HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Annual Report 2021

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2021 Statistics at a Glance

Top 10

The HPRA was among the top 10 contributors at EU level for lead assessment of centrally authorised human medicines and scientific advice

82

The number of EMA scientific advice procedures for human medicines co-ordinated by the HPRA

107

applications issued for clinical trials of human medicines

1,914

The total number of veterinary medicines authorised in Ireland at year-end

21

The number of assessments carried out by the HPRA under the centrally authorised route for human medicine approvals – 11 as rapporteur and 10 as co-rapporteur

542

new human medicines authorised during 2021

No. 1

The HPRA was the leading national competent authority in the EU for outgoing work related to new veterinary medicines authorisation

294

medical device economic operators registered with the HPRA – a significant increase on previous years

5,726

export and free sale certificates issued – 1,244 certificates for medicines and 4,482 free sale certificates for medical devices

25,622

suspected adverse reaction reports for human medicines received of which 17,946 were associated with the use of COVID-19 vaccines

1,855

medical device vigilance reports received and assessed

248

reactive surveillance cases initiated for cosmetic products

87

good manufacturing practice (GMP) inspections at sites that produce human medicines or active substances

56

the number of centrally authorised human medicines where the HPRA was EU rapporteur for the monitoring of any safety signals

439

reports of suspected adverse reactions associated with the use of veterinary medicines

882

market surveillance cases undertaken in respect of medical devices

124

medicine recalls consisting of 117 human medicines and 7 veterinary medicines

1,604,589

dosage units of fake (falsified) and other illegal medicines detained

Chairperson's Statement

I was very much honoured to be appointed Chairperson of the Health Products Regulatory Authority (HPRA) and I am pleased to present the 2021 Annual Report.

I wish to begin by acknowledging the huge contribution of my predecessor Ann Horan to the Authority of the HPRA over 10 years including the last five as Chairperson. I have benefited greatly from the highly effective and efficient governance structures and processes that were enhanced under Ann's guidance. Prior to the end of her term as Chairperson, she was also central to the development of the HPRA's new Strategic Plan 2021-2025. On behalf of the Authority members and myself, I want to both acknowledge Ann's significant contribution to the HPRA and wish her the best for the future.

2021 – Another Extraordinary Year

There is no doubt that 2021 was another extraordinary year not just for our country in general but for our broader health service and for the HPRA as an organisation. We have lived through the most remarkable of times since March 2020 when the World Health Organisation confirmed its decision to declare the COVID-19 outbreak a pandemic.

While we are all too aware of the subsequent terrible and often devastating effects of COVID-19, we have also witnessed an inspirational response from our frontline healthcare and service workers, and from so many others in communities all across Ireland. The pandemic also necessitated an immediate response from Government and from public health bodies and officials at both a national and global level. In Ireland, necessary and robust decisions were made and actions taken to contain, delay and ultimately alleviate the impact of the virus.

As it became clear during the first year of the pandemic that vaccines, therapeutics and testing would be among the primary public health interventions to mitigate the disease at a population level, focus also turned very quickly to scientists, researchers and the life sciences sector. The collective contribution of so many across these areas and their work during the pandemic must be acknowledged. Health product regulators around the world, including the HPRA, were also recognised as key contributors and enablers of the global response to the pandemic. As evidenced throughout this report, there is no doubting that this had a huge influence on the activities and operations of the HPRA.

HPRA Contribution to the COVID-19 Vaccination Programme

By the end of the 2021, an additional four vaccines had been authorised for use in Europe in addition to the first authorisation granted in late 2020. HPRA national experts contributed directly to the assessment of the newly authorised vaccines through membership of the relevant European Medicines Agency (EMA) committees and working groups. As always, working on behalf of Irish and European citizens, there was an absolute focus on ensuring appropriate levels of safety, efficacy and quality. Later in 2021, the same approach was taken in the assessment and authorisation of additional therapeutics to treat people with COVID-19, particularly those at greatest risk of becoming seriously ill.

Following the commencement of Ireland's national vaccination programme in late 2020, the HPRA immediately launched its dedicated system to monitor the safety of the vaccines. This included the receipt and assessment of side effect reports nationally and membership of the EMA's safety committee and other relevant global fora. Close to 18,000 reports of suspected side effects linked to COVID-19 vaccines were received and assessed throughout 2021 – a hugely important contribution by the organisation. Also, the very transparent and open way in which vaccine safety issues were addressed, working with national and European partners, was a key element in building public trust in the vaccination programme. I would like to take this opportunity to thank healthcare professionals and members of the public for reporting to the HPRA. The receipt of reports of suspected side effects is central to our monitoring system and helps us to increase our knowledge of the safety profile of all medicines, including vaccines.

Throughout 2021, and particularly as the rollout of vaccines nationally began to accelerate, the HPRA contributed expert regulatory support and guidance to colleagues across the health system working in partnership with the Department of Health, the HSE and healthcare professionals. This included our participation in the National Public Health Emergency Team (NPHET), the High-Level Taskforce on COVID-19 Vaccination and at the National Immunisation Advisory Committee (NIAC). These contributions were part of a coordinated approach across the national health system to address public concerns and encourage vaccine take-up. It is important to acknowledge the key impact of that planned approach in what would subsequently become one of the most successful vaccine rollouts in the world.

A New Strategic Plan

The year in review was also significant in that the HPRA launched and commenced delivery of its new Strategic Plan for 2021 to 2025. The five core strategic goals identified in the plan are outlined below.

The new plan builds on the successful completion and delivery of the previous five-year strategy and sets out an ambitious agenda for the next five years to deliver better outcomes for people and animals through value-driven regulation and partnerships. Key to the successful delivery of that agenda will be the dynamic growth of the organisation in addition to the significant evolution in the regulatory frameworks under which it operates. In turn, these elements must be informed by the ongoing innovation and development of the ever changing industries and sectors regulated by the HPRA and its global partners.

Together, all of these factors can ensure that the HPRA delivers outcomes that make a real difference in the lives of all who use medicines, medical devices, and other health products. Importantly, the focus of the plan reflects the key considerations and work areas highlighted during an extensive external and internal consultative process.

As regards the implementation of year one of the plan, I welcome the significant progress made against each of the five core strategic goals while recognising that considerable resource effort was required throughout 2021 for COVID-related activities (see page 13 for further details of the progress report for year one).

The Importance of Enhanced Patient Engagement

At the heart of the Strategic Plan are the themes of partnerships and collaboration, responsive and adaptive regulation, and support for innovation. Reflecting on 2021, I believe all of these important elements were clearly evident, not just in the context of the HPRA's response to the pandemic, but across all its various work programmes.

While the broader achievements are set out in detail in the progress report, I wish to highlight, in particular, the continued development of the HPRA's patient forum. The Authority is strongly supportive of the HPRA's commitment to widening its engagement with patients and patient organisations so as to enable a deeper understanding of patient perspectives and experiences in the context of health products regulation. We believe further development and advancement of this initiative is of immense value and importance to the organisation.

By year-end, considerable progress had been achieved with the adoption of the Terms of Reference and the proposed work plan for 2022, and these have since been published on the HPRA website. Moving from the initial pilot phase to a more established basis was a key milestone and I wish to thank all the members for their time and their expert contributions to the forum throughout the year. It is clear, as a public health agency, that we must continue to listen to and engage with patients to ensure their experiences and perspective are heard and incorporated into the regulatory processes for medicines and devices.

Acknowledgments

On behalf of the Authority, I thank the Minister for Health and the Minister for Agriculture, Food and the Marine, in addition to their advisors and the staff of their departments, for their engagement and support of the HPRA and its activities during 2021.

I would like to thank all my fellow members of the Authority for their commitment and for the advice and expertise provided throughout a very busy year. As well as my own appointment as Chair, we also welcomed Dr Paula Kilbane and Dr Sharon O'Kane as new members of the Authority during 2021. There remains an ongoing commitment to succession planning at Authority level and ensuring across the membership that we have continued access to the necessary diversity, skills and technical competencies required to deliver on the Authority's mandate.

I would also like to express my appreciation to those members who chair our advisory committees and sub-committees. The contribution of the committees is of great value to the HPRA, and even more so during periods of intense public health focus as witnessed during the on going pandemic. I wish to acknowledge all the independent experts who give freely of their time and knowledge.

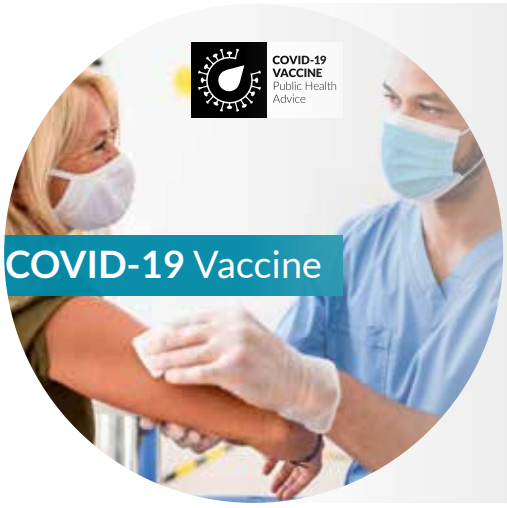
Finally, my sincere thanks to the Chief Executive, management and all the staff of the HPRA. They demonstrated an exceptional commitment to the protection of public and animal health throughout 2021 and I commend and thank them for their efforts. What has become abundantly clear to me since taking the role of Chair of the HPRA, is the quality, professionalism and commitment to public service of those who work across the organisation.

Reflections on 2021 and for the Future

In closing, while the pandemic has challenged us all in so many ways, it has also brought a focus to the invaluable contribution of so many people, professions and organisations that work and serve for the most part outside of the public eye. I believe this to be the case in respect of the HPRA but, arising from its key contribution to Ireland's public health response to the pandemic, I welcome the now greater understanding and recognition of the role it plays in regulating medicines and devices for the benefit of people and animals.

On behalf of the Authority, I look forward to the ongoing delivery of the HPRA's strategic goals and I am confident that through the unflinching commitment of the management and staff it will continue to focus on its clear vision of *excellence in health product regulation through science, collaboration and innovation.*

Michael Donnelly
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. The members of the Authority during 2021 were:

Mr Michael Donnelly
Chairperson
Appointed 19 April 2021

Mr Joe Collins

Dr Paula Kilbane
Appointed 28 June 2021

Mr David Holohan

Dr Sharon O'Kane
Appointed 15 July 2021

Mr Brian Jones

Dr Diarmuid Quinlan

Dr Elizabeth Keane

Prof Richard Reilly

Management Committee

The members of the Management Committee in 2021 included:

Dr Lorraine Nolan
Chief Executive

Ms Rita Purcell
Deputy Chief Executive

Dr J.G. Beechinor
Director of Veterinary Sciences

Ms Sinead Curran
Director of Human Products Monitoring

Mr Sean d'Art
Director of ICT and Business Services

Dr Caitríona Fisher
Director of Quality, Scientific Affairs and Communications
Retired 1 October 2021

Mr John Lynch
Director of Compliance
Retired 8 August 2021

Dr Niall MacAleenan
Director of Medical Devices

Ms Grainne Power
Director of Human Products Authorisation and Registration

Ms Elizabeth Stuart
Director of Human Resources and Change

Chief Executive's Report

As I reflect on what has been another busy and productive year for the organisation, I am incredibly proud and inspired by the level of dedication shown by everyone in the HPRA to ensure the continued protection of human and animal health during unprecedented times.

Pandemic Response

As expected, the pandemic response remained a key priority for the organisation in 2021. The continual authorisation of safe and effective vaccines and therapeutics as the year progressed provided new approaches and a renewed hope in our fight to protect public health. Indeed, thanks to the overwhelming success of the national vaccination campaign, supported by many stakeholders across the broader health system, including the HPRA, we have been able to decouple the relationship between SARS-CoV-2 infection and disease severity. As vaccination rates increased, severe disease, ICU admissions and deaths due to COVID steadily declined throughout the year despite initial concerns associated with the emergence of new variants.

Through participation at NPHET, NIAC, and the High-Level Task Force on COVID-19 Vaccination, experts from across our organisation provided regulatory updates and data to help inform and support both the pandemic response decision-making and the subsequent public health advice. The HPRA also contributed significantly on many fronts to the pandemic response effort at European level, including permanent representation on the EMA's Emergency Expert Task Force, which was a leading contributor in Europe to the evaluation and review of vaccines.

The initial oversight of the development of safe and effective vaccines was only part of the process. The regulatory system needed to demonstrate an incredible level of agility and foresight to ensure the continued safety and trust in vaccines during the extraordinary national, regional and global vaccination campaigns with billions of doses administered by the end of 2021. Indeed, our HPRA safety monitoring team demonstrated an incredible level of resolve, agility and diligence in processing almost 18,000 reports of suspected side effects associated with COVID-19 vaccines throughout 2021. The individual assessment of this volume of reports, and their subsequent inclusion in both national and European safety reviews, was a huge achievement for the organisation, and I would like to express my sincere thanks to everyone who worked tirelessly to ensure the continued safety of all approved COVID-19 vaccines and therapeutics throughout the year.

Exciting Future of Work

The pandemic demonstrated the importance of adopting an agile approach to how we work to achieve our goals of ensuring the protection of human and animal health. Specifically, the organisation continued to adapt to a new business environment as staff worked remotely throughout the year in line with public health recommendations. In an effort to capitalise on the very real benefits afforded by remote working, the organisation is introducing a hybrid-working model to include both office and remote based working. Such an approach will enable us to effectively meet our statutory obligations and deliver for our stakeholders, while at the same time preserving the unique ethos and culture of the organisation, and allowing for an enhanced work-life balance.

To establish how a hybrid model can be best implemented, a cross-organisational project was initiated to better understand the operational priorities, stakeholder needs, buildings and technology requirements, and current flexibilities. The organisation is now taking its first steps towards a progressive, exciting and flexible way of working.

Opportunities Afforded by New Legislative Changes

The past year was a time of significant evolution with regard to the implementation of new legislative frameworks, which will positively affect both human and animal health into the future. Indeed, developments occurred across a number of areas and will continue over the coming years. The introduction of the new Medical Devices Regulation (MDR) in May of this year represents a major step forward in the protection of public health, through its capacity to enable enhanced safety and performance of medical devices and its support to continued innovation within the sector. The successful implementation of this Regulation, and preparation for the new *in-vitro* diagnostic framework in 2023, continues to be a key focus for the organisation. In 2021, the finalisation of our preparations for the new European Clinical Trials Regulation and the Veterinary Medicines Regulation were also areas of intense focus. We look forward to the new opportunities that these developments will bring to each of the relevant sectors, including better support for the growth of clinical research in Ireland and for the availability, safety and optimum use of veterinary medicines.

The implementation of each new regulatory framework involves continued advancement of our partnership approach to working with other health system stakeholders both nationally and at European level. Each new framework also requires internal organisational development, and, in particular, the national integration into new European databases and IT infrastructure that underpin the legislative enhancements. Preparation is a true cross-organisational effort, encompassing not only our relevant technical teams, but also colleagues throughout the organisation including ICT, business services, human resources and communications. As this work was also conducted in 2021, in parallel with the national pandemic response, particular thanks are due to everyone involved for their contribution to the future proofing of the regulatory system.

Looking Forward

Science has provided us with new beginnings in our approach to tackling the pandemic and protecting public health, and it affords us the opportunity to look forward to 2022 with renewed optimism. Although the epidemiological situation improved throughout 2021, thanks to the authorisation and roll-out of safe and effective vaccines, the HPRA will continue to support health system partners as we transition to a new phase in the pandemic response. We will continue to provide regulatory support and closely monitor the safety of vaccines and therapeutics over the months and indeed years ahead, as booster campaigns and vaccine roll-out further evolve to meet needs. Moreover, it is critical we consolidate and strengthen both existing and newly established relationships to further enhance national systems to better regulate both human and animal health products.

The pandemic has demonstrated in a very meaningful way the opportunity, but also the feasibility, of safe and rapid acceleration in innovative product development, from concept to market authorisation and global uptake in a period of less than 12 months. This remarkable achievement was supported through the introduction of range of regulatory agilities, including, but not limited to, early access to scientific advice, rolling reviews and accelerated assessments of market authorisation applications. It is now important to reflect on these adapted regulatory processes to evaluate their success and identify ways of embedding these practices into routine work to support innovation now and into the future. The new pharmaceutical strategy for Europe is also influencing our thinking in this area. The strategy will frame the future regulatory and policy direction for medicines in Europe for many years. In collaboration with colleagues from across the medicines regulatory network, we are actively reviewing and analysing the objectives of this policy in combination with lessons learned from the pandemic so that medicines regulation continues to add value.

Something that became increasingly evident throughout 2021, was the need for a global and coordinated approach by health products regulators. While this has been driven over many years by an increasingly globalised industry, the response to the pandemic further emphasised the importance of a coordinated international approach. Such coordination has many benefits in terms of avoiding duplication, providing greater certainty to regulated sectors and making the best use of resources. Ultimately, however, greater efficiency and coherence in the regulatory process can deliver significant benefits for patients through the application of consistent safety, efficacy and quality standards.

Furthermore, where appropriate, this approach can also result in accelerated product availability to meet both existing and newly emerging public health challenges. The HPRA continues to position itself centrally not just within the established European regulatory network for medicines but also through its ongoing commitment to the International Coalition of Medicines Regulatory Authorities (ICMRA). In this forum, it engages and collaborates with the largest and most advanced regulatory authorities in the world ensuring that the Irish perspective is heard and recognised. Similarly, in respect of medical devices, in addition to ongoing European engagement, the HPRA continues to participate in initiatives to promote regulatory convergence and harmonisation globally through the International Medical Device Regulators Forum (IMDRF).

Acknowledgements

I want to take this opportunity to acknowledge the significant contribution of our former colleagues and members of the HPRA's leadership team, John Lynch and Caitriona Fisher. John and Caitriona both retired in 2021 after many years of service to the organisation. John was instrumental in establishing our Compliance Department and many of the HPRA's systems and procedures for its inspection, market surveillance and enforcement activities. Caitriona, meanwhile, was responsible for the establishment and the enhancement of our processes for governance and oversight, including our quality management and audit programmes, and our strategic and business planning functions. Both have been wonderful colleagues, leaders, mentors and friends to so many throughout the years. I feel very privileged to have worked with them on a professional basis but also to have known and engaged with them at a personal level.

I would like to thank the Authority for their support, leadership and drive to ensure the HPRA is continually striving for excellence across our entire remit.
In addition, I wish to acknowledge the Ministers and staff of the Department of Health and of the Department of Agriculture, Food and the Marine for the support, co-operation and collaboration with the HPRA on a range of activities throughout the year, particularly related to the pandemic response and introduction of new legislative changes.

Finally, I would like to thank all my HPRA colleagues who, throughout 2021, maintained their absolute commitment to both public and animal health protection. I am so proud of their work and contribution to the health system nationally during a period of immense challenge. It is a privilege to work as part of such an excellent and professional team.

Dr Lorraine Nolan
Chief Executive

Strategic Plan 2021-2025 – Key Achievements in 2021

Goal 1

Health system partnerships

Strengthening our collaborations across all areas of the health system

Worked with national and international partners to manage the public health impact from COVID-19 and the extremely high volume of regulatory and communication activities relating to vaccines and therapies.

With the Department of Health and HSE, monitored and managed any impacts on the supply of medicines and medical devices arising from the end of the Brexit transition period.

Completed a mapping exercise of existing sources of data exchange for medicines, as well as newly identified sources to be progressed in 2022.

Worked with national stakeholders to support the establishment of the new national research ethics committees.

Goal 2

Progressive regulation

Increasing our use of proportionate and adaptive approaches for better patient outcomes

Collaborated with the Department of Health and national partners to prepare national legislation for the EU Clinical Trial Regulation, the EU Medical Device Regulation and the national research ethics committees.

Briefed the Department of Agriculture, Food and the Marine on the new EU Regulations for veterinary medicines and commented on draft legislation to replace the existing Irish regulations.

Co-led an International Coalition of Medicines Regulatory Authorities (ICMRA) project on regulatory flexibilities to increase manufacturing capacity and post approval changes of COVID-19 vaccines and therapeutics.

Goal 3

Communication and engagement

Improving our models of engagement to strengthen public trust and confidence

Formally established the Patient Forum, chaired by a member of the Authority and with agreed terms of reference and a work plan now published on the HPRA's website.

Deepened our engagement with stakeholders through our contributions to the national pandemic response, providing extensive website and newsletter updates, and significant engagement with national media to explain the regulatory processes and outcomes to the general public.

Explored interactions and modalities with HSE quality and safety personnel as an initial step in developing an overall policy for interaction with the HSE and clinical leads on medical devices.

Goal 4

Enabling innovation

Enhancing our supports for innovation from discovery through to regulatory approval

Developed guidance for innovators of medical devices as well as updated guidance and a free pre-submission process for clinical investigators in relation to new EU requirements.

Provided guidance to national researchers on the EU Clinical Trials Regulation, and encouraged their engagement with STARS[1] outputs of specific benefit to academic researchers.

Increased our capacity to contribute to EMA scientific advice for veterinary medicines, ranking joint first in the number of procedures by year-end.

1. STARS is the EU-funded project on 'Strengthening Training of Academia in Regulatory Science.'

Goal 5

Great people, great processes

Developing our organisation and people to successfully achieve our goals

Agreed the future hybrid model of working which takes account of organisation's needs, current experience with remote working and wider societal changes, for implementation from 2022.

Focussed our digital transformation activities on consolidating case management in a number of new areas into one digital platform.

Launched a new energy and sustainability project for 2021-2030 to build on the 33% gain in energy efficiency realised under the energy project for 2015-2020.

Created a Diversity and Inclusion Committee and achieved a silver award in the Investors in Diversity 'Equality, Diversity and Inclusion Mark'.

COVID-19 Response

Overview of Regulatory Activities

All pre- and post-authorisation procedures associated with COVID-19 related medicines dominated the HPRA's regulatory response throughout the year, in addition to liaising with key stakeholders across the broader national healthcare system through participation at NPHET, NIAC and the High-Level Task Force on COVID-19 Vaccination.

While the first COVID-19 vaccine was authorised in Q4 of 2020, which initiated a new phase in the pandemic response, the European medicines regulatory network continued to prioritise the expedited review, and ultimately authorisation, of additional therapeutics and vaccines in 2021. Specifically, four additional COVID-19 vaccines (Spikevax [Moderna]; Vaxzevria [AstraZeneca]; Jcovden [Janssen]; and Nuvaxovid [Novavax]) based on a range of technologies, including mRNA, viral vector and protein nanoparticles, all received conditional marketing authorisations (CMA). The conditional authorisations were granted following reviews by the EMA's Committee for Medicinal Products for Human Use (CHMP). As a member of the CHMP, experts from the HPRA participated in the assessment of each vaccine, in addition to the authorisation and review of numerous therapeutics for the treatment of COVID-19, including, Kineret (anakinra); Regkirona (regdanvimab); RoActemra (tocilizumab); Ronapreve (casirivimab / imdevimab), Xevudy (sotrovimab) and Lagevrio (molnupiravir). In addition to the authorisation procedures, the CHMP conducted numerous complementary reviews aimed at providing a harmonised scientific opinion at EU level to support national decisions on the use of COVID-19 treatments prior to full authorisation.

Importantly, the authorisation of safe and effective vaccines and therapeutics is only one element in the life cycle of a medicine. Following authorisation, new medicines are closely monitored on a national, regional and indeed global level to ensure their continued safety. Following the authorisation of COVID-19 vaccines and therapeutics, and subsequent initiation of the national vaccination campaign, the HPRA issued a request to healthcare professionals and members of the public to submit reports of suspected side effects following vaccination. This is a critical step to ensuring the benefit-risk profile of any medicine is informed through real-world use and that it remains positive following authorisation. Submission of reports of suspected side effects enables regulators to monitor vaccine safety and take the most appropriate action required should new safety related information become available. As expected, reports of suspected side effects submitted to the HPRA and reviewed by our safety monitoring team increased substantially in 2021 and more than trebled when compared to the previous year. Of the 25,622 suspected adverse reaction reports received, 17,946 were associated with the use of COVID-19 vaccines. In addition to reviewing and onward submission of national reports of suspected side effects to the broader EU safety database (EudraVigilance), the HPRA contributed to EU coordinated reviews of monthly safety update reports submitted by the licence holders, as well as ad-hoc signal assessment reports, to ensure the benefit-risk profile for each vaccine and therapeutic remained positive.

In addition to pre- and post-authorisation procedures, experts from across the organisation continued to facilitate other aspects of the pandemic response. To support the continued supply of medicines, a range of risk-based flexibilities were retained, including distant and hybrid inspections, and the introduction of e-licences for import/export of controlled drugs. Moreover, the HPRA continued to engage extensively with key stakeholders concerning the use medical devices, with a particular focus on the provision of regulatory support regarding antigen tests.

Specific Areas of Focus

The HPRA introduced a range of cross-functional activities and work-related agilities to support the broader pandemic response from a regulatory perspective. There was also significant engagement and collaboration with colleagues from both the wider public health system nationally and the European and global regulatory networks. HPRA-specific COVID-19 related activities, contributions and collaborations during 2021 included:

Medicines Authorisation and Availability

- Supported the operation of the national vaccination programme through regular engagement with the Department of Health and the HSE's National Immunisation Office incorporating the provision of regulatory updates to NPHET and the High-Level Task Force on COVID-19 Vaccination.
- Worked in partnership with the Department of Health, HSE and supply-chain stakeholders to minimise and proactively address any risks posed to the ongoing supply of medicines to Irish patients.
- Collaborated with the Department and the National Office for Research Ethics Committees to support expedited regulatory review for COVID-19 related health research.
- Active engagement in the assessment of COVID-19 vaccines and therapeutics at the EMA's CHMP, scientific working parties, committees and through permanent representation in the COVID-19 EMA pandemic task force (COVID-ETF).

Safety Monitoring

- Receipt and onward reporting of 17,946 reports of suspected adverse reactions associated with the use of COVID-19 vaccines. Healthcare professionals and the public were encouraged to report any suspected adverse reactions to the HPRA and this is reflected in the level of stimulated reporting which enabled the close monitoring of COVID-19 vaccines at a national level. Training was also provided to HSE vaccinators and to general practitioners on the safety reporting process.
- Participated in the extensive and ongoing safety monitoring activities for COVID-19 vaccines and therapeutics as a member of the EMA's Pharmacovigilance Risk Assessment Committee (PRAC). This involved input into the review of risk management plans, and contribution to the ongoing assessment of cumulative safety data, including that submitted in monthly safety summary reports, periodic safety update reports or arising through signal procedures.
- Actively participated as a member of the ICMRA COVID-19 Vaccines Pharmacovigilance Network, facilitating the exchange of safety issues between international regulators.
- Facilitated safety communications through the publication of 14 separate safety update reports summarising the national reporting experience and a dedicated Drug Safety Newsletter, in addition to the regulatory approval of nine direct healthcare professional communications (DHPCs) issued by marketing authorisation holders.
- Provided regular briefings on safety monitoring activities to the Department of Health, NPHET and NIAC.
- Engaged proactively with media including national media interviews discussing vaccine safety.

Compliance

- Adopted a suite of extraordinary risk-based flexibilities to ensure the continued availability of medicinal products, including:
  - Manufacturing requirements;
  - Importation of finished products and active ingredients;
  - Variations requests;
  - Changes to good practice (GxP) inspections, transitioning from on-site to fully remote or hybrid inspections.
- Participated in the development of an ICMRA Reflection Paper on experience gained from remote inspections and distant assessments.
- Worked together with colleagues from An Garda Síochána and Revenue's Customs Service to proactively monitor the supply chain for unauthorised or falsified COVID-19 health products.
- Monitored and responded to the advertising and promotion of unauthorised/non-compliant treatments and medical devices purported to be for the detection, cure or prevention of COVID-19.

Medical Devices

- Worked as part of the HSE medical devices criticality assessment group, a subgroup of NPHET to provide regulatory advice and input on relevant medical devices. The HPRA was also a member of the NPHET subgroup on diagnostic testing approaches.
- Provided regulatory support to the Department of Health and the rapid antigen test Expert Group regarding the use of antigen diagnostic tests (ADTs) and rapid antigen diagnostic tests (RADTs).
- Contributed to European regulatory activity via regular meetings of Competent Authorities on the topic of COVID-19 and *in-vitro* diagnostic medical devices (IVDs) .
- Participated in international regulatory activity relating to COVID-19 and medical devices and IVDs.
- The HPRA contributed to expert groups established by HIQA to conduct rapid assessments of scientific literature relating to COVID-19.

Ongoing Pandemic Response and Future Contributions

The intensity of activities related to the national and European pandemic response have decreased in the early part of 2022 due to the improving epidemiological situation. Importantly, while vaccination against COVID-19 continues, the HPRA will maintain its close monitoring of the safety of the vaccines, whether for primary or booster doses. In addition to the processing national reports of suspected adverse reactions to COVID-19 related vaccines and the publication of regular safety update reports, the HPRA will continue to contribute to EU coordinated reviews and to the assessment of ad-hoc signal assessment reports.

As next-generation vaccines are developed in response to changing epidemiological conditions and circulating variants, we will participate in pre-authorisation procedures to assess the safety, effectiveness and quality of vaccine candidates, while also influencing vaccine and therapeutic development through the provision of scientific advice.

Finally, the HPRA will continue to support and engage with key health system partners ensuring the most up-to-date regulatory information and data is available to support the ongoing national pandemic response.

Human Medicines

The HPRA grants licences for medicines subject to a review of their safety, quality and effectiveness and continuously monitors 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 or advertising of medicines.

Authorisation and Registration

- Prior to a new medicine being placed on the Irish market, it must be assessed and authorised (licensed) by the HPRA or by the 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 several routes through which a product can be authorised by the HPRA. These include the national procedure, the mutual recognition procedure (MRP) and the decentralised procedure (DCP). Both MRP and DCP involve the simultaneous submission of applications in a number of EU Member States.

  The centralised route is co-ordinated by the EMA and results in an authorisation that is granted by the European Commission and is valid across Europe. 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.

  During the year in review, the total number of new medicines authorised in Ireland was 542. The 2021 figure incorporates:

  – 94 new national applications including 88 parallel import applications;

  – 72 applications made under the MRP and 177 applications made under DCP. The HPRA acted as reference (lead) Member State for the assessment of 19 of these DCP applications;

  – 11 rapporteurships and 10 co-rapporteurships under the centralised route;

  – An additional 175 medicines authorised through the centralised route where the HPRA was neither rapporteur nor co-rapporteur;

  – Three traditional herbal medicinal products under the simplified registration scheme.

- The EMA operates a scientific advice and protocol assistance procedure system to applicants on the appropriate tests and studies in the development of a medicine. This is designed to facilitate the development and availability of high quality, effective and acceptably safe medicines for the benefit of patients. During 2021, the HPRA acted as co-ordinator for 82 EMA scientific advice requests across a broad range of conditions.

  Our national scientific and regulatory advice procedure functions in a similar way and assists commercial and non-commercial entities making applications for clinical trial authorisation or marketing authorisations. This service complements advice that we provide on earlier stage product development through our Innovation Office. During the year, we completed seven requests under this procedure.

- Participation in clinical trials can enable patients to benefit from new and promising therapies. During 2021, we issued 107 new clinical trial applications, including five COVID-19 related trials, one of which was a voluntary harmonisation procedure with the HPRA acting as lead Member State.

- Reclassification of the legal status of medicines aims to increase the number of medicines available to patients without prescription where it is safe to do so. Of note in 2021, two medicines were authorised for non-prescription, general sale. Five new applications for the reclassification of medicines from prescription only to non-prescription pharmacy only status were received.

- The HPRA publishes and maintains a list of interchangeable medicines to facilitate generic substitution by pharmacists and to allow for reference pricing by the HSE. By year-end, the interchangeable medicines list included 118 active substances or combinations of active substances.

- The Medicines Shortages Framework brings together key players in the health sector with the aim of developing strategies to mitigate the effect of shortages in Ireland. A review of the first two years of the operation of the framework has shown the effectiveness of the framework in addressing shortages and identifying opportunities to further improve the prevention and management of shortages. Consideration and implementation of these opportunities will begin in 2022.

  The HPRA also continues to take a prominent role in European and International initiatives to address medicines shortages including the single point of contact network for medicines shortages and the structured dialogue on security of medicines supply organised by the European Commission.

- As the use of multilingual labelling remains an important means of minimising the impact of Brexit and supporting the availability of medicines in Ireland, the HPRA remains actively involved in progressing this initiative at the HMA level through the Coordination group for Mutual recognition and Decentralised procedures – human (CMDh). In 2021, the HPRA continued to lead the CMDh Multilingual Packaging Working Group, which prepared a further update of the best practice guide on multilingual packaging. The update takes into account discussions on issues arising and Member State feedback collected in a survey conducted during 2021. Concerns raised by interested parties and requests from Member States for clarification on practical aspects of the pilot on multilingual packaging were also considered. The pilot phase continued throughout 2021.

  The HPRA continues to actively contribute at the EMA QRD (Quality Review of Documents) group to agree labelling flexibilities for COVID-19 vaccines and labelling exemption requests to maintain availability of small volume medicines.

- To aid the continuity of supply to the marketplace in the event of a medicine shortage following Brexit, the HPRA granted 181 temporary 'batch-specific request' authorisations during 2021.

- The HPRA granted four market authorisations following the zero-day mutual recognition procedure to ensure the availability of medicinal products important for the Irish market.

- Relating to Brexit, the HPRA accepted 371 notifications for human medicines under the Commission Notice on 'Application of the Union's pharmaceutical acquis in markets historically dependent on medicines supply from or through Great Britain after the end of the transition period'.

Authorisation and registration: Key figures	2019	2020	2021
Classification queries/reviews	76	88	89
Scientific advice			
Lead in EMA scientific advice:	102	119	82
National scientific advice	20	11	7
Clinical trial applications	88	73	107
Voluntary Harmonisation Procedures (multinational clinical trials)			
Lead	2	4	3
Participating member state	8	7	7
New medicines applications for marketing authorisations			
National (including new parallel imports)	49	61	94
Mutual recognition and decentralised RMS	20	23	29
Mutual recognition and decentralised CMS	229	163	220
Centralised Rapp/Co-Rapp/Peer reviewer	17	18	28
Traditional herbal medicinal products under the simplified registration scheme	2	2	3
Homeopathic medicines under the simplified/national rules schemes	3	2	0
Variations to marketing authorisations (Type IA, IB, II)	14,957	12,026	9,665
Articles 45 and 46 - Variations to Update Product Information	0	1	6
Renewals of marketing authorisations	291	390	305
Transfer of marketing authorisation holder	1,583	202	468
Manufacturers	135	138	145
Manufacturers of investigational medicinal products	69	76	75
Wholesalers	385	379	391
Registrations for active pharmaceuticals ingredients			
Manufacturers	30	29	23
Importers	68	75	77
Distributors	92	102	99
Brokers	8	9	7
Export certificates	1,367	1,019	1,102
Exempt medicines programme for notification of unauthorised medicine import	2,586,120 packs	2,789,340 packs	2,758,650 packs

Safety and Quality

- Adverse reaction reporting assists the HPRA, in co-operation with pharmacovigilance professionals in Europe and further afield, to further characterise the safety profile of authorised medicines when in clinical use. Reports submitted to the HPRA in many instances arise from concerns due to an observation of an unexpected and / or unwanted event, in the context of use of a medicine. They can also include known adverse reactions, such as those described in the product information.

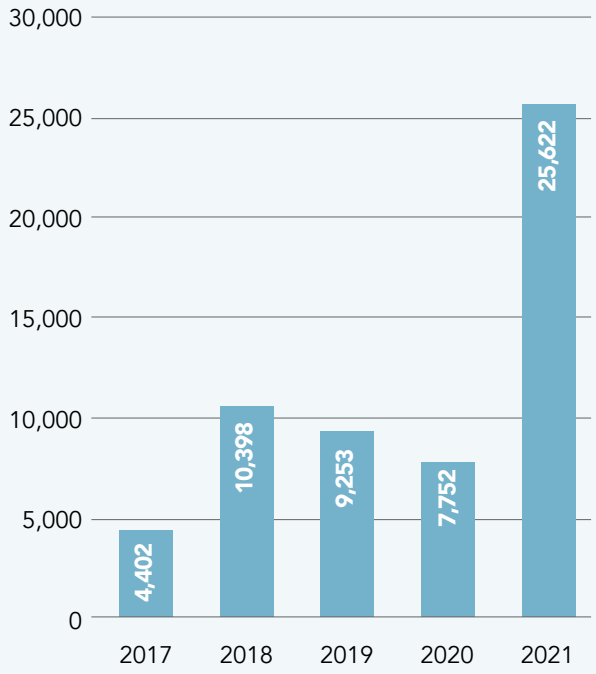
  This year:

  – A total of 25,622 suspected adverse reaction reports were received associated with the use of human medicines, which represents a significant increase of 331% in the total number of reports received compared to 2020.

  – Of the reports received, 17,946 were associated with the use of COVID-19 vaccines, with approximately 7.5 million doses administered in 2021. As part of the roll-out of vaccination programs, healthcare professionals and the public were strongly encouraged to report any suspected adverse reactions to the HPRA. This is reflected in the level of stimulated reporting and enabled the close monitoring of COVID-19 vaccines undertaken together with EU counterparts.

  – An additional 7,676 suspected adverse reaction reports were received in 2021 associated with the use of other human medicines (including other vaccines), which is largely unchanged as compared with 2020.

Adverse Event Reports



– Of the adverse reaction reports received by the HPRA in 2021, 45% were received from members of the public, 26% from healthcare professionals and 29% were reported by marketing authorisation holders.

The breakdown of reports submitted directly by members of the public and healthcare professionals (excluding marketing authorisation holders) was as follows

Sources of Suspected New Adverse Reaction Reports	%
Doctor	12
Patient/Consumer	63
Nurse	11
Pharmacist	9
Healthcare professional - Other	5

This represents a significant change in the reporting pattern from 2020, again largely attributable to COVID-19 vaccines, for which 62% of reports were from members of the public, a further 34% from healthcare professionals and 4% from marketing authorisation holders. For the remaining reports, the pattern for 2021 is similar to previous years, with 89% reported by marketing authorisation holders, with a further 0.5% reported by sponsors, in the context of

ongoing clinical trials. It is important to note that reports received by companies will have been initially notified to them by healthcare professionals or members of the public.

– Medicines subject to additional monitoring account for 74% of the reports submitted, of which 70% were associated with COVID-19 vaccines.

- The medicines most frequently included in reports to the HPRA accounted for approximately 92% of the adverse reaction reports received in 2021 (see below 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*
Vaccines, including COVID-19 vaccines	18,242
Antineoplastic medicines, including immune-modulating medicines, monoclonal antibodies and endocrine medicines	4,115
Anti-infective medicines, including antibacterials, antimycotics, antivirals and immunoglobulins	494
Psycholeptic medicines	470
Medicines for obstructive airway diseases	352
Medicines for the treatment of Parkinson's Disease	348
Medicines for the treatment of Diabetes Mellitus	312
Analgesics, including medicines for prevention and treatment of migraine	244
Medicines regulating parathyroid hormone levels	213
Hormonal medicines including contraceptives and hormone replacement therapies	205

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

- Of the new adverse reaction reports received by the HPRA in 2021, 229 patients were reported to have died following treatment with a suspect medicine. The following table outlines the medicines or class of medicines associated with the highest number of reports.

– 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.

– It can be expected that fatalities due to progression of underlying disease or natural causes will continue to occur during or after treatment with medicines. This does not mean that the medicine caused the death.

– Individual reports alone are rarely sufficient to establish causation, and it is essential that the totality of data are examined, including that from voluntary reporting systems, as well as from literature, epidemiological studies and clinical trials, to reach robust conclusions on causal relationship.

– In many cases, where a fatality is reported, the patient concerned was described as having significant underlying illness and were treated with multiple medicines and/or surgery.

– In respect of COVID-19 vaccines, the HPRA published safety updates throughout 2021. Each updated including information on reports received describing an individual who was known to have been vaccinated and subsequently passed away. The majority of such reports related to individuals aged 75 years and over. Further information is available on the HPRA website www.hpra.ie/covid19

Suspect Medicine(s)/ Class of Medicines	Number of Reports*
Vaccines including COVID-19 vaccines	104
Antineoplastic medicines, including immune-modulating medicines, monoclonal antibodies and endocrine medicines	72
Psycholeptic medicines	29
Anti-infective medicines, including antibacterials, antimycotics, antivirals and immunoglobulins	8
Cardiovascular medicines, including anti-hypertensive, anti-arrhythmic, and lipid lowering medicines	7
Antithrombotic medicines including anti-coagulant and anti-platelet medicines	7
Medicines for the treatment of Parkinson's Disease	7
Systemic medicines for treatment of acne	<5
Systemic corticosteroid medicines	<5
Respiratory medicines	<5
Analgesic medicines	<5

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

- The HPRA also plays a key role in monitoring the safety of medicines on the Irish market via our vigilance assessment and risk management activities. This incorporates our contribution to the work of t PRAC at the EMA. During 2021, the HPRA:
  - Continued our involvement in the work-sharing initiative for signal detection within the EU, acting as lead Member State for the monitoring of 70 nationally authorised active substances;
  - Serving as PRAC rapporteur, we were also responsible for the further management of any signals detected in relation to 56 centrally authorised medicines (containing 40 active substances / combination of active substances);
  - Participated in the EU periodic safety update report (PSUR) single assessment procedure and national assessments contributing to the evaluation of 837 PSURs and leading the single EU assessment for 53 procedures;
  - Serving as a PRAC Member State, participated in the assessment of 36 monthly safety summary reports as part of close safety monitoring of COVID-19 vaccines;
  - Participated as a concerned Member State in four ongoing safety referrals, two of which reached a conclusion during the year;
  - Contributed to the review of 440 risk management plans (newly approved or updated) submitted via national, mutual recognition, decentralised and centralised procedures;
  - We also provided assessment input to 603 post-authorisation safety procedures (including safety study protocols, reports and other post authorisation safety-related measures).
- The HPRA continues to communicate important safety information to facilitate clinical readiness at national level for new recommendations on the safe and rational use of medicines following EU benefit-risk reviews. During 2021, the HPRA:
  - Approved the content and communication plan for 23 Direct Healthcare Professional Communications (DHPCs), containing important new information on authorised medicines and highlighting the need for healthcare professionals to take certain actions or adapt their practices in order to minimise risks to patients and optimise safe use of medicines. DHPCs are distributed by marketing authorisation holders and are available on the HPRA website.
  - Approved the content and communication plan for 93 sets of new or updated additional risk minimisation measures for medicines. These measures are recommended only when necessary to manage an important safety issue and to optimise the risk-benefit balance of a medicine. This includes, for example, educational materials for healthcare professionals, patient guides and cards, pregnancy prevention programs, and controlled distribution systems. The materials are distributed by marketing authorisation holders and are available on the HPRA website.
  - Published and distributed five issues of the HPRAs Drug Safety Newsletter to registered healthcare professionals, all of which are accessible from the HPRA website. The Drug Safety Newsletter highlights important safety information to healthcare professionals with hyperlinks to product information and other relevant documents on the HPRA and EMA websites. A full index of topics covered during the past year is included in Appendix 3.

- Provided 21 articles for inclusion in the monthly MIMS (Ireland) publication in addition to two articles for the Irish Medicines Formulary. The full list of topics covered in these articles is included in Appendix 3.
- Highlighted the PRAC monthly agendas, minutes, meeting highlights, notifications of safety reviews and signals via our website.

- Also, in 2021, the HPRA progressed a research project, in collaboration with researchers from the Royal College of Surgeons in Ireland (RCSI), to assess the effectiveness of risk minimisation measures to prevent harms from teratogenic medicines. The project was funded through a Health Research Board Applied Partnership Award, bringing together the HPRA as knowledge user and the RCSI as academic researcher. This collaborative project resulted in the publication of a multi-stakeholder cross-sectional study relating to awareness, knowledge and practice of healthcare professionals following implementation of a pregnancy prevention program for sodium valproate in Ireland (Hughes JE, Buckley N, Looney Y, Kirwan G, Curran S, Doherty CP, Mullooly M, Bennett KE. Expert Opin Drug Saf. 2021 Aug;20(8):965-977). A summary of the results was included in the 106th edition of the HPRAs Drug Safety Newsletter.

- The HPRA's inspections programme focuses on ensuring compliance with relevant standards and legislation. This year, there were:
  - 87 good manufacturing practice (GMP) inspections at sites that produce human medicines or active substances;
  - 49 good distribution practice (GDP) inspections at wholesalers and distributors;
  - Five good clinical practice inspections at investigator or sponsor sites;
  - Six pharmacovigilance inspections;
  - One regulatory compliance inspection conducted at the premises of a marketing authorisation holder to determine the level of compliance with the legal requirements for the marketing and advertising of medicines.

- The risk-based sampling and analysis programme is part of the HPRA's monitoring of the quality and safety of medicines, both on the Irish market and pharmaceutical products manufactured in Ireland for export. It involves the analytical testing of products and the examination of their packaging and labelling, as well as product usability checks. In 2021, 422 cases were opened under the programme. These included:
  - Completion of analytical testing of 269 medicines and other product samples. Of those, 205 were authorised medicines with 64 relating to HPRA enforcement cases. One product was analysed at the HPRA's Official Medicines Control Laboratory (OMCL) as part of the European Directorate for the Quality of Medicines (EDQM) surveillance programme for centrally authorised products. With respect to non-enforcement samples, the majority were found to be compliant with their specifications. However, several out-of-specification results were obtained. The most frequent related to the presence of particulate matter in injectable products. A number of ineffective anti-tamper devices on outer cartons were also observed at the laboratory, as well as a small number of out-of-specification results for appearance. Appropriate follow-up actions were undertaken in each case.
  - Examination of the packaging and labelling of 142 medicines. Nineteen non-compliances were identified including cases where safety information/warnings were absent from the package leaflet. In addition, a number of non-compliances with the Falsified Medicines Directive were identified, including ineffective anti-tamper devices. Braille-related observations were also identified, such as low dot height issues, anti-tamper devices covering the Braille dots, Braille not in a format suitable for readers in Ireland, as well as other Braille non-compliances. Appropriate follow-up actions were undertaken in each case.
  - Product usability checks were performed on 11 products typically in response to earlier quality defect reports related to those medicines. None of the samples were found to be non-compliant.

- 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 pertaining to 2,033 medicines for human use were reported or identified in 2021. This represented a 44% increase over the 2020 figure (1,408), which in turn was a 49% increase over the 2019 figure (948). The risk classifications assigned, along with the corresponding figures for the previous years, are outlined in the following table:

Year	2019	2020	2021
Critical quality defects	259	312	396
Major quality defects	291	701	1,381
Minor quality defects	375	378	235
Number of reports not justified	23	17	21
Total Number Quality Defects	**948**	**1,408**	**2,033**

Most quality defect reports (39%) were submitted by pharmacists, mainly through the HPRA online reporting portal. This was a significant increase on 2020, when 20% of reports were received from pharmacists. Reports from pharmaceutical companies, including manufacturers, distributors and/or marketing authorisation holders accounted for 32% of cases in 2021, with 26% of coming from other competent authorities.

- In certain cases, it is necessary to withdraw, or recall, medicines from the Irish market in order to protect public health. During the year, 117 human medicines were recalled, for reasons outlined in the table below.

Cause of Recall	Number of Products
Contamination issues	33
Validated transport time excursions	26
Cold chain/temperature excursions	15
Non-compliance with specifications	13
Stability Issues	6
Erroneous distribution	6
Marketing Authorisation Non-compliance	5
Lack of Sterility Assurance	4
Barcode Issues	2
Unlicensed product on the market	2
Other miscellaneous issues	5

- Caution in Use Notifications and Dear Doctor Letters/Direct Healthcare Professional Communications are issued for medicines with a significant quality defect, but where a recall action should not be initiated. This includes where an out-of-stock situation for the medicine in question, arising because of a recall action, may pose more risk to patients than the quality defect issue. Forty-three such communications were approved during 2021.

- Three rapid alerts were issued during 2021 to notify other competent authorities of significant quality defect issues that may impact other markets.

- Throughout 2021, HPRA continued to receive responses from marketing authorisation holders to the 'call for review' established under the CHMP Opinion for the Article 5(3) referral on nitrosamines.

- The HPRA monitors the sale of certain consumer health products in outlets such as grocery shops, health food shops and, where necessary, pharmacies. During 2021, 16 cases were investigated, some of which involved multiple products. Of these:
  - Fifteen cases related to the sale of medicines that did not carry a valid registration number or authorisation number for the Irish market, resulting in 26 medicines being removed from sale and necessary follow-up actions being taken;
  - One case related to an investigation into a non-compliance with the paracetamol regulations as established by the Medicinal Products (Prescription and Control of Supply) Regulations 2003.

  In addition, 50 queries linked to the sale of health products in Ireland were addressed.

- The advertising compliance programme monitors and reviews the compliance of advertising and promotional activities carried out by the industry in relation to human medicines. In total, 66 advertisements were reviewed, and non-compliances, including both major and minor issues, were identified in six cases. Two advertising-related complaints were also received. In all cases, we oversaw the necessary corrective and/or preventative actions, where relevant.

- Under our enforcement programme:
  - The HPRA detained 1,604,589 dosage units (including tablets, capsules and vials) of falsified and other illegal medicines in 2021, compared to 1,610,295 dosage units in 2020. The products detained included sedatives (46%), anabolic steroids (13%), analgesics (10%) and erectile dysfunction medicines (6%). In total, 10,596 enforcement cases were initiated, compared to 8,043 in the previous year;
  - We initiated five prosecution cases and issued seven voluntary formal cautions. Prosecutions are taken where the HPRA considers that there is a significant risk to public health or where there are persistent non-compliances. Three prosecutions related to the unauthorised supply of anabolic steroids, one related to the unauthorised supply of sildenafil citrate and one related to the supply of medicinal products from a market stall. We also supported prosecutions brought by the Director of Public Prosecutions in relation to the illegal supply of medicines;
  - The Interpol-coordinated Operation Pangea XIV was a year-round operation designed to enhance worldwide cooperation between health products regulators and other government agencies. The continued joint agency cooperation between the HPRA, Revenue's Customs Service and An Garda Síochána at a national level was reflected in the HPRA detention figures for 2021;
  - In addition, the monitoring of websites, online marketplace advertisements and social media sites throughout the year resulted in the amendment or shutdown of 461 websites, e-commerce listings and/or social media pages.

Legislation and Regulation

- In the four-year period leading up to the Trade and Cooperation Agreement between the EU and UK in December 2020, the HPRA's key strategic objective in preparing and planning for Brexit was the protection of supply of medicines and medical devices for patients and animals. This remained a key focus in 2021 as the HPRA engaged with partners both nationally and at a European level to manage the outcome and implications of the Agreement and related derogations applying to medicines introduced by the EU Commission.

  Specifically, in late December 2020, the EU Commission published a notice on the 'application of the Union's pharmaceutical acquis in markets historically dependent on medicines supply from or through Great Britain after the end of the transition period'. Applying to Ireland, Malta, Cyprus and Northern Ireland, and taking into account the special characteristics of these markets for medicines supply, the notice facilitated derogations for those medicines which had not made the necessary regulatory changes to stay on the market for one year (to 31 December 2021). As 2021 progressed, it was apparent that some compliance issues in relation to the four small markets would persist into 2022 and the Commission proposed draft legislation published in December 2021 in relation to human medicines, which extended the derogations for a further three years with a deadline of 31 December 2024. In the interests of stability and predictability, the Commission confirmed a continuation of the existing derogations for human medicines pending the outcome of the proposed legislative package. However, companies are expected to make efforts to be in compliance before the extended deadline. The derogations in respect of the Northern Ireland are not time limited.

While Ireland has issued some exemptions, the market is substantially compliant and the HPRA will continue to work with companies to ensure that outstanding issues are addressed.

- The new Clinical Trials Regulation, Regulation EU No 536/2014, came into effect on 31 January 2022, after the Clinical Trial Information System (CTIS) developed by the EMA was deemed fully functional by the European Commission.

  The following national activities were progressed by the HPRA during 2021 to support clinical research:

  – Continued engagement with the Department of Health and the National Office for Research Ethics regarding the implementation of the Regulation and the development of national legislation;

  – Hosting a series of webinars on the implementation of the Clinical Trials Regulation with over 800 participants involved during the weeklong initiative. Presentations and guidance were made available on the HPRA website following the webinars;

  – The availability of a pilot project for simultaneous submission of applications to both the HPRA and the National Research Ethics Committee (NREC), which enables preparation for implementation of the Regulation;

  – Active participation in the European voluntary harmonisation project, which is similar to the approval process for clinical trials under the planned new legislation.

  Ongoing collaboration with the EMA and other Member States on the implementation of the new legislation.

- Since 9 February 2019, under the Falsified Medicines Directive, the outer packs of prescription medicines must carry safety features in the form of an anti-tamper device and a barcode containing unique identifiers, including a serial number to allow verification of the authenticity of the packs. In 2021:

  – Work on the national implementation and introduction of these measures continued in conjunction with the Irish Medicines Verification Organisation (IMVO), which was responsible for establishing and managing the repository and software systems;

  – We participated in the national oversight steering group of stakeholders which met regularly to monitor progress on implementation both nationally and across the EU;

  – We contributed to the EU Expert Group on Safety Features;

  – Notwithstanding these efforts, the plan for full implementation was put on pause due to the COVID-19 pandemic and the process remained in a 'use and learn' phase at year-end.

Stakeholders and Partners

- There has been significant engagement with a range of partners from across multiple levels of government, including key public health stakeholders, in response to the COVID-19 pandemic. Please refer to dedicated earlier section of this report for further detail.

- January 2021 marked a fundamental change to the EU's and Ireland's relationship with the UK. As part of the planning for Brexit, the HPRA had liaised with wholesalers and marketing authorisation holders to ensure that there was sufficient stock in the country to act as a buffer should delays occur at ports. In addition, at the start of the year, the HPRA participated in daily meetings with colleagues from the Department of Health and the HSE to monitor critical short-life medicines and medical devices arriving into the country. A memorandum of understanding between the HPRA and customs colleagues facilitated early intervention if critical medicines got delayed due to customs issues, which proved to be enormously beneficial. While some issues occurred, close cooperation between customs, suppliers, the Department, the HSE and the HPRA, ensured there was no impact for patients. Those initial limited issues were mainly driven by unfamiliarity with third-country imports and exports. This intense period of work lasted until March 2021 and, combined with the huge amount of regulatory planning and preparation that took place in the proceeding four years, resulted in a smooth transition to the new paradigm of the UK being outside the EU.

- In September, the HPRA's Chief Executive, accompanied by the Director of Compliance and the Health Products Distribution Manager, appeared before the Joint Committee on Health which was discussing the Medical Cannabis Access Programme (MCAP). The HPRA representatives provided an outline of the HPRA role in respect of MCAP as well as an update on product applications and reviews, and products subsequently placed in Schedule 1 of the Regulations (which permits them to be used under the MCAP). The HPRA, appearing before the Committee alongside representatives from the Department of Health and the HSE, also provided responses to a number of queries from the Committee members. MCAP was previously discussed by the Committee in July 2021 with HPRA representatives again participating and responding to member queries.

- As in recent years, the HPRA delivered a programme of presentations and talks at external stakeholder events such as meetings, seminars, conferences and training courses. Such presentations provide stakeholders, including healthcare professionals and regulatory professionals, with access to relevant, up-to-date regulatory and safety information. In addition, a programme of presentations was delivered to undergraduate and postgraduate students studying courses related to the role of the HPRA. A full list of all presentations delivered during 2021 relevant to human medicines is provided in Appendix 2. As a result of the public health measures introduced in response to the COVID-19 pandemic, presentations were generally delivered remotely.

- Publications and Information

  – The Medicinal Products Newsletter provides regulatory news and updates for those working in the pharmaceutical industry. Three editions were published on our website in 2021 and are available to download from the 'Publications' section.

  – HPRA guidance documents provide stakeholders, primarily from the industry sectors we regulate, with advice and direction in respect of legislation and regulatory requirements. Several existing guidance documents were updated during 2021 and are available to download from our website. This includes documents which were the subject of significant revision, including:

    - Scientific animal protection guidance on statistical returns and applications;

    - Veterinary medicines joint-labelling and leaflet standards;

    - Guides to renewals and variations of human medicines.

Medical Devices

As the national competent authority for medical devices, the HPRA carries out a range of registration, surveillance, assessment and compliance activities. Our aim is to ensure that these health products perform as intended and do not compromise the health and safety of the patient or the person using them.

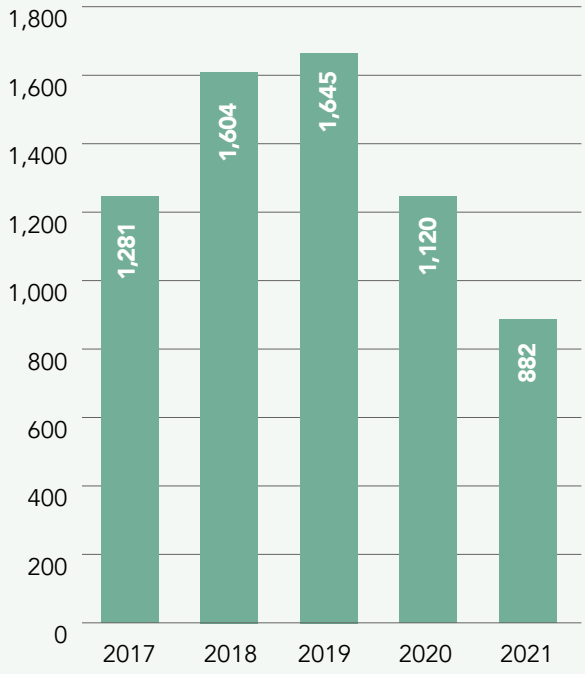
Authorisation and Registration

- The HPRA is focused on ensuring effective and consistent designation and oversight of notified bodies at a national and European level. In 2021, we:
  - Assessed an application for designation under Regulation (EU) 2017/746 on *in vitro* diagnostic medical devices (IVDR) which included the completion of a preliminary assessment report, an on-site assessment, and review of follow-up CAPA responses. This process will continue into 2022;
  - Continued our schedule of oversight of the notified body in Ireland based on ongoing assessment, surveillance and observed audits. We completed the first surveillance assessment under Regulation (EU) 2017/745 on medical devices (MDR);
  - Contributed as national experts as part of a European Joint Assessment Team (JAT) for a designation application under the IVDR for an Italian conformity assessment body;
  - Continued to support the development of EU coordination of notified body designation and oversight through participation in the EU Notified Bodies Oversight (NBO) group and the Medical Device Coordination Group (MDCG);
  - Worked with the European Commission and the Competent Authorities for Medical Devices (CAMD) on initiatives to gather data on notified body capacity and certification workload associated with MDR and IVDR.
- Supporting innovation and research of new technologies is a key strategic priority for the HPRA medical devices team. In 2021, this support included:
  - The review of applications to conduct clinical investigations of medical devices in Ireland. The number of clinical investigations increased with nine new applications and seven amendments to ongoing investigations. The HPRA anticipates that these numbers will increase further in the future;
  - A continued focus on ensuring regulatory requirements and processes are clear and accessible to potential applicants. As part of our commitment to encourage engagement during product development and innovation of medical technologies, we held pre-submission meetings with four groups of innovators to discuss potential clinical investigation applications in 2021;
  - The provision of technical, clinical and regulatory support to the work of the HPRA Innovation Office on medical devices queries received.
- Manufacturers of certain medical devices and in-vitro diagnostics (IVDs) are required to register with the HPRA. In 2021, the HPRA registered 294 medical device economic operators (for example manufacturers, authorised representatives) on the national database. 586 economic operators were validated on the European medical device database (Eudamed) by the HPRA. A total of 7,299 medical devices were also registered. This represented a significant increase in economic operator registrations when compared to previous years, some of which is attributable to the UK's exit from the European Union. During 2021, the HPRA estimates that around 35% of the economic operators registering in Ireland were due to Brexit.

Safety and Quality

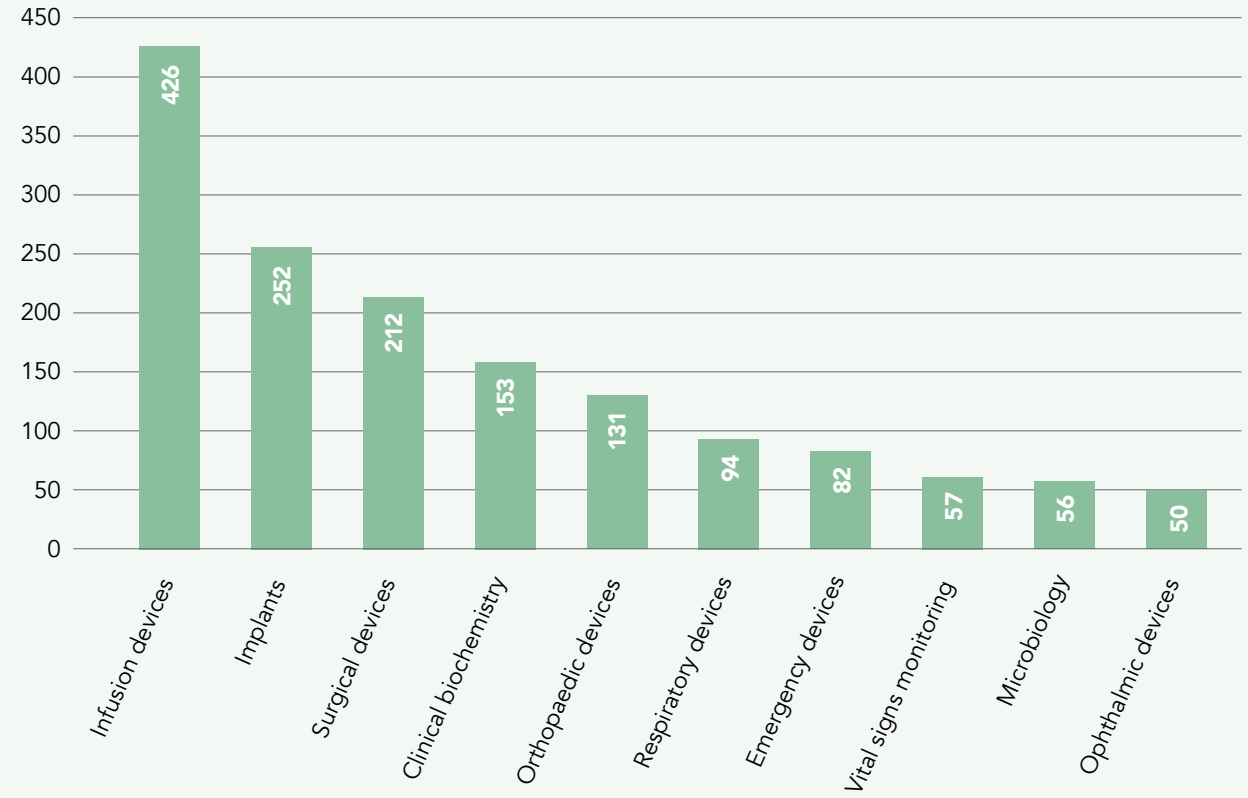
- We continue to develop and reinforce our market surveillance activities, with a particular emphasis on proactive rather than reactive actions. Of note in 2021:
  - We further developed our lifecycle market surveillance strategy and planning mechanism to allow for more effective management and reporting of these activities;
  - A total of 11 notifications were sent by the HPRA to the European network relating to medical device compliance concerns;
  - The HPRA supported the European network of authorities via the Market Surveillance Working Group to further develop coordination practices for market surveillance. The HPRA also participated in the newly formed joint inspectors group;
  - There were 882 market surveillance cases undertaken in 2021, a decrease compared to 2020 due to a significant reduction in the number of certificate notifications from notified bodies. The number of complex assessment and proactive market surveillance activities increased overall in 2021.

Market Surveillance Cases



- We continued to focus our vigilance activities during 2021 on the areas of user reporting and dissemination of HPRA medical device safety communications. This included:
  - The receipt and assessment of 1,855 medical device vigilance cases, an increase compared to 2020. Of the reports received in 2021, manufacturers accounted for 77%, 15% came from other competent authorities and 8% were received from users. Of the 1,133 incident reports notified directly to the HPRA, 13% came from users of medical devices;
  - There were 359 field safety corrective actions (FSCA) associated with the national market including 113 product removals conducted in Ireland during 2021;
  - We issued 141 national competent authority reports, one vigilance enquiry form and one notified body form to other European authorities;
  - We also issued eight safety notices in relation to medical device issues and 22 direct to healthcare professional communications;
  - Infusion devices, implants and surgical devices accounted for 48% of the total vigilance reports (see page 29). Reports continue to be received relating to in-vitro diagnostic devices in the area of clinical biochemistry (8% of reports) and medical devices in the areas of orthopaedic devices (7% of reports) and respiratory devices (5% of reports);
  - During the year, we also continued development work on signal detection of medical device issues.
- As part of its market surveillance activities, the HPRA undertakes proactive and 'for-cause' inspections of manufacturers, notified bodies, importers, distributors and authorised representatives with the objective of monitoring compliance of devices emanating from Irish based organisations. During 2021, 20 audits were performed at notified bodies, medical device manufacturers and authorised representative facilities, all of which were based on proactive market surveillance projects and notified body surveillance/assessment.

Vigilance Reports Received – Top 10 Product Types



Legislation and Regulation

- The Medical Device Regulation (EU) 2017/745 became fully applicable in May 2021. Our work during 2021 continued to help ensure an effective and timely implementation of the EU Device Regulations (EUDR) at a national and European level. Work also involved preparation for the implementation of Regulation (EU) 2017/746 on *In-vitro* Diagnostic Medical Devices. This included:
  - Ongoing work on the HPRA programme for continued development of appropriate resources, processes and systems to meet our obligations under the new regulations;
  - Engagement with key stakeholders in the sector to ensure awareness of the impact of the regulations incorporating the provision of information, the development of guidance and other communication initiatives;
  - Working with the Department of Health and relevant stakeholders on national policy and national provisions to ensure transposition of the national requirements into Irish law;
  - Contributing to the European Commission's development of the secondary legislation relating to both regulations;
  - Participating in the EU Medical Device Coordination Group (MDCG). Chaired by the EU Commission, this group is responsible for the overall coordination and governance of the regulatory system;
  - Participating in the EU Working Groups tasked with developing guidance for specific functional areas;
  - Identifying and proposing resolutions to issues posed by the ending of the Mutual Recognition Agreement (MRA) for medical devices between the EU and Switzerland.

- The HPRA continues to play a significant role in the development of EU regulatory systems and mechanisms to promote co-ordination, co-operation and consistency. In 2021, this included:
  - Continued participation in the Executive Group of the CAMD network;
  - Participation in the MDCG discussions on improving co-ordination and consistency of implementation of the new EU Regulations and prioritisation of implementation activities in the short, medium and long term. The HPRA prompted inclusion of this topic on the agenda at the MDCG meeting during 2021;
  - Continuing to lead the work of the clinical investigation and evaluation working group (CIEWG), acting as the co-chair along with the EU Commission.
- Throughout the year, our focus remained on identifying and promoting discussions and developing practical measures to ensure the regulatory system operates effectively in practice. Our core priority is on developing the European coordination of medical device safety issues. To this end, we participated in a number of Competent Authority workshops identifying key aspects to give effect to a coordinated approach to EU wide issues. The HPRA prompted inclusion of this topic on the agenda in October 2021.
- In 2021, the HPRA proposed the establishment of a core group on medical devices at the Heads of Medicines Agencies (HMA). Twelve heads of agencies have joined this core group to identify key objectives and priorities while also enhancing leadership support for the EU regulatory system for medical devices.
- At national level, we further developed our fee-based funding model for medical devices to recover costs associated with our medical device activities. However, fees were not increased during 2021 reflecting the impact of the COVID-19 pandemic on the sector.
- We continued to participate actively in initiatives to promote regulatory convergence and harmonisation of medical devices globally through the International Medical Device Regulators Forum (IMDRF). This involved:
  - Participation in the IMDRF Management Committee as part of the European delegation (along with the EU Commission and Germany);
  - Continuing to act as the IMDRF secretariat for the National Competent Authority Report (NCAR) Exchange programme;
  - Participation in the clinical evaluation working group of the IMDRF;
  - Contributing to discussions and development of the Medical Device Single Review Programme, which relates to product review.

Stakeholders and Partners

- In respect of COVID-19, we engaged with key stakeholders at both national and European level to address regulatory matters linked to medical devices. This included a particular focus on the provision of regulatory support related to antigen tests.
- We continued to engage with stakeholders to identify and resolve any challenges posed by Brexit in supplying the Irish market with critical medical devices.
- Our work to encourage the direct reporting of incidents and medical devices issues by device users and members of the public continued throughout 2021. We also continued our engagement with health services and healthcare professionals to encourage reporting and raise awareness of the roles and activities of the HPRA. In 2021, we initiated a specific project of work in this area to increase engagement and information on medical device issues to members of the public and healthcare professionals.
- The HPRA undertook a number of communication initiatives to raise awareness of the impact and requirements arising from the new EUDR. During 2021, we:
  - Hosted a training and education workshop for patients through collaboration with the Irish Platform for Patient Organisations, Science and Industry (IPPOSI), to highlight the value and importance of patient engagement for the regulatory system and to encourage user reporting;
  - Updated the HPRA website and social media channels to provide information and guidance regarding the new EU Regulations and COVID-19;
  - Delivered briefings, advice and workshops on the new Regulations to a range of different stakeholders including the HSE, notified bodies and distributors.
- Throughout the year, we engaged in ongoing strategic, operational and communication initiatives on a bilateral and multilateral basis with European and international authorities, and the EU Commission. We also further developed our bilateral partnerships with a number of these authorities. In addition, we participated in operational and strategic discussions on developing cooperation between the CAMD and the HMA networks.
- The HPRA continues to deliver a programme of presentations and talks to a range of external stakeholders. A full list of all presentations related to the regulation of medical devices that were delivered during 2021 is provided in Appendix 2.
- The HPRA contributed to a Horizon 2020 funded project (Co-ordination of Research and Evaluation of Medical Devices) CORE-MD. The HPRA are leading a work package and are part of the project board.

Medical devices: Key figures	2019	2020	2021
Lead Competent Authority role on specific vigilance issues	84	106	141
NCARs and vigilance related communications	118	142	172
Vigilance cases received/ opened	2,295	1,668	1,855
Field safety notices uploaded	461	362	382
Medical device safety / information notices	34	18	8
Medical device targeted healthcare professional communications	63	17	22
NCARs managed as IMDRF NCAR secretariat	8	10	4
COEF reports to EU network	9	18	11
Market surveillance cases	263	469	621
Notifications relating to notified body certificates	1,305	561	187
Classification requests	45	38	40
Compassionate use applications	24	34	23
Certificates of free sale	2,710	2,520	4,482
Medical device queries received	857	1,928	1,397

Blood, Tissues and Organs

The HPRA is responsible for monitoring the safety and quality of blood and blood components, and of tissues and cells intended for human transplantation. Along with the HSE, we are joint Competent Authority for organs intended for transplantation.

Authorisation and Registration

The authorisation of blood establishments, tissue establishments and organ procurement organisations/ transplantation centres permits those facilities to carry out specified activities. 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	2017	2018	2019	2020	2021
Blood establishments	3	3	3	3	3
Tissue establishments	25	26	27	25	26
Organ procurement/ transplantation	4	4	4	4	4

Safety and Quality

- Following collaboration with the National Haemovigilance Office (NHO), we submitted an annual report of serious adverse reactions and events to the EU Commission during 2021. The report reflected information received by the NHO in 2020 and included information on 59 serious adverse reactions and 120 serious adverse events that met the mandatory legislative reporting requirements.

- We also submitted an annual report on serious adverse reactions and events associated with tissues and cells to the EU Commission during 2021. The report reflected information received in 2020 and consisted of 24 reports, 17 of which met the legislative reporting requirements, including two serious adverse reactions and 15 serious adverse events.

- Updates to the common approach for defining reportable serious adverse reactions and events and other vigilance activities in Europe are continuing under the SoHO Vigilance Expert Sub-Group (VES) at which the HPRA is actively participating.

- We continued to liaise with the HSE lead and colleagues from Organ Donation and Transplant Ireland (ODTI) in relation to our respective roles under EU and national legislation on the Quality and Safety of Human Organs intended for Transplantation. During the past year, this included:
  - The exchange of relevant information on serious adverse reactions and events. In 2021, the HPRA received 14 reports of serious adverse reactions and events associated with organ donation/ transplantation;
  - Contribution to the review of the 'Framework for the Quality and Safety of Human Organs Intended for Transplantation'.

- We inspect relevant establishments, organisations and centres to monitor compliance with applicable national and EU legislation and guidelines on the quality and safety of blood, blood components, tissues and cells, and human organs intended for transplantation. Our inspection programme in 2021 included:
  - 17 tissue establishment inspections, the majority of which were routine;
  - Five blood establishments inspections;
  - Two inspections at organ procurement organisations/transplant centres.

Legislation and Regulation

- In relation to assisted human reproduction, we worked with the Department of Health on development of related legislation and engaged in respect of the commencement of parts 2 and 3 of the Children and Family Relationships Act 2015 which came into effect on 4 May 2020.

Veterinary Medicines

Our role is to grant licences for veterinary medicines subject to a review of their safety, quality and effectiveness. We continuously monitor the use of these products in animals once they become available on the market in addition to authorising clinical field trials and inspecting / licensing manufacturing sites.

Authorisation and Registration

- There are a number of procedures 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 total number of veterinary medicines authorised in Ireland at year-end was 1914.

  The 2021 figure incorporates:

  – Five new national (only) applications and one parallel importation.

  – 57 applications made under DCP. The HPRA acted as reference (lead) Member State (RMS) for the assessment of 30 of these DCP applications, including extensions.

  – 11 applications made under the MRP. The HPRA acted as RMS for the assessment of three of these MRP applications and also led a further six applications as RMS under the repeat use procedure.

  Based on the figures presented above, the HPRA was the leading national competent authority in the EU for outgoing work during 2021.

- The centralised authorisation procedure is another framework whereby veterinary medicinal products can be licensed for supply in Ireland. Experts from the HPRA acted as rapporteur or co-rapporteur in respect of three medicines that were authorised by this route.

- During 2021, the HPRA acted as co-ordinator or joint co-ordinator for five EMA scientific advice procedures.

Authorisation and registration: Key figures	2019	2020	2021
Classification enquiries	12	11	13
Clinical trials	4	5	3
New centralised as (co-)rapporteur	24	3	8
New MR/DCP as RMS	38	10	39
New MR/DCP as CMS	48	34	35
New homeopathic applications	3	0	0
New national applications	6	5	5
Renewals, national and MR	87	71	102
Variations, national and MR	2,153	789	2,362
Manufacturers of veterinary medicines	24	23	31
Export certificates	125	106	142

Safety and Quality

- The operation of a national pharmacovigilance system for veterinary medicines 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.

  Over the course of 2021, we received 439 national reports of suspected adverse events to veterinary medicines with the vast majority of reports, as in previous years, received from pharmaceutical companies.

Suspected adverse events	2017	2018	2019	2020	2021
Number of reports	397	394	347	391	439

- We processed 1,074 periodic safety update reports (PSURs) which incorporated the assessment of individual medicines on the market in Ireland as well as a work-sharing initiative where we led, or contributed to, the assessment of a class of veterinary medicines for the European Union.

- Containing the development of antimicrobial resistance (AMR) is essential for public and animal health. Our work in this area includes the collection of annual information on the sale of veterinary antibiotics from each marketing authorisation holder. This information, which is included in the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC), 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 shows that, due to a variety of factors, there are significant fluctuations in sales annually and, consequently, a clear trend is not identifiable.

Veterinary antibiotic use	2016	2017	2018	2019	2020
Tonnes sold	103.4	99.7	99.4	88.8	103.9

- The analytical testing and examination of veterinary medicines is a key component of our risk-based sampling and analysis programme. Forty-three veterinary medicines samples were included in the surveillance programme in 2021. Of these, 28 products were sent for analytical testing across a number of laboratories. This included microbiological testing and physiochemical testing. Products were also analysed at the HPRA's Official Medicines Control Laboratory (OMCL) as part of the EDQM's surveillance programme for centrally authorised products. There were no out-of-specification test results obtained for any analytical tests completed and reported during 2021. In addition, packaging and labelling checks were performed on 15 veterinary products. One non-compliance was observed where the product name detailed on the package leaflet did not conform exactly to the product name as listed on the summary of product characteristics (SmPC). Appropriate follow-up action was taken.

- Quality defects pertaining to 85 veterinary medicines were reported or identified in 2021. This represented a 9% annual increase (78 products in 2020). The risk classifications assigned, along with the corresponding figures for the previous two years, are outlined in the following table:

Year	2019	2020	2021
Critical quality defects	10	12	12
Major quality defects	19	36	35
Minor quality defects	38	29	37
Number of reports not justified	1	1	1

Almost half of the reports (49%) were submitted by pharmaceutical companies, which included manufacturers, distributors and marketing authorisation holders, while 51% of the reports were received from other competent authorities.

- 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.
  - Seven such recalls occurred during 2021.
  - Three of the recalls related to stability issues while there was one recall in each of the following categories - lack of sterility assurance, stability, non-compliance with specifications, and artwork/ SmPC non-compliance.

- One Caution-in-Use Notification was issued for a veterinary medicine to mitigate the risks presented by the quality defect.

- Our inspections programme focuses on ensuring compliance with relevant standards and legislation. In 2021, there were nine good manufacturing practice (GMP) inspections of manufacturers producing veterinary medicines and two routine pharmacovigilance inspections to determine compliance with pharmacovigilance obligations.

Legislation and Regulation

- The new veterinary regulation (Regulation 2019/6) came into effect on 28 January 2019 and will be applied from 2022. During 2021, we continued to meet and engage with the Department of Agriculture, Food and the Marine in respect of the preparations needed to support the new Regulation. Significant time and resources were also spent in providing input and advice to the Department in respect of the elaboration of new national legislation enacted in January 2022. Furthermore, the HPRA continued to engage with network preparations, including the following:
  - Preparations for the EMA's Union Product Database (UPD) of veterinary medicinal products;
  - Preparation for best practice guidelines being developed by the Coordination Group for Mutual Recognition and Decentralised Procedures - Veterinary (CMDv);
  - Preparations for the centralised management of signal detection of adverse reactions at the EMA;
  - Input into the development of changes to EMA procedures required by the legislation.
- Additionally, a project to implement the new requirements for HPRA procedures is ongoing, while there continues to be substantial ongoing work to modify internal IT systems to interface and communicate with the UPD. Furthermore, new HPRA training materials have been developed and training implemented.
- We continued to monitor developments regarding the judicial review proceedings taken against the Department of Agriculture, Food and the Marine. These proceedings contested that the labelling and packaging of veterinary medicines should be in both the Irish and English languages. A final judgment is awaited, even as the new legislation provides that national labelling can be either in Irish or in English.
- Concerning Brexit, in late December 2020, the EU Commission published a notice on the 'application of the Union's pharmaceutical acquis in markets historically dependent on medicines supply from or through Great Britain after the end of the transition period'. Applying to Ireland, Malta, Cyprus and Northern Ireland, and taking into account the special characteristics of these markets for medicines supply, the notice facilitated derogations for those medicines which had not made the necessary regulatory changes to stay on the market for one year (to 31 December 2021). While the Commission subsequently proposed draft legislation, published in December 2021, extending the derogations for human medicines for a further three years, this did not apply to veterinary medicines. The Commission did however issue a Communication extending the veterinary exemptions until the end of 2022.

Stakeholders and Partners

- As part of our ongoing stakeholder engagement, in 2021 we:
  - Held several webinars and an information day to keep stakeholders abreast of developments with the new veterinary Regulation;
  - Provided a monthly blog on HPRA implementation activities as well as those of the wider EU network on the HPRA website;
  - Participated in a number of seminars held by stakeholders in respect of the implications of the new legislation on the availability of veterinary medicinal products in Ireland;
  - Participated in the Department stakeholder group on antiparasitic resistance control measures;
  - Placed a series of public announcements in the farming press in July highlighting changes to the labelling of antiparasitic medicines for food-producing animals.
- In April 2021, the Director of Veterinary Sciences and the Veterinary Manager (CVMP) appeared before the Joint Committee on Agriculture and the Marine. The HPRA representatives delivered an opening statement on the regulation and availability of veterinary medicines before providing detailed responses to related questions from the Committee members.
- Concerning Brexit, we focused on the HPRA's key strategic aim of protecting the availability of veterinary medicines on the Irish market while also optimising our role within the European regulatory network. During the past year, this included:
  - Continued engagement with industry to identify potentially vulnerable products;
  - Continued dialogue with the UK's Veterinary Medicines Directorate regarding maintenance of common labelling for medicines post Brexit;
  - Liaising with stakeholders concerning the availability of veterinary medicinal products on the island of Ireland.

- Throughout 2021, we continued our involvement across the EU regulatory network, which includes active participation at the EMA and the HMA.
- As in recent years, we continued to deliver a programme of presentations to veterinarian students and veterinary nursing students on the role of the HPRA and the promotion of veterinary pharmacovigilance. We also presented at a number of industry stakeholder events. A full list of presentations for 2021, most of which were delivered remotely, is provided in Appendix 2.
- Our Medicinal Products Newsletter provides updates for those working in the veterinary medicines sector on Irish and European legislation, new/revised HPRA regulatory publications and stakeholder events such as information days. Three editions were published in 2021 and are available to download from the 'Publications' section on our website.

  We also contributed a number of articles to the Veterinary Ireland Journal and the It's Your Field publication. Details are included in Appendix 3.

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.

Authorisation and Registration

- The HPRA carries out evaluations of applications for the authorisation of research establishments and projects. In addition, we assess applications from individuals to allow them to manage projects or to conduct procedures or euthanasia of animals.

Authorisation and registration – Key 2021 figures	
Individual authorisations	220
Individual renewals	29
Project authorisations	95
Individual amendments	40
Project amendments	101
Establishment renewals	9
Retrospective assessments	32

The number of new individual and project authorisations issued during the past five years are outlined in the following graph.

- In December, we published the eighth annual statistical report on the use of animals for scientific purposes in Ireland. The HPRA is 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.

Inspections and Compliance

- During 2021, notwithstanding the restrictions of COVID-19 public health measures, there were 29 inspections completed to monitor animal welfare standards and compliance with legislation. Ten of these inspections were classified as breeder, supplier, or user establishment renewal inspections. These inspections are performed to ensure that establishments that breed/supply/use animals for research and testing meet the legal standards required for authorisation. The inspections performed as part of the authorisation renewal process are performed as announced inspections, as this allows for a comprehensive review of every aspect of the establishment's activities and operations under the scientific animal protection legislation. The remaining 19 inspections performed in 2021 were targeted compliance inspections. 63% of these compliance inspections were performed as unannounced inspections, with 37% performed on an announced basis.

- Of the 57 non-compliances recorded under the Scientific Animal Protection inspections and compliance programme, 51% were self-reported to the HPRA by authorised breeder/supplier/user establishment personnel. 35% were identified during the course of HPRA inspections, with the remaining 14% detected as a result of other HPRA activities including, for example, the review of end-of-project reports.

- Non-compliances are categorised as Type 1, Type 2 and Type 3, with Type 1 being the most serious and Type 3 being more minor in nature. Of the non-compliances identified in 2021:

  – 16% were Type 1

  – 60% were Type 2

  – 24% were Type 3

  The most common reason recorded for non-compliance was a breach of the terms and conditions of HPRA project authorisation, for example due to the performance of procedures on animals after the HPRA project authorisation had expired. The next most common reason recorded was a failure to comply with the requirements of Annex III to Directive 2010/63/EU in relation to the care and accommodation of animals. Non-compliances in relation to Annex III requirements were most frequently related to failures in maintaining environmental parameters (relative humidity and temperature levels) within the required specifications.

Legislation and Regulation

- Commission Implementing Decision 2020/569/EU sets out a common format for submitting information to the European Commission. One of the key requirements of this Decision is for Member State competent authorities to publish non-technical project summaries (NTS) on an open access European Union (EU) NTS database, rather than nationally. All NTS for projects that were granted approval by the HPRA from 1 January 2021 onwards are publicly accessible on this EU database. This marks a change in procedure from previous years.

- In November 2021, Member States formally endorsed European Commission guidance on writing NTS that had been developed by an expert working group led by the HPRA. The net effect is that the format and content of the reports differ from those required by the previous legislation.

Stakeholders and Partners

- We published and disseminated four 'Regulatory Updates' to provide stakeholders with the latest news and guidance from the HPRA including information on best practices in respect of the 3Rs and compliance with the legislation.

- We delivered a number of Laboratory Animal Science and Training (LAST) lectures in relation to the legislative and regulatory aspects of scientific animal protection.

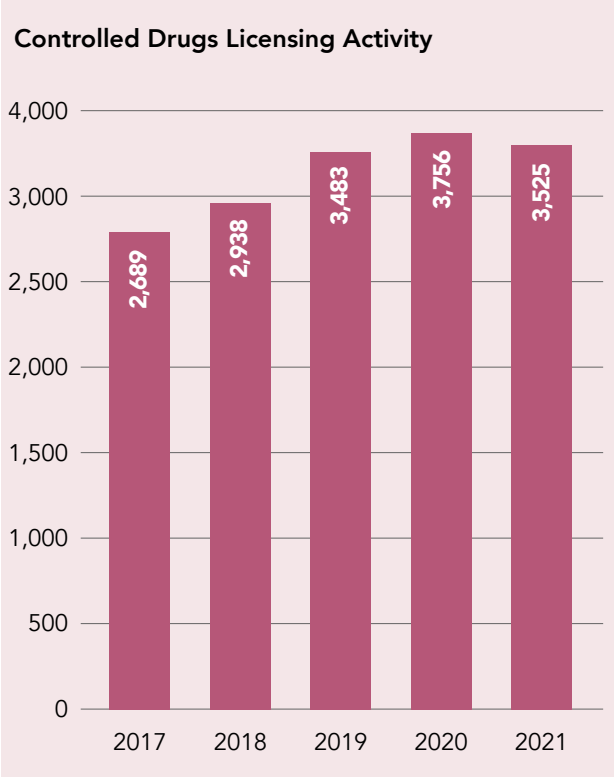
- Throughout 2021, we continued our active involvement in EU regulatory network, which includes active participation at National Contact Point meetings for the Implementation of Directive 2010/63/EU.

Controlled Drugs and Precursor Chemicals

The HPRA is responsible for reviewing the licence application for a controlled drug as listed in the schedule to the Misuse of Drugs Acts 1977 and 1984. Additionally, the HPRA regulates the movement of precursor chemicals used in the manufacture of licensed medicines, certain foodstuffs and for other scientific or laboratory uses.

Authorisation and Registration

- 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 graph.



- The following table shows the licensing activity for precursor chemicals since 20189

Precursor Chemicals Licensing Activity	2019	2020	2021
Total	13	14	14

- We process applications for licences to cultivate hemp on behalf of the Department of Health. A cultivation licence is valid for a period of one year from the date it is granted. The below table shows the number of licences issued during the past three years.

Hemp Cultivation Licensing Activity	2019	2020	2021
Total	74	94	78

Safety and Quality

- We carry out inspections of manufacturers and distributors of controlled drugs, as well as some other operators, as necessary, to monitor compliance with the relevant requirements. In 2021, five inspections were conducted linked to the possession and/or supply of controlled drugs. Operators were informed of any non-compliances identified and requested to implement corrective actions.

Legislation and Regulation

- Throughout 2021, the HPRA provided support to the Department of Health in the implementation and progression of the Medical Cannabis Access Programme (MCAP). The HPRA received nine applications from potential suppliers seeking to have their products included in the programme. From these applications, two additional cannabis products were considered to meet the specified requirements and were added to the programme. In total, six cannabis products have been accepted for use on the MCAP to date.

  The programme became fully operational during 2021, with consultants on the specialist medical register able to prescribe a cannabis-based treatment for patients with any of three specified conditions:

  – Spasticity associated with multiple sclerosis resistant to all standard therapies and interventions;

  – Intractable nausea and vomiting associated with chemotherapy, despite the use of standard anti-emetic regimes;

  – Severe, refractory epilepsy that has failed to respond to standard anticonvulsant medications.

  Further information is available on the Department of Health website.

Stakeholders and Partners

- In 2021 a new online platform, NDS7, was rolled out for controlled drug import and export licences. The new software platform allows users to apply electronically through NDS7 and upload all related documents required in a much more user-friendly way than the previous system. Multiple training sessions were provided to relevant industry stakeholders likely to use the new software platform to apply for such licences.

- Emergency electronic e-licences, which were introduced in 2020 to adapt to COVID-19 pandemic, continued to be issued in 2021 where needed to ensure ongoing processing of import and export licences for controlled substances. This e-licence can be issued within a short timeframe and allows for monitoring and tracking of the legitimate movement of controlled substances. Hard copy licences for controlled substances continued to be issued where possible.

Cosmetic Products

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

- We issued 122 cosmetics free sale certificates, requested by companies intending to export products to non-European Economic Area countries.

Safety and Quality

- As part of proactive market surveillance activities, we initiated two Product Information File (PIF) reviews, to assess compliance with the Cosmetics Regulation.

- Our reactive market surveillance includes investigation of quality-related complaints (compliance cases), reports of adverse events relating to the use of cosmetics (vigilance cases) and serious risk alerts received from other countries (Safety Gate RAPEX).

  During 2021, 248 market surveillance cases were initiated, including both proactive and reactive surveillance of cosmetic products.

Stakeholders and Partners

- There has been a substantial increase year on year since 2019 in the number of Responsible Persons (RPs) for cosmetic products located in Ireland. The cosmetic team provided additional guidance during 2021 via a webinar and updated Brexit related guidance to assist new RPs to navigate any changes required.

Other Regulatory Programmes

Inspections and Market Compliance

- Throughout 2021, HPRA contributions to the EU included participation in/leading on:
  - the drafting group for the new EU GMP Guide Annex 21 on importation;
  - the PIC/S drafting group for revision of the GMP guide for manufacture of veterinary medicines;
  - the ICMRA digital transformation of inspections working group which produced a reflection paper on the regulatory experience of digital approaches to GCP and GCP oversights during the COVID-19 pandemic;
  - the EU funded GAPP project to facilitate the development of a common and optimal approach to assess and authorise preparation processes in blood and tissues establishments;
  - the development of a new risk assessment tool for the selection of medicinal products and active substances for surveillance testing;
  - a new risk-based tool to support inspection and surveillance relating to heparin manufacturers and their related products;
  - the development of a communication toolkit for the Official Medicines Control Laboratory (OMCL) network.

Innovation Support

- The HPRA continues to focus on supporting innovation as one of our five strategic goals. This reflects our role not just to protect but also to enhance public and animal health. Our supports for innovation aim to facilitate safe and timely access to innovative health products and to increase and improve treatment options for patients. They also benefit the HPRA by helping to inform our future development and allowing us to identify novel product types and technologies that require new or adapted regulatory science approaches.

Our actions in 2021 included the following:

- The HPRA's Innovation Office continues to offer regulatory advice to anyone developing an innovative health product or technology.

  Over 65% of queries received came from academia or small and medium enterprises who may have limited access to specialist regulatory advice. Medical devices was the most frequent area addressed through Innovation Office queries followed closely by medicines;
- In our role as co-chair of the EU Innovation Network, the HPRA continued to take a prominent role in relation to activities to support innovation at European level. Initiatives progressed within the EU Innovation Network include pilots offering simultaneous national scientific advice and supports for non-commercial organisations involved in the repurposing of authorised medicines. The HPRA also continues to contribute to horizon scanning within both the EU Innovation Network and ICMRA;
- The HPRA also continued to participate along with other European medicines regulatory agencies in 'Strengthening regulatory sciences and supporting regulatory scientific advice' (STARS). This is a Horizon 2020 project to facilitate translation of academic medical research into approved health products by increasing regulatory knowledge and tailoring regulatory supports to academic researchers. A second EU stakeholder workshop was held in 2021, with participation by Irish representatives and a breakout session facilitated by the HPRA;
- Our national classification process continued to offer advice to stakeholders on the borderline between different regulatory frameworks including medicines, medical devices, cosmetics and other products. In 2021, the HPRA also took a lead role in establishing a subgroup of the EU Innovation Network to facilitate discussions in relation to borderline product classification at EU level with a view to ensuring consistency in relation to the regulatory frameworks to be applied to borderline innovative products.

Outreach and Engagement

The HPRA is committed to a strategic focus on outreach and engagement with key partners and stakeholders to enhance and maximise the effectiveness of the regulatory system.

- In our outreach activities to support education and innovation developments in Ireland:
  - The HPRA continued to meet and interact with a number of other state agencies and organisations who seek to support innovation in Ireland as well as representatives from third level institutions. We also met with individuals and organisations who are seeking to develop innovative health products and technologies to provide guidance on the regulatory requirements that will apply to their products.
  - As a result of our prominent role within the European network, the HPRA was invited to present on supports for innovation available from national competent authorities at the DIA Europe meeting and the DIA CMA Workshop. We also participated in a panel discussion at a joint HMA/EMA workshop on artificial intelligence in medicines regulation.
  - The HPRA continues to contribute to education programmes at both undergraduate and postgraduate levels. During 2021, we continued to implement a new policy related to our involvement in third level educational programmes. We also provided a training placement to a fourth year pharmacy student as part of the five-year integrated pharmacist training programme.
  - The HPRA's graduate training programme for medical devices continued throughout 2021 with training provided to a graduate of biomedical science as part of this initiative.
- Stakeholder communications and engagement:
  - We continued our public information campaign: Zero Gains. The campaign is focused on building awareness of the many and often serious side effects associated with the non-medical use of anabolic steroids. The rollout of the 2021 media plan was initially impacted due to COVID-19 but commenced in late November for a period of approximately five weeks. The highly targeted campaign incorporated a mix of social media, website and in-app advertising, and digital audio advertising. This latter element involved an audio advert featuring key campaign messages airing via podcasts, sports content and streaming music services. In respect of social media, the main platforms utilised were Snapchat and TikTok, reflecting high levels of use among our main target audience, in addition to Facebook and Twitter. Targeted in-gym and outdoor advertising, including both static and digital poster sites, also formed part of the campaign following the lifting of public health restrictions. The website - www.zerogains.ie - continued to be an important element of the campaign providing reliable and trustworthy information on the real risks of anabolic steroid use. Overall, the various channels continued to perform in line with expectations with strong engagement levels across key digital platforms.
  - Our media communications programme was dominated by matters relating to COVID-19, particularly in the first half of the year. During this period, the HPRA managed an unprecedented level of media interest and engagement in our authorisation and safety activities linked to COVID-19 vaccines. Our key messaging as we moved from initial authorisation to real-world use was focused mainly on the key role of the HPRA in monitoring the safety of the vaccines. Through highlighting the critical importance of the regulatory system, we also supported and complemented the communications activities of the Department of Health, the HSE, NIAC and other national partners across the health system.

- Our Chief Executive and our Vigilance Assessment Manager participated in a large number of national broadcast media interviews including RTE radio, Newstalk and Virgin TV.
- We engaged extensively with health correspondents and other journalists across print and online media. In total, we responded to more than 300 COVID-19 queries, follow-up queries and interview requests from across the Irish media.
- We participated in a number of NPHET COVID-19 press conferences (as hosted twice weekly by the Department of Health) delivering a HPRA opening statement as necessary.
- In addition to 14 vaccine safety updates reports published throughout 2021, we issued five media statements / press releases directly related to COVID-19 vaccines which resulted in extensive coverage across national and regional media (both broadcast and print), and online platforms.
- All of our communications activities were supported by social media content (Twitter and LinkedIn) and through the publication of relevant updates on our website. A number of separate social media and website updates were also published highlighting significant developments at an EMA level including authorisations of COVID-19 vaccines and therapeutics.

– Elsewhere, we continued to proactively communicate important safety messages (non COVID related) and to build awareness of the role of the HPRA. We issued a range of press releases and website statements concerning safety and regulatory matters to ensure consumers, healthcare professionals and other stakeholders received timely and accurate information and advice.

– The HPRA is committed to widening its engagement with patients and patient organisations, to enable a deeper understanding of patient perspectives and experiences in relation to the regulation of health products. To this end, following extensive preparatory work, we established our first ever patient forum on a pilot basis during 2020 with four meetings subsequently held during 2021. Participants include both patients and representatives of patient organisations while the HPRA is represented by our Chief Executive and members of our senior management team. By year-end, considerable progress had been achieved in the ongoing development of the forum with final Terms of Reference and the proposed work plan for 2022 agreed. Both documents have since been published on the HPRA website. The consolidation of the forum, which has now importantly moved from the initial pilot phase to a more established basis, represents an important and valuable approach to patient-centred regulation. As an organisation, our primary focus is to ensure enhanced outcomes for patients through access to safe and effective health products. Consequently, it is imperative we listen to and work with patients to ensure their voice is heard and their perspective is incorporated into regulatory decision-making.

– The HPRA participated in the sixth annual #MedSafetyWeek, an international social media campaign designed to raise awareness of the importance of reporting side effects from medicines. In 2021, the campaign focused on reporting side effects from vaccines, including COVID-19 vaccines. The messaging stressed the benefits of reporting in 'making vaccines better for everyone'. The campaign is a global initiative led by the Uppsala Monitoring Centre (UMC), the World Health Organisation Collaborating Centre for International Drug Monitoring. In total, 64 medicines regulatory authorities across the world took part. While UMC led the campaign, a planning committee comprising representatives from several medicines agencies, including for the first time, the HPRA, met regularly to develop

the campaign materials. The campaign consisted primarily of three short animated videos, available to view and download on our website, which were shared on our Twitter, LinkedIn and Instagram accounts. Following a request for support from the HPRA in advance of the launch, a large number of national patient and consumer organisations, health agencies and other public bodies promoted the campaign's important public health message on social media. Additionally, a press release promoting the HPRA's involvement in #MedSafetyWeek was issued and alerted to website subscribers. A review of performance at the end of the campaign showed a 26% increase on Twitter engagements compared to 2020.

– The HPRA website – www.hpra.ie – is a key communications channel and we continuously monitor and analyse analytics data and user feedback. During the second half of 2021, we published a user survey requesting feedback in respect of commonly used pages, areas for improvement and user profiles. Engagement levels for the survey were very positive with approximately 300 completed surveys received. As outlined in our Strategic Plan for 2021 – 2025, the HPRA is committed to the redevelopment of our current website. The feedback from the survey will be very relevant and informative as the redevelopment process commences in 2022 following completion of a public procurement process.

– The @TheHPRA Twitter account supports our communications activities and helps to direct additional traffic to the HPRA website. We continued to develop our Twitter activity during 2021 and by year-end we had grown our number of followers to almost 4,000, an increase of 33%.

– Our LinkedIn account continues to support the growth of our employer brand. In addition, it facilities the dissemination of important regulatory and safety information to health and industry professionals. By end 2021, our total number of followers had grown to more than 14,000.

– Also during 2021, we continued to utilise our corporate Instagram account to highlight and promote certain activities and events including #MedSafetyWeek.

- European and international contribution:

  – Throughout the year, the HPRA participated in a significant number of initiatives and working groups in respect of COVID-19, which included the EMA Pandemic Task Force and the EU Executive Steering Group on Shortages of Medicines caused by Major Events. Details of the extensive COVID-19 related work carried out by the HPRA during 2021 are outlined earlier in this report (see page 13).

  – We continued our participation in all EMA and all HMA management board/group meetings which were held virtually due to the COVID-19 pandemic:

    - The coordination of the regulatory response to COVID-19 was a key issue for the EMA Management Board throughout 2021. Other ongoing issues considered at its quarterly meetings included the new veterinary legislation and clinical trials regulation implementation, including the new Clinical Trials Information Systems (CTIS).

    - We continued our role as a member of the European HMA Management Group, which contributes to the direction and oversight of the HMA.

  – Additionally, as part of our ongoing contribution to the European regulatory system, HPRA scientific and technical staff participated in a broad range of committees and working parties at the European Commission, EMA, HMA, CAMD and other forums (see Appendix 4).

  – The HPRA continued its role as a member of the International Coalition of Medicines Regulatory Authorities (ICMRA) Executive Committee. COVID-19 was again a dominant topic for ICMRA in 2021 and the HPRA actively participated in a range of initiatives including those linked to the authorisation of vaccines and therapeutics, clinical trials, safety monitoring and inspection programmes.

  – In 2019, the EU Commission commenced its work in developing the new pharmaceutical strategy for the EU, and the HPRA continues to participate in the development of that strategy.

Key outreach and engagement figures	2021
Public consultations held: - Proposed regulatory fees for human products - Proposed regulatory fees for veterinary medicines - Proposed regulatory fees for clinical trials	3
Public consultations responded to: - Included Department of Health; Joint Oireachtas Committee on Health; Medical Council; and Health Information and Quality Authority (HIQA).	4
Events managed by HPRA events teams	6
Freedom of information requests	71
Freedom of information requests answered outside the FOI Act	25
Requests received in accordance with the Data Protection Acts	11
Parliamentary questions	46
Queries from Government departments or members of the Oireachtas	74
Protected disclosures received by external persons under section 7(2) of the protected Disclosures Act, of which investigation is: - Concluded - Ongoing	 7 5
Complaints	3
Customer service queries	2,173

Organisation 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.

Human Resources and Change

The HR and Change team continued to deliver across a number of workstreams in a responsive and agile manner throughout 2021. While continuing to support the organisation throughout the period of the COVID-19 pandemic, we focused on developing management capabilities, provided change management support where required and adopted a lead role in the Future of Work project. It was agreed that the development of the new HR and Change/ People Strategy would be postponed to 2022. This was due to changes to the HR and Change director role and the timing of the new strategic plan.

Both the HR and the learning and development teams progressed a number of key activities under each of the following headings during 2021.

Retention and Engagement:

- The second year of the HPRA recognition programme was completed facilitating peer and manager recognition as well as celebrating length of service.
- In support of the HPRA's commitment to 'inclusion' as a core value, our first Diversity and Inclusion committee was established, with the first 'investors in diversity' survey completed. A silver award was achieved from the Irish Centre for Diversity following our initial bronze award in 2019.
- Our health and wellbeing agenda continued as a key focus with a number of initiatives adapted to the remote environment. The HPRA was awarded 'Best in Class Mental Health' at The KeepWell Awards in recognition of our health and wellbeing initiatives during 2021. The HPRA was also listed in IBEC's 'Top 100 Companies Leading in Wellbeing'. Our health and wellbeing programme targeted the mental, physical and social impacts of the pandemic on employees.
- To aid employee retention and develop management skills, two management development courses launched, 'Managing Remotely' and 'Managing Others Through Change'. There was a high level of engagement from management with 85% and 93% attending these courses respectively.

Career Development:

- The third iteration of the HPRA graduate programme commenced in September 2021. Recruitment for the fourth iteration was also completed with graduate resources confirmed to commence in September 2022. In recognition of the programme, the HPRA was awarded 'Graduate Programme of the Year' at the HR Leadership awards in 2021.
- Eight new further education requests were supported and approved to commence in 2021, with eight continuing from 2020 and 2019.
- The reflective tool 'What, So What and Now What' was launched to all employees to encourage and support self-awareness and self-development across the organisation.

HR and Change:

- The HR business partners (HRBP) continued their advisory role to provide department specific supports and advice in conjunction with the learning and development team throughout 2021.
- HR and Change assumed a lead role in the business continuity subgroup and relevant activities.
- There was continued enhancement of the HPRA employer brand including the promotion of social media content.
- Resources and support were provided on a timely basis to assist employees and managers with working and managing remotely.
- Interim department management plans were put in place to ensure smooth continuation of business-as-usual and progression of strategic goals during Director maternity leave.

Organisation Design:

- To ensure the HPRA can respond accordingly to future needs, the 'Future of Work' project commenced to analyse the possible impact of more flexible working models on the organisation. The HR and Change team took a lead role in a number of the project work streams.
- The Medical Devices / Compliance scope extension project concluded.

Talent Management:

- An agile recruitment process was adopted to support remote recruitment while the recruitment and appointment of a number of key senior appointments was supported.
- The management development process was redefined with a series of courses rolled-out in 2021. The 'New Manager Training' programme was developed and launched while the 'Train the Trainer' programme was adapted and facilitated virtually in 2021.

Change Management:

- Training, tools and supports were developed, curated and provided to managers to aid their ability to manage remotely and ensure any people-related issues or concerns were managed appropriately.
- A bespoke video was also created for all staff to provide support for change projects.
- Ongoing change management support was delivered to various projects across the organisation.

Public Sector Equality and Human Rights Duty

The HPRA seeks to meet obligations under Section 42 of the Irish Human Rights and Equality Act 2014. Work continues to ensure that consideration is given to human rights and equality in the development of policies, procedures and engagement with stakeholders in fulfilling our mission to regulate medicines and medical devices for the benefit of people and animals.

IT Developments

The HPRA's Digital Transformation Strategy (2021-2025) was launched at the beginning of 2021 establishing an application and technology direction to support the organisation in achieving its objectives in the coming years. The strategy focuses on building existing capabilities, while also introducing innovative technologies that will support new ways of working. It integrates a series of objectives to ensure a performant and secure technology platform and to and enhance the efficiency and effectiveness of the organisation.

The strategy is constructed around six core themes:

- Optimising Transaction Applications: providing efficient core transaction capability to support day to day process.
- Enhancing Digital Integration: automating the transfer of data between systems and across the organisation boundary without the need for manual intervention.
- Improving Data Management and Decision Support: ensuring availability, integrity and security of data to enable efficient organisation processes.

- Enhancing Client Computing: provide facilities and user productivity applications to enable staff fulfil their roles and collaborate effectively.
- Enhancing Technology Infrastructure: provide a performant and resilient technology infrastructure and connectivity to distributed workforce.
- Improving Governance: provide oversight and control over information technology activities to ensure alignment with the business strategy.

A series of initiatives have been mobilised to deliver on the strategic objectives. In addition to this, progress has been made integrating with systems hosted by the EMA, including the Union Project Database, and upgrading the Common European Submissions Portal (CESP) hosted and managed by the HPRA on behalf of the European regulatory network.

Quality Management

- The HPRA's quality management team was responsible for the continued implementation of policies and procedures relating to the General Data Protection Regulation (GDPR). There were 11 data subject requests received in 2021. All requests were managed within the required timelines.
- In the HPRA's continued commitment to the quality management system, 13 internal audits were completed in 2021 throughout various departments.
- Quality induction training courses were redeveloped to support the culture of continuous improvement within the HPRA.
- The quality management team worked closely with various departments to prepare for the implementation of the new veterinary medicines and clinical trials regulations.

Finance

- The HPRA is committed to the highest standards of corporate governance. During 2021, the financial statements for the previous year were prepared and submitted for audit to the Comptroller and Auditor General and subsequently published in the HPRA's 2020 Annual Report. All financial transactions during the period were reflected and reported upon in these statements.
- The annual review of regulatory fees for 2022, incorporating a public consultation, was completed followed by the publication of the updated fees.
- Two internal audit reviews took place and reports were issued on ICT cybersecurity, and on procurement.

Energy Usage

- 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 2021, the HPRA consumed 533.6 MWh of energy consisting of:
  - 270.2 MWh of electricity;
  - 283.4 MWh of fossil fuels;
  - 0 MWh of renewable fuels.

According to the Sustainable Energy Authority of Ireland (SEAI) Annual Report 2021 on Public Sector Energy Efficiency Performance, total energy reduction achieved by the HPRA since baseline was 62.4%* exceeding the public sector target of 33% by 2020.

* Data in the 2021 report should not be compared on a like for like basis to the data for previous years due to the impact of COVID-19.

Authority and Committees

The Authority (Board) 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. In addition to the Authority, there are three advisory committees: The Advisory Committee for Human Medicines, the Advisory Committee for Veterinary Medicines and the Advisory Committee for Medical Devices.

- The Authority of the HPRA met six times in 2021 and considered a number of strategic matters including the response to COVID-19, the outcome of Brexit, strategic planning and financial matters. The latter included monthly management accounts, annual budgets and the financial statements for 2020. The Authority also reviewed update reports from the Statutory Advisory Committees and the Audit and Risk 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 2021 was as follows:

- The Audit and Risk Committee, a subcommittee to the Authority, met five times in 2021. Further details are provided in the HPRA's Financial Statements.
- The Advisory Committee for Human Medicines met on two occasions in 2021. The Clinical Trials Sub-Committee is a sub-committee to the Advisory Committee for Human Medicines and it met twelve times in the past year.
- The Advisory Committee for Veterinary Medicines met three times.
- The Advisory Committee for Medical Devices met once.
- 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 2021.

Authority Member	Number of meetings held during the period the member was on the Authority	Number of meetings attended during the period the member was on the Authority
Mr Michael Donnelly (Chairperson)	5	4
Dr Joe Collins	6	6
Mr David Holohan	6	4
Mr Brian Jones	6	6
Dr Elizabeth Keane	6	6
Dr Diarmuid Quinlan	6	6
Prof Richard Reilly	6	6
Dr Sharon O'Kane	3	3
Dr Paula Kilbane	3	3

- 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 and Risk 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 significant amendments to the pension benefits of the Chief Executive and staff

  – 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.

Financial Statements

for the Year Ended 31 December 2021

Authority Members and Other Information

Authority:	*Most recent appointment date*	*Expiry date*
Mr. Michael Donnelly (Chairperson)	19/04/2021	31/12/2025
Mr. Joe Collins	28/09/2020	31/12/2024
Mr. David Holohan	27/01/2021	26/01/2026
Mr. Brian Jones	27/01/2021	26/01/2026
Dr. Elizabeth Keane	22/05/2019	21/05/2022
Dr. Paula Kilbane	28/06/2021	31/12/2025
Dr. Sharon O'Kane	15/07/2021	31/12/2025
Dr. Diarmuid Quinlan	22/05/2019	21/05/2024
Prof. Richard Reilly	01/01/2020	31/12/2024

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

KBC Bank Ireland
Sandwith Street
Dublin 2

Solicitors:

Eugene F. Collins
Temple Chambers
3 Burlington Road
Dublin 4

Byrne Wallace
88 Harcourt Street
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

Governance Statement and Authority Member's Report

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 chairperson and eight non-executive members. The Authority is accountable to the Minister for Health and is responsible for ensuring good governance, and performs this task by setting strategic objectives and targets and taking strategic decisions on all key business issues. The regular day-to-day management, control and direction of the HPRA are the responsibility of the Chief Executive and the Management Committee. The Chief Executive and the Management Committee must follow the broad strategic direction set by the Authority, and must ensure that all Authority members have a clear understanding of the key activities and decisions related to the HPRA, and of any significant risks likely to arise. The Chief Executive acts as a direct liaison between the Authority and management of the HPRA.

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.

Authority Responsibilities

The work and responsibilities of the Authority are set out in the Irish Medicines Board Act, 1995 (as amended), as well as in the 'Terms of Reference and Rules of Procedure' of the HPRA, which also contains the matters specifically reserved for Authority decision. Standing items considered by the Authority include:

- declaration of interests,
- reports from committees,
- financial reports/management accounts,
- performance reports, and
- reserved matters.

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 financial position 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,
- prepare the financial statements on a going concern basis unless it is inappropriate to presume that the HPRA will continue in existence, and
- state whether applicable accounting standards have been followed, subject to any material departures disclosed and explained in the financial statements.

The Authority is responsible for keeping adequate 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. The maintenance and integrity of the corporate and financial information on the HPRA's website is the responsibility of the Authority.

The Authority is responsible for approving the annual plan and budget. 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.

The Authority considers that, except for the non-compliance with the requirements of FRS102 in relation to retirement benefits, the financial statements of the HPRA give a true and fair view of the financial performance and the financial position of the HPRA at 31 December 2021.

Audit and Risk Committee

The HPRA has an audit and risk committee comprising three Authority members, which met on 5 occasions during 2021. 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 2021, the internal auditor carried out internal audit reviews on the areas of ICT cybersecurity and procurement. The audit and risk committee has also been involved with the review of the quality systems as described below.

Quality Systems

During 2021, 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 Chairperson receives remuneration as directed by the Minister for Health in accordance with the Irish Medicines Board Act, 1995. Other Authority members receive remuneration under the terms of the Health (Miscellaneous Provisions) Act 2017. All Authority members are entitled to 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 remuneration of the Chief Executive and Executive Directors are 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 Chairperson's report on pages 55 to 56.

Disclosures Required by Code of Practice for the Governance of State Bodies (2016)

The Authority is responsible for ensuring that the HPRA has complied with the requirements of the Code of Practice for the Governance of State Bodies, as published by the Department of Public Expenditure and Reform in August 2016. The following disclosures are required by the Code, and are contained in the notes to the financial statements:

- employee short term benefits breakdown,
- consultancy costs,
- legal costs and settlements,
- travel and subsistence expenditure, and
- hospitality expenditure.

Statement of Compliance

The Authority has adopted the Code of Practice for the Governance of State Bodies (2016) and has put procedures in place to ensure compliance with the Code. The HPRA was in full compliance with the Code of Practice for the Governance of State Bodies for 2021.

Performance Review

The Authority carried out a self-assessment evaluation of its own performance and its committees for the year ended 31 December 2021.

On behalf of the Authority

Mr. Michael Donnelly
Chairperson

Mr. David Holohan
Authority Member

Date: 11 May 2022

Statement on Internal Control

Scope of Responsibility

I, as Chairperson, acknowledge the Authority's responsibility for ensuring that an effective system of internal control is maintained and operated. This responsibility takes account of the requirements of the Code of Practice for the Governance of State Bodies (2016).

Purpose of the System of Internal Control

The system of internal control is designed to manage risk to a tolerable level rather than to eliminate it. The system can therefore only provide reasonable and not absolute assurance that assets are safeguarded, transactions authorised and properly recorded and that material errors or irregularities are either prevented or detected in a timely way.

The system of internal control, which accords with guidance issued by the Department of Public Expenditure and Reform, has been in place in the HPRA for the year ended 31 December 2021 and up to the date of approval of the financial statements.

Capacity to Handle Risk

The HPRA has an audit and risk committee comprising three Authority members, which met on 5 occasions during 2021.

The HPRA has outsourced the internal audit function to an independent professional firm, who conduct a programme of work as agreed with the audit and risk committee. During 2021 two internal audit reviews were conducted.

The HPRA have developed a risk management framework, which sets out its risk appetite, the risk management processes in place and details the roles and responsibilities of staff in relation to risk. This framework has been made available to all staff, who are expected to work within the HPRA's risk management policies, to alert management on emerging risks and control weaknesses, and assume responsibility for risks and controls within their own area of work.

Risk and Control Framework

The HPRA has implemented a risk management system which identifies and reports key risks and the management actions being taken to address, and to the extent possible, to mitigate those risks.

A risk register is in place which identifies the key risks facing the HPRA, and these have been identified, evaluated and graded according to their significance. The register is reviewed and updated by management, considered by the audit and risk committee twice per year and presented to the Authority. The outcome of these assessments is used to plan and allocate resources to ensure risks are managed to an acceptable level.

The risk register details the controls and actions needed to mitigate risks and responsibility for operation of controls assigned to specific staff. I confirm that a control environment containing the following elements is in place:

- procedures for all key business processes have been documented,
- financial responsibilities have been assigned at management level with corresponding accountability,
- there is an appropriate budgeting system with an annual budget, which is kept under review by senior management,
- there are systems aimed at ensuring the security of the information and communication technology systems, and
- there are systems in place to safeguard the assets.

Ongoing Monitoring and Review

Formal procedures have been established for monitoring control processes, and any control deficiencies are communicated to those responsible for taking corrective action, and to management and the Authority, where relevant, in a timely manner. I confirm that the following ongoing monitoring systems are in place:

- key risks and related controls have been identified, and processes have been put in place to monitor the operation of those key controls and report any identified deficiencies,
- reporting arrangements have been established at all levels where responsibility for financial management has been assigned, and
- there are regular reviews by senior management of periodic and annual performance and financial reports, which indicate performance against budgets.

Procurement

I confirm that the HPRA has procedures in place to ensure compliance with current procurement rules and guidelines, and that during 2021 the HPRA complied with those procedures.

Review of Effectiveness

I confirm that the HPRA has procedures to monitor the effectiveness of its risk management and control procedures. The HPRA's monitoring and review of the effectiveness of the system of internal control is informed by the work of the internal and external auditors, the audit and risk committee which oversees their work, and the senior management within the HPRA, responsible for the development and maintenance of the internal control framework.

I confirm that the Authority conducted an annual review of the effectiveness of the internal controls for 2021. This review was carried out at its meeting on 11 May 2022. Prior to this meeting, a document outlining the effectiveness of the internal controls in the HPRA for 2021 was circulated to the Authority members by e-mail. This document was circulated on 24 March 2022.

Internal Control Issues

No weaknesses in internal control were identified in relation to 2021 that require disclosure in the financial statements.

COVID-19 Pandemic

Due to the impact of COVID-19, the HPRA carried out a review of its control environment, based on a guidance document issued by the Office of the Comptroller and Auditor General. Many of the controls in place pre-COVID continue to apply in the current environment. This review document was considered by the Audit and Risk Committee at its December 2020 meeting, who were happy with the content.

All staff are predominately working offsite, with many resources diverted to managing implications of the pandemic. This has had little or no effect on internal controls already in place, many of which were not dependent on physically being in the office.

Mr. Michael Donnelly
Chairperson to the Authority

Date: 11 May 2022

Comptroller and Auditor General

Report for presentation to the Houses of the Oireachtas

Qualified opinion on the financial statements

I have audited the financial statements of the Health Products Regulatory Authority (the Authority) for the year ended 31 December 2021 as required under the provisions of section 18 of the Irish Medicines Board Act, 1995. The financial statements have been prepared in accordance with Financial Reporting Standard (FRS) 102 – *The Financial Reporting Standard applicable in the UK and the Republic of Ireland* and 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, including a summary of significant accounting policies.

In my opinion, except for the non-compliance with the requirements of FRS 102 in relation to retirement benefit entitlements referred to below, the financial statements give a true and fair view of the assets, liabilities and financial position of the Authority at 31 December 2021 and of its income and expenditure for 2021 in accordance with FRS 102.

Basis for qualified opinion on financial statements

In compliance with the directions of the Minister for Health, the Authority accounts for the costs of retirement benefit entitlements only as they become payable. This does not comply with FRS 102 which requires that the financial statements recognise the full cost of retirement benefit entitlements earned in the period and the accrued liability at the reporting date. The effect of the non-compliance on the Authority's financial statements for 2021 has not been quantified.

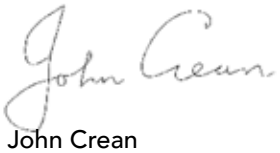
I conducted my audit of the financial statements in accordance with the International Standards on Auditing (ISAs) as promulgated by the International Organisation of Supreme Audit Institutions. My responsibilities under those standards are described in the appendix to this report. I am independent of the Authority and have fulfilled my other ethical responsibilities in accordance with the standards.

I believe that the audit evidence I have obtained is sufficient and appropriate to provide a basis for my opinion.

Report on information other than the financial statements, and on other matters

The Authority has presented certain other information together with the financial statements. This comprises the annual report, the governance statement and Authority members' report and the statement on internal control. My responsibilities to report in relation to such information, and on certain other matters upon which I report by exception, are described in the appendix to this report.

I have nothing to report in that regard.



John Crean

For and on behalf of the
Comptroller and Auditor General

17 May 2022

Appendix to the report

Responsibilities of Authority Members

As detailed in the governance statement and Authority members' report, the Authority members are responsible for

- The preparation of annual financial statements in the form prescribed under section 18 of the Irish Medicines Board Act 1995
- Ensuring that the financial statements give a true and fair view in accordance with FRS 102
- Ensuring the regularity of transactions
- Assessing whether the use of the going concern basis of accounting is appropriate, and
- Such internal control as they determine is necessary to enable the preparation of financial statements that are free from material misstatement, whether due to fraud or error.

Responsibilities of the Comptroller and Auditor General

I am required under section 18 of the Irish Medicines Board Act 1995 to audit the financial statements of the Authority and to report thereon to the Houses of the Oireachtas.

My objective in carrying out the audit is to obtain reasonable assurance about whether the financial statements as a whole are free from material misstatement due to fraud or error. Reasonable assurance is a high level of assurance, but it is not a guarantee that an audit conducted in accordance with the ISAs will always detect a material misstatement when it exists. Misstatements can arise from fraud or error and are considered material if, individually or in the aggregate, they could reasonably be expected to influence the economic decisions of users taken on the basis of these financial statements.

As part of an audit in accordance with the ISAs, I exercise professional judgement and maintain professional scepticism throughout the audit. In doing so,

- I identify and assess the risks of material misstatement of the financial statements whether due to fraud or error; design and perform audit procedures responsive to those risks; and obtain audit evidence that is sufficient and appropriate to provide a basis for my opinion. The risk of not detecting a material misstatement resulting from fraud is higher than for one resulting from error, as fraud may involve collusion, forgery, intentional omissions, misrepresentations, or the override of internal control.
- I obtain an understanding of internal control relevant to the audit in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the internal controls.
- I evaluate the appropriateness of accounting policies used and the reasonableness of accounting estimates and related disclosures.
- I conclude on the appropriateness of the use of the going concern basis of accounting and, based on the audit evidence obtained, on whether a material uncertainty exists related to events or conditions that may cast significant doubt on the Authority's ability to continue as a going concern. If I conclude that a material uncertainty exists, I am required to draw attention in my report to the related disclosures in the financial statements or, if such disclosures are inadequate, to modify my opinion. My conclusions are based on the audit evidence obtained up to the date of my report. However, future events or conditions may cause the Authority to cease to continue as a going concern.
- I evaluate the overall presentation, structure and content of the financial statements, including the disclosures, and whether the financial statements represent the underlying transactions and events in a manner that achieves fair presentation.

I communicate with those charged with governance regarding, among other matters, the planned scope and timing of the audit and significant audit findings, including any significant deficiencies in internal control that I identify during my audit.

I report by exception if, in my opinion,

- I have not received all the information and explanations I required for my audit, or
- The accounting records were not sufficient to permit the financial statements to be readily and properly audited, or
- The financial statements are not in agreement with the accounting records.

Information other than the financial statements

My opinion on the financial statements does not cover the other information presented with those statements, and I do not express any form of assurance conclusion thereon.

In connection with my audit of the financial statements, I am required under the ISAs to read the other information presented and, in doing so, consider whether the other information is materially inconsistent with the financial statements or with knowledge obtained during the audit, or if it otherwise appears to be materially misstated. If, based on the work I have performed, I conclude that there is a material misstatement of this other information, I am required to report that fact.

Reporting on other matters

My audit is conducted by reference to the special considerations which attach to State bodies in relation to their management and operation. I report if I identify material matters relating to the manner in which public business has been conducted.

I seek to obtain evidence about the regularity of financial transactions in the course of audit. I report if I identify any material instance where public money has not been applied for the purposes intended or where transactions did not conform to the authorities governing them.

Statement of Income and Expenditure and Retained Revenue Reserves
For the year ended 31 December 2021

	Note	2021	2020
		€	€
Fee Income	3	**30,035,513**	29,712,923
Department of Health Funding	3	**5,200,000**	4,975,000
Other Income	4	**648,438**	803,196
		35,883,951	35,491,119
Salaries and Wages	5	**27,291,731**	25,436,125
Other Operating Costs	6	**5,609,084**	5,059,018
Depreciation	2	**1,122,662**	1,080,820
		34,023,477	31,575,963
Surplus for the year before write back of Superannuation contributions		**1,860,474**	3,915,156
Staff Superannuation Contributions		**643,824**	637,287
Surplus for the year		**2,504,298**	4,552,443
Balance brought forward		**35,658,707**	31,106,264
Balance carried forward	12	**38,163,005**	35,658,707

The Statement of Income and Expenditure and Retained Revenue Reserves includes all gains and losses recognised in the year. The Statement of Cash Flows and the notes on pages 63 to 73 form part of the financial statements.

On behalf of the Authority

Mr. Michael Donnelly
Chairperson

Mr. David Holohan
Authority Member

Date: 11 May 2022

Statement of Financial Position
As at 31 December 2021

	Note	2021	2020
		€	€
Fixed Assets			
Property, Plant and Equipment	2	24,360,470	24,665,841
Current Assets			
Debtors and Prepayments	7	1,642,061	2,846,261
Inventory of Stationery		5,099	4,936
Cash and Cash Equivalents	9	25,236,105	22,629,442
Short Term Deposits	10	-	-
		26,883,265	25,480,639
Current Liabilities - Amounts falling due within one year			
Creditors and Accruals	8	12,575,719	13,814,425
Mortgage	13	168,337	168,337
		12,744,056	13,982,762
Net Current Assets		14,139,209	11,497,877
Long Term Liabilities - Amounts falling due after more than one year			
Mortgage	13	336,674	505,011
NET ASSETS		38,163,005	35,658,707
Reserves			
Retained Revenue Reserves	12	20,913,896	21,053,422
Superannuation Reserve	12	17,249,109	14,605,285
		38,163,005	35,658,707

The Statement of Cash Flows and the notes on pages 63 to 73 form part of the financial statements.

On behalf of the Authority

Mr. Michael Donnelly
Chairperson

Mr. David Holohan
Authority Member

Date: 11 May 2022

Statement of Cash Flows
For the year ended 31 December 2021

	Note	2021	2020
		€	€
Cash flows from Operating Activities			
Surplus for financial year		2,504,298	4,552,443
Depreciation of property, plant and equipment		1,122,662	1,080,820
(Profit)/Loss on Disposal of property, plant and equipment		0	0
(Increase)/Decrease in Debtors		1,204,200	(331,277)
(Increase)/Decrease in Stock		(163)	597
Increase/(Decrease) in Creditors - amounts falling due within one year		(1,238,706)	1,521,338
Deposit Interest		0	(5,508)
Bank Interest		146,739	349,040
Cash from Operations		3,739,030	7,167,453
Bank Interest Paid		(146,739)	(349,040)
Net Cash generated from Operating Activities		3,592,291	6,818,413
Cash flows from Investing Activities			
Deposit Interest Received		0	5,508
(Increase)/Decrease in Bank Deposits		0	17,658,240
Payments to acquire property, plant and equipment		(817,291)	(850,207)
Receipts fom sales of property, plant and equipment		0	0
Net cash from Investing Activities		(817,291)	16,813,541
Cash flows from Financing Activities			
Repayment of Borrowings		(168,337)	(3,293,332)
Net cash used in Financing Activities		(168,337)	(3,293,332)
Net increase/(decrease) in Cash and Cash Equivalents		2,606,663	20,338,622
Cash and Cash Equivalents at beginning of year		22,629,442	2,290,820
Cash and Cash Equivalents at end of year	9	25,236,105	22,629,442

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 have been prepared in compliance with the applicable legislation, and with FRS 102 (the Financial Reporting Standard applicable in the UK and the Republic of Ireland), issued by the Financial Reporting Council in the UK, as modified by the directions of the Minister for Health in relation to superannuation. In compliance with the directions of the Minister for Health, HPRA accounts for the costs of superannuation entitlements only as they become payable (see K). This basis of accounting does not comply with FRS102, which requires such costs to be recognised in the year in which the entitlement is earned. On the advice of its solicitors, the HPRA is not disclosing the specific amounts of the legal provisions provided for by it, as disclosure of such amounts might prejudice seriously its position in relation to disputes with other parties on the subject matter of the provision. In all other respects, the financial statements comply with FRS 102.

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 reporting 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.

(b) Bad and Doubtful Debts

The HPRA makes an estimate of the recoverable value of trade and other receivables. The HPRA uses estimates based on historical experience in determining the level of bad debts, which the Authority believes will not be collected. These estimates include such factors as the current credit rating, the ageing profile, historical experience of the particular trade receivable and objective evidence of impairment of the asset. Any significant reduction in the level of bad debt provision would have a positive impact on the annual surplus/deficit. The level of provisioning required is reviewed on an on-going basis and has been disclosed in the notes to the financial statements.

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 reporting date or at a contracted date. Exchange differences are dealt with in the statement of income and expenditure and retained revenue reserves.

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.

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 scheme is a defined benefit scheme for employees. No provision has been made in respect of benefits payable. Pension payments under the scheme are charged to the statement of income and expenditure when paid. Contributions from employees who are members of the scheme are credited to the statement of income and expenditure when received. The surplus/(deficit) for the year is shown both before and after superannuation deductions.

HPRA also operate the Single Public Service Pension Scheme. All new entrants into the public sector with effect from 1 January 2013 are members of this scheme, where all employee pension deductions are paid to the Department of Public Expenditure and Reform.

By direction of the Minister for Health, no provision has been made in respect of benefits payable in future years in relation to the Local Government (Superannuation Revision) (Consolidation) Scheme 1986 or the Single Public Service Pension Scheme.

In order to help meet the cost of benefits payable in future years, reserves have been split between retained reserves and superannuation reserves, which consist of employee superannuation contributions. Since 2018 the HPRA Audit and Risk Committee have also recommended further transfers from retained revenue reserves to the superannuation reserve, as a result of a number of recent and upcoming retirements, where the costs are quite significant. This split is shown in note 12 - Movement on Income and Expenditure Reserves.

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 Statement of Income and Expenditure and Retained Revenue Reserves 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.

2. Property, plant and equipment	Fixtures and Fittings	Computer Equipment	Leasehold Improvements	Improvements To Premises	Premises	Total
	€	€	€	€	€	€
Cost						
Balance as at 1 January 2021	1,320,148	17,101,791	866,055	4,374,608	23,156,037	46,818,639
Additions for the year	27,029	790,262	-	-	-	817,291
Disposals for the year	(15,819)	(228,300)	-	-	-	(244,119)
As at 31 December 2021	1,331,358	17,663,753	866,055	4,374,608	23,156,037	47,391,811
Depreciation						
Balance as at 1 January 2021	1,233,092	16,155,734	565,907	4,198,065	-	22,152,798
Charge for the year	36,369	967,612	36,361	82,320	-	1,122,662
Disposals for the year	(15,819)	(228,300)	-	-	-	(244,119)
As at 31 December 2021	1,253,642	16,895,046	602,268	4,280,385	-	23,031,341
Net Book value at 31 December 2021	77,716	768,707	263,787	94,223	23,156,037	24,360,470
Net Book value at 1 January 2021	87,056	946,057	300,148	176,543	23,156,037	24,665,841

3. Income	2021	2020
	€	€
Fee Income		
Human Medicine - National Fees	11,690,298	11,701,344
Human Medicines - Centralised Fees	6,563,095	6,014,748
Veterinary Sciences - National Fees	3,316,202	3,159,413
Veterinary Sciences - Centralised Fees	502,203	870,180
Compliance Department	5,525,818	5,878,330
Medical Devices	2,393,218	1,989,240
	29,990,834	29,613,255
Movement in deferred revenue	44,679	99,668
	30,035,513	29,712,923
Dept Of Health Funding (Vote 38 Subhead E1)	5,200,000	4,975,000
Other Income (Note 4)	648,438	803,196
Total Income	35,883,951	35,491,119

The 2020 figures for Fee Income have been restated in line with the recategorisation of the Fee Income headings.

Fees received by the Authority under Section 13 of the Irish Medicines Board Act 1995 and Section 29 of the Animal Remedies Act 1993, totalling €21,720,962 in 2021, 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.

4. Other Income

	2021	2020
	€	€
Deposit Interest	-	5,508
IT Income	648,438	797,688
	648,438	803,196

5. Salaries and Wages

Basic Pay	21,765,662	20,785,092
Overtime	33,563	9,270
Allowances	172,045	190,173
Staff Short Term Benefits	21,971,270	20,984,535
Retirement Benefit Costs	1,636,878	1,044,800
Employer's Contribution to Social Welfare	2,300,829	2,123,813
Employer's Contribution to Single Scheme Pension	1,382,754	1,282,977
	27,291,731	25,436,125

The average number of staff employed during the year was 370 (2020 - 353).
Payroll numbers at 31 December 2021 can be analysed across the following departments:

Chief Executive	7	4
Compliance	67	71
Finance, Corporate & International	31	26
Human Products Authorisation & Registration	101	105
Human Products Monitoring	44	35
Human Resources & Change	8	10
IT & Business Services	18	17
Medical Devices	44	43
Organisational Excellence & Quality	7	11
Veterinary Sciences	36	39
Staff	363	361
Authority Members	8	5
Pensioners	51	47
	422	413

No termination or severance payments were made during the year.

Additional superannuation contributions for Public Servants of €694,361 were deducted from staff during the year and paid over to the Department of Health. On 1 January 2019, in accordance with DPER circular 21/2018, the pension related deduction (PRD) was replaced by an additiona superannuation contribution (ASC).

Pension deductions for Public Servants who are members of the Single Public Service Pension Scheme of €501,255 were deducted from staff during the year and paid over to the Department of Public Expenditure and Reform. In agreement with our parent department and DPER, the HPRA have also paid over Single Scheme employer contributions since January 2019 for employees not employed in exchequer funded areas.

Employee's short term benefits are categorised into the following bands:

Salary Band	2021	2020
€0 to €60,000	206	206
€60,001 to €70,000	64	74
€70,001 to €80,000	25	19
€80,001 to €90,000	15	15
€90,001 to €100,000	20	21
€100,001 to €110,000	20	15
€110,001 to €120,000	8	6
€120,001 to €130,000	3	4
€130,001 to €140,000	1	-
€140,001 to €150,000	-	-
€150,001 to €160,000	-	-
€160,001 to €170,000	1	1
	363	361
Average Salary	€56K	€55K

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.

For the purposes of this disclosure, short-term employee benefits in relation to services rendered during the reporting period include salary, overtime, allowances and other payments made on behalf of the employee, but exclude employer's PRSI.

6. Operating Costs

	2021 €	2020 €
Accommodation Costs	1,470,181	1,498,976
Travel, Representation and Training	513,945	365,503
Bank Charges and Interest	151,424	353,621
Legal Fees	171,302	147,150
Audit Fees (External and Internal)	35,481	34,323
Stationery, Publications, Postage and Communications	400,713	336,144
Consultancy	555,654	332,980
Sampling and Analysis	250,482	240,179
IT Costs	1,812,010	1,591,951
Document Storage	137,087	124,379
Telephone and Telecommunications	90,445	107,972
Movement on Bad Debt Provision	20,360	(74,160)
	5,609,084	5,059,018

Travel costs include an amount of €36,146 related to hospitality, and an amount of €79,181 related to travel and subsistence, of which €75,992 is national and €3,189 is foreign.

No costs were incurred in relation to client hospitality. Legal fees are in relation to ongoing legal proceedings, and do not include any amounts in relation to conciliation, arbitration or settlement payments.

Consultancy costs comprise €194,277 related to public relations/marketing, €255,637 related to human resources/ pensions and €105,740 related to other.

7. Debtors (all due within one year)	2021	2020
	€	€
Trade Debtors	1,341,833	2,505,431
Prepayments	228,775	244,562
Other Debtors	71,453	96,268
	1,642,061	2,846,261

Trade debtors are shown net of the bad debt provision.

8. Creditors (amounts falling due within one year)		
Trade Creditors	118,175	402,819
Credit Balances on Debtor Accounts	4,515,049	5,570,223
Accruals	5,596,816	5,506,511
Deferred Revenue	1,593,950	1,638,629
Revenue Commissioners	751,729	696,243
	12,575,719	13,814,425

9. Cash and Cash Equivalents		
Cash at Bank and in Hand	13,134,899	10,472,026
Demand Deposits (Convertible to Cash on Demand)	12,101,206	12,157,416
	25,236,105	22,629,442

10. Short Term Deposits		
Short Term Deposits (not immediately convertible to cash)	-	-
	-	-

11. Administration Expenses		
Surplus for the year was calculated having charged:		
Auditor's Remuneration	22,000	20,000

12. Movement on Income and Expenditure Reserves

	As At 01/01/2021 €	Income & Expenditure €	Transfer to Superann Reserve €	As At 31/12/2021 €
Retained Revenue Reserves	21,053,422	1,860,474	(2,000,000)	20,913,896
Superannuation Reserve	14,605,285	643,824	2,000,000	17,249,109
	35,658,707	2,504,298	0	38,163,005

Our Audit and Risk Committee recommended the transfer of a further €2,000,000 in 2021 from retained revenue reserves to the superannuation reserve as a result of a number of recent and upcoming retirements, where the costs are quite significant.

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 :

	2021 €	2020 €
- within one year	168,337	168,337
- between one and five years	336,674	505,011
- after five years	-	-
	505,011	673,348

On 30 December 2020 the HPRA made a partial redemption of its mortgage with Bank of Ireland, paying €2,500,000 off the outstanding balance. This will result in lower quarterly repayment amounts over the remaining years of the mortgage.

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.

15. Financial Commitments

Accommodation Costs (Note 6) includes expenditure of €655,861 in relation to operating leases.

On 28 January 2005 the HPRA signed a leasehold interest in respect of the 5th floor, 6 Earlsfort Terrace, Dublin 2. At 31 December 2021 this lease had 131 days remaining.

	2021	2020
	€	€
The amounts due under this lease are as follows:		
- within one year	103,620	285,984
- between one and five years	-	95,328
- after five years	-	-
	103,620	381,312

On 12 May 2022 the HPRA signed a lease renewal in respect of the 5th floor, 6 Earlsfort Terrace, Dublin 2. This renewal will run for 3 years to 11 May 2025.

The amounts due under this lease are as follows:		
- within one year	226,353	-
- between one and five years	832,862	-
- after five years	-	-
	1,059,215	-

On 11 June 2019 the HPRA signed a leasehold interest in respect of the 4th floor, 6 Earlsfort Terrace, Dublin 2. The lease included a 7 month rent free period to 10 January 2020.

At 31 December 2021 this lease had 12 years and 5.5 months remaining.

The amounts due under this lease are as follows:		
- within one year	371,421	365,246
- between one and five years	1,485,683	1,460,983
- after five years	2,770,179	3,089,372
	4,627,283	4,915,601

16. Capital Commitments

	2021	2020
	€	€
Contracted For (Contract Signed)	479,002	20,963
Contracted For (Contract Not Signed)	-	93,436
	479,002	114,399

17. Authority Remuneration

	Fees	Expenses
	€	€
Michael Donnelly (Chairperson)	8,439	-
Joe Collins	7,695	-
David Holohan	7,695	-
Brian Jones	7,695	-
Elizabeth Keane	7,695	-
Paula Kilbane	3,936	-
Sharon O'Kane	3,560	-
Diarmuid Quinlan	7,695	-
Richard Reilly	-	-
	54,410	-

Up to the 15th February 2017, other than the Chairperson, no other Authority Member received a salary. On 16th February 2017, the Health (Miscellaneous Provisions) Act was enacted, which made provision for payment of fees to other Authority members, provided that they were in compliance with the 'one person one salary' principle. One Authority member does not receive a fee under this principle.

18. Key Management Personnel Remuneration

	2021	2020
	€	€
Chief Executive	163,327	160,524
Senior Management	1,072,759	940,884
	1,236,086	1,101,408

All payments to key management personnel were in respect of salaries and short term employee benefits. No post-employment benefits or termination benefits were paid.

The Chief Executive's and senior management's pension entitlements do not extend beyond the standard entitlements in the model public sector defined benefit superannuation scheme.

19. Related Party Transactions

The HPRA adopts procedures in accordance with the guidelines issued by the Department of Public Expenditure and Reform (DPER) covering the personal interests of Authority members. A register of such interests is maintained. In addition to the DPER guidelines, as a regulator the HPRA has strict conflict of interest and disclosure requirements in relation to any interactions with a regulated body, which are updated annually. 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 payment of accounts.

21. Exchange Rates

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

2021	€1 = STG £0.83939
2020	€1 = STG £0.90453

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. On the advice of its solicitors, the HPRA is not disclosing the specific amounts of the legal provisions provided for by it, as disclosure of such amounts might prejudice seriously its position in relation to disputes with other parties on the subject matter of the provision.

23. Going Concern

The HPRA has a reasonable expectation, at the time of approving 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.

The COVID-19 pandemic has impacted how the HPRA operates, with all staff substantially moved offsite since March 2020. From March 2022, staff have begun to return to the office on a phased basis, and the HPRA is moving towards a hybrid working model.

24. Approval of Financial Statements

The financial statements were approved by the Authority of the HPRA on 11 May 2022.

Appendix 1

2021 Committee Members

Management Committee

Dr Lorraine Nolan
Chief Executive

Ms Rita Purcell
Deputy Chief Executive

Dr Gabriel Beechinor
Director of Veterinary Sciences

Ms Sinead Curran
Director of Human Products Monitoring

Mr Sean d'Art
Director of ICT and Business Services

Dr Caitríona Fisher
Director of Quality, Scientific Affairs and Communications
(Retired 1 October 2021)

Mr John Lynch
Director of Compliance
(Retired 1 October 2021)

Dr Niall MacAleenan
Director of Medical Devices

Ms Elizabeth Stuart
Director Human Resources and Change
(Appointed 12 May 2021)

Ms Grainne Power
Director of Human Products Authorisation and Registration

Authority (Board)

Mr Michael Donnelly – Chairperson
(Appointed 19 April 2021)

Dr Joe Collins

Mr David Holohan

Mr Brian Jones

Dr Elizabeth Keane

Dr Paula Kilbane
(Appointed 28 June 2021)

Dr Sharon O'Kane
(Appointed 15 July 2021)

Dr Diarmuid Quinlan

Prof Richard Reilly

Audit and Risk Committee

Prof Elizabeth Keane – Chair

Mr David Holohan

Mr Brian Jones

Advisory Committee for Human Medicines

Dr Diarmuid Quinlan – Chair

Prof Brian Cleary

Prof Desmond Corrigan

Dr Paul Gallagher

Ms Fionnuala King

Dr Fionnuala Ní Ainle

Dr Brian O'Connell

Ms Margaret O'Doherty

Ms Siobhan O'Sullivan

Dr Patrick Sullivan

Advisory Committee for Veterinary Medicines

Dr Joe Collins – Chair

Dr Patrick Paul Corkery

Dr Abina Crean

Dr Caroline Garvan

Dr John Gilmore

Dr David Graham

Dr Andrew Hillan

Dr Orla Keane

Dr Edward Malone

Dr Bryan Markey

Dr Robert Shiel

Dr Christina Tlustos

Advisory Committee for Medical Devices

Prof Richard Reilly – Chair
Prof Robert Byrne
Mr Ger Flynn
Dr Vida Hamilton
Dr Tanya Mulcahy
Dr Fergal McCaffrey
Ms Margaret O'Donnell
Prof Sean Tierney
Prof Pat Twomey

Clinical Trial Sub-Committee of Advisory Committee for Human Medicines

Dr Patrick Sullivan – Chair
Dr Liam Bannan
Dr Patrick Morris
Dr Thomas Peirce
Prof Catherine McHugh
Dr Amjad Hayat

Experts Sub-Committee of the Advisory Committee for Human Medicines

Dr Diarmuid Quinlan – Chair
Dr Fionnuala Breathnach
Dr Linda Coate
Dr Peter Coakley
Mr James Colville
Dr Noreen Dowd
Dr Stephen Eustace
Prof Stephen Flint
Dr Tim Fulcher
Dr Joseph Galvin
Dr Sheila Galvin
Dr Patrick Gavin
Dr Paul Gallagher
Dr Kevin Kelleher
Dr Catherine Kelly
Dr Mary Keogan
Dr Mark Ledwidge
Dr Frank Murray
Dr Yvonne O'Meara
Dr Cormac Owens
Dr Jogin Thakore
Dr Gerry Wilson

Advisory Sub-Committee for Herbal Medicines

Prof Des Corrigan – Chair
Dr James Barlow
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

Appendix 2

Presentations 2021

Educational/Professional Development Presentations and Training

Institution	Course / Subject	Presentation Title
Atrium	Module on Biopharmaceuticals	Biosimilars - Quality, Non-Clinical and Clinical Requirements
Criminal Assets Bureau	Proceeds of Crime and Asset Investigation (Postgrad Diploma)	Investigations and Emerging Trends – HPRA Enforcement Section
Criminal Assets Bureau	Proceeds of Crime and Asset Investigation (Postgrad Diploma)	Remit of HPRA Enforcement Section
Criminal Assets Bureau	Proceeds of Crime and Asset Investigation (Postgrad Diploma)	Remit of the HPRA Controlled Operations Team in conjunction with Revenue's Customs Service
DCU/TCD	Bioprocess Engineering	Regulation of Biological Medicinal Products
DCU/TCD	Bioprocess Engineering	Regulation of Medicinal Products
GAPP/Italian National Transplant Centre	GAPP Advanced Inspector Training	Development of Overall Guidance on Organisation of PPA System
HSE	Vaccinator Training Programme	Safety Monitoring of COVID-19 Vaccines
IPPOSI	IPPOSI Education Programme	Quality Defect and Recall Programme
LAST	Laboratory Animal Science and Training	Implementation of Scientific Animal Protection Legislation in Ireland (multiple presentations)
LYIT	Veterinary Nursing	Authorisation and Monitoring of Veterinary Medicines
RCSI	Nurse Prescribing	The Role of the HPRA and Safety Monitoring of Medicines
RCSI	Pharmacy	Quality Defect Investigations and Product Recalls
St. John's Central College, Cork	Veterinary Nursing	Authorisation and Monitoring of Veterinary Medicines
Swissmedic	Training Event for GMP Inspectors	The 2019 Revision of ISPE's C&Q Baseline Guide and how it relates to Annex 15

TCD	Immunology	Regulation of Medicines
TCD	ImmunoTherapeutics	Regulation of Biological Medicinal Products
TCD	ImmunoTherapeutics	Regulation of Medicinal Products
TCD	Pharmaceutical Medicine	Advanced Therapy Medicinal Products
TCD	Pharmaceutical Medicine	Collection and reporting of Adverse Events/Reaction Reports arising from Clinical Trials
TCD	Pharmaceutical Medicine	Biostatistical Aspects of Regulation
TCD	Pharmaceutical Medicine	Communication of Drug Safety Data
TCD	Pharmaceutical Medicine	Early Access to Medicines
TCD	Pharmaceutical Medicine	EU Medical Devices Regulation
TCD	Pharmaceutical Medicine	GCP Inspections
TCD	Pharmaceutical Medicine	Medicines Regulation: International Quality Standards and Pharmacopoeias
TCD	Pharmaceutical Medicine	Nonclinical Drug Development
TCD	Pharmaceutical Medicine	Overview of Clinical Trials Legislation in Europe
TCD	Pharmaceutical Medicine	Overview of Pharmacovigilance Risk Assessment Committee
TCD	Pharmaceutical Medicine	Pharmacovigilance Inspections
TCD	Pharmaceutical Medicine	Quality Defects, Product Recalls and MA Withdrawals
TCD	Pharmaceutical Medicine	Regulation of Biological Medicinal Products
TCD	Pharmaceutical Medicine	The Paediatric Regulation
TCD	Pharmaceutical Medicine	The Role of CHMP (EMA)/CP
TCD	Pharmaceutical Medicine	The role of CMD(h)
TCD	Pharmacy	Quality, Safety and Risk Management
TCD	Qualified Person Forum	Regulatory Update
TUD	Medical Device Decontamination (CPD)	Medical Device Legislation
TUD	Medical Device Decontamination (CPD)	Practical Aspects of Medical Device Regulation for Healthcare Institutions
TUD	Pharmaceutical Quality Assurance and RegulationPharmaceutical QA and Regulatory Affairs	A Regulator's Perspective on Quality Risk Management
UCC	Industrial Pharmaceutical Technology and Quality Systems	Regulatory Update
UCC	Pharmacy	Quality Defect Investigations and Product Recalls
UCD	Prescription of Medication	The Role of the HPRA and Safety Monitoring of Medicines

Regulatory Presentations

Event/Organiser	Presentation Title
American Institute of Chemical Engineers (AIChE)	Data Analytics in Pharmaceutical Manufacturing – Regulatory Considerations
Animal and Plant Health Association	Industry Implications of Regulation 2019/6
Cancer Retreat – Clinical Trials Ireland	Roles and Obligations of Academic Sponsors
CT Legal	GCP inspections during (and after) COVID-19
Cystinosis Ireland Workshop	The HPRA and the Regulation of Clinical Trials in Ireland
Department of Agriculture, Food and the Marine – Webinar for Veterinary Surgeons	Veterinary Medicines Landscape Post-2022
DIA Accelerating CMC Workshop	Regulatory Flexibilities and Post-Approval Changes – Lessons Learned from the Pandemic
DIA China	Application and Implementation – PIC/S
DIA Europe	EMA Toolbox Guidance for PRIME products
DIA Europe	Evolving Regulation of IMP – Intersection between GCP and GMP
DIA Europe	Experience on Virtual Inspection
DIA Europe	Vaccination: Exploring Risk Communication Needs
EDQM (Council of Europe)	HPRA Project - Detention of Unauthorised Medicines from the US
EFSPI	Biostatistical Aspects of Regulation
EMA Committee for Advanced Therapies (Interested Parties Meeting)	Comprehensiveness Criteria for Marketing Authorisation Applications for ATMPs
ESWI	COVID-19 Response in Ireland: Vaccine Risk Communication
European Healthcare Distribution Association (GIRP)	Regulatory Flexibility for GDPs
European QP Association	Specific Requirements for IMPs – The Inspector's View
Hitech Health	ATMPs – A Regulatory Update and Lessons Learned So Far
HSE Webinar	Medical Device Regulation 2017/745
ICGP	COVID-19 Vaccines – Safety Monitoring and Reporting of Suspected Adverse Reactions
IFPAC	Personal Considerations Regarding Use of Models in Module 3
IFPMA	Overview of GMP Harmonisation – Role of PIC/S
INAB	The In-Vitro Diagnostic Regulation and In-House Devices
ISPE China	PIC/S Pre-Accession
ISPE Global Summit	PIC/S Remote/Distant Assessments
National Clinical Pathology Programme	The In-Vitro Diagnostic Regulation and In-House Devices

Oireachtas Committee on Agriculture and the Marine	Regulation of Veterinary Medicines
PDA / FDA Regulatory Conference	Quality Risk Management – An Update on the Ongoing Revision of ICH Q9
PDA Asia Pacific Conference	Quality Risk Management – An Update on the Ongoing Revision of ICH Q9
PDA Ireland Chapter	Annex 1 – Regulatory Process
Pharmachem Skillnet/BPCI	Human Error in GMP – A Regulator's Perspective
Pharmacovigilance World	Pharmacovigilance Inspections – A Regulatory Perspective
Protein Expression in Animal Cell (PEAce)	Regulatory Flexibility in the Context of the COVID-19 Pandemic
QRM Summit	A Regulator's Perspective on Quality Risk Management
The Cattle Association of Veterinary Ireland	Changes to the Prescribing and Supply of Animal Remedies in 2022
TOPRA	An Introduction to Regulatory Affairs
TOPRA	Managing Lifecycle and Variations Effectively
TOPRA	The SmPC – The Regulator's Perspective
Veterinary Ireland	Regulation of Veterinary Medicinal Products in 2022

Appendix 4

Publications and Articles 2021

Drug Safety Newsletters

Edition	Articles
February 101st Edition	Special Edition on COVID-19 Vaccines Safety Monitoring Activities: - COVID-19 Vaccines – What is authorised? - Importance of reporting suspected adverse reactions - How to report suspected adverse reactions to the HPRA - Information on European safety monitoring for COVID-19 vaccines - How to register with the HPRA for alerts
March 102nd Edition	COVID-19 Vaccine AstraZeneca® – Conclusion of EMA review of thromboembolic events following vaccination
April 103rd Edition	COVID-19 Vaccine Janssen® – EMA review of very rare cases of thrombosis in combination with thrombocytopenia following vaccination
August 104th Edition	COVID-19 Vaccines Pharmacovigilance Update: - Myocarditis and pericarditis – Comirnaty® and Spikevax® - Thrombosis with thrombocytopenia syndrome (TTS) - Vaxzevria® and COVID-19 Vaccine Janssen® - Capillary Leak Syndrome – Vaxzevria® and COVID-19 Vaccine Janssen® - Guillain-Barré Syndrome (GBS) – Vaxzevria® and COVID-19 Vaccine Janssen - Direct Healthcare Professional Communications published on the HPRA website since the last update
September 105th Edition	- Pregabalin – Respiratory depression without concomitant use of opioids or other CNS depressants - Direct oral anticoagulants (DOACs) – Reminder of the importance of adhering to product information and existing measures to minimise the known risk of haemorrhage - Reporting of suspected adverse reactions - Direct Healthcare Professional Communications published on the HPRA website since the last Drug Safety Newsletter

Human Medicines Safety Articles – External Publications

Month	Publication	Topic
January	MIMS	Adverse Reaction Reporting
February	MIMS	COVID-19 Vaccines – Safety Monitoring Activities
	MIMS Respiratory Supplement	Clarithromycin – Updates to PI regarding important interactions, use in pregnancy and lactation and contraindication in hypomagnesaemia
March	IMF	COVID-19 Vaccines – Safety Monitoring Activities
	MIMS	Implanon NXT – updated insertion and removal instructions due to risk of neurovascular injury and implant migration
April	MIMS	Leuprorelin-containing depot medicines – Risk of lack of efficacy due to incorrect reconstitution and administration
	MIMS Cardiac Supplement	COVID-19 Vaccine AstraZeneca – Conclusion of EMA review of thromboembolic events following vaccination
May	MIMS	Imfinzi▼ (durvalumab) – Risk of myasthenia gravis
	MIMS Womens Health Supplement	Optimising the safe and effective use of medicines in clinical practice through proactive risk management
July/August	MIMS (July/August combined issue)	Paracetamol – Reminder of the risk of hepatotoxicity in patients with risk factors
	MIMS Respiratory supplement	Clarithromycin – Updates to PI regarding important interactions, use in pregnancy and lactation and contraindication in hypomagnesaemia
September	IMF	Direct acting oral anticoagulants (DOACs) : Update on recent studies and reminder of the importance of adhering to product information, including existing measures to minimise the known risk of haemorrhage
	MIMS	Paracetamol – Reminder of the risk of hepatotoxicity in patients with risk factors
October	MIMS	Adverse Reaction Reporting
	MIMS Respiratory Supplement	Clarithromycin – Updates to PI regarding important interactions, use in pregnancy and lactation and contraindication in hypomagnesaemia
November	MIMS	Polystyrene sulfonate and risk of GI stenosis & ischaemia
	MIMS Diabetes Supplement	Canagliflozin (Invokana & Vokanamet) – PI updates regarding complicated UTIs
December	MIMS	IL-17 inhibitiors – PI updates on inflammatory bowel disease (IBD)
	MIMS Compendium	Pregabalin – Respiratory depression

Veterinary Medicines Articles – External Publications

Month	Publication	Topic
September	Veterinary Ireland Journal	Tips for developing best practice protocols for use of antiparasitic drugs on farms in Ireland
October	Veterinary Ireland Journal	The New Veterinary Regulation – Key Changes
November	Veterinary Ireland Journal	Best practice protocols for use of antiparasitic drugs on farms in Ireland
March	It's Your Field	The New Veterinary Regulation and its impact on the distribution of veterinary medicines
August	It's Your Field	The New Veterinary Regulation – Wholesale and retail of veterinary medicines

Appendix 4

Standing Committee/ Working Group Participation

Committee/Working Group	Organisation	Meetings in 2021
Controlled Drugs Cross Border Group	Care Quality Commission (UK)	3
Counterfeiting of Medical Products (CMED)	Council of Europe	3
International Network on the Control of Precursors Diversion	Council of Europe	1
iNAP (Ireland's National Action Plan on AMR) Animal Health Implementation Committee	Department of Agriculture, Food and the Marine	3
Children and Family Relationships Act	Department of Health	3
Early Warning and Emerging Trends Group	Department of Health	3
Medical Cannabis Access Programme	Department of Health	7
National Clinical Effectiveness Team	Department of Health	2
National Public Health Emergency Team – COVID-19	Department of Health	26
Medicines Criticality Assessment Group	Department of Health / HSE	7
Connecting for Life Strategy	Department of Health / National Office of Suicide Prevention / National Suicide Research Foundation	3
Borderline Product Network (medicines)	EDQM	1
Committee for Cosmetics and Consumer Health	EDQM	1
Committee for Cosmetics and Consumer Health / European Network of OCCLs	EDQM	1
EU OCABR (Official Control Authority Batch Release) Network	EDQM	1
European Network of Official Cosmetics Control Laboratories (OCCL)	EDQM	1
OMCL Network Active Pharmaceutical Ingredient Working Group	EDQM	1
OMCL Network Advisory Group	EDQM	4
OMCL Network General Annual meeting	EDQM	1
OMCL Network MRP/DCP/CAP Annual Meeting	EDQM	1
Clinical Trials Information System (CTIS) – Member State Training	EMA	1

Committee/Working Group	Organisation	Meetings in 2021
Committee for Advanced Therapies (CAT)	EMA	12
Committee for Medicinal Products for Human Use (CHMP)	EMA	25
Committee for Medicinal Products for Veterinary Use (CVMP)	EMA	11
Committee for Orphan Medicinal Products (COMP)	EMA	11
COVID-19 EMA Pandemic Task Force	EMA	100+
Efficacy Working Party - Veterinary	EMA	3
ESVAC (European Surveillance of Veterinary Antimicrobial Consumption) Annual Network meeting	EMA	1
ESVAC Change Liaison Network for Antimicrobials Sales and Use Data (ASU)	EMA	1
GCP IWG / CMDh Joint Meeting	EMA	2
GMP / GDP Inspectors Working Group – GMP Responsibilities of MA holders	EMA	7
Good Clinical Practice (GCP) Inspectors' Working Group	EMA	6
Good Manufacturing and Distribution Practice (GMDP) Inspectors' Working Group	EMA	4
IRIS Change Champions group	EMA	1
IWG Sub-Group on Article 123 of the new EU Veterinary Regulation 2019/6	EMA	3
Management Board	EMA	4
New Veterinary Regulation Expert Group – Drafting of Veterinary Inspection Procedures	EMA	3
Paediatric Committee (PDCO)	EMA	11
Pharmacovigilance (PV) Inspectors' Working Group (Human and Veterinary)	EMA	1
Pharmacovigilance Business Team	EMA	5
Pharmacovigilance Risk Assessment Committee (PRAC) - Organisational, Regulatory and Methodological Matters (ORGAM)	EMA	11
Pharmacovigilance Risk Assessment Committee (PRAC) – Plenary	EMA	19
Pharmacovigilance Working Party - Veterinary	EMA	6
Quality Review of Documents Working Groups	EMA	4
Safety Working Party – Veterinary	EMA	2
Scientific Advice Working Party - Human	EMA	11
Signal Management Review Technical Working Group (Methods) – PRAC	EMA	4
Signal Management Review Technical Working Group (SMART) Processes – PRAC	EMA	2
EMA/IWG/EDQM Sub-group – Sartan Lessons Learnt Report	EMA / EDQM	1
Revision of ICH Q9 Guideline	EMA / ICH	26

Committee/Working Group	Organisation	Meetings in 2021
Eudralex Volume 4, Annex 21 Working Group	EMA / National Competent Authorities	1
Pharma Legislation Revision – Inspections	EMA / National Competent Authorities	4
Competent Authorities for Blood	European Commission	1
Competent Authorities for Organ Donation and Transplantation	European Commission	1
Competent Authorities for Tissues and Cells	European Commission	1
DG SANTE F5 Fact Finding Study Team	European Commission	2
European Product Compliance Network (EUPCN) – Market Surveillance	European Commission	2
European Product Compliance Network (EUPCN) – Market Surveillance	European Commission	2
European Union Intellectual Property Office (EUIPO)	European Commission	1
Expert Group on Precursor Chemicals	European Commission	2
Expert Sub-Group on Vigilance for Blood, Tissues and Cells, and Organs (VES)	European Commission	10
GAPP Advanced Inspector Training	European Commission	4
Horizontal Drugs Group (HDG)	European Commission	1
Joint European Product Compliance Network (EUPCN) / Consumer Safety Network (CSN)	European Commission	1
Medical Device Coordination Group (MDCG) (MDR / IVDR)	European Commission	8
MDCG – WG1 Notified Body Oversight (NBO)	European Commission	4
MDCG – WG2 Standards	European Commission	1
MDCG – WG3 Clinical Investigation and Evaluation (CIE)	European Commission	2
MDCG – WG4 Market Surveillance and Vigilance (PMSV)	European Commission	3
MDCG – WG5 Market Surveillance	European Commission	2
MDCG – WG6 Borderline and Classification	European Commission	1
MDCG – WG8 Eudamed	European Commission	4
MDCG – WG9 Unique Device Identification (UDI)	European Commission	1
MDCG – WG10 International Matters	European Commission	2
MDCG – WG11 In Vitro Diagnostic (IVD)	European Commission	2
MDCG – WG12 Nomenclature	European Commission	1
MDCG – WG 13 Annex XVI	European Commission	2
National Contact Points for the Implementation of Directive 2010/63/EU	European Commission	2
New Veterinary Regulation – Implementing Acts re Pharmacovigilance	European Commission	2
Pharmaceutical Committee	European Commission	5

Committee/Working Group	Organisation	Meetings in 2021
Platform of European Market Surveillance Activities in Cosmetics (PEMSAC)	European Commission	1
Revision of Blood, Tissues & Cells Legislation	European Commission	14
Standing Committee on Cosmetic Products	European Commission	3
Standing Committee on Veterinary Medicinal Products	European Commission	3
Working Group on Cosmetic Products	European Commission	3
Working Group on Good Distribution Practice for Active Pharmaceutical Ingredients and Veterinary Medicinal Products	European Commission	1
Operation Shield	Europol	2
Food Fraud Task Force	Food Safety Authority of Ireland (FSAI)	1
Clinical Trials Facilitation Group (CTFG) Decentralised Trials	HMA	1
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
EU Innovation Network (EU-IN)	HMA	10
EU-IN Borderline Products Classification Subgroup	HMA	9
Heads of Agency Meeting	HMA	5
Joint GCP IWD/ CMDh Working Party	HMA	7
Pharmacovigilance Work-sharing Procedures Working Party	HMA	10
Supply Chain Working Group	HMA	2
Working Group of Communications Professionals (EU Presidency)	HMA	2
Working Group of Enforcement Officers (WGEO)	HMA	11
Working Group of Quality Managers	HMA	3
Risk Assessment Tool for Surveillance Testing	HMA / EDQM	6
COVID-19 Communications Meetings	HMA / EMA	50
HSE COVID-19 Vaccination Monitoring and Evaluation Meeting	HSE / HPSC	25
National Cosmetics Surveillance Forum	HSE Environmental Health Service (EHS)	2
ICH Q3E Expert Working Group on Extractables and Leachables	ICH	1
ICMRA COVID-19 Vaccine Pharmacovigilance Network	ICMRA	18
ICMRA Plenary Meeting	ICMRA	2
ICMRA Vaccine Confidence Working Group	ICMRA	1
Working Group on Digital Transformation of Inspections	ICMRA	2
Safety Features Oversight Group	IMVO / PSI / Department of Health	8
Operation Pangea	Interpol	3

Committee/Working Group	Organisation	Meetings in 2021
Overprescribing Working Group	Medical Council	3
Expert Group on Pharmaceuticals and Medical Devices	OECD	1
PFIPC Liaison Meetings	Permanent forum on International Pharmaceutical Crime (PFIPC)	3
Pharmaceutical Inspection Co-Operation Scheme (PIC/S) Executive Bureau	PIC/S	1
PIC/S Expert Circle on Controlling Cross Contamination in Shared Facilities	PIC/S	25
PIC/S Expert Circle on Quality Risk Management	PIC/S	19
PIC/S Sub-Committee on Harmonisation	PIC/S	3
PIC/S Working Group on ICH Q12 Training	PIC/S	3
International Strategic Working Group on Nitrosamines	Regulatory Authorities	1
National Immunisation Advisory Committee (NIAC)	Royal College of Physicians of Ireland (RCPI)	5
NIAC COVID-19 Working Group	RCPI	50
Anti-Doping Committee	Sports Council	1
European Region Workshop – National Focal Points for substandard and falsified medical products	WHO	1
International API Program	WHO	12
Internet Working Group	WHO	4
Member State Mechanism on Substandard and Falsified Medical Products	WHO	1
Operation STOP II	World Customs Organisation	1

HPRA
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Health Products Regulatory Authority

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