HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Public Consultation on
Annual Review and Proposal for Fees – Financial Year 2025

Human Medicines, Compliance Activities, Blood, Tissue Establishments and Organs and Medical Devices

OCTOBER 2024

CONTENTS

1 INTRODUCTION

The Health Products Regulatory Authority (HPRA), since its establishment in 1996, has successfully run its regulation of human medicines authorisation, manufacturer and wholesaler operations without recourse to exchequer funding, and has established sufficient reserves to allow it to fund capital and IT expenditure and deal with unexpected costs as these arise. This is both a requirement under the Irish Medicines Board Act and a stated objective of the Authority[1] of the HPRA. Since 2004, the HPRA has implemented a policy of annual fee reviews following consultation with industry. For medical devices, cosmetics, blood, tissues and cells, the HPRA receives a partial subvention from the Department of Health but also commits to ensure that the income received matches the costs of those functions.

As stated in previous consultations, it is a priority for the HPRA to match resources from fee income, with current work volumes and to plan for future activity. The second aim, in respect of fee income, is to provide predictability, stable timelines and ability to fund the cost of the regulatory system that we operate.

To ensure that we manage the business properly, we have agreed to review our fees on an annual basis to reflect changes to our cost base and service levels. This document summarises the outcome of our review of fees, and it sets out the current operating environment, the service levels and activities and expected changes in service levels and activities for 2025.

2 THE OPERATING ENVIRONMENT

In 2024 the HPRA operating environment stabilised after a number of challenging years following the COVID-19 pandemic. Hybrid working is established within the organisation, enabling 400 staff to return to the office while continuing to facilitate homeworking. While the hybrid model continues to be reviewed, the organisation is adapting to the new way of working.

2024 was a busy year where the activity levels reached or exceeded pre-pandemic levels. Volumes of transactions were high across all areas of the organisation, and this was combined with significant project work and the implementation and development of significant new legislative packages. In relation to Brexit, work continued preparing for the implementation of the Windsor Framework in January 2025 and the expiry for the Brexit exemptions. Shortages remained a feature of both the national and European market and consumed considerable resources. Preparing for the inquiry into sodium valproate and preparing a review of codeine containing medicines were also resource intensive. Overall, human medicine income and other income categories are

[1] The term 'Authority' is used to refer to the persons appointed under section 7 of the Irish Medicines Board Act, 1995, and previously referred to as the 'Board' of the IMB.

performing well in 2024. In 2025, authorisation and inspection volumes are expected to be consistent with 2024 and costs are expected to increase. Payroll costs were significantly less than planned in 2024 due to delays in approvals which meant that positions were unfilled for a large part of the year. This was further impacted by full employment in the market with related resource constraints. In 2024, we experienced significant payroll increases arising out of the national State sector pay deal which will also impact 2025. In 2025, we also expect substantial increases in the cost of payroll related to increases in staff numbers. This increase is due to delays in recruiting in 2024 and greater staff turnover. However, additional staff are also required to reflect the increased volume of activity and increased complexity of regulation. For 2025 we must continue to deliver on the Clinical Trial Regulation (CTR), address the level of Mutual Recognition Procedures (MRP) and Decentralised Procedures (DCP) in the system and the need for more centralised assessors. The medical device department continues to need additional staff as the Medical Device and *In Vitro* Medical Device Regulations (MDR and IVDR) are rolled out across Europe. Big projects such as the website redevelopment, the pharmaceutical legislative project, the sodium valproate inquiry, and the implementation of the Critical Entity Resilience (CER) Directive will also impact resourcing. The ESG requirements required an investment in the building and work practices to better contribute to the environment and sustainability. Costs in 2024 increased in line with inflation. General inflation has stabilised and is expected to be between 2 and 3% in 2025 but wage inflation remains significantly higher.

Pensions continue to be a growing cost and for the single service scheme, the employer contribution is up to 17% of the payroll cost of those employees. By its nature, this cost will increase exponentially as all new staff are covered by this obligation and this means that as longer serving employees leave, they are replaced by a more expensive resource. It is appropriate, in common with all pension schemes that the employer makes a contribution, and all staff in this scheme will have their pension funded from the central exchequer. However, staff from pre 2013 are part of the local government superannuation scheme which is an unfunded pension scheme, and this pension liability continues to impact on fees.

A particular area of concern is increased litigation, in the areas of both personal injury and judicial review. This unfortunately results in increased costs and resources dedicated solely to work which delivers nothing under our public health remit.

Public scrutiny and the role of the regulator in relation to medicines has increased in the areas of global supply and shortages, vaccines and vaccine hesitancy, availability and access to innovative therapies.

3 STRATEGIC DIRECTION OF THE HPRA

During 2020-2021, the HPRA developed a new strategic plan for the period 2021-2025. Following extensive consultations and a detailed review of the environment within which we operate, we have identified the themes and activities which we believe are relevant to the development of our

regulatory activities over the next five years. The high-level strategic goals under the current plan are as follows:

- **Health system partnerships** (strengthening our collaborations across all areas of the health system)
- **Progressive regulation** (increasing our use of proportionate and adaptive approaches for better patient outcomes)
- **Communication and engagement** (improving our models of engagement to strengthen public trust and confidence)
- **Enabling innovation** (enhancing our supports for innovation from discovery through to regulatory approval)
- **Great people, great processes** (developing our organisation and people to successfully achieve our goals)

In 2025, our key objectives under the strategic plan include:

General
- Participation in the sodium valproate national inquiry.
- Develop, agree and sign off the next iteration of the HPRA's strategic plan for the period 2026 to 2028 (3 years).
- Cross-organisational readiness and engagement with the Benchmarking of European Medicine Agencies (BEMA) V assessment in March 2025.

Strategic goal 1
- Progress activities in line with the HPRA strategic proposal for medicines availability/shortages.
- Strengthen and increase the scientific animal protection inspections programme, enhancing the role the HPRA as an advocate for the 3R principles.

Strategic goal 2
- Continue preparations to support Ireland holding the 2026 EU presidency.
- Continue to support the review of the new pharmaceutical legislation package.
- Engage in the implementation of the CER Directive.
- Implement a marketing surveillance strategy for in-house and custom-made device manufacturers to ensure MDR and IVDR requirements are met.
- Initiate preparations as needed for the Substances of Human Origin (SoHO) legislation.

Strategic goal 3
- Continue the communications and engagement strategy implementation.
- Develop transparency polices in the Compliance and Medical devices functions.

Strategic goal 4
- Implement additional innovation supports at EU and national levels.

- Plan capacity and expertise needed for national regulation and innovation support in Medical Devices.

Strategic goal 5
- Deliver the new HPRA website.
- Continue to work on initiatives to support the People Strategy, especially focusing on the career and capability framework project.
- Continue the implementation of the Digital Transformation Strategy, including:
  - Progression of an organisation wide 'time recording' project
  - Delivering further Eolas implementation projects and determining an approach for the assessment of Eolas future direction options
  - Developing a future data approach and enhancing our skills and use of automation.
- Progress building enhancements and other energy efficiency initiatives based on the HPRA climate action roadmap, including the move of Compliance to the main HPRA building.

All the above initiatives will provide real and tangible benefits to our stakeholders.

4 THE OUTLOOK FOR 2025

Operating environment for 2024
While inflation has stabilised, the volume of work has increased and the need for additional resources has resulted in a challenging operating environment.

New legislation
In 2023, the HPRA implemented three new regulations: the New Veterinary Regulation (NVR), the CTR and the IVDR. The HPRA will continue to implement these regulations in 2025 as the transition provisions expire. The SoHO Directive was finalised in 2024 and will move to implementation in 2025. The extensive pharmaceutical package containing a directive and regulation is being negotiated in the Council of Europe, and the HPRA is supporting the Department of Health in these negotiations.

The CER Directive has been published and has implications for medicines and medical devices. The HPRA has been appointed as the competent authority and will commence implementation in 2025 as part of the Compliance department. Medicines shortages will continue to be a priority. Inspection levels were high in 2024 and issues around import of medicines outside of the legitimate supply chain continued to be resource intensive.

The workload of the medical device department has increased significantly. The importance of the role that medical devices play in healthcare delivery, and the related challenges in their regulation is recognised. The MDR and IVDR are both applicable although transitional provisions still apply. Significant work remains in providing support to stakeholders to aid their understanding and support their implementation of the regulations.

The new regulations place very explicit obligations on regulatory authorities in relation to their activities, resources and capabilities. In addition, growth in specific technological areas, such as digital health products and *in-vitro* diagnostics will necessitate reallocation, re-purposing and development of our staff. This means that further staff increases in 2024/2025 are required to manage this increased workload. This will impact on the funding model, which is currently subvented by the Department of Health.

Implementation of new legislation does not just impact the departments concerned. The impact is felt across the organisation as management, legal, HR, IT and financial support is necessary for the successful delivery of the new legislation.

Financial outturn for 2024
The outturn for 2024 will be positive. This reflects the income levels operating as expected or above expectations and significantly lower costs, principally around payroll caused by the inability to bring the expected levels of staff on board in the first half of 2024.

Financial impacts on 2025
It is expected that there will be a substantial increase in costs for 2025. This reflects the high level of recruitment in Q3/Q4, planned additional staff in 2025 and a continuing increase to costs reflecting the increased workloads. Income levels are expected to be similar to those of 2025.

Payroll
The key driver of payroll increases in 2025 will be the impact of the new pay deal which was finalised in January 2024 and resulted in pay awards in 2024 and 2025 as follows:

Year 2024
- 2.5% or €1,125 whichever is higher in January 2024
- 1% in June 2024
- 1% or €500 whichever is higher to be paid in October 2024

Year 2025
- 2% or €1,000 whichever is higher to be paid in March 2025
- 1% to be paid in August 2025
- 1% to be paid in September 2025 (local bargaining)

The increases in 2024 were not included in costings for 2024 and will be in place for a full year in 2025. There will also be additional staff numbers related to expanded functions, increased levels of work and increased pension costs.

Other costs
Other costs continue to increase as activity levels are returning to pre-pandemic levels. The current energy crisis significantly increased costs in 2024 and will have a knock-on impact in 2025, although there is evidence of steadying energy costs. While inflation (which has been running as

high as 3% in 2023) has reduced to 2.6% in 2024, it will still have a significant impact on projected costs.

The HPRA expects that 2025 will be another challenging year in managing costs for the reasons outlined above.

4.1 Risks and uncertainties in relation to the fee model

The fee proposal outlined above is based on the volumes and patterns of submissions seen in the first seven months of 2024. The nature of regulatory income is that it is dictated by industry activity, which can change significantly over a period of time.

As with previous years, the HPRA commits to review the proposed fees during the planning cycle in 2025 and further amend the fees and fee structure, if required, for 2025.

5 PROPOSED FEES

In 2024, the HPRA increased the fees by only 1.5% notwithstanding the level of inflation experienced in 2023 and the pay deal that was implemented in 2024. The cost base of the HPRA will increase in 2025, and to reflect this, the HPRA propose to impose a general increase of 5% in 2025 which is significantly less than the combined payroll and inflationary increases and equates to 3.25% p.a. over the last two years.

6 DETAILED CHANGES TO FEES

6.1 General change to fees

As outlined above, there will be a 5% adjustment to fees for the year 2025.

6.2 Other proposed adjustments to fees – clinical trials

6.2.1 Clinical trial fees under the Clinical Trials Regulation (CTR) – the HPRA fee and National Office fee

A single fee is charged by Ireland (the HPRA and the National Office for Research Ethics Committees ('National Office')) for each clinical trial application or substantial modification (previously known as substantial amendment). The sponsor pays the total fee to the HPRA at the time of application and following validation the HPRA transfers the corresponding portion to the National Office.

The HPRA proposes to increase the current CTR fees (see section 6.2.2 below). The National Office intends to review its fees and conduct an independent consultation on clinical trial fees that may

impact the total single fee for CTR clinical trials. Following the National Office consultation, the HPRA will publish any changes to the single fee for CTR clinical trials in our fee documents. For information on the National Office fees, see https://www.nrecoffice.ie/apply/fees/

The National Office and the HPRA will continue not to charge for non-commercial/academic clinical trials to encourage non-commercial research.

Please note that substantial amendments to clinical trials authorised under the Clinical Trials Directive 2004 cannot be made after the 30 January 2025.

6.2.2 Clinical trial fees

The HPRA proposes to increase the following clinical trial fees by 15% to align with other member states and to ensure clinical trials are sufficiently resourced. However, it is proposed not to increase the RMS fee for new clinical trial applications.

New clinical trial applications

Fee code	Description	Current HPRA fee	Proposed fee
1001	Applications with IMPD: Mono-national applications (i.e. Ireland only)	1,920	2,210
1003	Applications with IMPD: IE is a concerned member state for initial, or additional applications	1,700	1,955
1007	Mono-national (no IMPD, simplified IMPD or low interventional CT)	905	1,040
1009	IE is a concerned member state for initial, or additional applications (no IMPD, simplified IMPD or low interventional CT)	635	730

Substantial modification (Parts 1 and 2 or Part 1 only with the addition of a new IMPD)

Fee code	Description	Current HPRA fee	Proposed fee
1011	Applications with new IMPD: Mono-national (i.e. Ireland only)	980	1,125
1012	Applications with new IMPD: IE is the reporting member state	1,200	1,380
1013	Applications with new IMPD: IE is a concerned member state	925	1,065
1015	Other modifications: Mono-national (i.e. Ireland only)	510	585
1016	Other modifications: IE is the reporting member state	810	930

Fee code	Description	Current HPRA fee	Proposed fee
1017	Other modifications: IE is a concerned member state	430	495

The general increase will apply to all other clinical trial fees.

6.2.3 Drug Safety Update Reports – review of annual safety data

It is proposed to remove this fee as full transition to the CTR on the 30 January 2025 will make this fee redundant.

6.3 Other proposed adjustments to fees – Human

6.3.1 Line extensions, first additional strength

It is proposed to bring the fees for the first additional strength where Ireland is the RMS in line with the current fee levels for a new pharmaceutical form.

Fee code	Description	Current HPRA fee	Proposed fee
182	Decentralised application where IE is a concerned member state – first additional strength (existing form)	3,385	3,385
XXX	Decentralised application where IE is the reference member state – first additional strength (existing form)	3,385	8,800

6.4 Other Proposed adjustments to fees – Medical Devices

6.4.1 Designation fee for a Notified Body

It is proposed to apply a fee of €5,435 (fee code 485) for the work associated with the reinstatement of a restriction or suspension of a designation.

It was also proposed that in the case that a notified body's designation is fully or partially withdrawn, any future applications are considered *de novo* and will be subject to the relevant fee.

6.5 Other Proposed adjustments to fees – Compliance

6.5.1 Drug precursors

It is proposed to increase and restructure the drug precursor fees to cover the work involved in processing these applications. The existing fee was set in legislation in 2009 and there has been no increase since.

Fee code	Description	Current HPRA fee	Proposed fee
309	Import/Export, new annual licence/registration for possession and/or for intermediary activities. Renewal of annual licence/registration with amendments.	63.50	110
XXX	New annual licence/registration to place on the market (supply)		300
XXX	Renewal of annual licence/registration with no amendments		85

If applying for more than one activity, the highest fee will apply.

7 CONSULTATION

The HPRA welcomes comments on these proposals and invites respondents to comment.

Contributions to the consultation on these proposals may be provided to the HPRA by 30 October 2024. Contributions should be sent by email to feesconsultation@hpra.ie.

APPENDIX I SERVICE LEVELS – HUMAN PRODUCTS AUTHORISATION, REGISTRATION AND SAFETY MONITORING

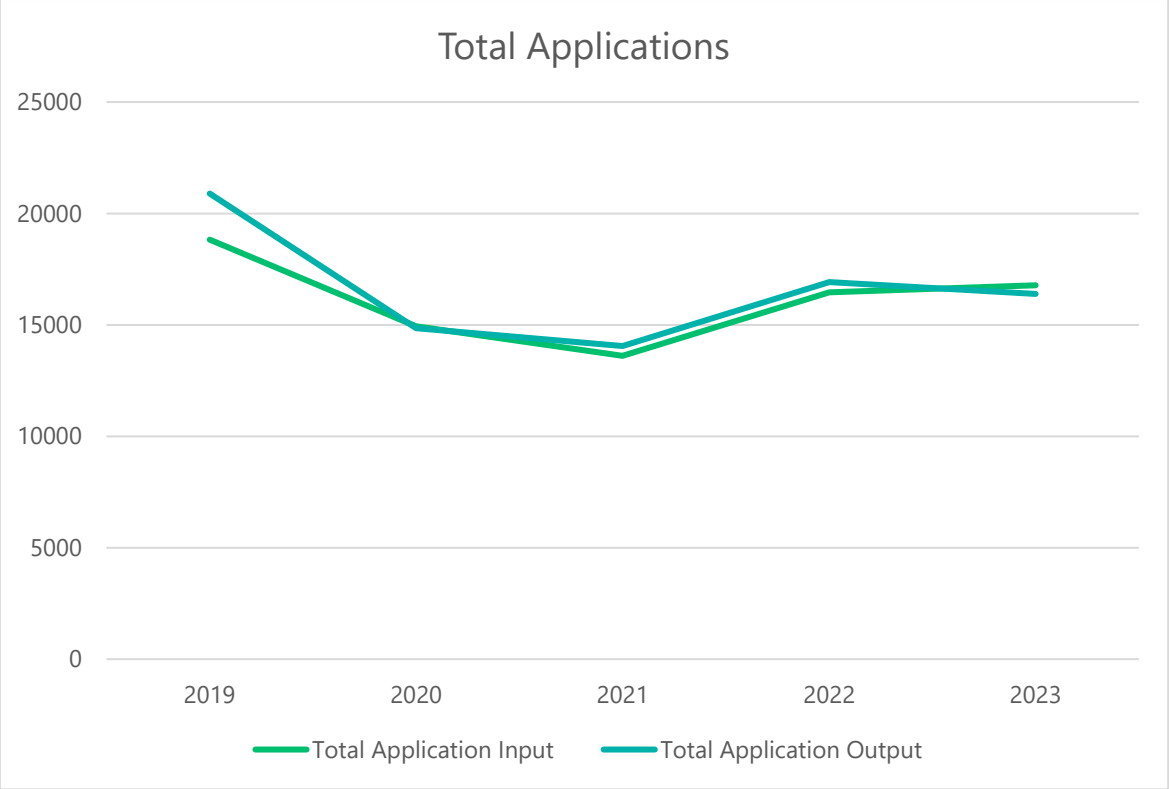
The most significant projects undertaken by the HPRA in the last number of years were driven by the requirement to maintain and further improve patient safety, protect access to medicines and service levels to industry.

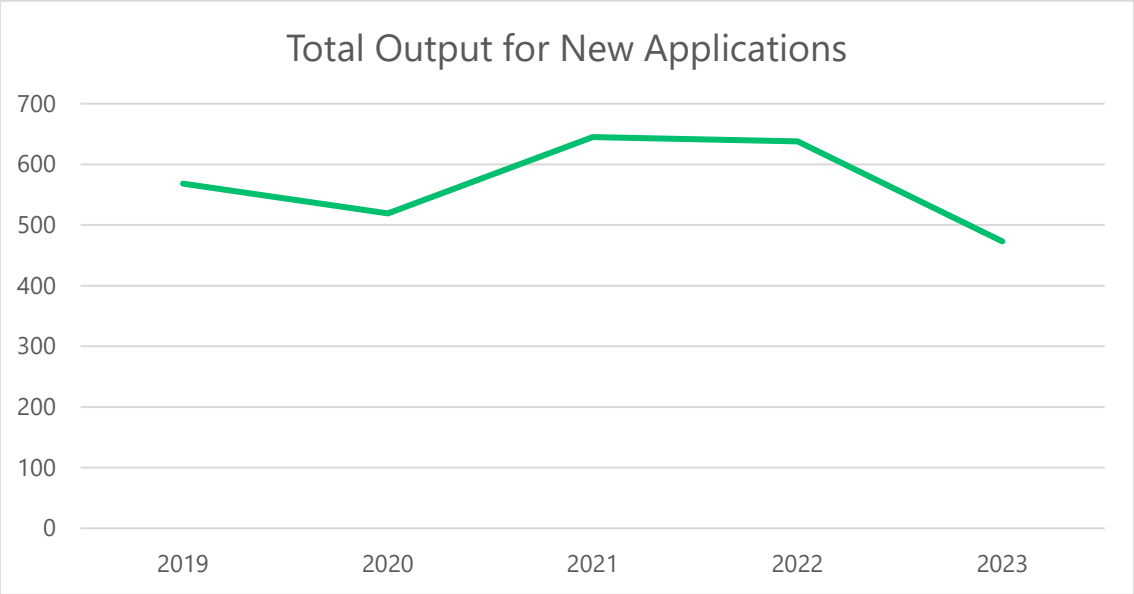
These projects include in summary:

- Readiness to operate as Reference Member State for both MRP and DCP new procedures.
- Introduction of a booking system for MRP, DCP and national procedures to better plan resource utilisation.
- A national scientific advice procedure was introduced in 2016 and was expanded to include a swift national scientific advice procedure in 2023. This assists applicants in the development of new or existing human medicinal products by taking into account the current knowledge of a given condition, targeted patient population, existing treatment modalities and specificities of the product being developed.
- Progress has been made in the development of a new HPRA workflow system. Our focus is now on further optimisation of this workflow technology to ensure ongoing delivery of continued benefits to the organisation and stakeholders in the tracking and managing of workloads. Further development of capabilities in using key performance indicators to allow for more effective monitoring of timelines will improve utilisation of resources and drive further efficiencies.
- Integration of the online reporting system for adverse reactions with the HPRA adverse reaction database which is accessible to patients and health care professionals. Further streamlining of adverse reaction processing procedures is also underway to improve efficiency in this area. This work supported the significant increase in adverse reaction reports related to vaccines and therapeutics which were submitted directly to the HPRA arising from the COVID-19 pandemic.
- Enhanced monitoring of vaccines and therapeutics related to COVID-19. Direct reports to the HPRA continue to be made available to marketing authorisation holders (MAH) via EudraVigilance.
- Continued customer-focused approach.
- Work on the list of interchangeable medicines to support generic substitution by pharmacists in line with the Health (Pricing and Supply of Medical Goods) Act 2013 continues, and is a routine component of assessment work. We review substances as requested by the Minister for Health or the HSE. In addition, we review applications made by industry to have their products incorporated on to the list.
- Focus on the continued provision of guidance and support to industry stakeholders in areas undergoing evolving regulatory development, including new requirements from the CTR and MDR.

- A proactive approach to reclassification of the legal status of medicines (switching) continues. The HPRA is open to discussing innovative switches.
- Raising awareness of the regulation of medicines and important safety considerations via publications and contributions to undergraduate programmes in the medical and paramedical fields.
- Enhanced patient engagement through the Patient Forum which facilitates dialogue and exchange on topics relevant to patients regarding the regulation of medicines and medical devices.

The following graphs outline the output across all application types up to the end of 2023.




Total Output for New Applications
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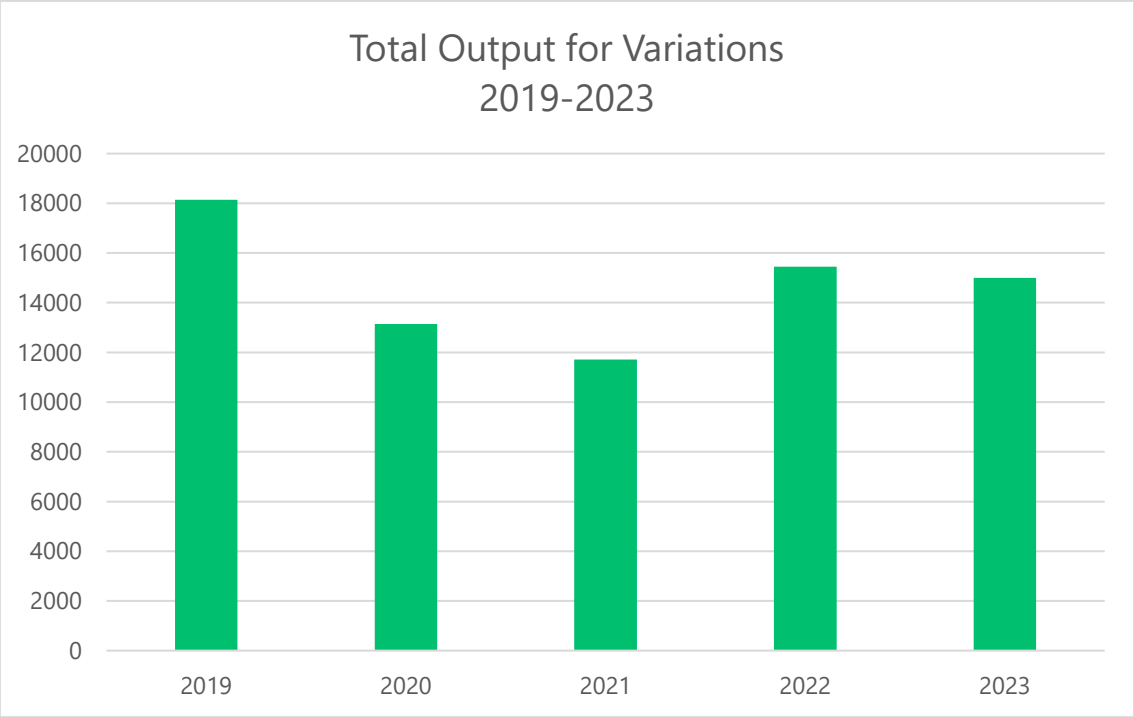
600
500
400
300
200
100
0
2019
2020
2021
2022
2023


Total Output for Variations
2019-2023
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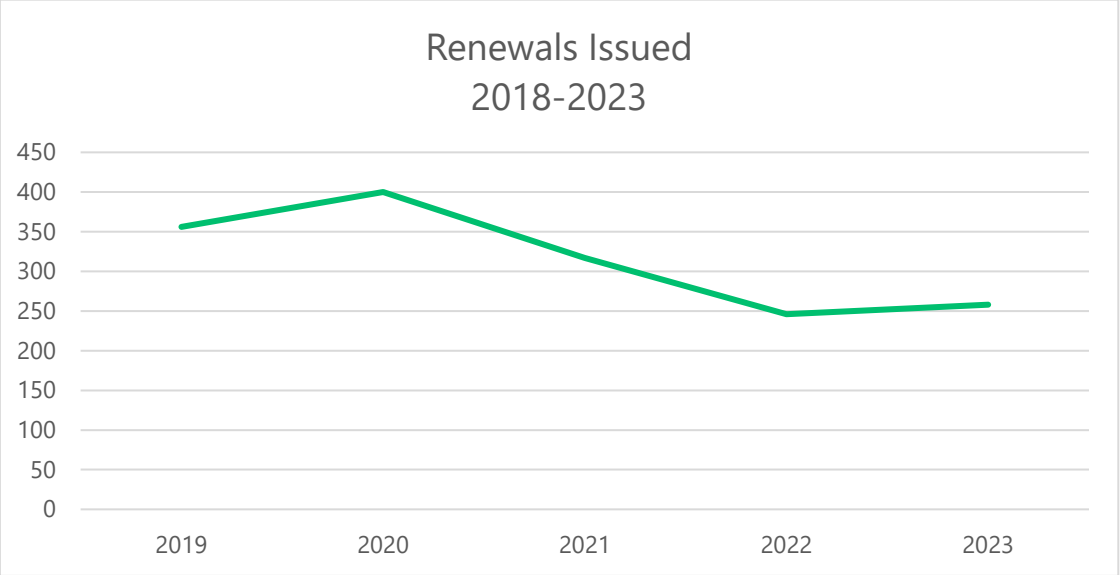
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
2019
2020
2021
2022
2023


Renewals Issued
2018-2023
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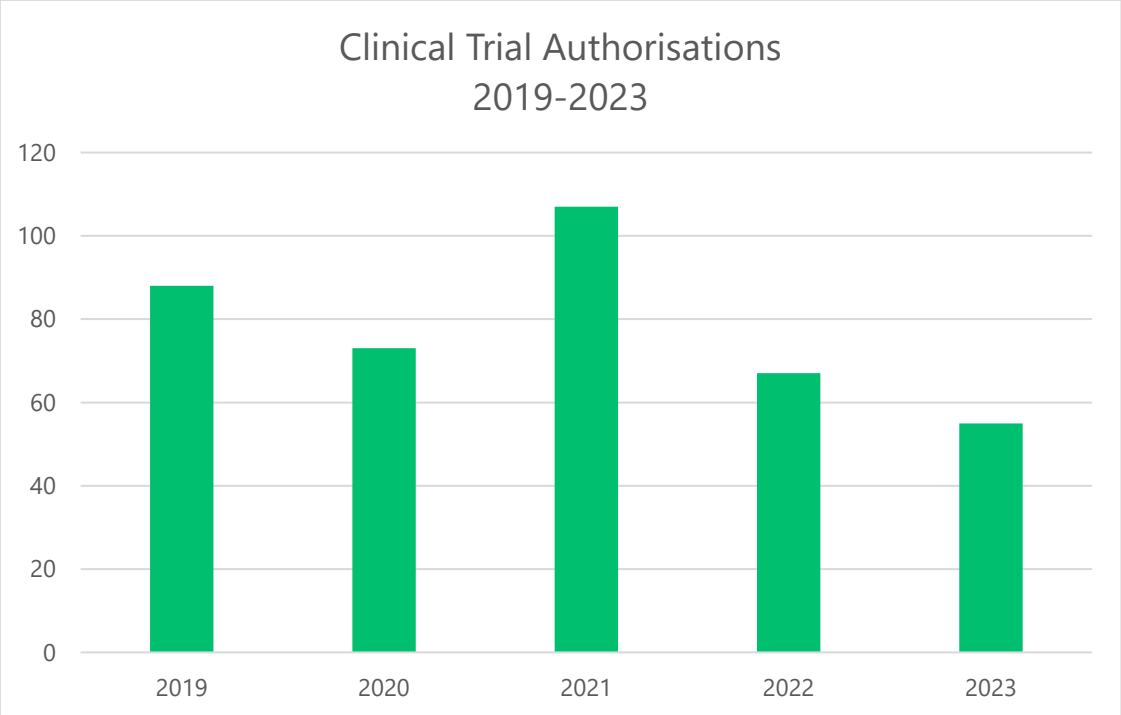
400
350
300
250
200
150
100
50
0
2019
2020
2021
2022
2023


Clinical Trial Authorisations
2019-2023
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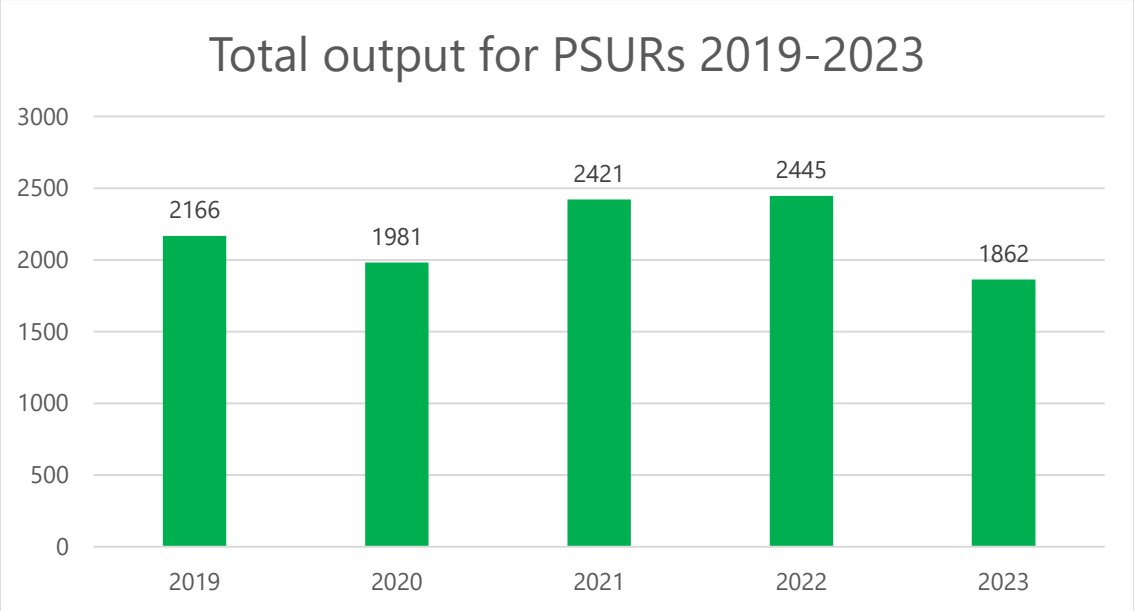
100
80
60
40
20
0
2019
2020
2021
2022
2023


Total output for PSURs 2019-2023
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1500
1000
500
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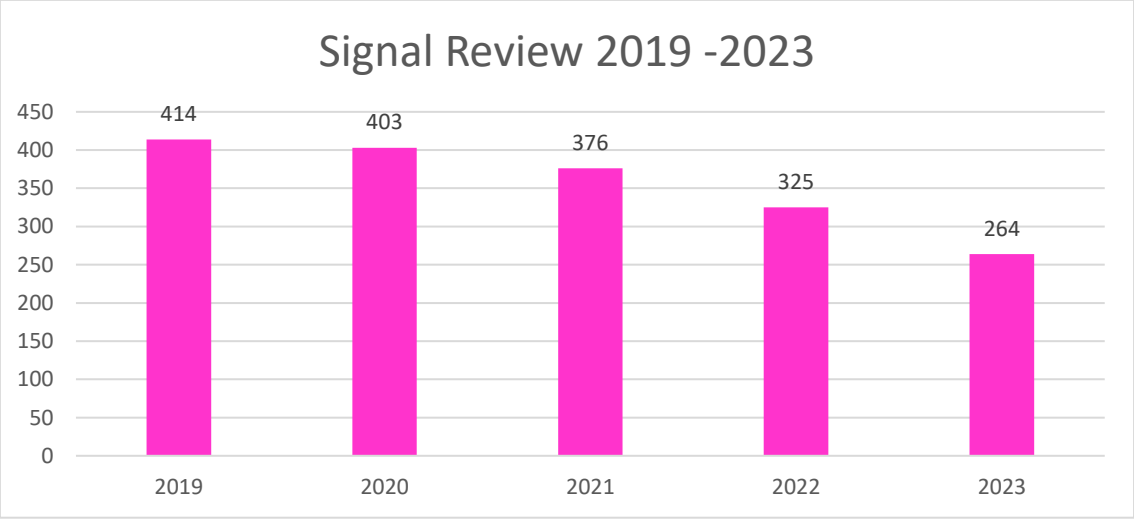
2421
2445
1862
2019
2020
2021
2022
2023


Signal Review 2019 -2023
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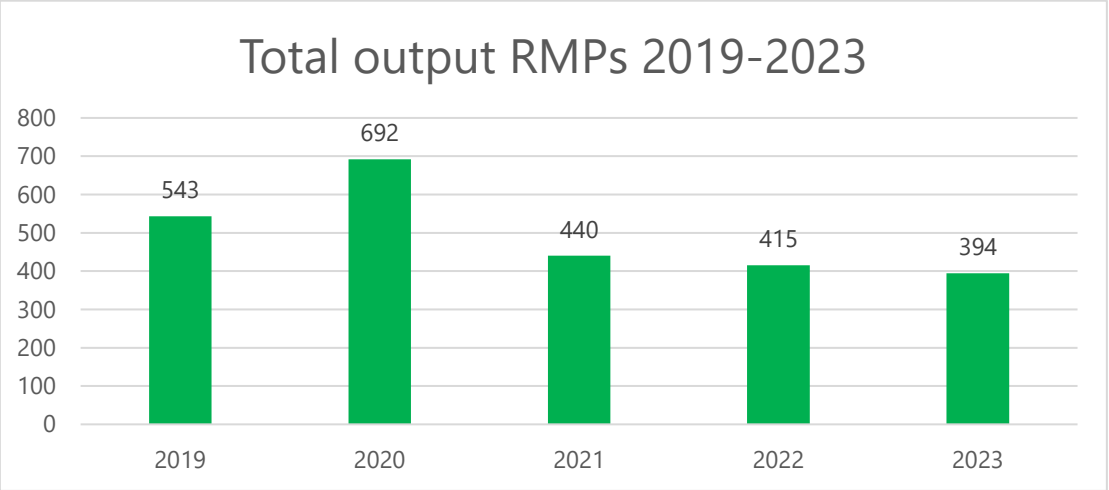
2019
2020
2021
2022
2023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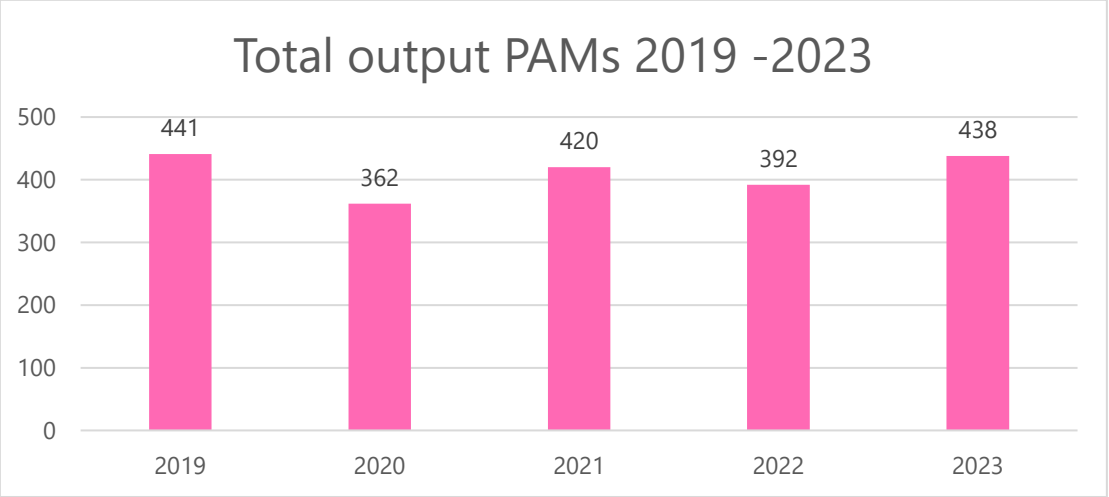
2020
2021
2022
2023


Total output PAMs 2019 -2023
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400
300
200
100
0
441
362
420
392
438
2019
2020
2021
2022
2023


Referrals 2019-2023
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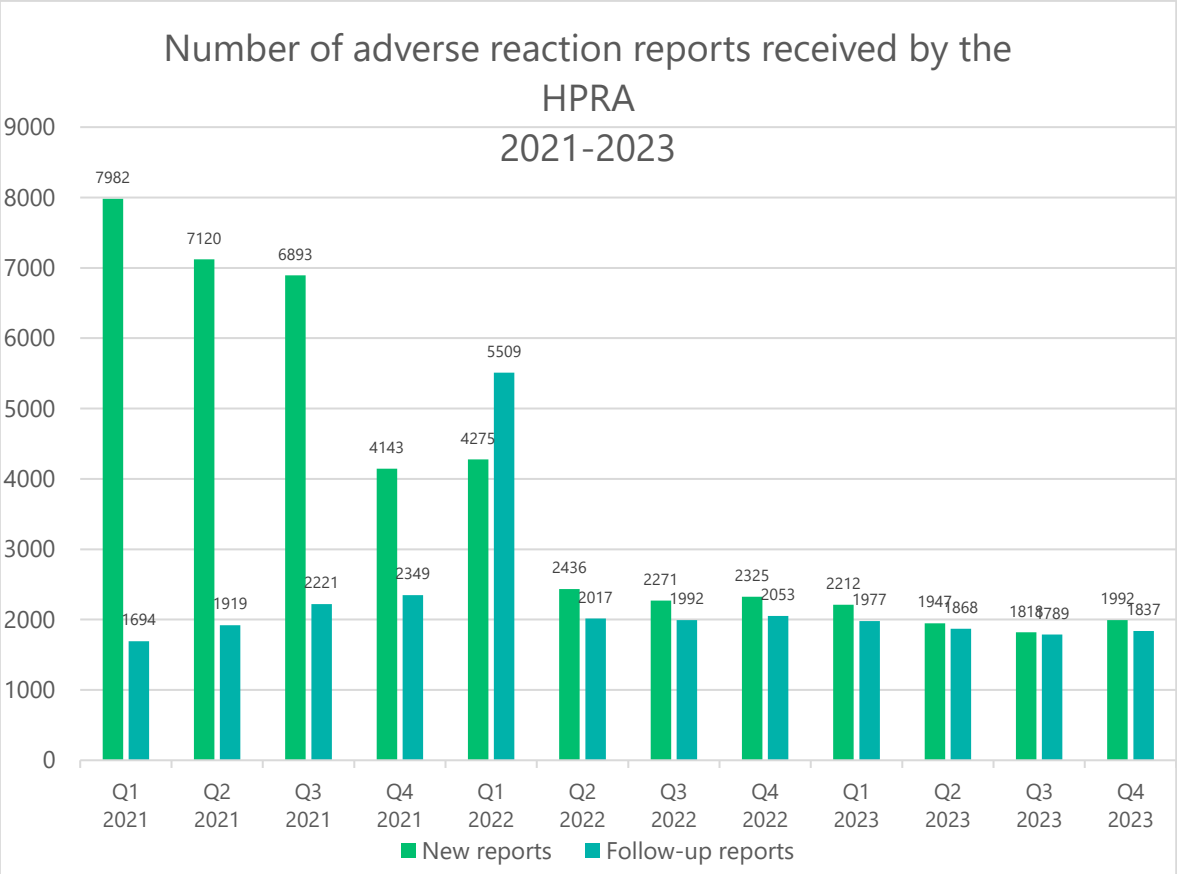
5
4
3
2
1
0
5
5
2
5
2
2019
2020
2021
2022
2023


Number of adverse reaction reports received by the HPRA
2021-2023
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
7982
1694
7120
1919
6893
2221
4143
2349
4275
5509
2436
2017
2271
1992
2325
2053
2212
1977
1947
1868
1818
1789
1992
1837
Q1 2021
Q2 2021
Q3 2021
Q4 2021
Q1 2022
Q2 2022
Q3 2022
Q4 2022
Q1 2023
Q2 2023
Q3 2023
Q4 2023
New reports
Follow-up reports

APPENDIX II SERVICE LEVELS – COMPLIANCE DEPARTMENT

Initiatives undertaken/further developed in 2023/2024 included:

- Preparations for the end of certain derogations arising from Brexit and preparing for the implementation of Regulation (EU) 2023/1182 arising from the Windsor Framework have included:
  - Continued engagement with stakeholders with the primary purpose of maintaining supplies of health products.
  - Continued meetings with companies to discuss their Brexit related plans and to clarify issues arising. Such meetings and liaison will continue to be an important focus.
  - Meetings with industry representative bodies, and attendance at workshops organised by some of those bodies, to consider and clarify Brexit related questions.
  - Advising potential applicants for authorisations and licences of the requirements and processing of a number of new applications.
  - Provision of support to the Department of Health and the Department of Agriculture, Food and the Marine (DAFM), including participation in regular meetings of the Brexit Operations Group and the Brexit Medicines Review Group, both convened by the Department of Health.
  - Liaison with other agencies, including the HSE and Revenue's Customs Service, on issues of mutual interest.
- Annual updates to registrations of manufacturers, importers and distributors of active substances and brokers of medicines for human use were processed during 2023 and 2024.
- Continued provision of support to the Irish Medicines Verification Organisation (IMVO) on the implementation of national legislation aimed at preventing the entry of falsified medicines into the legal supply chain – implementation of Directive 2011/62/EU (Falsified Medicines Directive).
- HPRA staff continued to participate in an expert group on safety features convened by the European Commission. A Commission Delegated Regulation, which sets out the requirements around safety features on the majority of prescription medicines for human use, was implemented by relevant MAHs and manufacturers on 9 February 2019. In relation to this, the HPRA has liaised closely with the IMVO to implement the systems. This has included the development of a national database (repository) for batches of human medicines bearing safety features that are placed on the Irish market and a system for authentication of packs at various points in the supply chain, principally at point of dispensing. The purpose is to guard against falsified medicines reaching patients.

  While the HPRA are not part of the governance structure of the IMVO, we continue to liaise closely with the organisation. The HPRA has an oversight role in relation to the repository and has taken the lead role of the EU working group on supervision of the repositories. We also participate in a National Oversight Group made up of key stakeholders and convened by the IMVO. Implementation of authentication was not straightforward and, accordingly, was approached in a 'use and learn' mode. Gradual transition to full implementation, as per the

Delegated Regulation, commenced during the first quarter of 2021 but was postponed due to the COVID-19 pandemic. The 'use and learn' phase officially concluded on the 30 May 2023.

- Continued upload of wholesale distribution authorisations and post-inspection good distribution practice (GDP) certificates to the EudraGMDP database.
- Continued upload of manufacturers and Importers authorisations) and post inspection good manufacturing practice (GMP) certificates to the EudraGMDP database.
- The NVR (2019/6) was implemented in January 2023. Work is ongoing with colleagues from the Veterinary Sciences department, the legal section and the DAFM to ensure smooth implementation of the new regulation.
- Provision of support to the Department of Health on the implementation of national legislation relating to the Children and Family Relationships Act, Human Tissue Bill and Health (Assisted Human Reproduction) Bill which overlaps with the human tissues and cells legislation for which HPRA are the designated competent authority.
- Continued support to the Department of Health on the implementation of national legislation regarding quality and safety of human organs intended for transplantation from Directive 2010/53/EC. This included monitoring of authorised procurement and transplant centres, via inspections and other follow up measures. The framework for quality and safety of organs for human transplantation, developed in conjunction with Organ Donation and Transplant Ireland (ODTI), is used in evaluating these centres.
- A system for reporting and assessment of serious adverse events/reactions relating to organs for human transplantation remains in place.
- Continued support to the Department of Health on the development and implementation of national legislation regarding controlled drugs. An upgraded system for processing of licence applications and collation of statistics became fully operational in Q1 2022 and has provided a much-improved service to stakeholders since then.
- Continued provision of support to the Department of Health in relation to the access programme for cannabis for medical use. The HPRA continue to receive and review applications for inclusion of products under the programme. A number of products have been recommended to the Department for inclusion under the programme. This work is ongoing.
- Monitoring, via inspections, of the implementation of GMP and GDP requirements, Good Clinical Practice (GCP) and Good Pharmacovigilance Practice (GvP) standards, and of the required controls relating to controlled drugs and precursor chemicals. A full return to on-site inspections has been made following the COVID-19 pandemic.
- Monitoring, via inspections, of the activities of MAH companies with respect to their obligations under the Medicinal Products (Control of Placing on the Market) Regulations, 2007 to 2019.
- Active participation in harmonisation of standards and inspection practices through European Medicines Agency (EMA) working groups and the Pharmaceutical Inspection Co-operation Scheme (PIC/S) Committee and its Expert Circle meetings.
- Active participation in the work of the Official Medicines Control Laboratories (OMCL) network to promote risk-based approaches to surveillance programmes and effective work-sharing programmes. The HPRA has continued to lead on an initiative within the Heads of Medicines Agencies (HMA) Group on developing the risk-based approach to the sampling and analysis of mutual recognition, decentralised and centralised medicines.

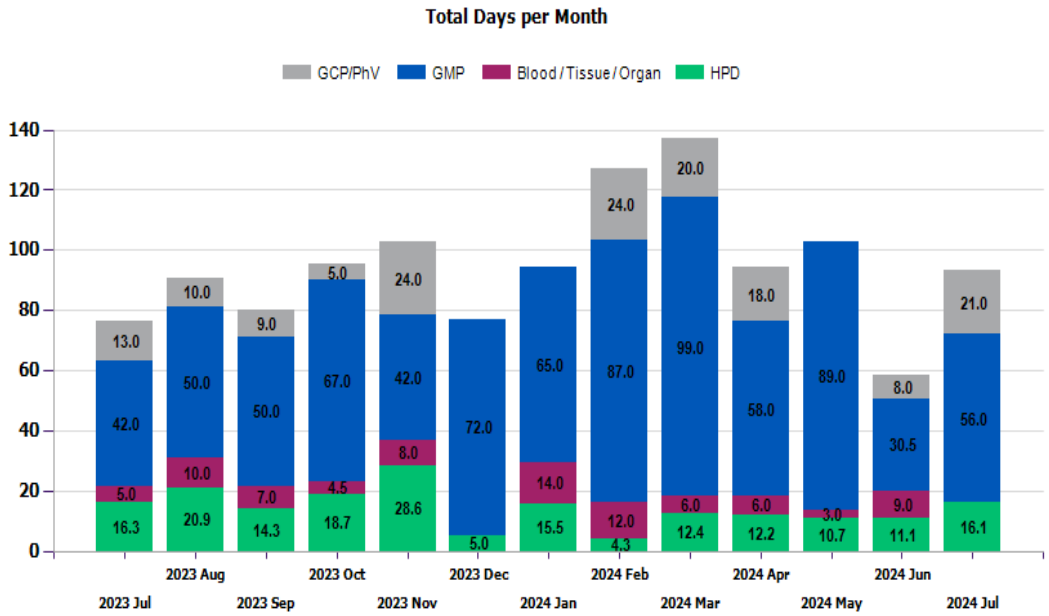
- The HPRA continues to participate in optimisation of the processes used by EEA medicines competent authorities for the management of quality defects, recalls and rapid alerts. This includes implementation of revised (more risk-based) versions of the relevant EEA procedures.
- Continued focus on the advertising compliance programme which includes regular liaison with industry to outline HPRA requirements and clarify our interpretation of the legislation.
- Further development of the monitoring of the availability of medicines in non-pharmacy retail outlets with appropriate follow up where unauthorised or pharmacy confined/prescription only medicines are identified and on-going public communication regarding the risks of purchasing prescription medicines on-line.
- Continued development of our role as competent authority for cosmetics. This includes maintenance of effective working relationships with the Department of Health, HSE and the Competition and Consumer Protection Commission, and the implementation of a coordinated national approach to market surveillance and testing of cosmetics.
- The National Cosmetics Safety Forum was continued by the HPRA and the HSE for the purpose of reviewing the safety of cosmetic products available within the Irish marketplace. The forum develops the market surveillance programme in line with risk-based principles and takes account of new legislative and technical progress.

Other activities included:

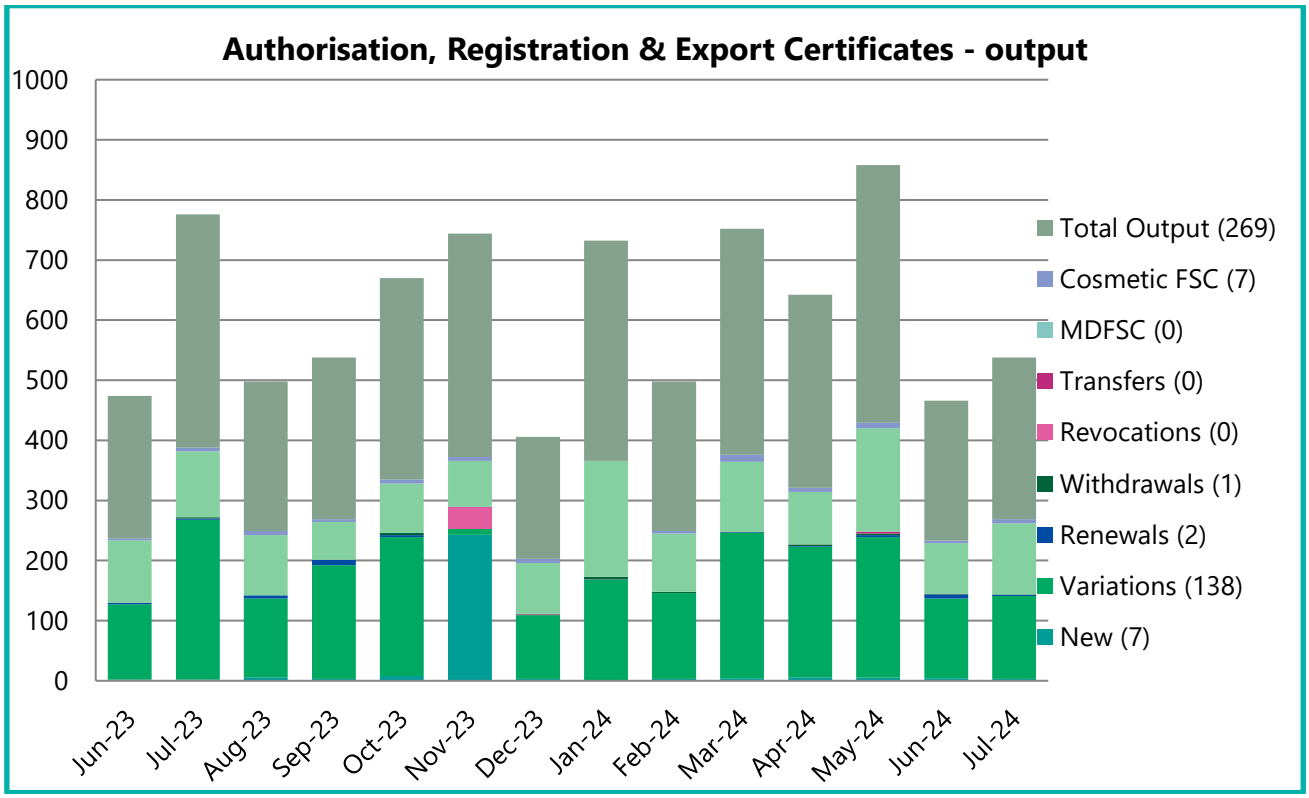
- Continued interaction and communication with stakeholders, including industry and other representative groups. These included meetings (virtual) with industry representative bodies and individual companies.
- Continued management of the controlled drugs licensing function on behalf of the Department of Health.
- Continued management and use of the exempt medicinal products importation/supply data that are notified to the HPRA by wholesalers sourcing exempt products. These data continue to serve as a source of relevant information for the quality defect and recalls programme.
- Processing of applications for variations to manufacturers and wholesalers authorisations, and for export certificates (medicines, medical devices and cosmetics) and controlled drugs licences.
- Further development of good clinical practice, bioequivalence and pharmacovigilance inspections.
- Full programme of good practice inspections of blood, tissue and organ establishments.
- Continued strong focus, through good distribution practice inspections and enforcement activities, on the legitimate supply chain to prevent infiltration of falsified products.
- Continued monitoring of the parallel trading of medicines by wholesalers based in Ireland, particularly relative to ensuring that the needs of Irish patients are met.
- Focus on illegal trade in anabolic steroids and associated products has continued.
- In co-operation with Revenue's Customs Service, ongoing detection and detention of illegal supply, including mail-order importations of prescription-only medicines.
- Co-operation with Revenue's Customs Service, An Garda Síochána, Sport Ireland, and the Food Safety Authority of Ireland (FSAI) to identify and disrupt medicinal products/food supplements supply among sport and leisure participants that are considered to present a risk to human health.

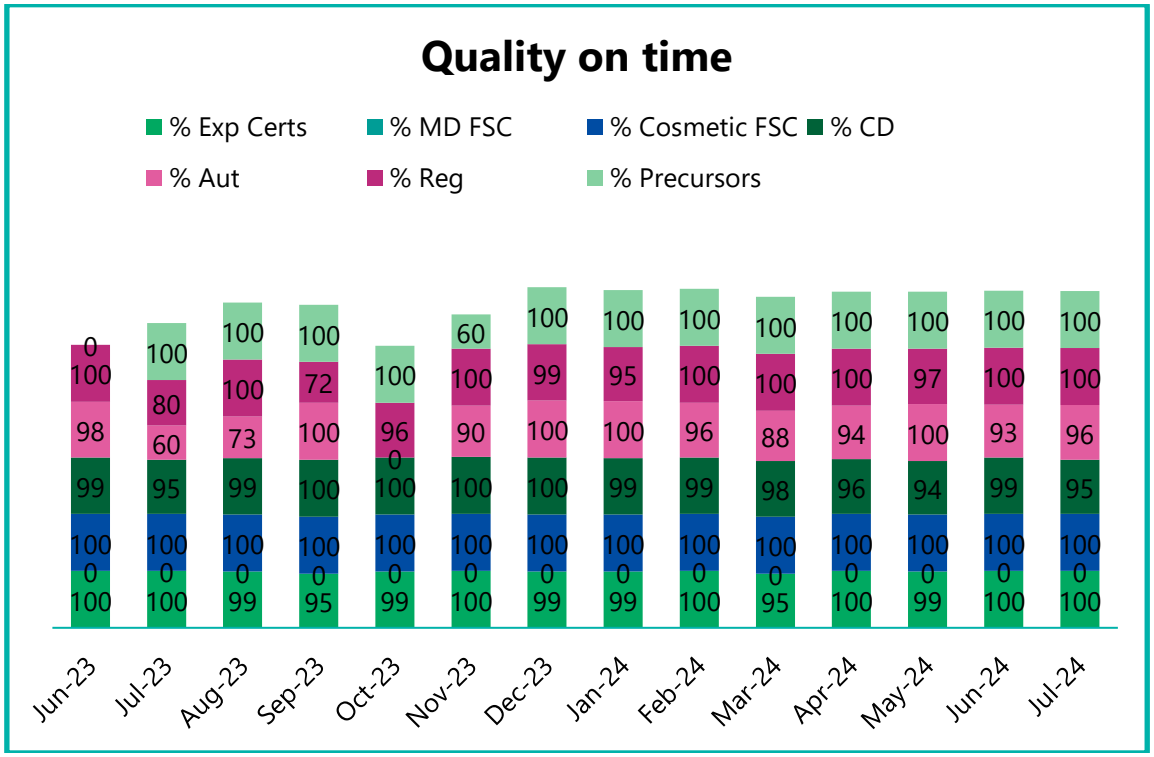
- Co-operation with An Garda Síochána and the Pharmaceutical Society of Ireland (PSI) to detect and stem the flow of unauthorised medicinal products and leakage of authorised medicinal products from the legitimate supply chain for illicit supply and use.
- Enhanced level of intelligence-led enforcement operations with An Garda Síochána, Revenue's Customs Service and enforcement agencies worldwide on Operation Pangea XIII, an Interpol-coordinated international operation against illegal supplies, including trafficking, of unauthorised prescription medicines and medical devices via online and social media activities.

The graph below shows the level of inspection activity for the period July 2023 to July 2024 inclusive. HPD refers to Health Product Distribution inspections which includes GDP and Controlled Drugs inspections.

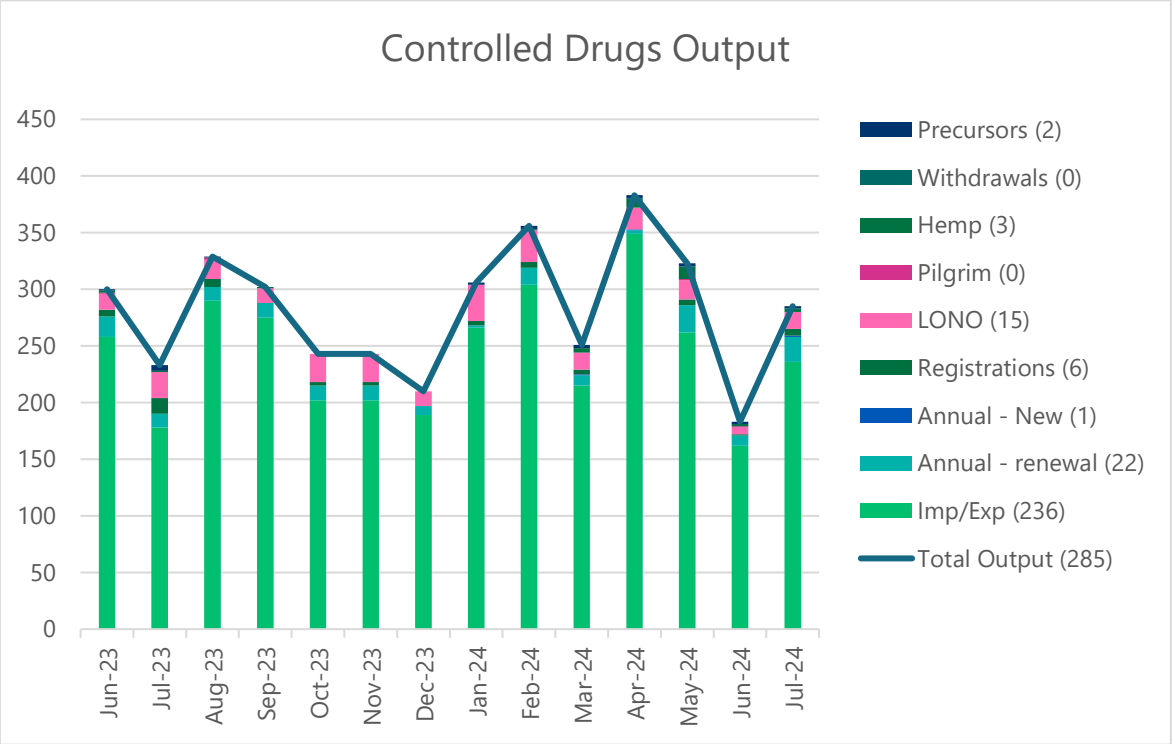


The following graphs show the numbers issued and the percentages issued on time, for export certificates, controlled drugs licences and GDP, GMP and IMP licences, over the period July 2023 to July 2024, inclusive.

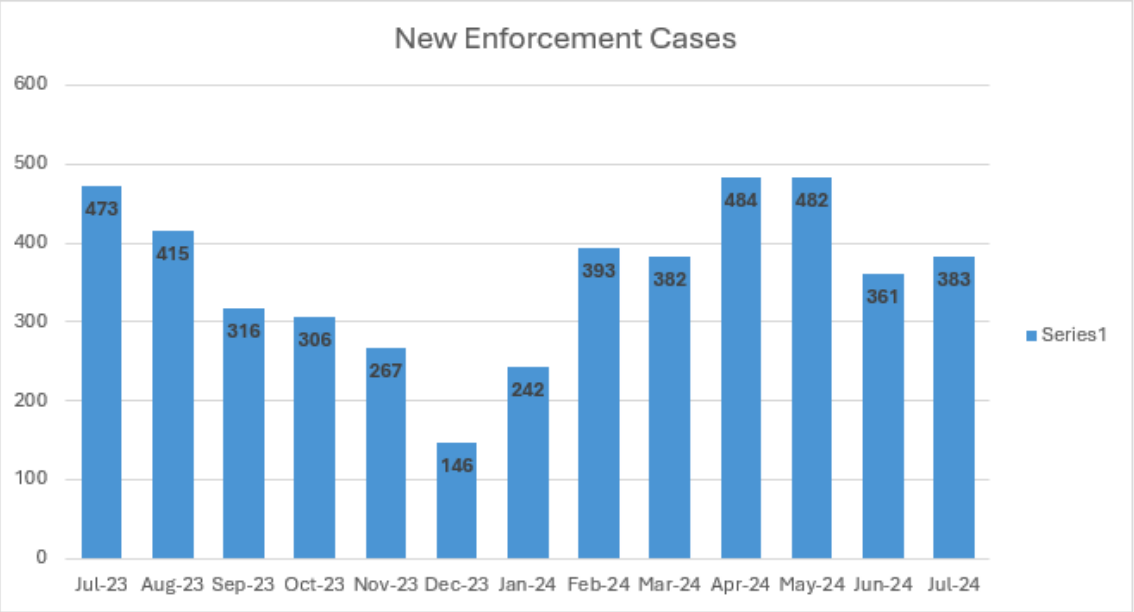



Quality on time
% Exp Certs
% MD FSC
% Cosmetic FSC
% CD
% Aut
% Reg
% Precursors
Jun-23
Jul-23
Aug-23
Sep-23
Oct-23
Nov-23
Dec-23
Jan-24
Feb-24
Mar-24
Apr-24
May-24
Jun-24
Jul-24

The graph below shows the output of licensing of controlled drugs, by category of licence.



The graph below shows the number of enforcement cases for the period July 2023 – July 2024 inclusive. The majority of these relate to attempts to illegally import prescription-only medicines, an amount of which are falsified. The remainder involve the supply by wholesale and retail sale of falsified medicines and prescription-only medicinal products which are authentic, but diverted from the legal supply chain.



Blood, tissues and cells

During 2023 and 2024 to date, a full inspection programme for blood establishments (i.e. involved in the collection, testing, processing, storage and distribution of blood) was carried out. Annual reports from all blood banks were received and reviewed during both years.

The HPRA continued its interaction with the National Haemovigilance Office (NHO) in relation to haemovigilance reporting requirements and updates.

The tissues and cells legislation requires all sites involved in the procurement, testing, processing, storage and distribution of tissues and cells to be authorised. A programme of inspections of tissue establishments has been carried out.

The HPRA continued to operate the tissues and cells vigilance system and participates at EU activities and training to support development of further harmonisation initiatives across the EU.

Human organs for transplantation

Directive 2010/53/EC was transposed into Irish legislation via Statutory Instrument No. 325 of 2012. Under this legislation, the HPRA is the competent authority responsible for the inspection and authorisation of organ procurement and transplant centres and for serious adverse event and reaction reporting. The HSE (via ODTI) also has competent authority functions in the areas of standards and traceability/registries.

The organs legislation applies to the donation, procurement, testing, characterisation, transport and transplantation of organs. A programme of inspections of procurement and transplant centres was carried out with follow up, as appropriate. The HPRA continued to liaise with the HSE lead and ODTI colleagues in relation to the vigilance system in place for reporting of suspected serious adverse reactions and events, in accordance with the legislative provisions in place.

Controlled drugs

The HPRA continues to be responsible for management of the application and issuing processes for all controlled drugs licences, with the Department of Health retaining a signatory role for all official documentation. In 2019, the HPRA took on responsibility for managing applications for products to be included within the Medical Cannabis Access Programme (MCAP), on behalf of the Minister of Health. The Minister retains the final decision to include a product within the MCAP and this requires the schedule to a statutory instrument to be amended. Inspections related to import, export and holding of controlled drugs and drug precursors continue.

Exempt medicinal products

Notifications of importation of exempt (unauthorised) medicines continued through 2023 and 2024, to date. The HPRA has an electronic system for notifications and continues to work closely with notifying companies to ensure data has been uploaded correctly. The notifications are an important source of information, mainly when checking on whether products recalled in other countries have been supplied as exempt medicines in Ireland.

APPENDIX III SERVICE LEVELS – MEDICAL DEVICES

As the national competent authority for medical devices, the HPRA is the authority responsible for notified bodies and the market surveillance authority for medical devices in Ireland. The HPRA carries out a range of classification, registration, surveillance, assessment and compliance activities. We also review clinical investigations, inspect manufacturing sites and authorised representative facilities, designate and oversee notified bodies, and investigate activities associated with non-compliant supply and manufacture of medical devices. 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.

Caseload volume continued in line with recent trends observed since the application of the MDR in 2021. There continues to be a focus on vigilance cases and field actions (recalls, device modifications, etc.) relating to devices on the Irish market. These cases are increasing in complexity and significance in terms of assessing the impact on public health. In addition, the HPRA has developed its activities relating to medical device market surveillance, notified body oversight and technical and clinical assessment. Another key area of focus during the past year has been our contribution to ongoing legislative and policy initiatives aimed at developing the regulatory framework as well as our involvement in supporting the Department of Health, the HSE and industry in managing the transition to the new medical device regulations. Further details on these issues are outlined below.

AUTHORISATION AND REGISTRATION

- The HPRA is focused on ensuring effective and consistent designation and oversight of notified bodies at national and European level. In 2022, we:
    - Concluded an application for designation under Regulation (EU) 2017/746 on *in vitro* diagnostic medical devices with the completion of the formal designation and notification steps of the process in early 2023.
    - Continued our schedule of oversight of the notified body in Ireland based on ongoing assessment, surveillance and observed audits. This included an on-site surveillance assessment in January 2023 and a further on-site assessment in November 2023.
    - Contributed as a national expert as part of the European Joint Assessment Team for notified body designation applications in other member states under the MDR and IVDR.
    - Continued to support the development of EU coordination of notified body designation and oversight through participation in the EU Notified Bodies Oversight group and the Medical Device Coordination Group (MDCG). Chaired by the EU Commission, the MDCG is responsible for the overall coordination and governance of the regulatory system.
    - Worked with the European Commission and the Competent Authorities for Medical Devices (CAMD) on initiatives to gather data on notified body capacity, certification and device availability associated with MDR and IVDR.

- Supporting innovation and research of new technologies is a key strategic priority for the HPRA medical devices team. In 2023, this support included:
  - The review of applications to conduct clinical investigations of medical devices in Ireland under the new medical device regulations. We continued to review clinical investigations for innovative devices from both multi-national and academic sponsors with 11 new applications,15 amendments to ongoing investigations and 7 post-marketing clinical investigations. The HPRA devices team also reviewed7 applications for performance studies for new IVD devices under the recently implemented IVD regulation were received and reviewed in 2023. It is anticipated that these numbers will increase 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 offer pre-submission meetings. Activity in this area increased again in 2023, with 12 groups of innovators engaging with the HPRA to discuss potential clinical investigation and performance study applications in 2023.
  - The provision of technical, clinical and regulatory support in respect of medical devices related queries received by of the HPRA Innovation Office.

  Manufacturers of certain medical devices and *in-vitro* diagnostics are required to register with the HPRA via the European medical device database (EUDAMED). In 2023, 263 economic operators were validated on EUDAMED by the HPRA. For those entities registering at national level only, the HPRA registered 114 medical device economic operators (for example, manufacturers and authorised representatives) on the national database.

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 2023:
  - 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 eight 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 and led on an initiative to develop common evaluation principles for market surveillance.
  - There were 317 market surveillance cases undertaken.

- We continued to focus our vigilance activities on the areas of user reporting and dissemination of HPRA medical device safety communications. In 2023, this included:
  - The receipt and assessment of 3,065 medical device vigilance cases. Of the reports received, manufacturers accounted for 80%, 5% were from users and 13% came from other competent authorities. Of the 2,205 incident reports notified directly to the HPRA, 7% came from users of medical devices.
  - There were 391 field safety corrective actions (FSCA) associated with the national market.

- We issued 114 national competent authority reports to other European authorities.
- We also issued one safety notice in relation to a medical device and 25 direct to healthcare professional communications.
- Infusion devices, implants, surgical devices, vital signs monitoring, and in vitro diagnostic medical devices together accounted for 70% of the total vigilance reports received (see accompanying table).

Product types (Top 5)	Number of reports
INFU - Infusion devices	763
IMPL - Implants	418
SURG - Surgical devices	379
VSM - Vital signs monitoring	297
In-vitro diagnostic medical devices	290

- The HPRA adopted the role of co-chair of the European Working Group on Post-market Surveillance and Vigilance, a subgroup of the Medical Devices Coordination Group.
- 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 2023, 18 such inspections were performed all of which were based on proactive market surveillance projects and notified body surveillance/assessment.

During 2023 we also continued development work on signal detection of medical device issues.

LEGISLATION AND REGULATION

- Our work during 2023 focused on progressing implementation and application of EU Device Regulations for both medical devices and *in vitro* diagnostic medical devices at a national and European level particularly with regard to gathering data on the challenges with implementation. This included:
  - Working with the Department of Health on escalating mechanisms, identifying and proposing solutions for the lack of regulatory system readiness.
  - Supporting the Department of Health in preparing for EPSCO interventions calling out the need for focused solutions to the lack of system readiness and the need for a targeted discussion on the root causes of the longer-term challenges.

  - Engagement with key stakeholders in the sector to ensure awareness of the impact of the regulations. This includes the provision of information and the development of guidance and specific information sessions/webinars on MDR and IVDR implementation.
  - Participating and providing input into the EU4Health initiatives on governance and innovation and medical device availability as part of our role as MDCG members.
  - Participating in the EU Working Groups tasked with developing guidance for specific functional areas including orphan medical devices.

- 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 2023, this included:
  - Continued participation in the Executive Group of the CAMD network.
  - Participation in MDCG discussions on improving the coordination and consistency of the implementation of the new EU Regulations and prioritising implementation activities in the short, medium and long term, including priority areas such as governance and coordination, safety and access to critical devices.
  - Continuing to take a lead role in a number of taskforces of the MDCG working groups to help identify solutions to key practical challenges with implementation.

- Throughout 2023, our focus remained on identifying and promoting discussions and developing practical measures to ensure the regulatory system operates effectively in practice. We were also engaged in ensuring that medium- and long-term issues are prioritised and discussed within the EU network to work towards a sustainable effective implementation of the regulations.
- In 2023, the HPRA chaired a number of meetings of the medical devices core group of the HMA. The focus of the core group was to prioritise the capacity challenges for Notified Bodies in the EU network and to work together on identifying solutions to these challenges.
- 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)
  - 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

Our work to encourage the direct reporting of incidents and medical devices issues by device users and members of the public continued throughout 2023. 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.

- The HPRA undertook a number of communication initiatives to raise awareness of the impact and requirements arising from the new EU Device Regulations. During 2023, we:
  - Hosted a webinar for custom made device manufacturers on MDR requirements.
  - Updated the HPRA website and social media channels to provide information and guidance regarding the new EU Regulations.
  - Delivered briefings, advice and workshops on the new regulations to a range of different stakeholders including the HSE, industry and clinical associations.
- Throughout 2023, 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, workshops and talks to a range of external stakeholders.
- The HPRA are contributing to a Horizon 2020 funded project (Co-ordination of Research and Evaluation of Medical Devices) CORE-MD. The project runs from 2021-2024 and the HPRA is leading a work package and is also part of the project board. A number of project deliverables were presented and published in 2023.
- In 2023, a new EU4Health Joint Action on Market Surveillance 2.0 was launched with the HPRA participating in three of the technical work packages on market surveillance.

Case workloads

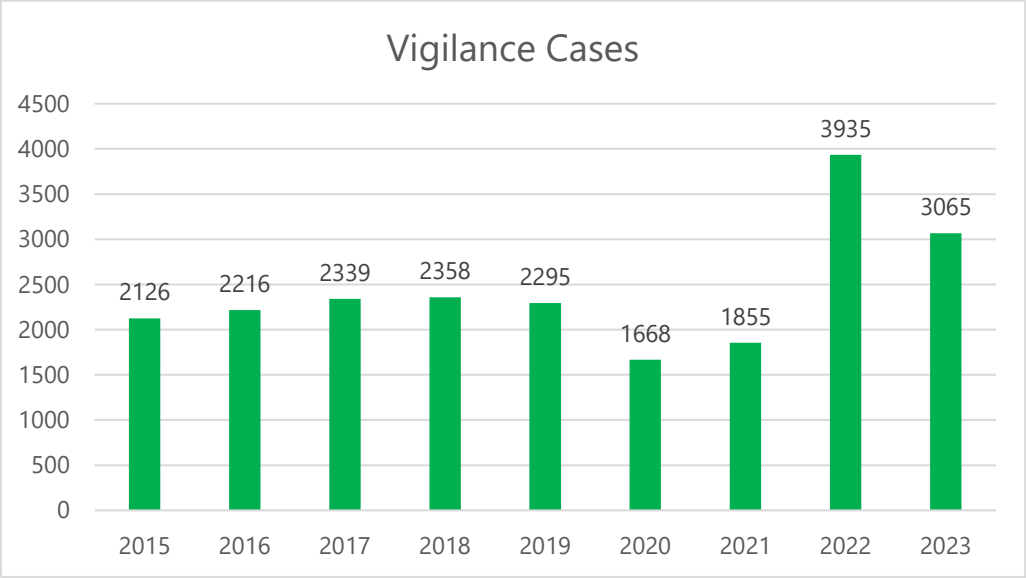
Vigilance and Compliance

There has been ongoing work with the HSE in various National Incident Management Teams during 2019- 2023 and case work continues to lead to the identification of significant issues that require increased monitoring and oversight by HPRA.

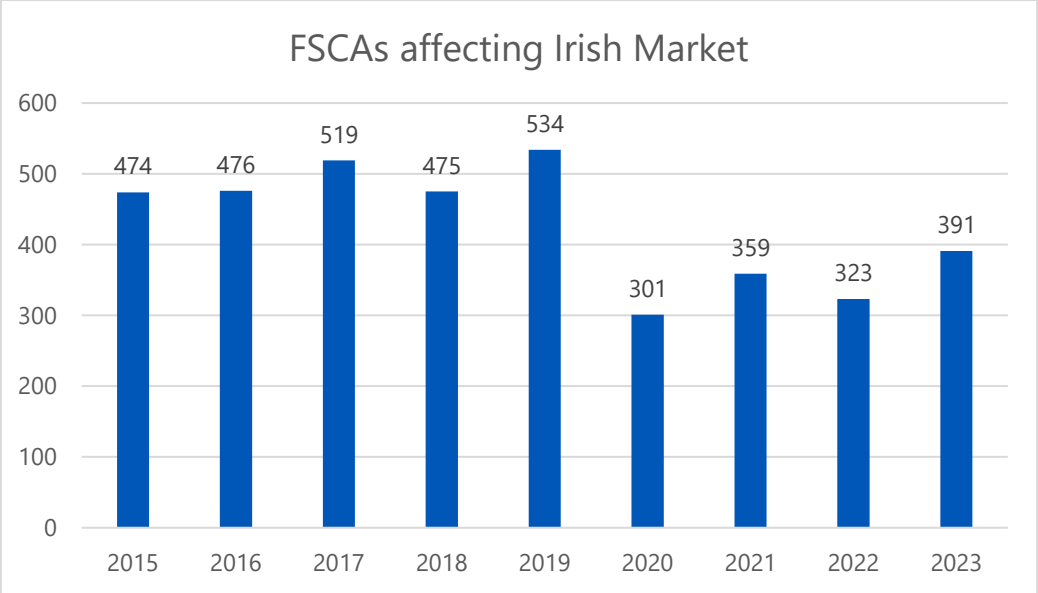
Our vigilance workload continues at consistent levels. In 2023, 3065 vigilance cases were opened and reviewed. Also in this period, among other communications, 114 NCAR's were issued nationally, across Europe and internationally. The HPRA continues to be very active at a European level in the area of vigilance.

Work has continued to enhance the vigilance function through the introduction of a signal detection and trend analysis system on medical device vigilance data. The aim of this system is to analyse the data on all vigilance reports received to identify trends, patterns or signals relating to medical devices at an earlier stage and to further enhance the contribution of the vigilance function to the overall regulatory system for medical devices.

See charts showing activity levels below.



Graph 1: Number of vigilance reports received (2015 to 2023)



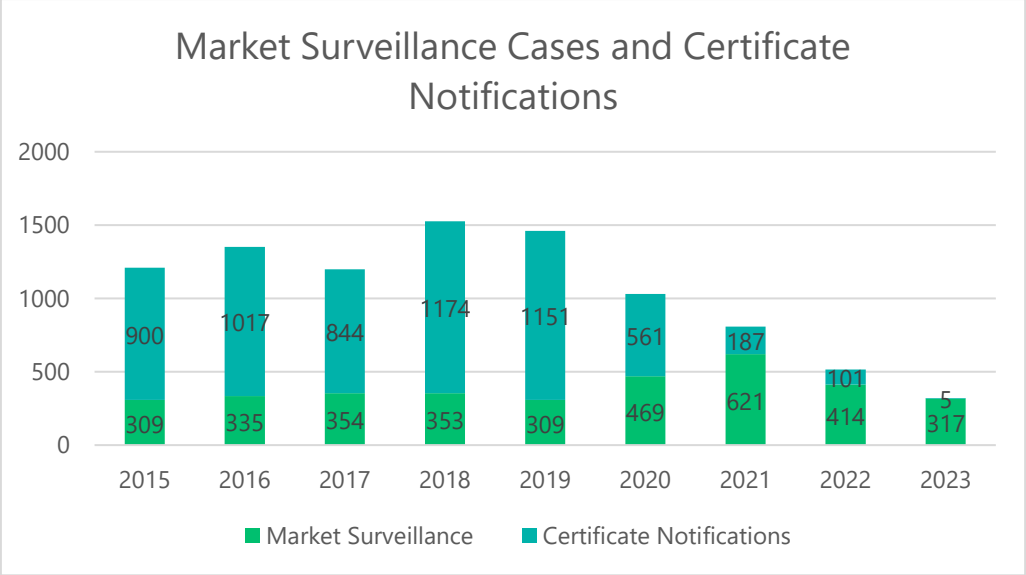
Graph 2: Number of field actions affecting the Irish market (2015 to 2023)

Designation and monitoring of notified bodies

Surveillance cases

During 2023, the HPRA continued to develop its lifecycle approach to market surveillance and investigated 317 market surveillance cases and received five* certificate notifications from notified bodies.

*In 2023, a new process was piloted to focus HPRA review on certificate notifications from the Irish notified body resulting in a decrease in the volume of notification cases.



Graph 3: Number of market surveillance cases and certificate notifications (2015 to 2023)

The HPRA has increased its level of proactive market surveillance activities to check conformance of marketed medical devices with the essential requirements defined in the legislation to help ensure performance and safety and to protect public health. In addition to documentation and labelling checks, this has also included an increased emphasis on sampling and analysis of products from the marketplace and detailed reviews of technical and clinical documentation. These proactive activities include assessment of specific devices, groups of devices or issues identified through the review of scientific data and literature.

The HPRA intends to continue to increase its level of proactive market surveillance activity for medical devices to help ensure that all medical devices placed on the Irish and European market are safe and meet the requirements of the legislation and to help prepare and provide guidance on new legislative requirements arising from the new EU Regulations.

As part of its market surveillance activities, the HPRA undertakes proactive and 'for-cause' audits of manufacturers, notified bodies and authorised representatives with the objective of monitoring compliance of devices emanating from Irish based organisations. During 2023, inspections 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.

Clinical evaluation review

The HPRA has increased its activities further in the assessment of clinical data presented by manufacturers to support the safety and performance of their device. The work was undertaken both reactively in response to a number of specific device issues and proactively as part of our ongoing market surveillance activities. This work also formed a significant part of our notified body designation and oversight activities both at national and European levels as part of EU joint assessment activities.

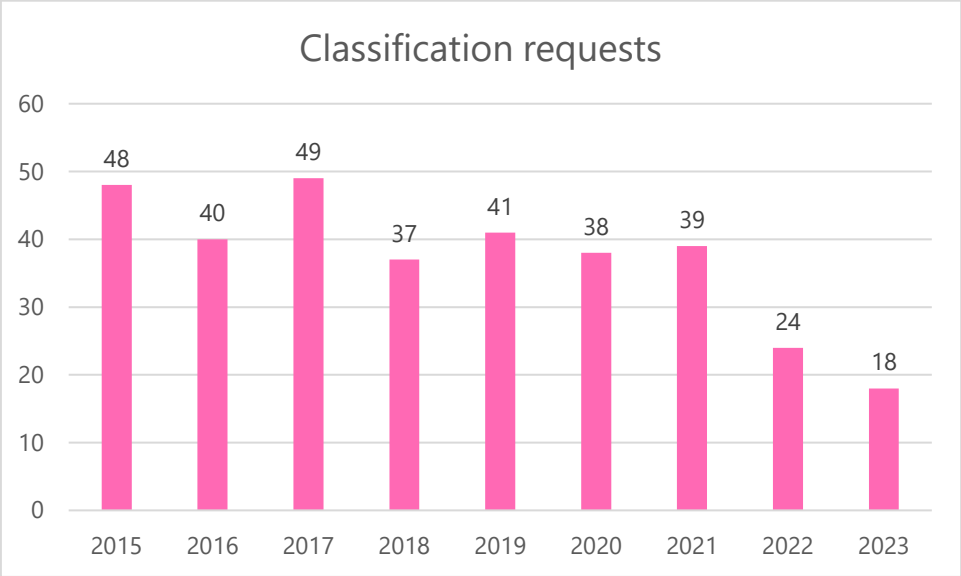
Economic Operator Registrations

In 2023, 114 medical device economic operators have registered with the HPRA. 263 economic operators have been validated on Eudamed. With EUDAMED development progressing, product registrations under the MDR and IVDR are expected to progress once EUDAMED becomes mandatory.

Classification requests

The HPRA received 18 applications for classification of medical devices or products queried as medical devices in 2023. This included many complex queries relating to borderline or combination products. The queries emanated from other medical device competent authorities in Europe, from medical device manufacturers, distributors and legal firms.

On foot of a number of these enquiries and as a result of HPRA investigations, a number of products were given a higher device classification.



Graph 4: Classification requests (2015 to 2023)

Clinical investigation applications

In 2023, the HPRA received 11 applications for clinical investigations, 15 amendments to clinical investigations of medical devices to be conducted in Ireland and 2 post-marketing clinical investigations. In addition, 27 compassionate use procedures were completed in this period.

Queries

During 2023, the HPAR medical devices team received 804 queries relating to medical devices.

Certificates of free sale

During 2023, the HPRA issued 5507 certificates of free sale compared with 5361 in 2022.