

**Public Consultation on  
Annual Review and Proposal for Fees –  
Financial Year 2022**

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

---



## CONTENTS

1	INTRODUCTION	3
2	THE OPERATING ENVIRONMENT	3
3	STRATEGIC DIRECTION OF THE HPRA	4
4	PROPOSED CHANGES FOR 2022	6
5	PROPOSED FEES	8
6	DETAILED CHANGES TO FEES	8
7	CONSULTATION	9
APPENDIX I	SERVICE LEVELS - HUMAN PRODUCTS AUTHORISATION, REGISTRATION AND SAFETY MONITORING	10
APPENDIX II	SERVICE LEVELS – COMPLIANCE DEPARTMENT	18
APPENDIX III	SERVICE LEVELS – MEDICAL DEVICES	28

## 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<sup>1</sup> of the HPRA. Since 2004, the HPRA has implemented a policy of annual fee reviews following consultation with industry.

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 2022.

## 2 THE OPERATING ENVIRONMENT

2021 has been a challenging year for both the HPRA and the industry. As with all companies, the COVID-19 pandemic continues to require the HPRA to work in a different way. As a health agency with responsibility for medicines and medical devices, 2021 has been particularly challenging with the authorisation and the roll out of the COVID-19 vaccines. The HPRA has provided a wide variety of support to the Government and Health Services across a range of activities. In addition, there was a unique challenge in managing the post authorisation supervision of the vaccines following the very successful and largest vaccine campaign in the history of the State. In relation to Brexit, while Ireland benefited from Commission regulatory exemptions, the start of 2021 brought a new set of challenges as companies' negotiated issues in relation to supplying the Irish market following the actual departure of the UK from the EU. The HPRA dedicated resources to Brexit and continued in 2021 the work with stakeholders to minimise the impact of Brexit and to ensure continued supply of medicines to the Irish Market. With the exception of inspection activity and related income, regulatory activity has continued at expected levels during the COVID-19 crisis.

In 2021 overall income is expected to be less than the previous year and costs are expected to increase. Payroll reflects an increase in staff numbers due to managing COVID-19,

---

<sup>1</sup> 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.

therapeutics and vaccines, the Clinical Trial regulation (CTR), implementation of the Medical Devices regulations (MDR, IVDR), pensions and the reversal of Haddington road / cost of living increases. Other costs however have remained at previous levels or at below normal levels due to working from home. General inflation remains low although the COVID-19 crisis has caused uncertainty in relation to costs and income and there is expectation that fuel costs will increase in 2022 with a knock-on impact for other costs.

Due to increased complexity of regulation and enhanced regulatory and public health offerings, staff numbers continue to increase. As noted above, the biggest impact on activities in 2021 was COVID-19 and work on implementing the new regulations.

As noted previously, since 2019, the HPRA makes an employer contribution in respect of staff employed since 2013, under the single service scheme. This contribution is up to 17% of the payroll cost of those employees. By its nature, it 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 we have flagged in previous fee consultations the long-term impact of an unfunded pension scheme. 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. An unfortunate result of this is increased costs and resources dedicated 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, and availability and access to innovative therapies. Compliance activity in relation to third country manufacture is also increasing (although challenging as a result of COVID-19). The HPRA expects staff levels to increase in 2022.

### 3 STRATEGIC DIRECTION OF THE HPRA

During 2020-2021, the HPRA has developed a new strategic plan for the period 2021 - 2025. Following extensive consultations, 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 & 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)

The key projects for 2022 will include:

- Managing the continued impact of COVID-19 as vaccines and therapeutics are authorised/rolled out.
- Maintaining the post-authorisation systems in response to any COVID-19 vaccines
- The further development of the innovation office and support for early innovation on a global basis
- Implementation of the IT strategy to ensure longevity and resilience in the system. Including facilitating new ways of working resulting from the COVID-19 pandemic
- Managing the return to office based work.
- European and international projects in pharmacovigilance, crisis management and GMP
- Increasing our regulatory offering both centrally and in the decentralised system
- Implementation of the Clinical Trials Directive
- Implementation of the Medical Devices and IVD regulations

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

## 4 PROPOSED CHANGES FOR 2022

### *Operating environment for 2021*

The HPRA is operating in a challenging environment, particularly in light of COVID-19, Brexit and the Medical Device Regulation (MDR) / In vitro Diagnostic Medical Devices Regulation (IVDR). As outlined above, we are committed proactively to supporting public health in relation to COVID-19, to support the industry and to manage its regulatory obligations in Europe following the outcome of the EU-UK Brexit negotiations.

### *New legislation*

2022 is unique in that the HPRA will be implementing 3 new regulations, veterinary (NVR), clinical trials (CTR) (subject to a separate fee consultation) and the medical device *in-vitro* diagnostics regulation (IVDR). The Medical Device Regulation, which commenced in May 2021, will also still be in the process of being fully implemented in 2022. The IVDR due to be implemented in May 2022 will make a profound change to the regulatory system for the area of *in-vitro* diagnostics and significant work will be necessary in this area at national and international level. These 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, repurposing and development of our staff.

Implementation of new legislation does not just impact the departments concerned, their 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 implications for 2022*

With income being maintained and costs being below normal in 2021, HPRA have absorbed increases in payroll costs that have occurred in 2021. However in 2022, it is expected that costs will increase significantly as it is planned that staff will return to work on a hybrid basis from 1 January. Implementing the hybrid model will itself bring additional costs to both IT and facilities.

### *Payroll*

Payroll will increase in 2022 due to:

- The impact of the new pay deal (Building Momentum) will result in pay awards of approximately 1%
- HPRA receives no funding for pensioners under the local government superannuation scheme (LGSS). Previously as a 'young' agency, this did not affect the HPRA significantly, but we have seen significant increases in pension costs in the last two years and it now accounts for 4% of payroll.

- COVID-19: Increased staff numbers brought on board 2021 will be kept on in 2022 as even though it is hoped that the pandemic will become an epidemic, it is still a novel disease and it is expected that there will still be considerable activity in 2022. From a regulatory perspective, in 2022 more therapeutics are expected and the issue of boosters/new vaccines and updated vaccines will also form part of the regulatory landscape.
- Implementation of new legislation; CTR, NVR, MDR and IVDR
- New projects under the new strategy.

#### *Other Costs*

While other costs have been below average during the lock down, this will change on 1 January 2022 with the planned return to the office. While inflation has been low, the current energy crisis has the potential to significantly increase costs in 2022 and the impact on the economy from the last 24 months pandemic response is uncertain but is likely to result in increased costs.

The HPRA expects that 2022 will be very challenging for the reasons outlined above however, in recognition of the income and cost levels of 2020 and 2021 which allowed the organisation generate a surplus, we propose a general fee freeze for 2022. This freeze will be subject to some amendments arising from submissions or changing circumstances in the preceding 12 months.

#### **General fee proposal**

- No general fee increase

#### **Compliance Fees**

- New fee for expedited variations to Annex 3 & 4 for Human MIA's.
- Removing the inspection booking fee and introducing an inspection cancellation fee
- New fee for processing and approving/rejection of non-routine import and export notifications for blood & tissue establishments and organ authorisations.
- Reduction of the number of products covered by the classification request fee for wholesalers from 20 products to 10.

#### **Medical Device Fees**

- Application of the current fees to the notification of clinical investigations detailed under Article 82 of the MDR.
- Reduction and alignment of the notification fees.

### **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 2021. The nature of regulatory income is that it is dictated by industry activity, which can change significantly over a period of time. In addition, the uncertainty from COVID-19 means that forecasting is extremely difficult and subject to change.

As with previous years, the HPRA commits to review the proposed fees during the planning cycle in 2022 and further amend the fees and fee structure, if required, for 2023.

## **5 PROPOSED FEES**

As outlined above there will be a freeze on fees for the year 2022.

## **6 DETAILED CHANGES TO FEES**

### **6.1 General change to fees**

It is proposed that there will be a freeze on fees for the year 2022.

### **6.2 Other Proposed adjustments to fees – Compliance activities**

#### **6.2.1 Expedited variations to Annex 3 & 4 – Human & Vet MIA's**

It is proposed to charge the current fast track variation fee (€1,225) to expedited assessments of Human & Veterinary MIA variations for Annex 3 & 4.

Where the same expedited variation applies to two or more authorisations, the second and subsequent applications will be charged at the admin variation fee (€310 -fee code 315).

#### **6.2.2 Inspections – Cancellation/rescheduling fee**

It is proposed to remove the inspection booking fee (€1,000) and introduce a cancellation/reschedule fee. The cancellation/rescheduling fee (€500) will apply to companies who give less than 3 weeks cancellation/rescheduling notice.

#### **6.2.3 Non-routine Import and Export Notifications (BTO)**

It is proposed to introduce a new fee for processing and approving/rejecting import and export notifications. The administrative fee of €310 will apply to these notifications.

#### **6.2.4 Classification request for wholesalers – up to 20 products - €335**

It is proposed to reduce the number of products that is covered by this fee from 20 products to 10.

### **6.3 Other Proposed adjustments to fees – Medical Devices**

#### **6.3.1 Clinical Investigations and Performance Studies**

It is proposed to apply the current notification fee to notifications of clinical investigations detailed under Article 82 of the MDR.

It is also proposed to align the notification fees (codes 450, 455 and 448) and reduce the fee to reflect the current manner in which these activities are being processed.

Clinical Investigations and IVDR Performance Studies	Current fee	Proposed fee
Active implantable medical devices clinical investigations	4,300	4,300
Class III and Class IIb medical devices, including relevant MDR Annex XVI clinical investigations	4,300	4,300
Class IIa and Class I medical devices, including relevant MDR Annex XVI clinical investigations	1,900	1,900
Notifications associated with MDR article 74(1) & Article 82 and IVDR Article 58(2)	310	200
Application for authorisation of In vitro diagnostic medical device (IVD) performance study under IVDR Article 58(1) (first submission)	2,500	2,500
Notification of Performance study involving Companion Diagnostic IVD using left over samples (IVDR Article 58(2))	265	200
PMPF study under IVDR Article 70	2,500	2,500
Substantial modifications and technical amendment to a previously approved clinical investigation / performance study	1,240	1,240
Non Substantial amendment to a previously approved clinical investigation/performance study	225	200
Resubmission of a clinical investigation/performance study following a withdrawal or objection or if the application has lapsed	1,900	1,900
Resubmission of a clinical investigation/performance study – Academic Sponsor	510	510

## 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 29 October 2021. Contributions should be sent by email to [feesconsultation@hpra.ie](mailto: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:

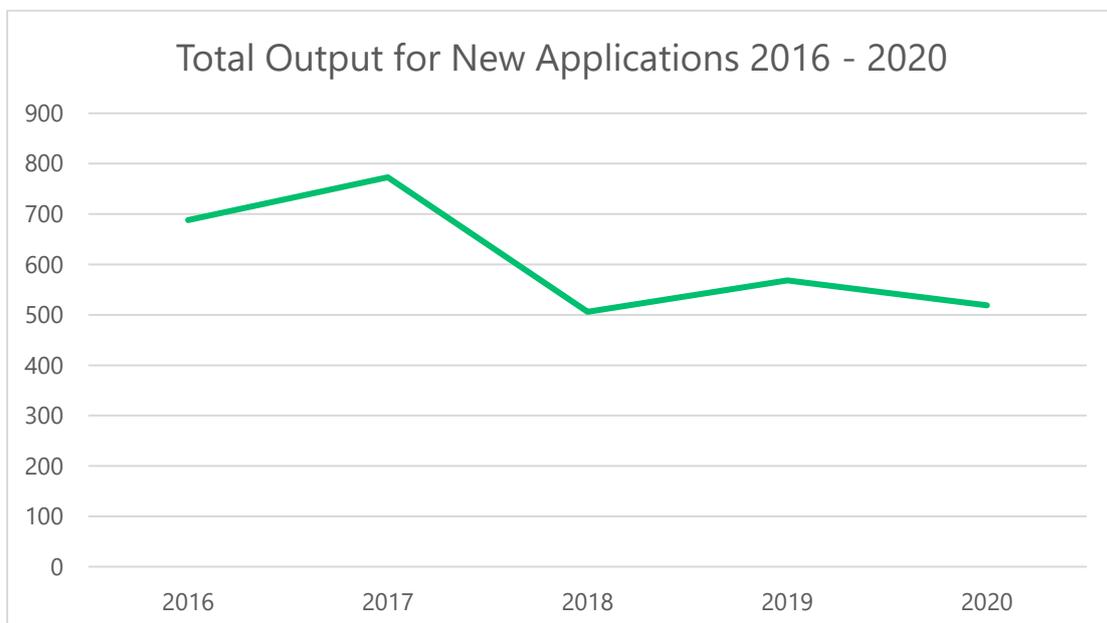
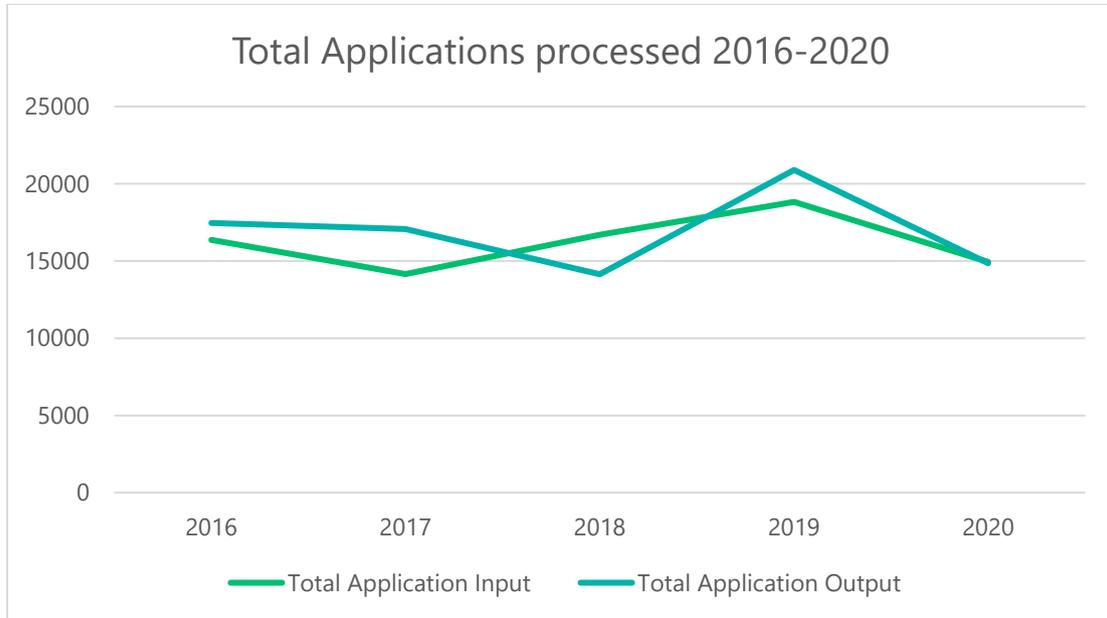
- Readiness to operate as Reference Member State for MR/DCP procedures for both new procedures and those transferring as a result of Brexit related activity.
- A national scientific advice procedure was introduced in 2016. This is to assist applicants in the development of new or existing human medicinal 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.
- Introduction of online reporting for adverse reaction and quality defects, accessible to patients, health care professionals and industry.
- Significant system upgrade to the adverse reactions database needed to meet the revised electronic reporting requirements standard (E2B R3 revision).
- Substantial increase in complexities associated with reporting of adverse reactions through the EudraVigilance system following the introduction of the centralised reporting requirements in November 2017 impacting on workload and interactions to support case processing and data quality.
- Continued customer-focused approach.

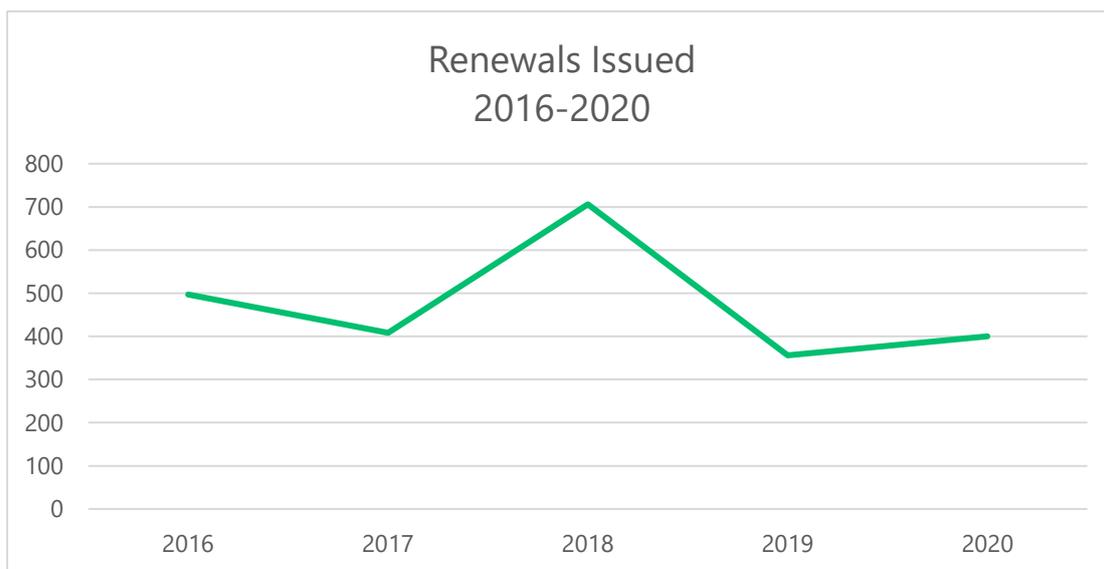
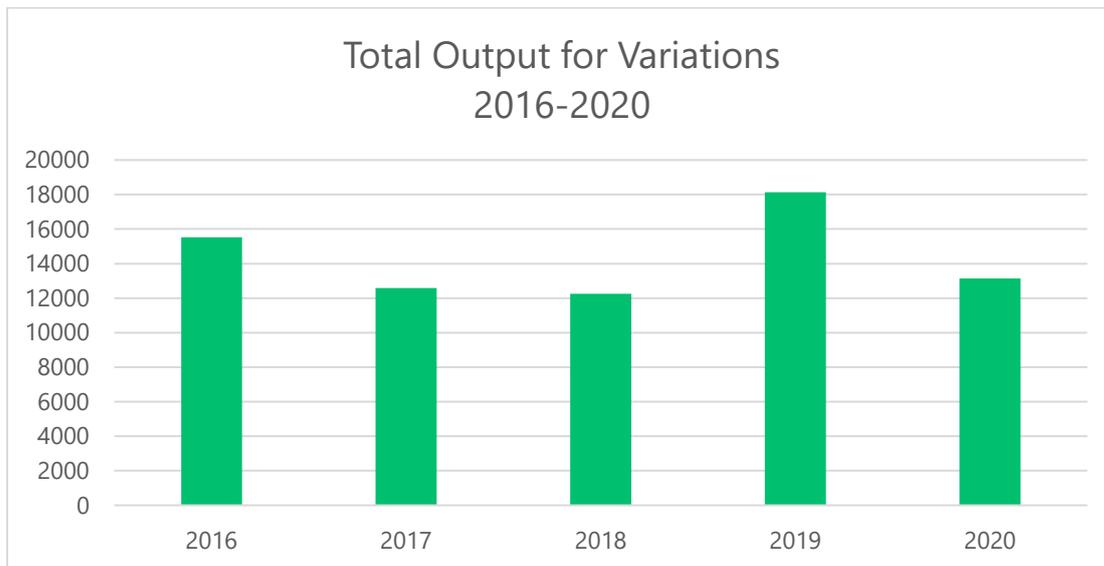
The work on the development of interchangeable medicines to support generic substitution by pharmacists in line with the Health (Pricing and Supply of Medical Goods) Act 2013, has progressed well. Of the 71 priority substances identified by the Minister for Health or the HSE for inclusion, 70 are now incorporated into the list. The remaining one is being assessed. The development of the interchangeable list will continue as a routine component of our assessment work, whereby industry can proactively make applications to have their product

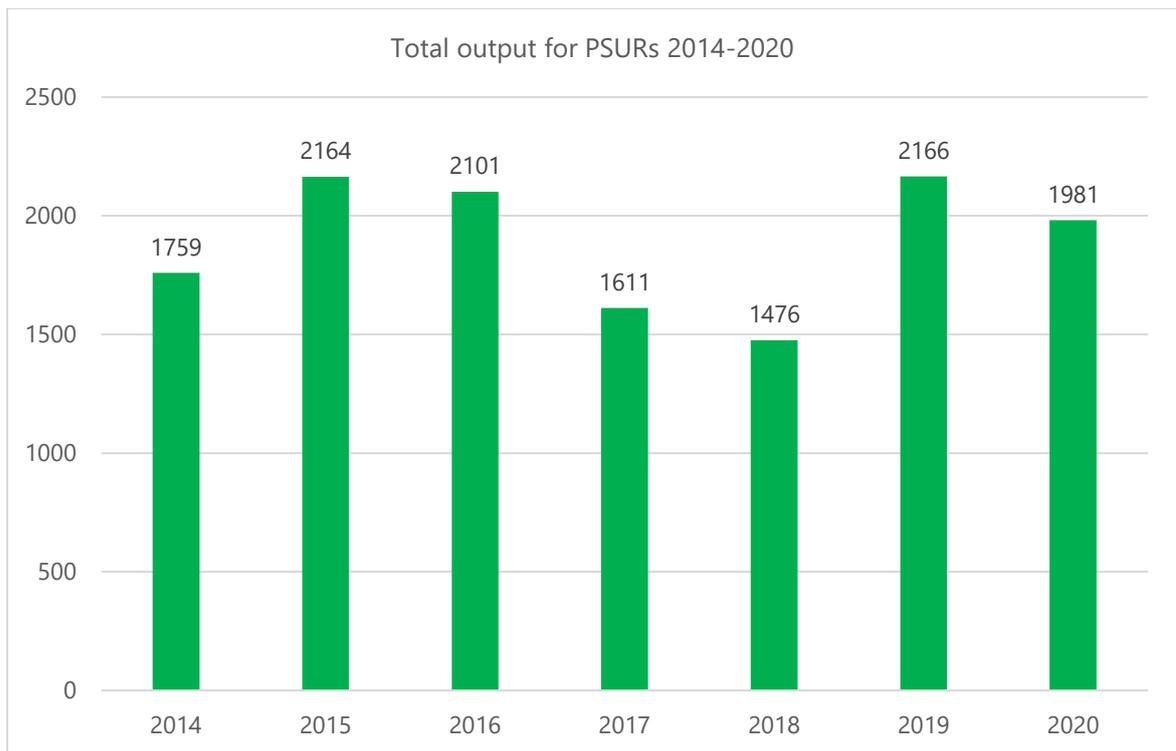
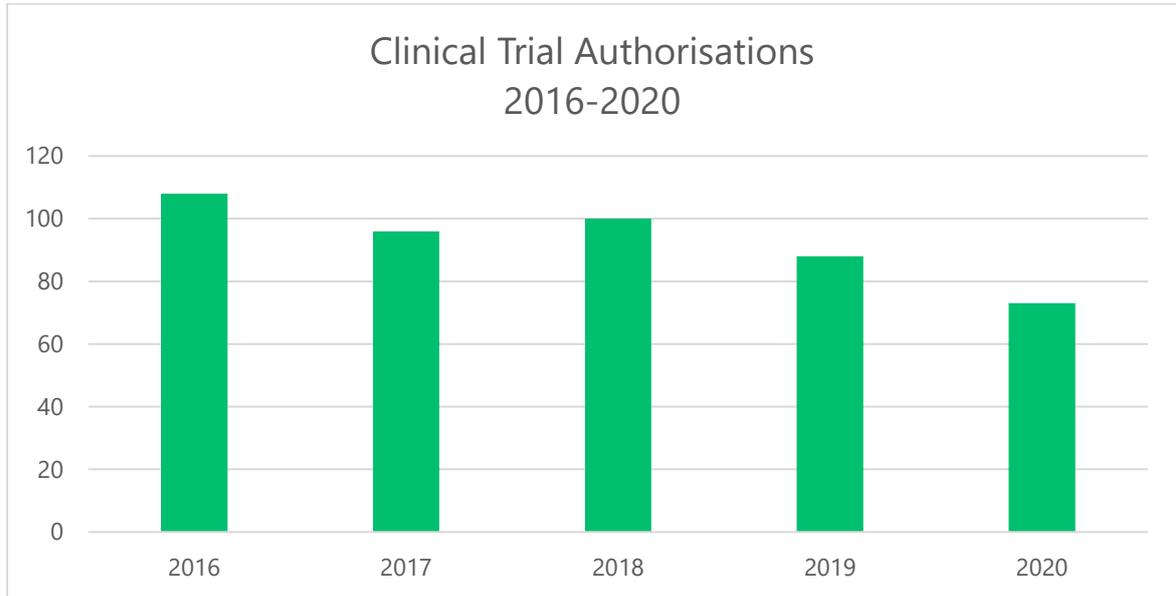
incorporated on to the list; we will also continue to work to include further substances as may be requested by the Minister for Health or the HSE.

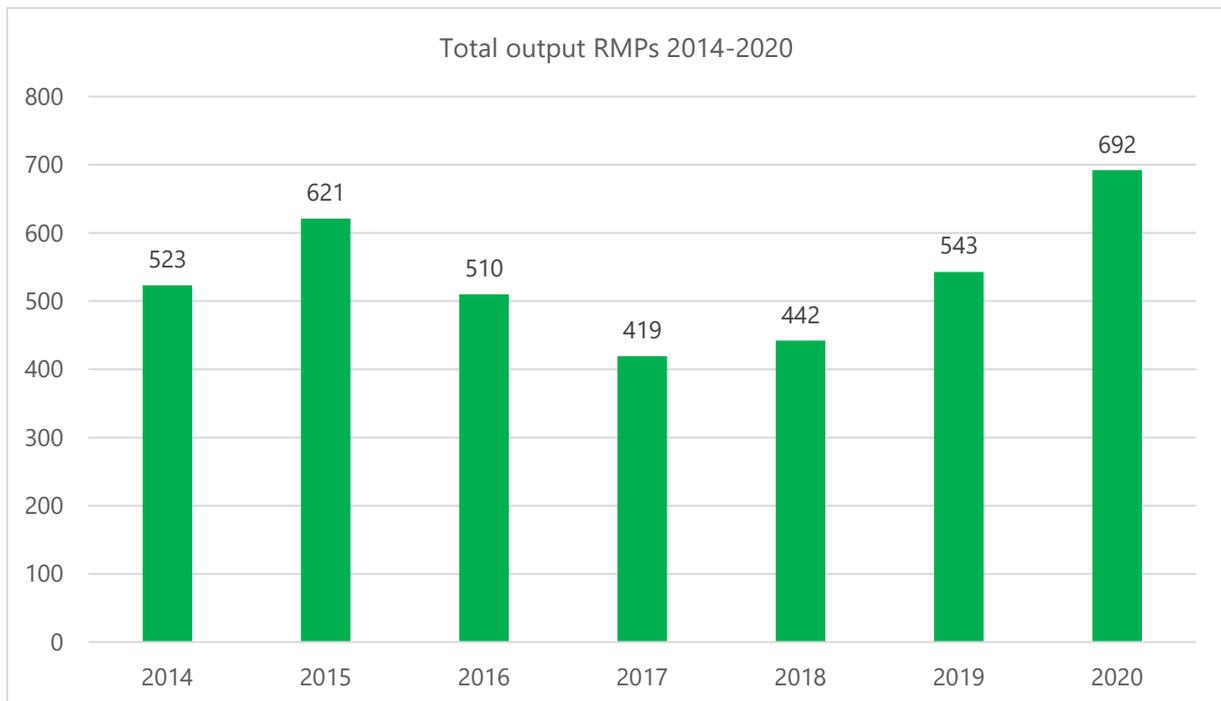
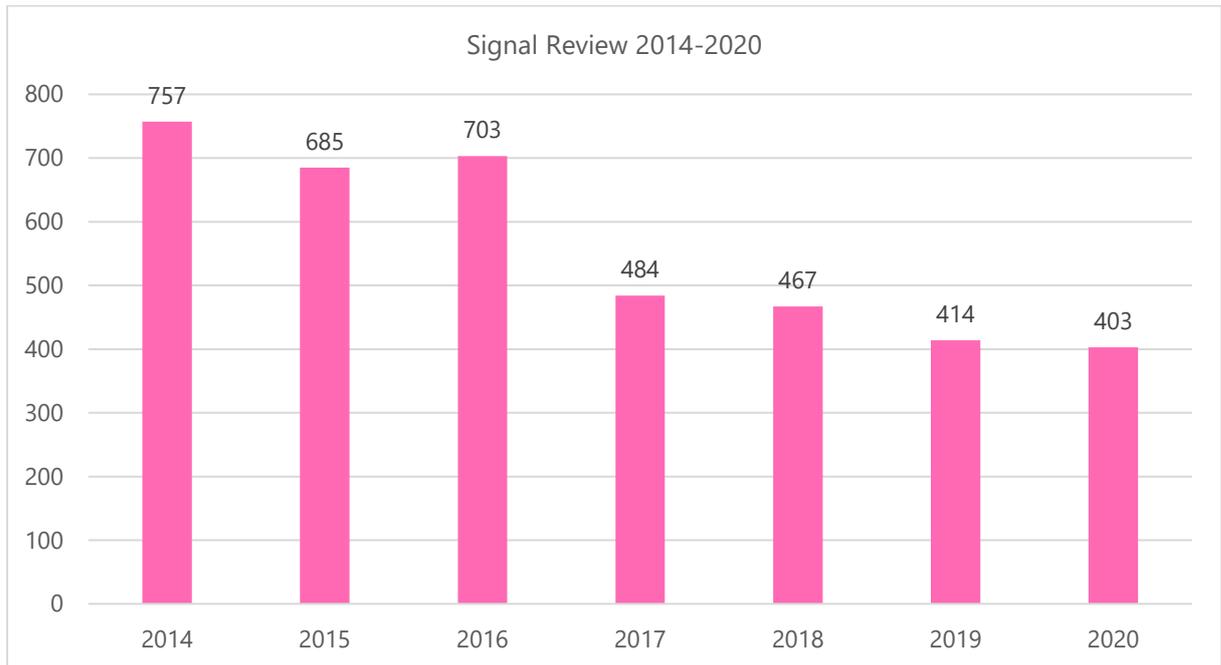
- Focus on the continued provision of guidance and support to industry stakeholders in areas undergoing evolving regulatory development, including:
  - o the new requirements of the Clinical Trials Regulation
  - o the new requirements of the Medical Devices Regulations
  
- A proactive approach to switching continues. Following a review of policies in this area, and after liaison with the Department of Health, the HSE Health and Wellbeing Directorate and healthcare professionals, the HPRA has taken a proactive approach to the reclassification of medicines since 2014. This has included the publication of a list of active substances currently classified as prescription-only medicines which the HPRA considers could be safely switched from prescription-only medicine to over the counter (OTC) pharmacy sale (not subject to medical prescription). The response from the marketing authorisation holders to this initiative has been disappointing, commercial reasons cited most often. The HPRA continues to engage directly with the industry to establish their interest in submitting applications for the reclassification of prescription medicines and reclassification of medicines currently available for sale through pharmacies, to make these available, where it is considered safe to do so, in general retail outlets. 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 monitoring of vaccines and therapeutics related to COVID-19 including substantial increase in the number of direct reports to the HPRA, which are then made available for MAHs via Eudravigilance.

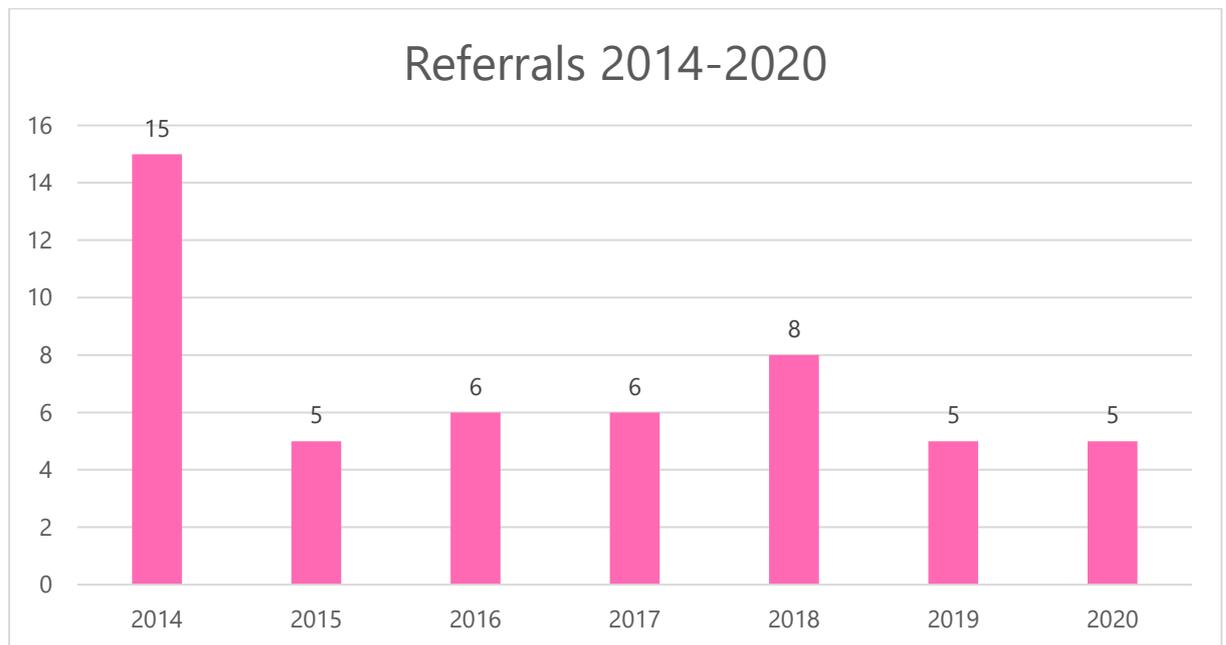
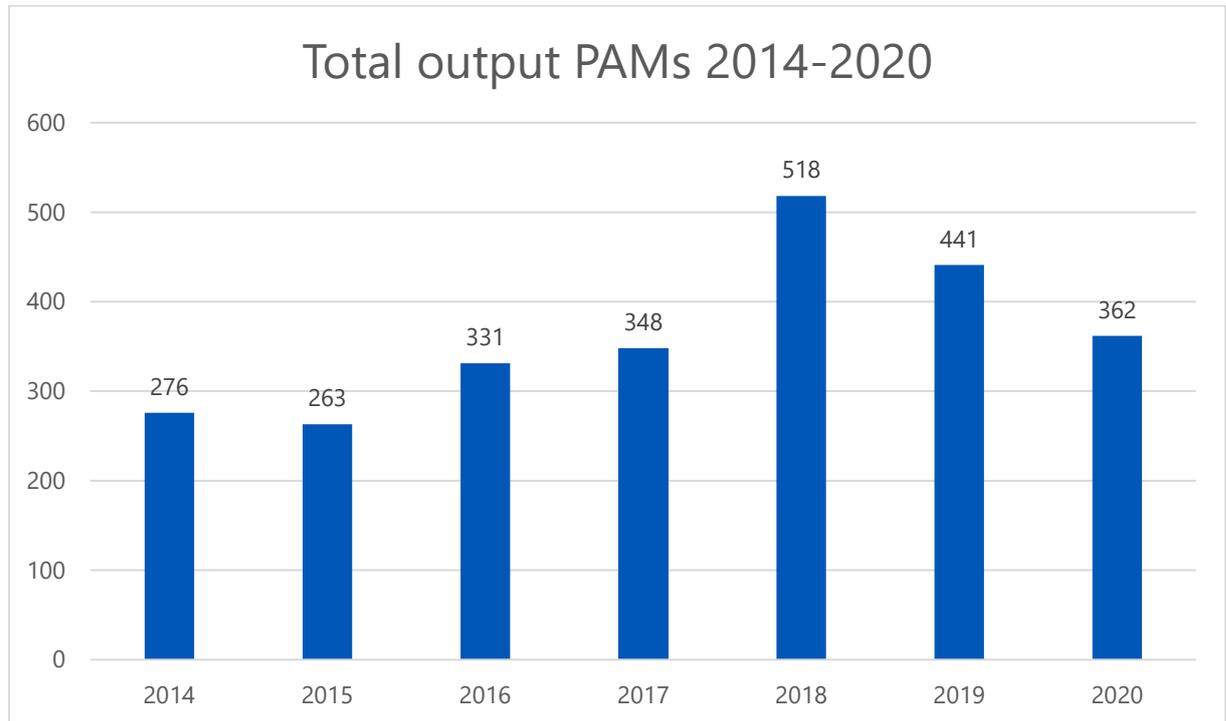
The following graphs outline the output across all application types up to the end of 2020.



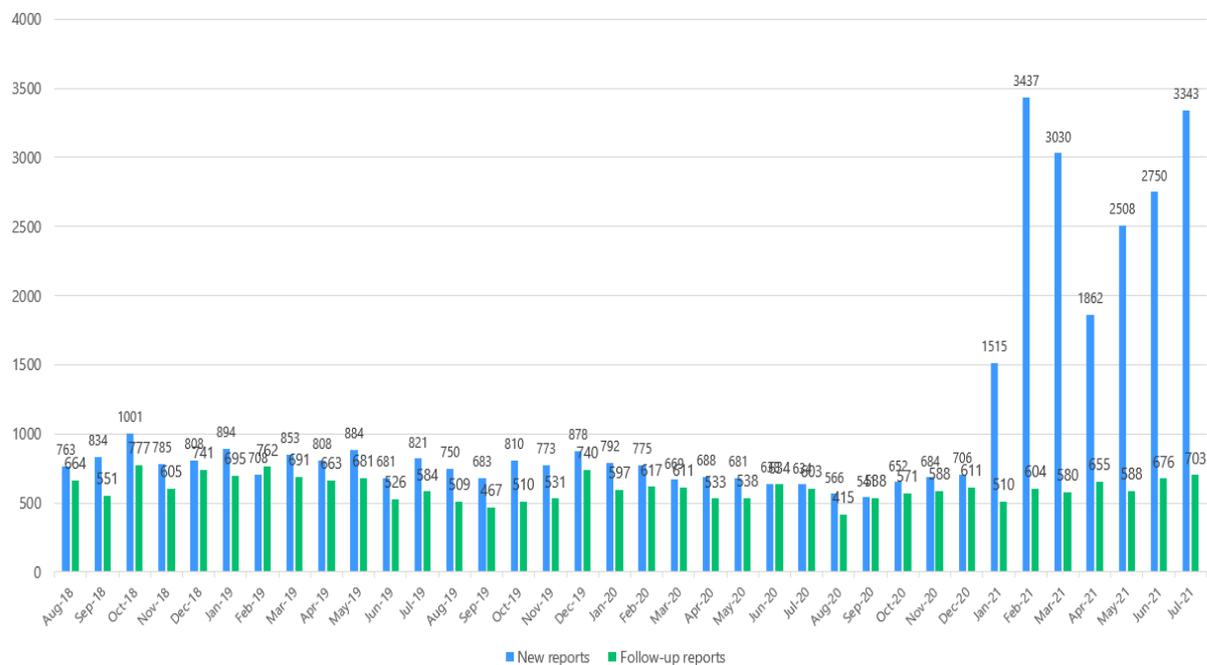








Number of adverse reaction reports received by the HPRA  
2018-2021



## APPENDIX II SERVICE LEVELS – COMPLIANCE DEPARTMENT

### Compliance Department General Activities

Initiatives undertaken/further developed in 2020/2021 included:

- Preparations for Brexit, in conjunction with other departments across the organisation, have included:
  - o Continued engagement with stakeholders with the primary purpose of maintaining supplies of health products through and beyond Brexit.
  - o Meetings continued with stakeholder companies in order to discuss their Brexit related plans and to clarify issues arising. Such meetings and liaison will continue to be an important focus.
  - o Regular liaison with key wholesalers to clarify ongoing stock levels of medicines, plans for replenishment, identify any particular difficulties in the supply chain and, if necessary, to assist in remediating those.
  - o Meetings with industry representative bodies, and attendance at workshops organised by some of those bodies, in order to consider and clarify Brexit related questions.
  - o Advising potential applicants for authorisations and licences of the requirements and processing of a number of new applications.
  - o Provision of support to the Departments of Health and Agriculture, Food and the Marine, including participation in regular meetings of the Brexit Operations Group and the Brexit Medicines Review Group, both convened by the Department of Health.
  - o Liaison with other agencies, including the Health Service Executive and Revenue's Customs Service, on issues of mutual interest.
- Since July 2019 when the EU – US mutual recognition agreement (MRA) on GMP inspection became fully operational, the HPRA has responded to a significant number of requests from the US Food and Drug Administration (FDA) for inspection reports relating to manufacturing sites in Ireland that are supplying human medicines into the US. This has led to a considerable reduction in the number of FDA inspections of Irish manufacturing facilities. In relation to importation of human medicines manufactured in the USA, the requirement for retesting of each batch on importation to the European Economic Area has been removed by virtue of the MRA becoming operational.
- Continued development of a workflow database for compliance case management to improve efficiency in processing of authorisations/licences/registrations, organisation and follow-up of inspections, quality defects and recall management and other compliance monitoring cases.
- Continued provision of support to the Department of Health 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' (FMD)).

- Under the FMD, annual updates to registrations of manufacturers, importers and distributors of active substances and brokers of medicines for human use were processed during 2019 and 2020.
- Also under the FMD, 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 marketing authorisation holders (MAHs) and manufacturers on 09 February 2019. In relation to this, the HPRA has liaised closely with MAHs, manufacturers, wholesale and retail stakeholders which have come together as the Irish Medicines Verification Organisation (IMVO) to implement the so called 'stakeholder model'. 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 not part of the governance structure of the IMVO, we continue to liaise closely with it. We have an oversight role in relation to the repository and have taken on the role of lead of the EU working group on supervision of the repositories.

We also participate in a National Oversight Group, convened by the IMVO, and including other key stakeholders. 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, had commenced during the first quarter of 2020 but had to be postponed due to the advent of the COVID-19 pandemic. It is now planned that this transition will be resumed in September 2021 and 'use and learn' will end on a phased basis concluding at the end of Q1 2022.

- Continued upload of post-inspection good distribution practice (GDP) certificates to the EudraGMDP database. All existing Wholesale Distribution Authorisations (WDAs) had already been uploaded to the database and upload of new or varied WDAs continued.
- Continued upload of Manufacturers'/Importers' Authorisations (MIAs) and post inspection good manufacturing practice (GMP) certificates to the EudraGMDP database.
- The Veterinary Regulation, 2019/6, is due for implementation in January 2022. Work is ongoing with colleagues from the Veterinary Sciences department, the legal section and the Department of Agriculture Food and the Marine with a view to ensuring smooth implementation.
- 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 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 – 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. Review and updating of this framework, in conjunction with ODTI, continued in 2019/20.

- 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 was installed and tested during quarters two and three of 2020. This system became fully operational in Q1 2021.
- Provision of support to the Department of Health in the development and implementation of an access programme for cannabis for medical use. In late June 2019, the Minister for Health signed Regulations to establish the access programme. Following that, the HPRA received and reviewed 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 Good Manufacturing Practice requirements, Good Distribution Practice, Good Clinical Practice, and Good Pharmacovigilance Practice standards, and of the required controls relating to Controlled Drugs and Precursors.
- Provision of support to the Department of Health in implementing two European Regulations relating to precursor chemicals.
- Monitoring, via inspections, of the activities of Marketing Authorisation Holder 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 EMA working groups, the Pharmaceutical Inspection Co-operation Scheme (PIC/S) Committee and its Expert Circle meetings. The HPRA's Inspection Manager assumed the Chair of the PIC/S, which has 54 member regulatory authorities, drawn from all continents, for 2020 – 2021.
- 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 also led on an initiative within the Heads of Medicines Agencies Group on developing a new risk-based approach to the sampling and analysis of mutual recognition, decentralised and centralised medicines which was finalised during 2018 and was implemented during 2019. Work on extending this initiative to the post marketing phase began in 2020
- 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 has included implementation of revised (more risk-based) versions of the relevant EEA procedures during 2019 and 2020.

- Continued development of the advertising compliance programme which includes regular liaison with the industry to outline HPRA requirements and to clarify our interpretation of the legislation.
- Further development of the monitoring of availability of medicines in non-pharmacy retail outlets with appropriate follow up where unauthorised or pharmacy confined/prescription only medicines are identified.
- Continued development of our role as competent authority for cosmetics. This has included 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 market place. The Forum develops the market surveillance programme in line with risk based principles and to take account of new legislative and technical progress.

#### COVID-19 pandemic:

- Processing of controlled drugs licences, export certificates and the various authorisations continued throughout
- The pandemic meant that all inspection activities had to be suspended during March 2020. Since then the HPRA has led on development of an EU guidance on remote inspections/distant assessments. A programme of remote inspections is in place across the GXP inspection activities of the organisation
- Guidance was drawn up for safe return of inspectors to regulated sites and training was completed. A hybrid inspection model, comprised of remote and focused onsite elements has been used, where necessary, during quarter three of 2020.
- All other activities of the Compliance department continued as normal throughout the pandemic
- In conjunction with colleagues from the Medical Devices department, the Enforcement section monitored for illegal supplies of test kits for diagnosis of COVID-19 and treatments for the virus. Monitoring for illegal supplies of medicines continued. Co-operation from Revenue Customs and An Garda Síochána was of great assistance in this monitoring and, where necessary, investigation of suspected illegal activities.

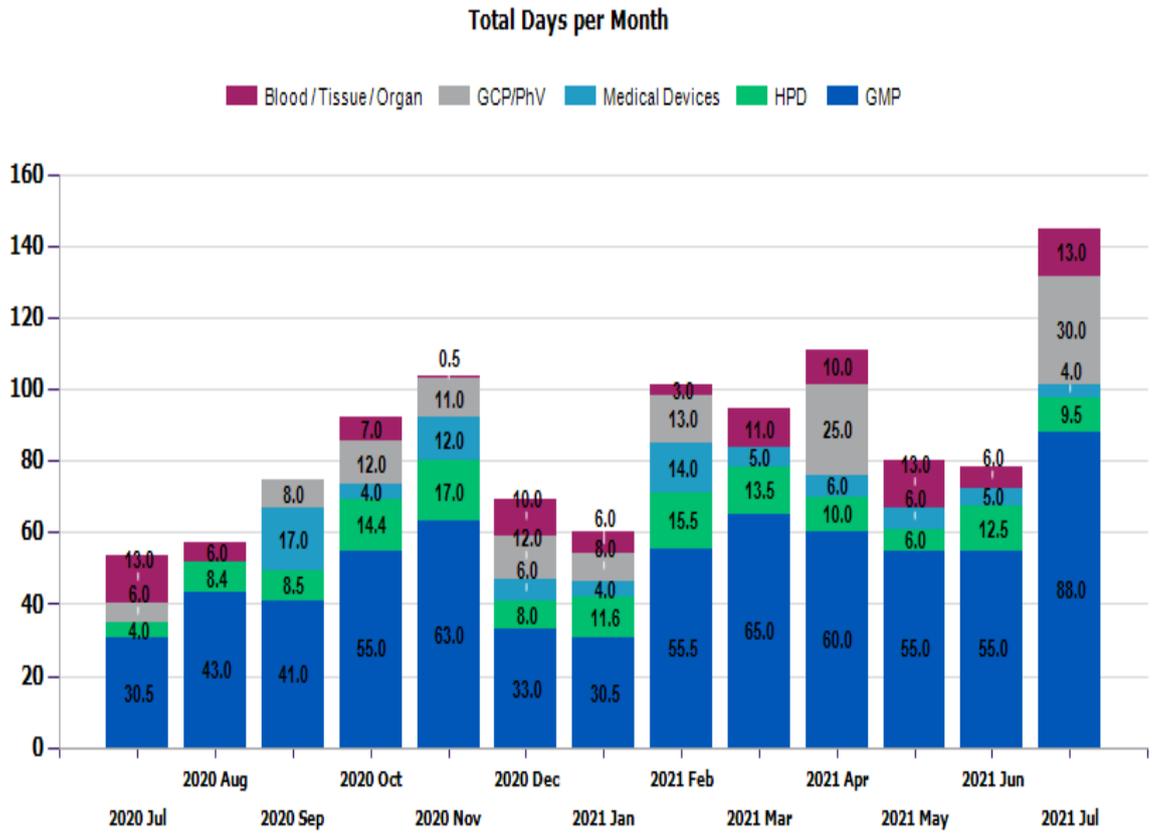
#### Other activities included:

- 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 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

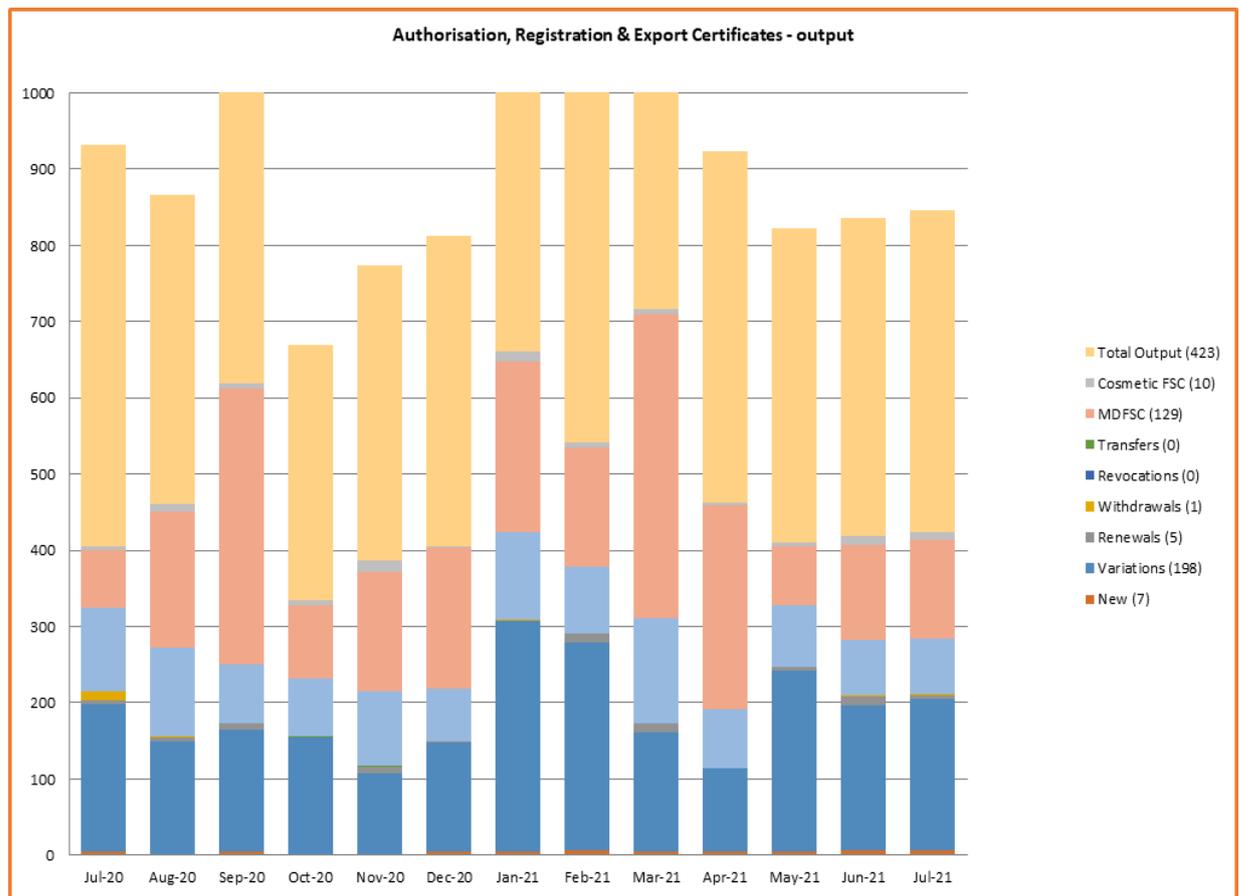
continue to serve as a source of relevant information for the Quality Defect and Recalls programme.

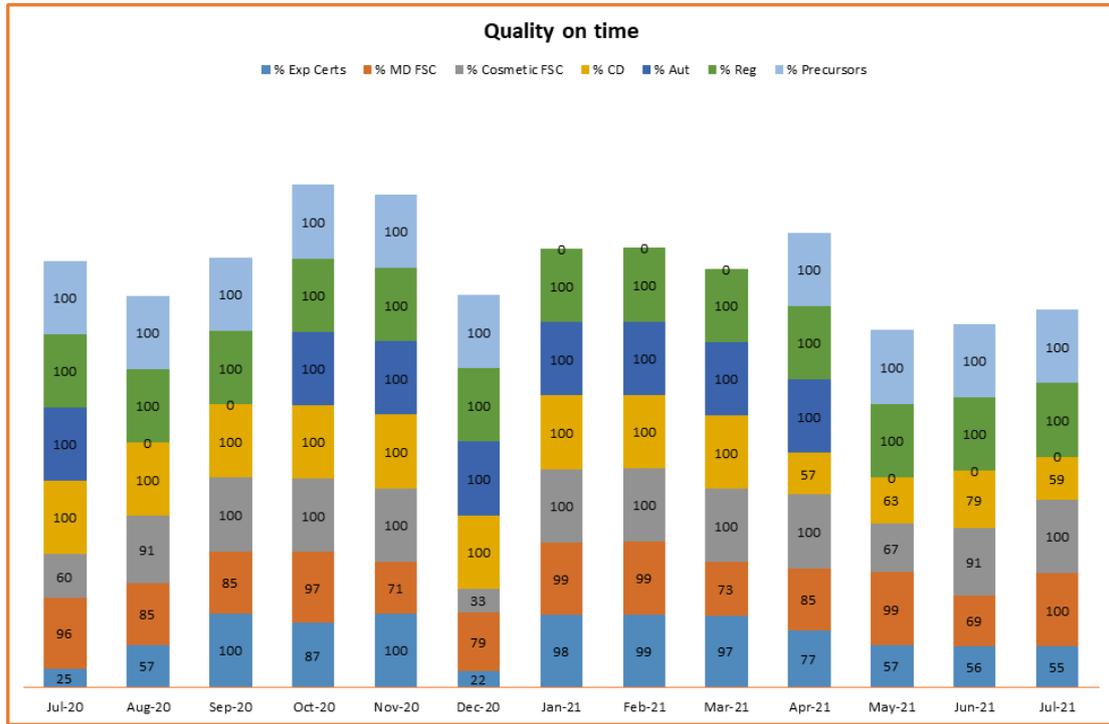
- Efficient turnaround of applications for variations to manufacturers' and wholesalers' authorisations, and for export certificates (medicines, medical devices and cosmetics) and controlled drugs licences.
- Further development of good clinical practice, bioequivalence and pharmacovigilance inspections.
- 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.
- The particular focus on the illegal trade in anabolic steroids and associated products 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, in particular, considered to present a risk to human health.
- Co-operation with An Garda Síochána and the Pharmaceutical Society of Ireland 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 over the period July 2020 to month-end July 2021.

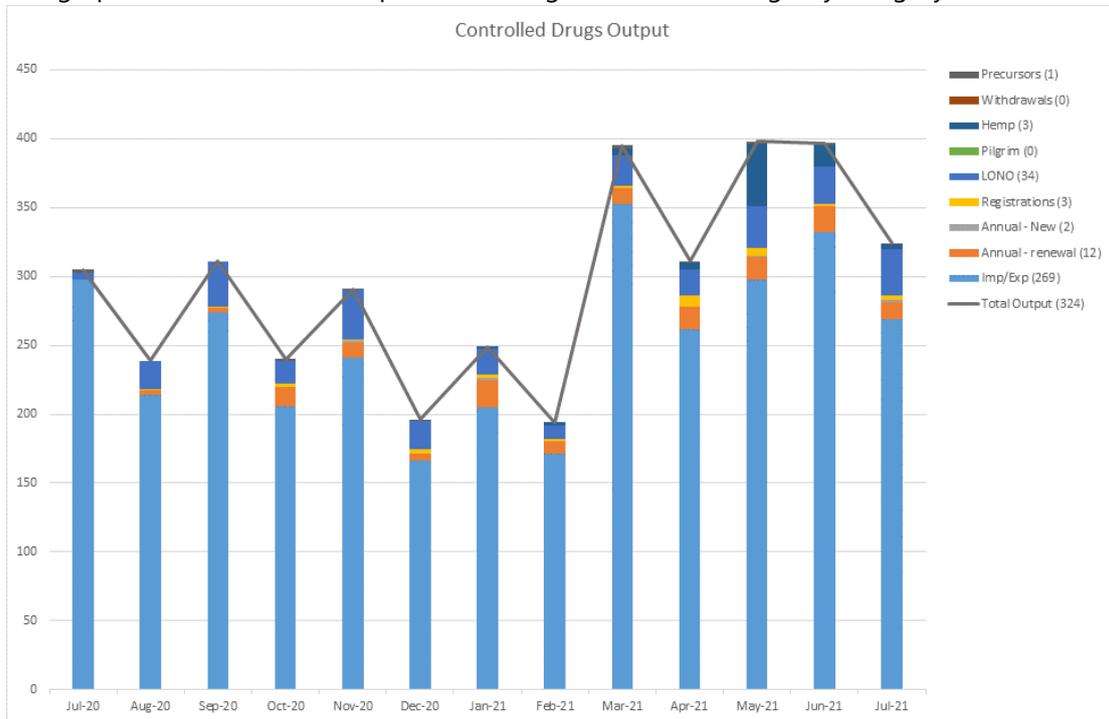


The following graphs show the numbers issued and the percentages issued on time, for export certificates, controlled drugs licences and GDP, GMP and IMP licences, over the period July 2020 to July 2021, inclusive.

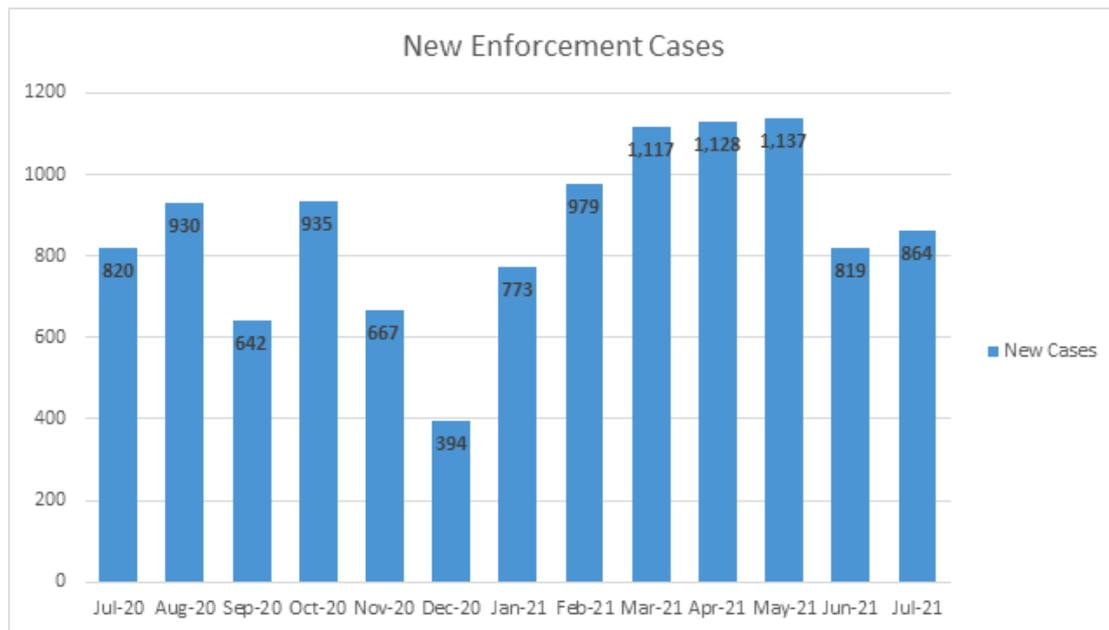




The graph below shows the output of licensing of controlled drugs, by category of licence.



The graph below shows the number of enforcement cases for the period July 2020 – July 2021 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 prescription only medicinal products which are authentic, but diverted and falsified medicines.



### **Blood and Tissues & Cells**

During 2020 and 2021 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 also 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 also continued to operate the Tissues and Cells vigilance system, participating 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 Organ Donation and Transplant Ireland (ODTI)) also has competent authority functions in the areas of standards and traceability/registries.

The Organs legislation applies to 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 as this requires the Schedule to a statutory instrument to be amended. Inspections related to import, export and holding of controlled drugs and drug precursors have been implemented and continue to be developed. The significant increase in applications for licences to cultivate hemp, first seen in 2019, has continued in 2020.

### **Exempt Medicinal Products**

A significant level of notifications of importation of exempt (unauthorised) medicines continued through 2019 and 2020, to date. Notifications increased during the early part of the Covid-19 pandemic and decreased towards mid-year, illustrating a peak in demand at the height of the crisis. We have an electronic system for notification and we continue to work closely with the notifying companies to ensure that data have been uploaded correctly. The notifications are an important source of information particularly when checking on whether products, recalled in other countries, have actually been supplied as exempt 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, monitoring 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 2015 in medical devices across the HPRA. 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 engaged significantly and 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 DOH, the HSE and industry in managing medical device related aspects of the COVID-19 pandemic. 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 2020, we:

- Designated a notified body in Ireland under the new EU Medical Device Regulation.
- Continued our schedule of oversight of the notified body in Ireland based on ongoing assessment, surveillance and observed audits;
- Continued to support development of EU coordination of notified body designation and oversight through participation in the EU Notified Body Operations Group (NBOG) and the Medical Device Coordination Group (MDCG);
- Worked along with the European Commission and the Competent Authorities for Medical Devices on initiatives to gather data on notified body capacity and certification workload associated with MDR.

Supporting innovation and research of new technologies is a key strategic priority for the HPRA medical devices team. In 2020, this involved:

- The review of applications to conduct clinical investigations of medical devices in Ireland. Nine new applications for clinical investigations and six amendments to ongoing investigations were assessed. The HPRA anticipates that these numbers will increase when the new EU Regulations are implemented;

- Continued focus on this area to ensure regulatory requirements and processes are clear and accessible to potential applicants;
- Encouraging engagement during product development and innovation of medical technologies. We met with 11 groups of innovators to discuss potential clinical investigation applications in 2020;
- Provided 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 are required to register with the HPRA. In 2020, the HPRA registered 183 new medical device economic operators (for example manufacturers, authorised representatives). A total of 20,757 medical devices were also registered. This represented a significant increase in registrations when compared to previous years, some of which is attributable to the UK's exit from the European Union. During 2020, HPRA estimate that 52 of the 183 economic operators registering in Ireland were as a consequence of Brexit.

### Safety and Quality

We continue to develop and reinforce our market surveillance activities, with particular emphasis on proactive rather than reactive actions. Of note in 2020:

- We further developed our lifecycle market surveillance strategy and planning mechanism to allow for more effective management and reporting of these activities;
- We concluded work in leading the EU Joint Action on Market Surveillance (JAMS) of medical devices initiative which is funded by the European Health Programme and aims to develop market surveillance activities at European level. The work programme was completed over a 3 year plan and was presented at a European stakeholder conference attended by 15 organisations representing patients, clinicians and other stakeholders, along with 23 competent authorities and the EU Commission.
- A total of 18 COEN notices were sent by HPRA to the European network relating to medical device compliance concerns;

There were 1,120 market surveillance cases undertaken in 2020, a decrease compared to 2019 due to a significant decrease in the number of certificate notifications from notified bodies. The number of complex assessment and proactive market surveillance activities substantially increased overall in 2020.

- Significant market surveillance activities were undertaken in the area of medical devices and IVDs used in response to the COVID-19 pandemic, including thermometers, ventilators, surgical / medical face masks, surgical gowns, IVDs utilising PCR (polymerase chain reaction), antibody and antigen technology.
- We continued to focus our vigilance activities during 2020 on the areas of user reporting and dissemination of HPRA medical device safety communications. This included:
- The receipt and assessment of 1,668 medical device vigilance cases, a decrease compared to 2019. Of the 956 incident reports notified to the HPRA, 11% came from users of medical

devices. Manufacturers accounted for 76% of all reports received in 2020 while 17% came from other competent authorities;

- There were 301 field safety corrective actions (FSCA) associated with the national market including 77 product removals conducted in Ireland during 2020;
- We issued 106 national competent authority reports, four notified body forms and one vigilance enquiry form;
- We also issued 14 safety notices in relation to medical device issues and 17 direct to healthcare professional communications; Implants, infusion devices, surgical devices and orthopaedic devices accounted for 56% of the total vigilance reports. Reports continue to be received relating to *in-vitro* diagnostic devices in the area of clinical biochemistry (10% of reports) and medical devices in the areas of vital signs monitoring (7% of reports) and respiratory devices (3% of reports). During the year, we also continued development work on signal detection of medical device issues.

### COVID-19 pandemic

The COVID-19 crisis highlighted the essential role that medical device technologies play in the diagnosis and treatment of disease. The availability for supply of medical devices, including accurate diagnostic tests for SARS-CoV-2, intensive care equipment such as ventilators and basic protective equipment for healthcare workers such as surgical masks, gloves and gowns came under intense and sustained pressure in response to unprecedented demand across the globe.

The Medical Devices Department has worked closely with the Department of Health and the Health Service Executive to assist in the national response to COVID-19 (SARS-CoV-2) in Ireland. The HPRA devices team worked as part of the Medical Devices Criticality Assessment Group (CAG), a subgroup of NPHET to provide regulatory advice and input on relevant medical devices. The devices team were also members of the NPHET subgroup on diagnostic testing approaches.

The HPRA also worked directly to provide guidance to manufacturers and suppliers on regulatory requirements for medical devices and IVDs and the HPRA continues to provide support on the regulatory framework to HSE and to manufacturers/distributors to ensure confidence in the long-term supply chain.

The regulatory support provided by the Devices Department during this pandemic has also resulted in cross-agency cooperation and collaboration with regulatory peers. The HPRA worked with HIQA in the area of Rapid Health Technology Assessment of alternative diagnostic testing for coronavirus 2 (SARS-CoV-2), as well as working with the Health & Safety Authority (HSA), the Competition and Consumer Protection Commission (CCPC) and the National Standards Authority of Ireland (NSAI), in relation to products such as face masks, gowns and gloves.

At a European level, the HPRA participated in the EU Commission established taskforce of the Medical Device Coordination Group (MDCG) market surveillance working group to share and exchange information on the challenges presented by COVID-19 in different EU countries. The devices team also participated in an international forum with regulators from Australia, Brazil, Canada, EU, Japan, Singapore, South Korea and the US to exchange experiences on emerging issues with essential devices on the market place.

The devices team working along with colleagues from the enforcement team continued to conduct surveillance of new devices coming on to the market in Ireland. The HPRA, working with customs colleagues and other stakeholders detected a number of falsified and counterfeit devices as well as incorrectly CE marked devices. Examples of falsified devices included fake or counterfeit tests and non-compliant thermometers. [Safety notices](#) and social media have been used to highlight these issues and to ensure the information reaches the stakeholders concerned.

To reflect the needs of internal and external stakeholders, a number of COVID-19 specific webpages have been published on the medical devices [webpage](#) to facilitate consolidation of key information and resources.

### Legislation and regulation

The Medical Device Regulation<sup>2</sup> (MDR) was due to become fully applicable in May 2020. Due to the impact of COVID-19, and the unprecedented pressure on the health services and the medtech sector, the date of application of this regulation was deferred to May 2021. We continued our work during 2020 to help ensure an effective and timely implementation of the EU Device Regulations<sup>3</sup> (EUDR) at national and European level. This included:

- Continued work on the HPRA programme plan 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 to the impact of the regulations and the development of guidance and communication initiatives;
- Working with the Department of Health and key 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 involving implementing and delegating acts;
- 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;

---

<sup>2</sup> Regulation (EU) 2017/745 on medical devices

<sup>3</sup> Regulation (EU) 2017/745 on medical devices and Regulation (EU) 2017/746 on *in vitro* diagnostic medical devices

- Participating in the EU Working Groups tasked with developing guidance for specific functional areas.

We continued to engage with the Department of Health throughout 2020 on policy and legislative issues arising from implementation of the new EU Regulations. At national level, we further developed our national fee-based funding model for medical devices to recover costs associated with our medical device activities. The model was revised in 2020 to streamline the approach and ensure new activities under the MDR are accounted for when MDR becomes fully applicable in May 2021.

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. This included:

- Re-election to the Executive Group of the Competent Authorities for Medical Devices (CAMD) network. This group has successfully worked in partnership with the EU Commission over the last number of years to help develop the regulatory system in Europe;
- Participation in the CAMD's Implementation Task Force (ITF) and Transition Subgroup (TSG) which aim to improve co-ordination and consistency of implementation of the new EU Regulations and published guidance on what it means to be compliant by the date of application of the Regulations as well as proposing key areas for the Joint Plan on MDR Implementation;
- Continuing to lead the work of the clinical investigation and evaluation working group (CIEWG), acting as the co-chair with the EU Commission.

In early 2020, HPRA led calls in Europe for a readiness check for implementation of the MDR, which resulted in the Commission's Joint Implementation Plan agreed in March 2020. Throughout the year, our focus remained on identifying and promoting discussions on practical measures for implementation of the system to ensure the system operates effectively in practice.

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, France and Germany);
- Continuing to act as the IMDRF secretariat for the National Competent Authority Report (NCAR) Exchange programme.
- Contributing to discussions and development of the Medical Device Single Review Programme, which relates to product review.

## Brexit Preparations

Preparations for Brexit, in conjunction with cross organisational departments, have continued in 2020 and have included participation in stakeholder meetings, development of website and guidance material, registering new organisations establishing in Ireland as a result of Brexit. The HPRA has continued to have extensive communication with manufacturers and authorised representatives at national level to ensure appropriate awareness of the implications of a no-deal Brexit for medical devices. We have also led on EU work with other competent authorities to promote awareness and to prevent adverse impacts on medical devices used in Ireland. HPRA has provided support to the HSE and the Department of Health in the Brexit operations groups.

## Stakeholders and partners

The advent of the COVID-19 pandemic had an unprecedented and significant impact on all stakeholders – patients, health services, industry, notified bodies and on government departments and agencies. The HPRA worked with key stakeholder groupings to provide guidance on the regulatory framework for devices and IVDs in the context of COVID-19. Interagency processes were developed to ensure CE marked critical medical devices were available to Irish health services and available to Irish patients. A specific medical devices COVID-19 webpage was launched and updated regularly with guidance and information on key aspects of medical device regulation linked to managing the treatment of patients with COVID-19.

In January 2020 Brexit was formalised with the UK departure from the EU and our work to ensure preparedness for the end of the withdrawal agreement between the EU and the UK continued throughout 2020. A number of stakeholder briefings and guidance materials were developed specific to the medical device sector as well as participating in relevant EU taskforces on the certification capacity of notified bodies following the withdrawal of UK notified bodies.

Our work to encourage direct reporting of incidents and medical devices issues by device users and members of the public continued throughout 2020. 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 EUDR. During 2020, we:

- Hosted a webinar series on medical devices and *in vitro* diagnostic medical devices for manufacturers, authorised representatives, distributors and importers. The series which ran over the course of a week, had a daily average attendance of between 350 – 450 participants;

- Continued to update the HPRA website and social media channels to provide information and guidance regarding EUDR;
- Information releases on the HPRA website and social media platforms relating to both COVID-19 and the new EU Regulations were some of the most frequently visited sites across HPRA in 2020.
- Provided briefings, advice and workshops on the new Regulations to a range of different stakeholders including 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 those authorities. In addition, we participated in operational and strategic discussions on developing cooperation between the CAMD and the Heads of Medicines Agencies (HMA) networks.

The HPRA continues to deliver a programme of presentations and talks to a range of external stakeholders.

The HPRA also continued, during 2020, on the development of the medical devices department with the further introduction of organisational improvement and efficiencies. These included the seamless introduction of remote working for the majority of the team during the COVID-19 crisis.

### **Fee based funding**

Fees for medical devices were introduced in January 2017 following extensive consultation with industry to cover the costs of the HPRA's medical device regulatory activities. The model was amended during 2018 to reflect feedback received from affected stakeholders and is now based on a cost recovery model which relies on subventions from the Department of Health.

### **Case Workloads**

#### **Vigilance and compliance**

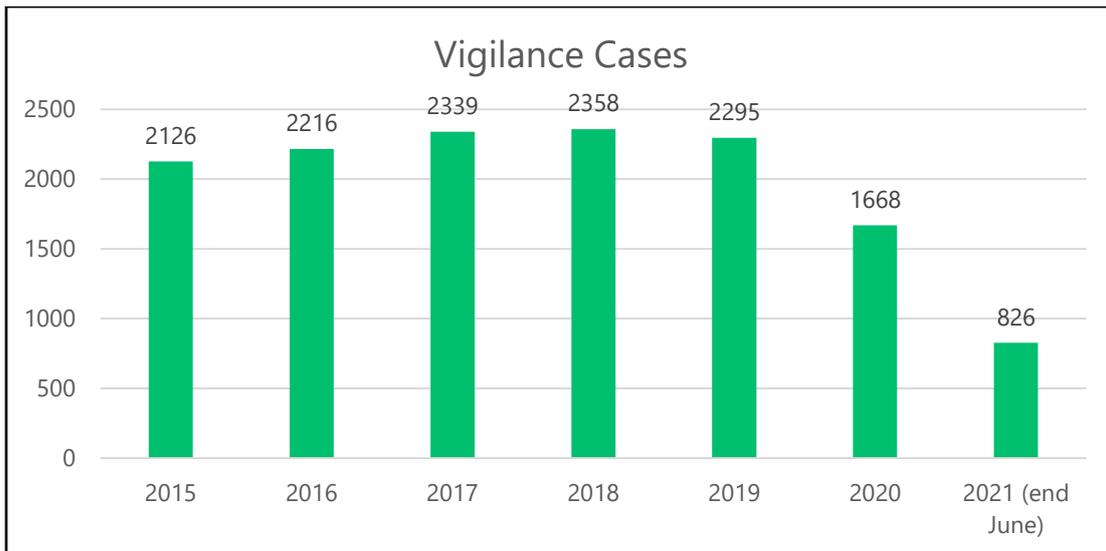
There has been ongoing work with the HSE in various National Incident Management Teams during 2019- 2020 and case work continues to lead to the identification of significant issues that require increased monitoring and oversight by HPRA.

To date in 2021, the vigilance workload continues at consistent levels, with an increase in complexity in relation to vigilance cases. Year to date (January to end June), 826 vigilance cases were opened and reviewed. Also in this period, among other communications, five HPRA safety notices and 67 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.

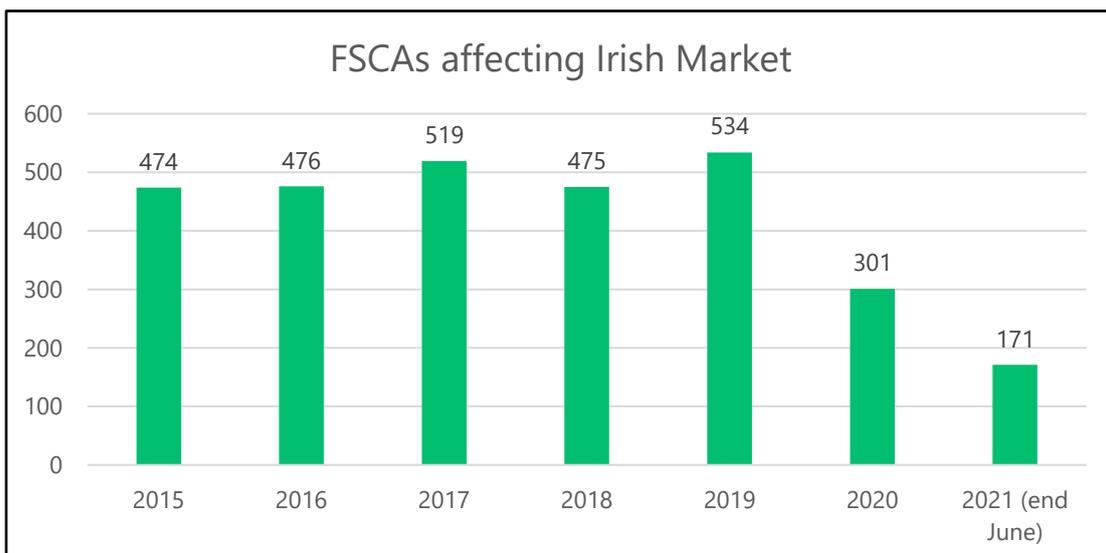
Work has continued to enhance the vigilance function through the introduction of a signal

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 end of June 2021)**

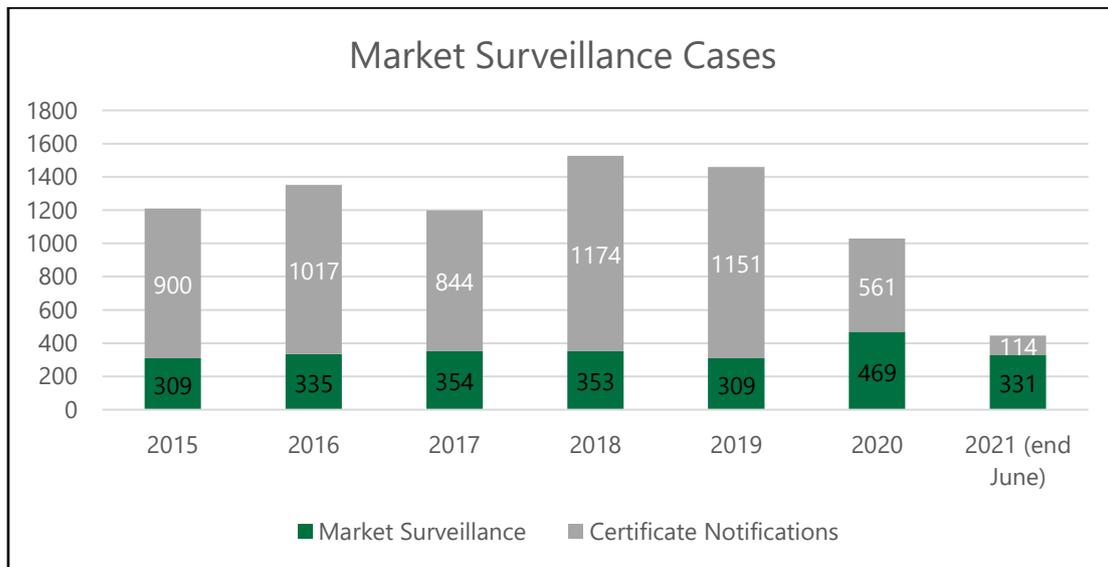


**Graph 2: Number of Field Actions affecting Irish Market (2015 to end of June 2021)**

### Designation and Monitoring of Notified Bodies

#### Surveillance cases

During 2020, the HPRA continued to develop its lifecycle approach to market surveillance and investigated 469 market surveillance cases and received 561 certificate notifications from Notified Bodies.



**Graph 3: Number of Market Surveillance Cases (2015 to end of June 2021)**

The HPRA has, in particular since 2014, 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 market place 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 2020, ten audits were performed at notified bodies, medical device manufacturers and authorised representative facilities, of which:

- one was a for cause audit:
- nine were based on proactive market surveillance projects and notified body surveillance/assessment.

### Clinical Evaluation Review

Since 2015, 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 reactively in response to a number of specific device issues highlighted during the year and proactively as part of our ongoing market surveillance activities. This work also formed a significant part of our notified body designation and oversight activities both at national level and European level as part of EU joint assessment activities.

### Product registrations

In 2020, the HPRA received 20,757 notifications of new medical devices to the medical device register, with 454 device amendments received. In addition, 90 new organisations as Irish-based manufacturers or authorised representatives for class I, custom-made, *in-vitro* diagnostic medical devices, as manufacturers of system or procedure packs, or as sterilisers of medical devices, have been notified. Registration of these devices in the Member State in which the manufacturer or its authorised representative is based is required by legislation as there is a self-declaration of conformity made by the manufacturer.

This increase in new organisations registering has already impacted on the number of market surveillance activities undertaken with regard to the register and it is expected that it will continue to be an ongoing focus of the market surveillance activity.

In the first six months of 2021, 37 medical device economic operators have registered with the HPRA under the MDD/IVDD and 174 medical device economic operators have registered directly with HPRA under the MDR/IVDR. 309 Economic operators have been validated on Eudamed.

### Classification Requests

The HPRA received 38 applications for classification of medical devices or products queried as medical devices in 2020. 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 up-classified to a higher device classification.



**Graph 4: Classification Requests (2015 to end of June 2021)**

#### Clinical Investigation Applications

The HPRA received nine applications for clinical investigations and six amendments to a clinical investigation of a medical device to be conducted in Ireland in 2020. In addition, 34 compassionate use procedures were completed in this period.

#### Queries

During 2020, the HPRA medical devices team received 1928 queries relating to medical devices. The majority of the queries related to COVID-19 related matters, the provision of guidance and interpretation of the legislation and registration. In addition, a large number of queries have been received in the first six months of 2021 the department received 698 queries.

#### Certificates of Free Sale

During 2020, the HPRA issued 2,520 certificates of free sale compared with 2,710 in 2019.