutical Medicine	Product Recalls and MA Withdrawals
TCD	Pharmaceutical Medicine	Traditional Herbal Medicinal Products
TCD	Pharmaceutical Medicine	Collection and Reporting of Adverse Events in Clinical Trials
TCD	Pharmaceutical Medicine	Pharmacovigilance – Where Are We Now?
TCD	Pharmaceutical Medicine	Communication of Drug Safety Data
TCD	Pharmaceutical Medicine	Risk Management Plans
TCD	Pharmaceutical Medicine	International Quality
Standards and Pharmacopoeias		
TCD	Pharmaceutical Medicine	Falsified Medicines Directive
TCD	Pharmaceutical Medicine	Recent Developments in Pharmacovigilance – A Perspective from PRA
TCD	Pharmaceutical Medicine	Regulation of Medical Devices
TCD	Pharmaceutical Medicine	Application of Quality Risk Management to Quality Defects and Recalls
TCD	Pharmacy	An Overview of Pharmacovigilance
TCD	Pharmacy	Investigation of Quality Defects
TOPRA	Autumn Introductory Course	Module 2 of the CTD

UCC	Medicine	Notification of Adverse Reactions
UCC	Pharmacy / Pharmaceutical Technology and Quality Systems	Quality Defect Investigations and Product Recalls
UCC	Medicine	Notification of Adverse Reactions
UCD	Association for Veterinary Teaching and Research Work	Implementation of Scientific Animal Protection Legislation
UCD	Veterinary Medicine / Veterinary Nursing	Regulation of Veterinary Medicines
UCD	Nurse / Midwife Prescribing	(1) The Role of the HPRA and (2) Pharmacovigilance
UCD	Clinical and Translational Research	Medical Devices – Principles and Practices of Clinical Research (two presentations)
University of Hertfordshire	Pharmacovigilance	Update on the EU Pharmacovigilance Legislation

Regulatory Presentations

Event / Organiser	Presentation Title
Advanced Manufacturing Ireland / Sligo IT	Regulation of Medical Devices and Collaborative Robots
Animal and Plant Health Association: Animal Health Conference	Surveillance and Monitoring of Veterinary Medicines
Annual OMCL Network Meeting	A New Risk-based Approach to Medicines Surveillance Testing (2 presentations)
Annual OMCL Network Meeting	Work of the Communications Working Group
Association for Veterinary Teaching and Research Work	Regulation of Animal Research using Non-Rodent Models
BioPharma Ambition Conference (IBEC)	The Regulator's Perspective on the future of Biopharma Manufacturing
Biosimilars 360° Symposium (RCPI)	Evolving Landscape on Regulatory Data – Requirements to Demonstrate Biosimilarity
China International Medical Device Regulators Conference	Regulatory developments in Europe and the new EU Regulations
Cosmetic, Toiletry and Perfumery Association Cosmetovigilance Seminar	Working with Regulation (EC) 1223/2009, as amended – A Regulator's Viewpoint
Drug Information Association (DIA)	International Regulatory Convergence, Collaboration and Cooperation
DIA Conference on Falsified Medicines	Considerations related to Falsified Medicines
DIA Workshop: Regulation of Veterinary Medicinal Products	Safety Surveillance in the Market: Pharmacovigilance
DIA	Pharmaceuticals and Globalisation
EMA Focus Group on Anthelmintic Resistance	Impact of Specific Formulations on Anthelmintic Resistance

EMA Tenth Stakeholder Forum on the Pharmacovigilance Legislation	Pharmacovigilance Impact Evaluation – For Better Pharmacovigilance
European Validation Week Meeting	Risk Based Validation Activities (two presentations)
Future Health Summit	Regulation of Standalone Software as a Medical Device
French Refrigeration Association (AFF) Cold Chain Conference	Inspection Findings for Cold Chain Products
Health Research Board CRCI Official Launch	HPRA – Supporting Clinical Research in Ireland
HSE Healthcare User Group Meeting	Introduction to the new Medical Device Regulation and Unique Device Identification (UDI)
HSE National Distribution Centre	Medical Devices Regulations: New Distributor Requirements
HSE Workshops: Medical Device Equipment QA+I tool	Medical Device Vigilance (multiple presentations)
ICMRA	The EU System of Pharmacovigilance and Risk Management
IFPAC Cortona Conference	Continuous Manufacturing – Some Assessment and GMP Considerations
IMSTA Distributor Breakfast Briefing	Medical Device Distributor Pilot Inspections (two presentations)
Institute of Validation and Technology Complaints Congress and Recalls Summit	Application of Quality Risk Management to Quality Defect Investigations
International Development Ireland: Saudi Arabian Delegation	Regulation of Medical Devices in Ireland and Europe
International Society for Pharmaceutical Engineering (ISPE)	Continuous Manufacturing – Some Assessment Considerations
Irish Clinical Embryologists (ICE) Association	Presentation on new Directive Requirements for Coding of Tissues
Irish Cardiac Society	Medical Device Vigilance
Irish Decontamination Institute	Best Practice in Decontamination
Irish Medtech Association Global Access Conference	Overview of the International Medical Device Regulators Forum (IMDRF)
Irish Medtech Association Global Access Conference	Introduction to new Regulations for Medical Devices and IVDs
Irish Medtech Association Additive Manufacturing Workshop	Regulation of Additive Manufacturing for Medical Devices
ISPE International Conference on Pharmacoepidemiology	PRAC Experience on Risk Management Plans
ISPE International Conference on Pharmacoepidemiology	Real World Effectiveness – How Effective is it?
ISPE International Conference on Pharmacoepidemiology	Pharmacoepidemiology and Risk Management Planning
Life Sciences Product Complaints Congress	The Evaluation from a Quality Risk Management Perspective of Quality Defects

Macedonian OMCL	Quality Risk Management in the GMP Environment
Market Surveillance Forum	Overview of new Regulations for Medical Devices and IVDs
Medtec Annual Conference	Introduction to new Regulations for Medical Devices and IVDs
Medtech Week (RCSI and Irish Medtech Association)	Clinical Research of Medical Devices
National Steering Group for Collaborative Robotics	Regulation of Medical Devices and Collaborative Robots
Parenteral Drug Association (PDA)	GMP Inspectors – Benefits of Interacting with Pharmaceutical Assessors
PDA	Formal and Informal Quality Risk Management
Pharma-Bio Serv Human Error Workshop	The Evaluation from a Quality Risk Management Perspective of Quality Defects
Pharmaceuticals and Medical Devices Agency, Japan	GMP Inspection Planning using Risk-based Principles
Pharmaceuticals and Medical Devices Agency, Japan	Performing a Mock GMP Inspection
Q1 Productions Conference	Competent Authority Perspective – Medical Device Regulation
Regulatory Science Ireland	Quality Defects Research Project
SCOPE Training: Lifecycle Pharmacovigilance	Work Package 8: Practical Guidance on PSUR/ PSUSA assessment
SCOPE Workshop: Risk Communication	Work Package 6, Topic 2: Impact Assessment
Society of Chief and Principal Dental Surgeons	Medical Device Vigilance
Swissmedic	Output of the Defect Best Practices Working Group
The Pharmaceutical Managers' Institute	The Role of the HPRA and our Key Areas of Focus
TOPRA Annual Symposium	Authorisation of Veterinary Medicinal Products Containing (potential) PBT or vPvB Substances
Technology Sciences Group Europe	Market Surveillance of Cosmetic Products in Ireland
WHO Workshop: Post-Market Surveillance of IVDs	What is Expected of Regulators?

Appendix 3
Human Medicines Safety: Publications and Articles

Drug Safety Newsletters

Edition	Topics
February 73rd Edition	- Educational materials – Optimising the safe and effective use of medicinal products - Adverse reaction reporting – A reminder - New Direct Healthcare Professional Communications published on the HPRA website
April 74th Edition	- High strength insulin preparations - Antiretroviral medicines – Updated advice on lipodystrophy and lactic acidosis - Natalizumab (Tysabri) – Updates to progressive multifocal leukoencephalopathy (PML) risk minimisation measures - Fingolimod (Gilenya) – Risks related to its immunosuppressive effects - New Direct Healthcare Professional Communications published on the HPRA website
May 75th Edition	- Withdrawal of fusafungine-containing medicinal products - Updated advice on the risk of diabetic ketoacidosis during treatment with SGLT2 inhibitors - Risk of pneumonia with inhaled corticosteroids for chronic obstructive pulmonary disease (COPD) - Risk of hepatitis B reactivation with BCR-ABL Tyrosine Kinase Inhibitors (TKIs) - Aflibercept (Zaltrap) – Minimising the risk of osteonecrosis of the jaw (ONJ) - New Direct Healthcare Professional Communications published on the HPRA website
August 76th Edition	- Valproate containing medicines – Additional educational materials available for healthcare professionals and patients - Miconazole and warfarin – Reminder of the potential for interaction - Levonorgestrel releasing intrauterine devices-Recommendation to prescribe by brand name - Implanon NXT-Risk of migration in vasculature and lung - New Direct Healthcare Professional Communications published on the HPRA website

October 77th Edition	- Direct-acting antivirals for hepatitis C – Advice on interaction potential with warfarin and other vitamin K antagonists leading to a reduced international normalized ratio (INR) - Advice on potential interaction between cobicistat-containing products and corticosteroids primarily metabolized by CYP3A – Risk of adrenal suppression - Adverse reaction reporting during 2015 - New Direct Healthcare Professional Communications published on the HPRA website
December 78th Edition	- Otezla (apremilast) – Important advice regarding suicidal ideation and behaviour - Lenalidomide (Revlimid) – Advice regarding viral reactivation - Levetiracetam 100mg/ml oral solution – Global reports of medication errors resulting in the administration of higher than intended doses of levetiracetam - Improved access to educational materials on the HPRA website - New Direct Healthcare Professional Communications published on the HPRA website

Articles in External Publications

Month	Publication	Topics
January	MIMS	- Bisphosphonates – Small risk of osteonecrosis of the external auditory canal
February	IMF	- Reminder – Oral methotrexate and risk of unintentional overdose due to medication errors
February	MIMS / MIMS Respiratory Supplement	- HPRA commences publication of educational materials and tools for medicines
March	MIMS / MIMS Cardiac Supplement	- Reminder – Oral methotrexate and risk of unintentional overdose due to medication errors - Ibuprofen – Review confirms small increased cardiovascular risk with daily doses at or above 2400mg
April	MIMS	- High strength insulin preparations
May	MIMS / MIMS Oncology Supplement	- Fingolimod (Gilenya) – Risks related to its immunosuppressive effects - HPRA commences publication of educational materials and tools for medicines
June	MIMS / MIMS Respiratory Supplement	- Withdrawal of fusafungine-containing medicinal products - Risk of pneumonia with inhaled corticosteroids for chronic obstructive pulmonary disease (COPD)
July	MIMS / MIMS Diabetes Supplement	- Risk of pneumonia with inhaled corticosteroids for chronic obstructive pulmonary disease (COPD)
August	IMF	- Valproate-containing medicines – New educational materials available for healthcare professionals and patients

August	MIMS	- Miconazole and warfarin – Reminder of the potential for interaction
September	MIMS / MIMS Rheumatoid Arthritis Supplement	- Valproate-containing medicines – Additional educational materials available for healthcare professionals and patients - Reminder – Oral methotrexate and risk of unintentional overdose due to medication errors
October	MIMS / MIMS Women's Health Supplement	- Implanon NXT – Risk of device migration in vasculature and lung
November	MIMS / MIMS Diabetes Supplement	- Fingolimod (Gilenya) – Risks related to its immunosuppressive effects - High strength insulins
December	MIMS / MIMS Compendium	- Direct-Acting Antivirals for Hepatitis C – Advice on interaction potential with warfarin and other vitamin K antagonists leading to a reduced international normalised ratio (INR) - Valproate-containing medicines – Additional educational materials available for healthcare professionals and patients

Appendix 4
European and National Committee / Working Group Participation

Committee/Working Group	Organisation	Meetings in 2016
Competent Authorities for Medical Devices (CAMD)	CAMD	2
Competent Authorities for Medical Devices – Executive Group	CAMD	4
Medical Device Compliance and Enforcement Working Group (COEN)	CAMD	2
Notified Bodies Operations Group (NBOG)	CAMD	2
Cross Border Controlled Drug Regulatory Meeting	Care Quality Commission	4
Committee of Experts on Minimising Public Health Risks Posed by Counterfeiting of Medical Products and Similar Crimes	Council of Europe	2
National Meeting on Endocrine Disruptors	Department of Agriculture	1
Early Warning and Emerging Trends	Department of Health	2
Medication Safety Forum	Department of Health	3
Chemicals Interdepartmental / Agency group	Department of Jobs, Enterprise and Innovation	2
Market Surveillance Forum	Department of Jobs, Enterprise and Innovation	2
Active Pharmaceutical Ingredients (API) Working Group of the OMCL Network	EDQM	1
Annual OMCL Network Meeting	EDQM	1
Centrally Authorised Products (CAP) OMCL Network Meeting	EDQM	1
Counterfeit Products Working Group of the OMCL Network	EDQM	2
MRP/DCP OMCL Network Meeting	EDQM	2
OMCL Network Communications Group	EDQM	2
Committee for Advanced Therapies (CAT)	EMA	11
Committee for Herbal Medicinal Products (HMPC)	EMA	6
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
GCP Inspectors Working Group	EMA	4
GMDP Inspectors Working Group	EMA	4
Heparin Working Group (Telecon)	EMA	2
Immunological Working Party - Veterinary	EMA	3
Paediatric Committee (PDCO)	EMA	12
Pharmacovigilance Inspectors Working Group (Human and Veterinary)	EMA	3
Pharmacovigilance Risk Assessment Committee (PRAC)	EMA	11
Pharmacovigilance Working Party - Veterinary	EMA	6
Quality Defects / Rapid Alerts Meetings	EMA	2
Quality Working Party	EMA	4
Safety Working Party – Veterinary	EMA	4
Scientific Advice Working Party – Veterinary	EMA	11
Signal Management and Review Team (SMART)	EMA	13
Statement of Non-compliance with GDP Process Drafting Group	EMA	2
EU Pharmacovigilance Business Team	EMA / National Competent Authorities	12
Health Advisory Committee	Environmental Protection Agency	3
Clinical Investigation and Evaluation Working Group	European Commission	4
Competent Authorities for Blood	European Commission	2
Competent Authorities for Organs for human transplantation	European Commission	1
Competent Authorities for Tissues and Cells	European Commission	2
Cosmetic Standing Committee and Working Group	European Commission	3
Drafting Group for GMP Guide for Advanced Therapy Medicinal Products (ATMPs)	European Commission	17
Drug Precursor Working Group	European Commission	2
European Commission Sub-working Group on Cosmetovigilance	European Commission	1
In Vitro Diagnostic Technical Group (IVDTG)	European Commission	2
MDR Eudamed Steering Committee	European Commission	2
MDR/IVDR Implementing Legislation	European Commission	2
Medical Device Expert Group (MDRG) – EU IMDRF Coordination	European Commission	2
Medical Device Vigilance Experts Group	European Commission	4
Medical Device Vigilance Monthly Teleconference	European Commission	12
Meeting of Expert Group on Safety Features	European Commission	4
Platform of European Market Surveillance Authorities for Cosmetics (PEMSAC) Market Surveillance	European Commission	1

Platform of European Market Surveillance Authorities for Cosmetics (PEMSAC) Analytical Methods	European Commission	1
Precursor Drafting Group	European Commission	2
Single European Code Working Group Meeting	European Commission	2
VISTART Project on Guidance for Regulators of Blood, Tissues and Cells, and Organs	European Commission	7
SCOPE Work Package Meetings	European Commission / National Competent Authorities	22
Working Party on Pharmaceuticals and Medical Devices	European Council	13
Food Fraud Task Force	FSAI	1
Zika Scientific Advice Committee	Health Protection Surveillance Centre	4
Clinical Trials Facilitation Group (CTFG)	HMA	6
Co-ordination Group for Mutual Recognition and Decentralised procedures – Human (CMDh)	HMA	11
Co-ordination Group for Mutual Recognition and Decentralised procedures – Veterinary (CMDv)	HMA	11
Drafting Group on Risk Based Surveillance Testing	HMA	5
Meeting of Heads of Medicines Agencies under EU Presidency	HMA	4
Pharmacovigilance Procedures Work Sharing Working Party	HMA	8
Working Group of Communications Professionals	HMA	2
Working Group of Enforcement Officers	HMA	3
Working Group of Quality Managers	HMA	2
National Cosmetics Surveillance Forum	HPRA / HSE	3
National Blood Glucose Meter Guidelines Group	HPRA / HSE / Pharmacists	4
Environmental Health Service Steering Committee and Operational Group	HSE Environmental Health Service	6
Sub-group for Drafting of ICH Q12	ICH	3
Supply Chain Integrity Drafting Group (Telecon)	ICMRA	11
International Medical Device Regulators Forum (IMDRF) Management Committee	IMDRF	1
IIWA Organising Committee	Interpol	1
Pangea Liaison	Interpol	2
HPRA and UK Department for Business Innovation and Skills	Ireland / UK Working Group	3
Forum on the Advertising of Medicines (FOAM) Network Meeting	MHRA	1
Cosmetic Standards Advisory Group	NSAI	2
PIC/S Committee of Officials Meeting	PIC/S	2

PIC/S Executive Bureau Meeting	PIC/S	2
PIC/S Quality Risk Management (QRM) Expert Circle	PIC/S	1
National Immunisation Advisory Committee	RCPI	6
National Medicines Forum	RCPI	1
Point of Care Consultative Group Meetings	RCPI	4
Present and Future of Countering Pharmaceutical Crime – Project ALPhA	University of Osnabruck	1
Annual National Pharmacovigilance Centres Meeting	WHO	1
Board of the WHO/UMC Collaborating Centre	WHO	3
Member State Mechanism on Substandard / Spurious / Falsely-labelled / Falsified / Counterfeit Medical Products	WHO	1
Notify Project Technical Meeting	WHO / Italian National Transplant Centre	1

Appendix 5
Glossary

AED	Automated External Defibrillator
AMR	Antimicrobial Resistance
APMI	Association of Pharmaceutical Manufacturers in Ireland
ART	Assisted Reproductive Technology
BEMA	Benchmarking of European Medicines Agencies
BPCI	BioPharmaChem Ireland
CAMD	Competent Authority for Medical Devices
CD	Controlled Drug
CESP	Common European Submission Portal
CHMP	Committee for Medicinal Products for Human Use
CMC	Chemistry, Manufacturing, and Controls
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
COEN	European Compliance and Enforcement
CVMP	Committee for Medicinal Products for Veterinary Use
DCP	Decentralised Procedure
DHPC	Direct Healthcare Professional Communications
DJEI	Department of Jobs, Enterprise and Innovation
EDQM	European Directorate for Quality of Medicines
EEA	European Economic Area
EMA	European Medicines Agency
EPA	Environmental Protection Agency
EUDAMED	European Database on Medical Devices
FOAM	Forum on the Advertising of Medicines
FVD	Food and Veterinary Office
FSAI	Food Safety Authority of Ireland
GCP	Good Clinical Practice
GDP	Good Distribution Practice
GMP	Good Manufacturing Practice

GVP	Good Vigilance Practice
HEA	Healthcare Enterprise Alliance
HIQA	Health Information and Quality Authority
HMA	Heads of Medicines Agencies
HMPC	Committee on Herbal Medicinal Products
HSE	Health Service Executive
HSS	Health Systems Strengthening
IAHS	Irish Association of Health Stores
IBTS	Irish Blood Transfusion Service
ICH	International Conference of Harmonisation
ICDA	Irish Cosmetics, Detergent & Allied Products Association
ICMRA	International Coalition of Medicines Regulatory Authorities
ICSR	Individual Case Safety Reports
IDA	Industrial Development Authority
IDMP	Identification of Medicinal Products
IGMA	Irish Generic Medicines Association
IHTA	Irish Health Trade Association
IMDRF	International Medical Device Regulators Forum
IMF	Irish Medicines Formulary
IMSTA	Irish Medical and Surgical Trade Association
IMVO	Irish Medicines Verification Organisation
IPHA	Irish Pharmaceutical Healthcare Association
IVD	In-Vitro Diagnostics
JAP	Joint Audit Programme
JRC	Joint Research Centre
LDP	Leadership Development Programme
MAH	Marketing Authorisation Holder
MDSAP	Medical Device Single Audit Program
MHRA	Medicines and Healthcare products Regulatory Authority
MIMS	Monthly Index of Medical Specialities
MS	Member State
MRP	Mutual Recognition Procedure
NBOG	Notified Body Operations Group
NCAR	National Competent Authority Report
NHO	National Haemovigilance Office
NSAI	National Standards Authority of Ireland
OMCL	Official Medicines Control Laboratories
OPW	Office of Public Works
OTC	Over-the-Counter
PASS	Post Authorisation Safety Studies
PIP	Paediatric Investigational Plans

PDP	Performance Development Programme
PHECC	Pre-Hospital Emergency Care Council
PIC/S	Pharmaceutical Inspection Co-operation Scheme
PIP	Paediatric Investigational Plan
PL	Package Leaflet
PMO	Project Management Office
PPC	Pay-per-click
PRAC	Pharmacovigilance Risk Assessment Committee
PSI	Pharmaceutical Society of Ireland
PSUR	Periodic Safety Update Report
PSUSA	EU Single Assessment Procedures
QRM	Quality Risk Management
RCPI	Royal College of Physicians in Ireland
RMP	Risk Management Plan
RMS	Reference Member State
RPS	Regulated Product Submission
SCOPE	Strengthening Collaboration for Operating Pharmacovigilance in Europe
SEAI	Sustainable Energy Authority of Ireland
SI	Statutory Instrument
SmPC	Summary of Product Characteristics
THMP	Traditional Herbal Medicinal Product
TOPRA	The Organisation for Professionals in Regulatory Affairs
UMC	Uppsala Monitoring Centre
VFC	Voluntary Formal Caution
VHP	Voluntary Harmonisation Procedure
VISTART	Safety of Transfusion, Assisted Reproduction and Transplantation
WHO	World Health Organization
ZAMRA	Zambian Medicines Agency

An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

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

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