HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Public Consultation on
Annual Review and Proposal for Fees – Financial Year 2021

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

01 OCTOBER 2020

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.

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 2021.

2 THE OPERATING ENVIRONMENT

2020 has been a challenging year for both the HPRA and the industry. As with all companies, the COVID-19 pandemic has resulted in the HPRA adapting to a different way of working and providing a wide variety of support to the Government and Health Services. Brexit has continued to bring considerable uncertainty to the regulatory framework and both industry and the HPRA have expanded their resources in preparation for Brexit. With the exception of inspection activity and related income, regulatory activity has held up well during the COVID-19 crisis.

2019 saw an increase in some regulatory activities related to Brexit, such as transfers and variations. Some of this has continued into 2020 but not at the levels seen previously. In terms of costs, the Haddington road reductions have been re-instated and salaries are subject to general public service pay increases of approximately 2% per annum. General inflation remains low although the COVID-19 crisis has caused uncertainty in relation to costs and income. While the impact of Brexit is unknown, it is becoming clear that regulatory alignment and a free trade agreement are unlikely and 2021 will see the real impact of a hard Brexit.

[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.

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 2020 was COVID-19 and Brexit.

COVID-19 has impacted all departments in the HPRA. In 2021 it is hoped that, in addition to more therapeutics, authorised vaccines will be available and administered across the State. This is likely to have a huge impact on our work nationally, with the EMA, International colleagues and the Department of Health. A significant challenge will be developing an appropriate national post-authorisation pharmacovigilance approach in respect of any COVID-19 vaccines.

Since Brexit was announced, the HPRA committed to the industry that we would work with them to minimise the regulatory burden where possible, to progress Brexit related changes in an expedited manner and to actively work with industry to deliver pragmatic solutions, where possible. In addition, we agreed to take over as Reference Member State (RMS) for any product that the UK previously was RMS and where Ireland was a Concerned Member State (CMS). We are happy that we delivered on and continue to deliver on these commitments but it has also had an impact on resources. Of significance to the financial model are products where we have taken over as RMS without a corresponding uplift in income.

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.

The impact of new legislation continues to be rolled out across the organisation. The Clinical Trials Regulation will be implemented in 2021/2022, and the EU Medical Device Regulation (MDR) will be implemented in 2021. The regulatory model is becoming increasingly complex, there are more complex medicines and Pharmacovigilance legislation has led to an increase in the number of referrals, and regulatory action arising from the outcome of these referrals.

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 2021.

3 STRATEGIC DIRECTION OF THE HPRA

The HPRA has commenced the process of developing its new strategy for the period 2021 - 2025. We continue to deliver under our current strategic plan for the years 2016 – 2020, which also aligns with the EMA and HMA joint strategic plan. The high-level strategic goals under the current plan are as follows:

- **Access to medicines** (enhancing regulatory support to patient access to medicines)
- **Better informed users** (providing current information to inform choices and decisions made by patients and their healthcare professional)
- **Optimised regulatory system** (keeping pace with product, manufacturing and supply chain developments)
- **Supporting innovation** (providing regulatory support and advice to research and development centres)
- **Internal capabilities** (ensuring strong internal systems, resource and expertise)

The plan for 2021 to 2025 will be published in Q4 2020. Many of the themes from the previous plan will be reflected in the new strategic plan while incorporating changes to the regulatory environment past and future, identified over the last five years. While this plan is still under consultation, key projects for 2021 will include:

- Managing the public health crisis arising from COVID-19 as it relates to medicines and medical devices
- Enhancing the post-authorisation systems in response to any COVID-19 vaccines
- Managing the impact of Brexit across all our strategic initiatives and in particular with our stakeholders, seeking to minimise the impact of Brexit on 31 December 2020
- Dedicated project and resources to manage medicines shortages from a regulatory view point, incorporating both the impact of COVID-19 and Brexit
- 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
- 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 2021

The HPRA is operating in a challenging environment, particularly in light of COVID-19 and Brexit. 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 still yet unknown outcome of the EU-UK Brexit negotiations.

Overall income and costs have performed well in 2020. Income has remained steady across a number of categories despite the impact of COVID-19, although the time line for regulatory submissions is such, that much of the income to date relates to work that would have been substantially progressed pre COVID-19. The longer-term impact of COVID-19 on the business is unclear and while we recognise that in a health crisis, there is an increased demand for certain medicines, this was not the case across the board. We expect that the effective shutdown of countries at the early stage of COVID-19 may have an impact on regulatory submissions downstream.

Brexit has also continued to have a positive impact on income as companies continued to make Brexit related regulatory submissions in 2020. This income will be depleted in 2021 and there will be fee income issues related to products that have failed to make the necessary regulatory changes. In addition, the commercial impact of Brexit on the industry has not yet happened and as such, the impact on regulatory activity and fees is unknown.

Costs as a result of COVID-19 have not behaved as expected in 2020. The HPRA offices have been closed for five months and consequently, many consumables related to a large office building have significantly reduced. Other costs such as travel, training and meetings have also significantly reduced as meetings were cancelled or delivered virtually. Predicted staffing levels are also below expected levels as recruitment was put on hold. While recruitment has recommenced, it is a challenging process and it will take some time to achieve optimal staffing levels.

Despite the positive impact on costs arising from Covid, payroll which is up to 82% of total costs continues to increase, with further increases expected in 2021 for the following reasons:

- The impact of the new Public Service Pay increases will result in pay awards of approximately 2%
- 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.
- Brexit: While the final shape of Brexit is still unknown, it is likely that managing the aftermath of Brexit will still be a significant workload for the HPRA. A longer-term effect will be our commitment to taking over a significant amount of work previously carried out

by the UK. This will affect the mix of work HPRA undertakes with a much greater emphasis on outgoing work.

The HPRA expects that 2021 will be very challenging for the reasons outlined above and that income levels may be challenged by COVID-19 and Brexit while payroll costs increase. However, in recognition of the income and cost levels of 2020, we propose a general fee freeze for 2021. 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

Human Medicines Fees

- Amendment of the outgoing MRP supplement where the outgoing MRP is applied for within six months of the national procedure ending to twelve months of the national procedure ending.
- Alignment of the fees for classification requests between Human Medicines and Medical Devices

Compliance Fees

- Application of the inspection fees to trainee inspectors for productive inspection time

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 2020. 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 Brexit and 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 2021 and further amend the fees and fee structure, if required, for 2022.

5 PROPOSED FEES

As outlined above there will be a freeze on fees for the year 2021.

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 2021.

6.2 Other proposed adjustments to fees - Human Medicines

6.2.1 New Applications

It is proposed to amend the outgoing MRP supplement where the outgoing MRP is applied for within six months of the national procedure ending to 12 months of the national procedure ending in order to bring the fees in line with the Decentralised outgoing fees for new products.

6.2.2 Classifications

It is proposed to introduce a new complex classification request fee that relates to novel products or products that incorporate elements from different regulatory frameworks. It is also proposed to remove the reduced fee relating to the submission of other products at the same time.

Classification Requests	Current Fee	Proposed Fee
Borderline Products – Classification Request	€280	€280
Borderline Products – Classification Request – other products at same time	€225	€0
Complex classification request	€0	€1,020
Borderline Products – Appeal to a Classification	€280	€280

6.3 Other Proposed adjustments to fees – Compliance activities

6.3.1 Fee for inspectors undergoing accreditation

It is proposed to charge the current inspection fees for trainee inspections for productive inspection time.

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 31 October 2020. 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 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. Following some reduction in output upon implementation, the organisation has returned to and is exceeding previous levels. Our focus is on improving our current workflow technology to ensure ongoing delivery of benefits to the organisation 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 increases in adverse reaction reporting following the introduction of centralised reporting requirements in November 2017, with additional complexities associated with reporting through the EudraVigilance system 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. Further efficiencies will be introduced during 2020-2021 to allow marketing authorisation holders, where appropriate, to incorporate an application for inclusion in a group on the list as part of their marketing authorisation application.

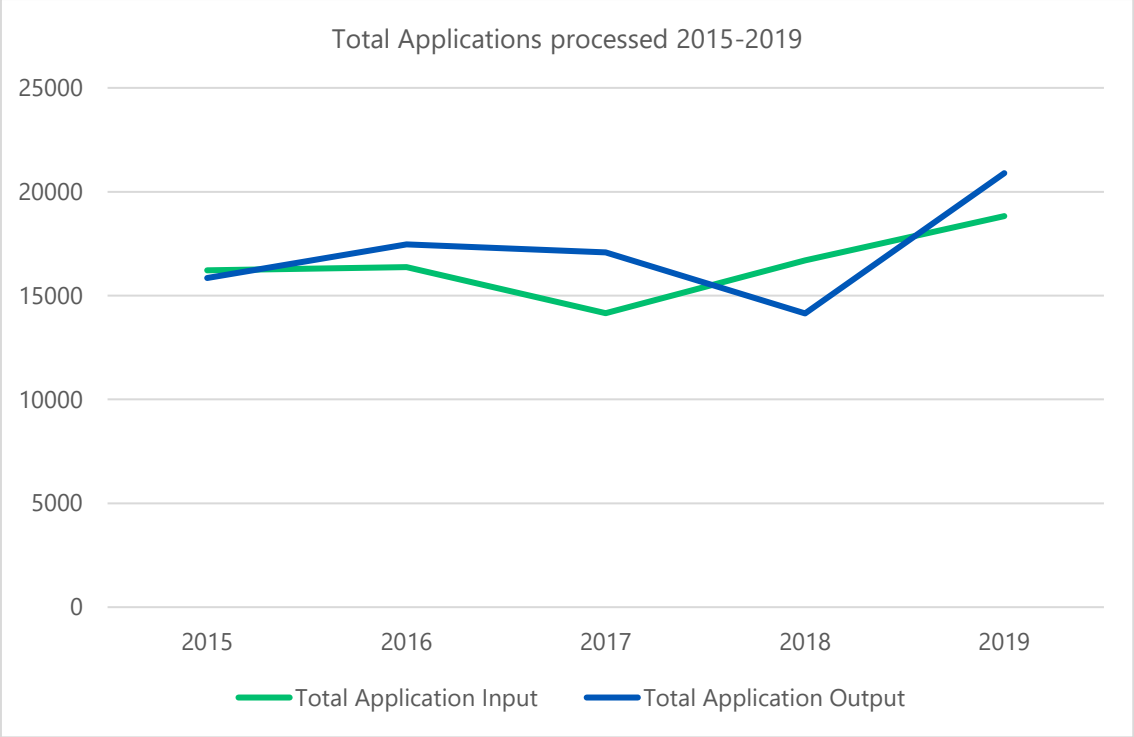
- Focus on the continued provision of guidance and support to industry stakeholders in areas undergoing evolving regulatory development, including:
  - the new requirements of the Clinical Trials Regulation
  - the new requirements of the Medical Devices Regulations
  - the registration of traditional herbal medicinal products

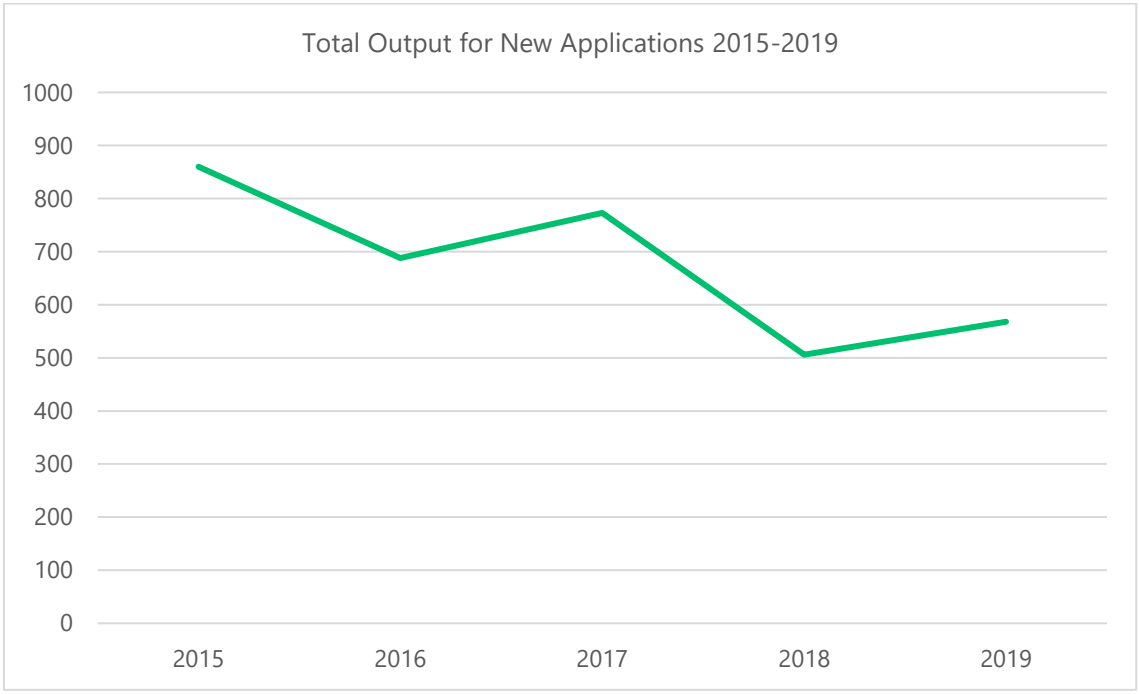
- Continued progression of a public health initiative focused on providing important online information about all medicines licensed by the HPRA. This includes maintaining publication of the summary of product characteristics document, patient information leaflets, ATC codes, interchangeable lists and the legal classification status of all human medicines on the HPRA website (www.hpra.ie). Since December 2015, all educational materials are published on the website.

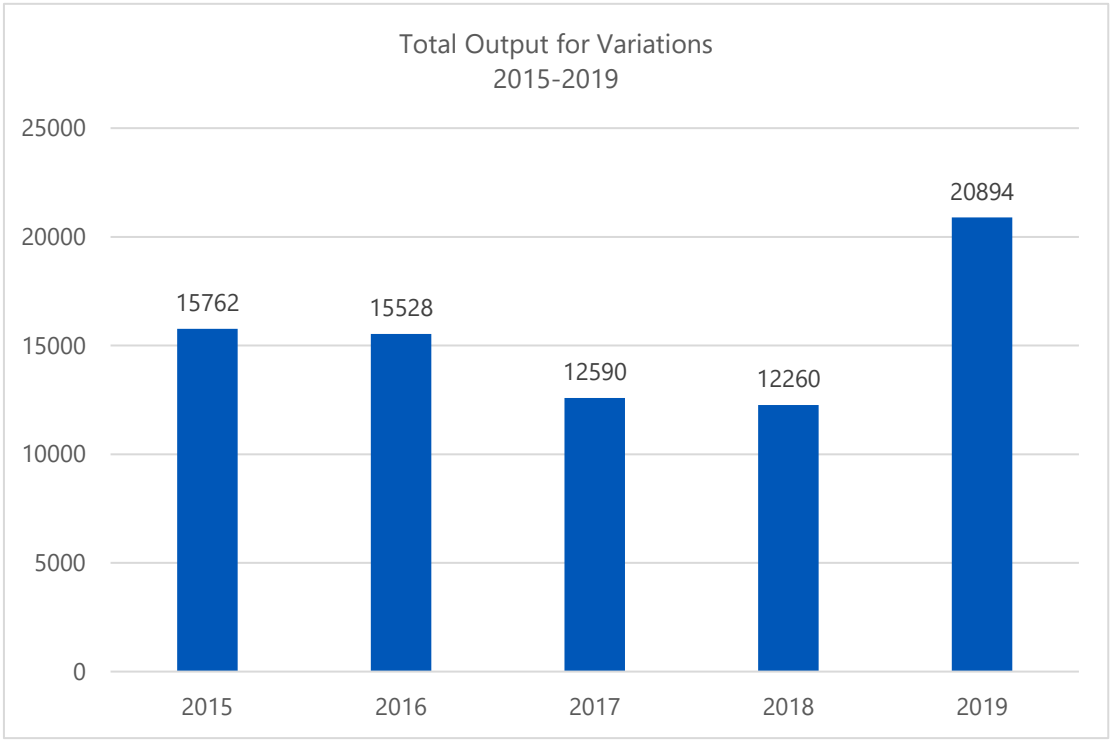
- A proactive approach to switching is ongoing. Following a review of policies in this area, and after liaison with the Department of Health, the HSE Health and Wellbeing Directorate and healthcare professionals, the HPRA has taken a proactive approach to the reclassification of medicines since 2014. 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.

The following graphs outline the output across all application types up to the end of 2019.




Total Output for New Applications 2015-2019
1000
900
800
700
600
500
400
300
200
100
0
2015
2016
2017
2018
2019


Total Output for Variations
2015-2019
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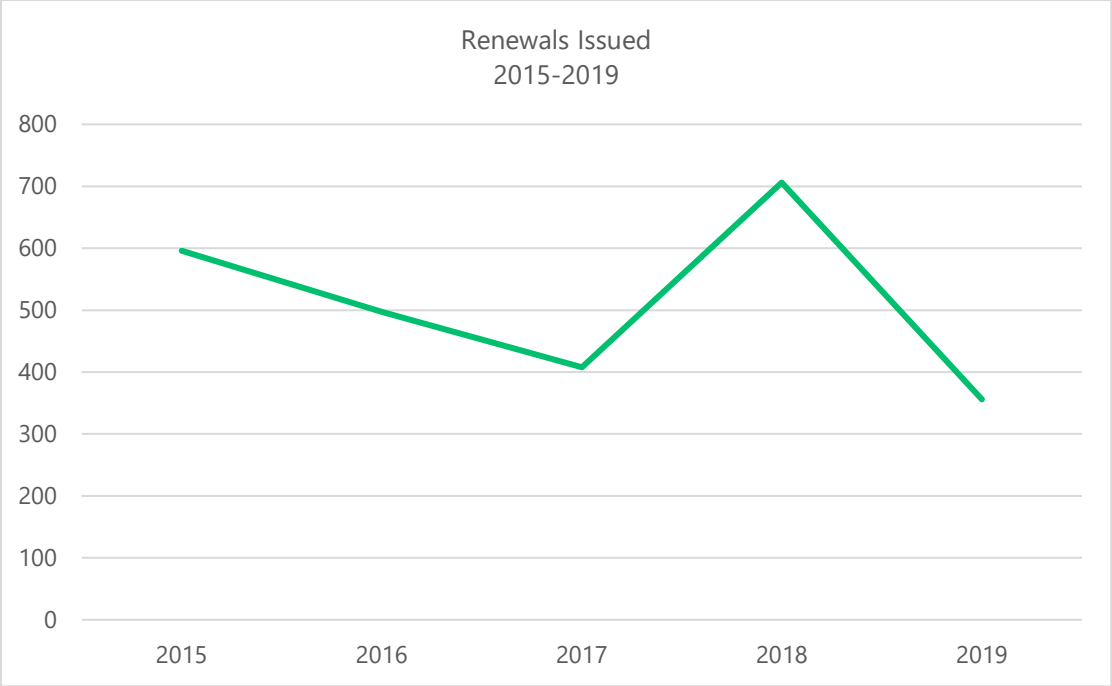
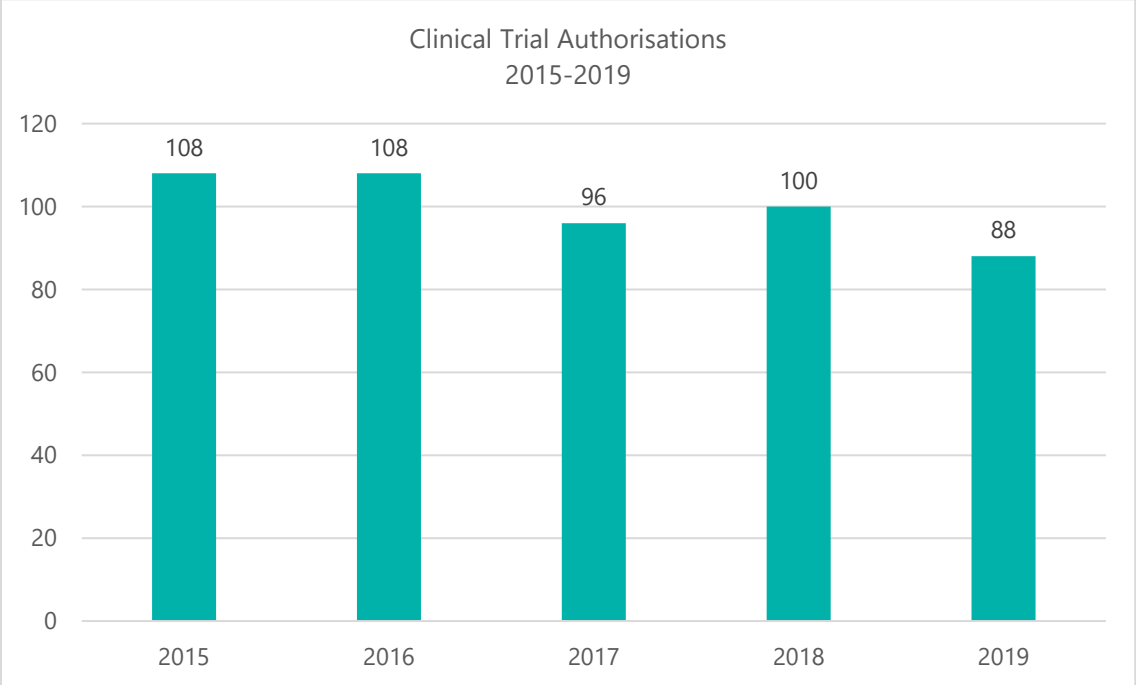
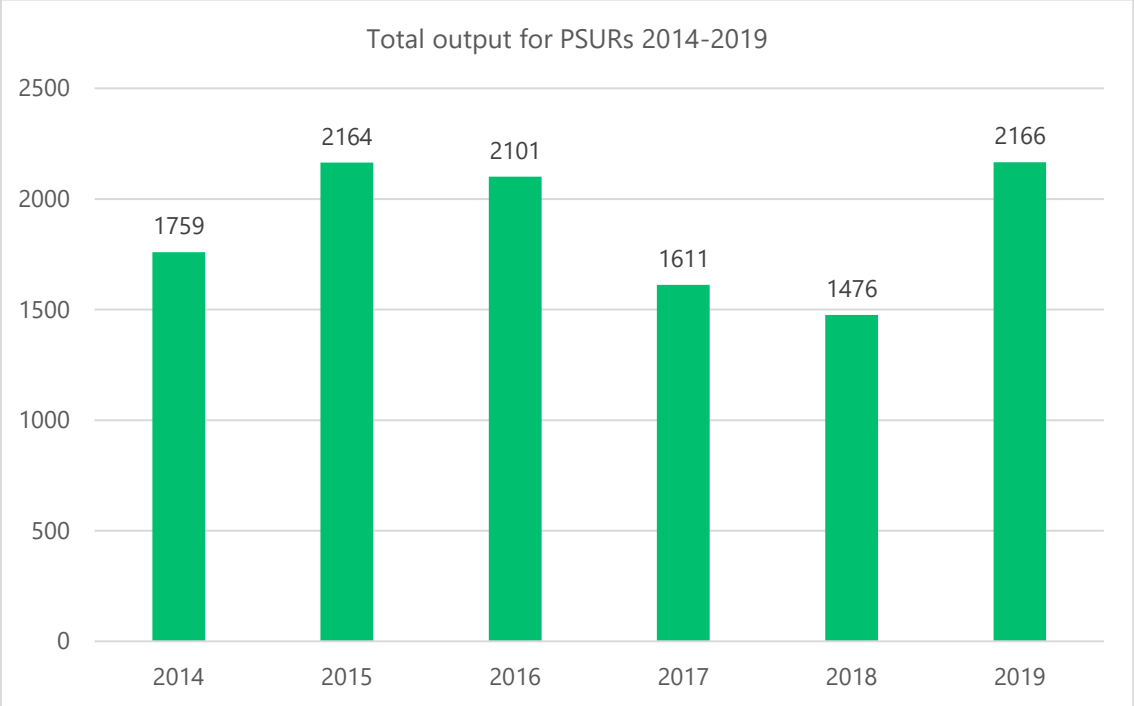
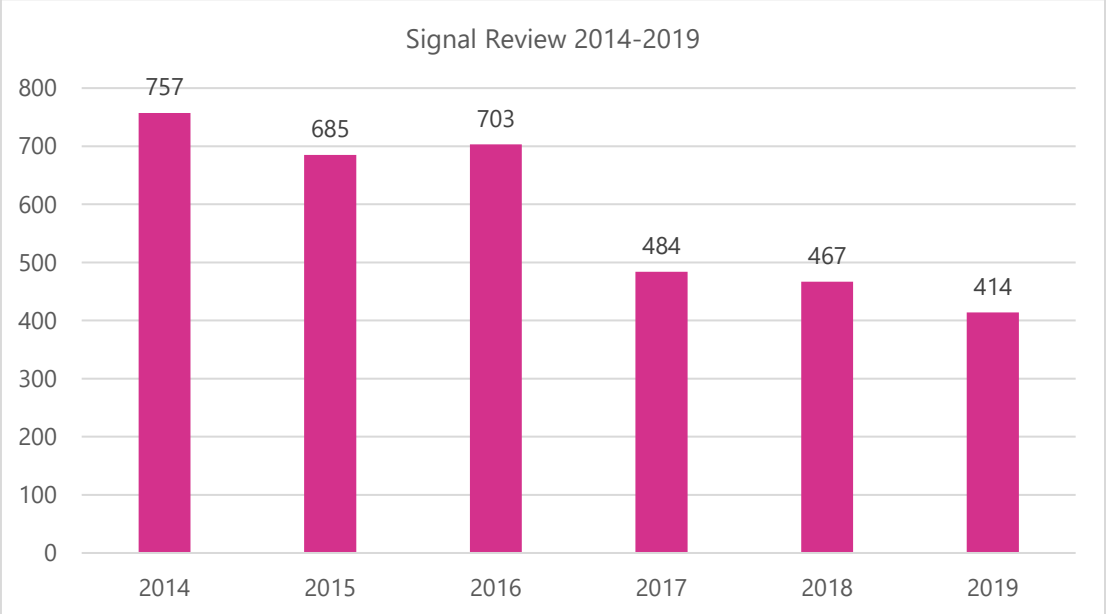
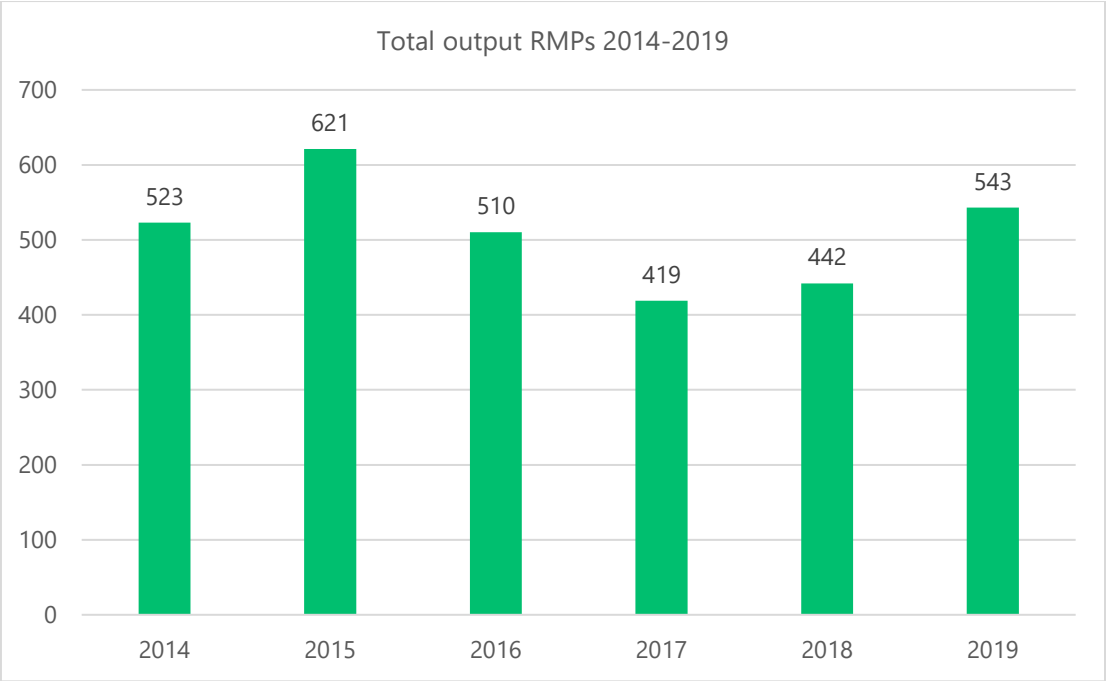
20000
15000
10000
5000
0
15762
15528
12590
12260
20894
2015
2016
2017
2018
2019


Renewals Issued
2015-2019
800
700
600
500
400
300
200
100
0
2015
2016
2017
2018
2019


Clinical Trial Authorisations
2015-2019
120
100
80
60
40
20
0
108
108
96
100
88
2015
2016
2017
2018
2019


Total output for PSURs 2014-2019
2500
2000
1500
1000
500
0
1759
2164
2101
1611
1476
2166
2014
2015
2016
2017
2018
2019


Signal Review 2014-2019
800
700
600
500
400
300
200
100
0
757
685
703
484
467
414
2014
2015
2016
2017
2018
2019


Total output RMPs 2014-2019
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500
400
300
200
100
0
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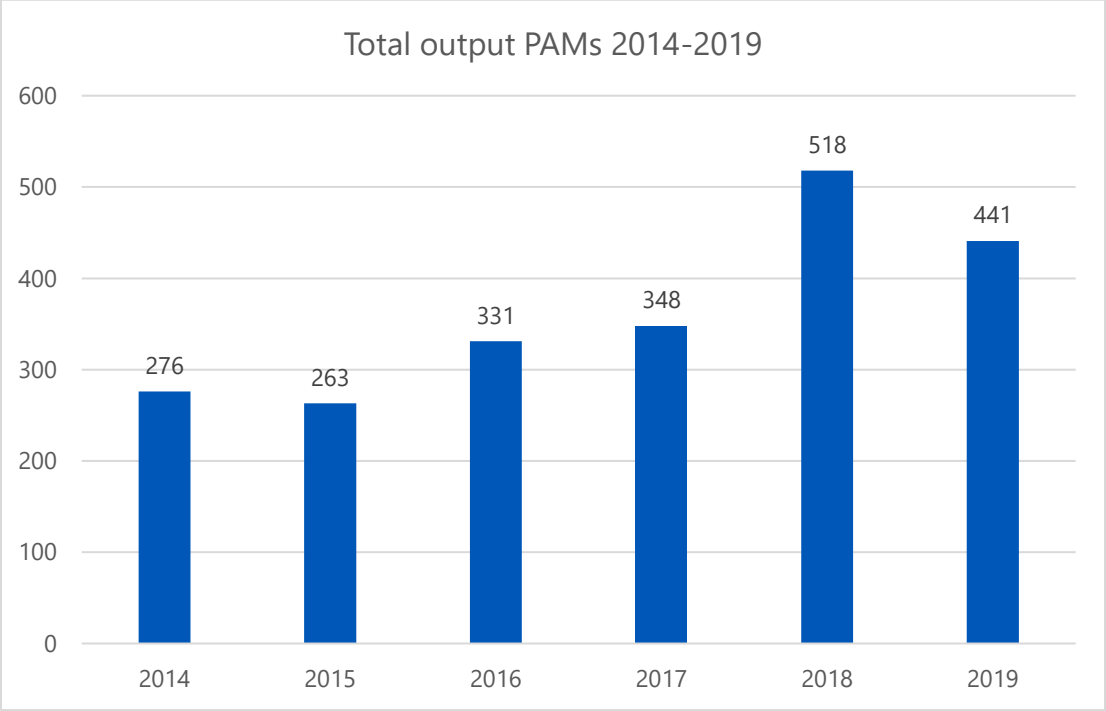
621
510
419
442
543
2014
2015
2016
2017
2018
2019


Total output PAMs 2014-2019
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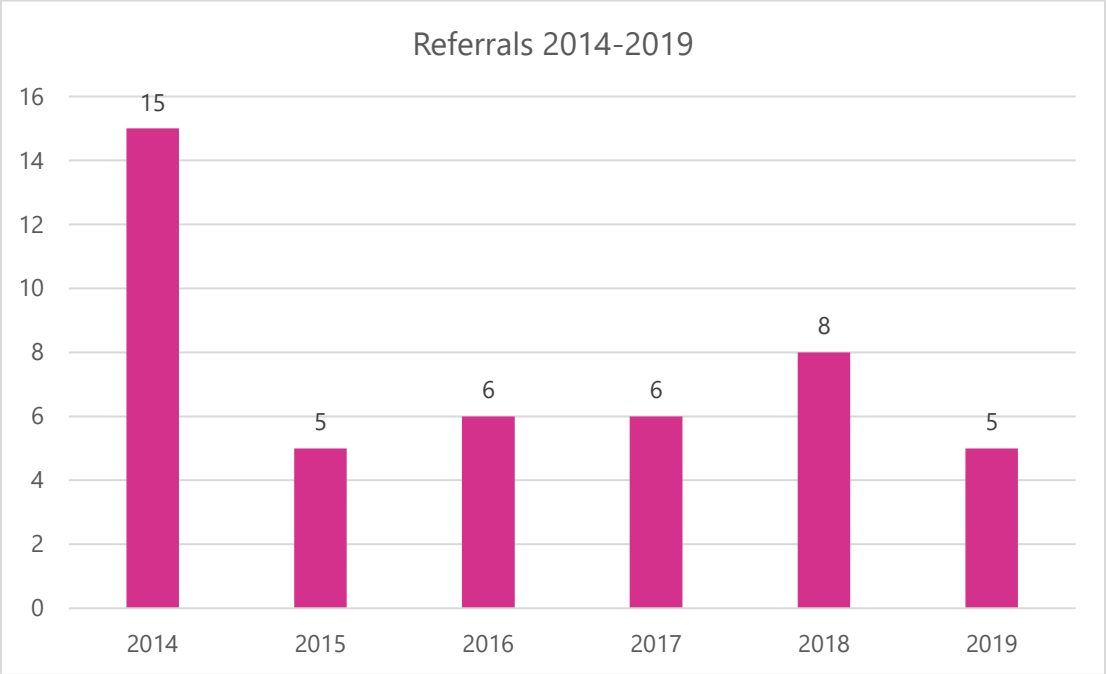
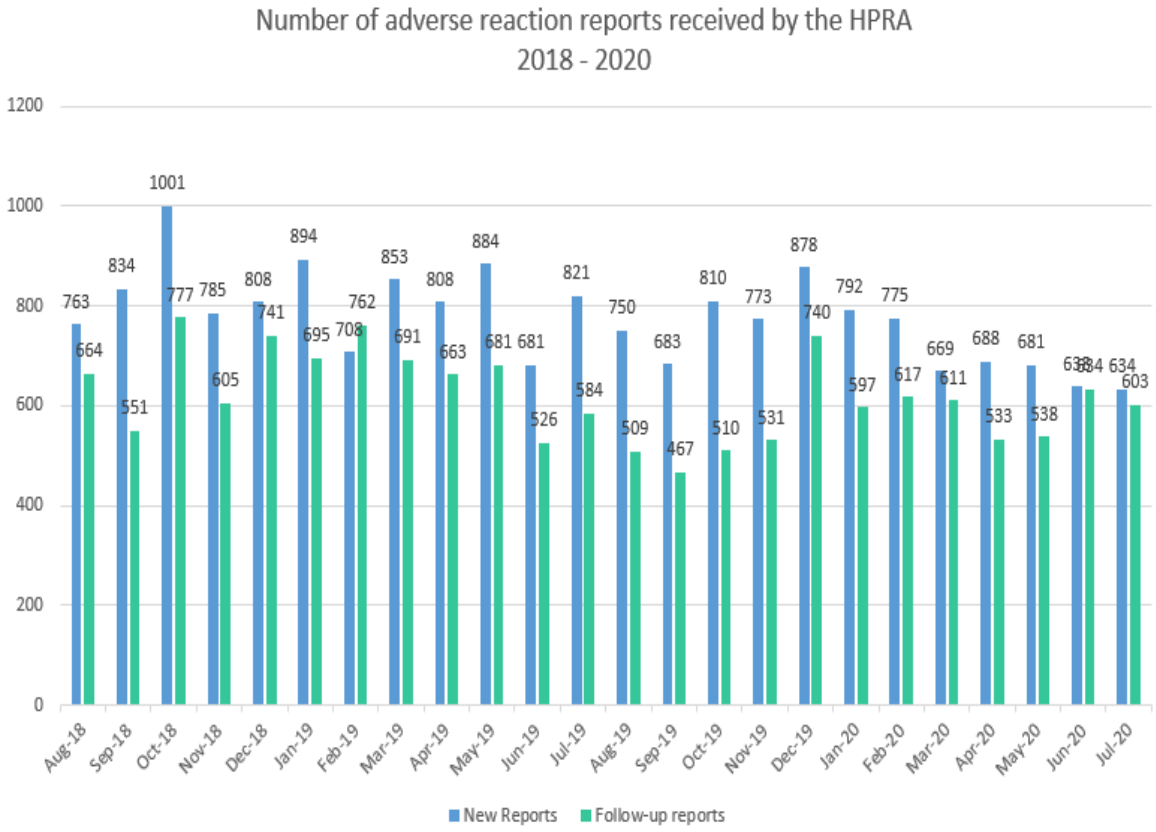
500
400
300
200
100
0
276
263
331
348
518
441
2014
2015
2016
2017
2018
2019


Referrals 2014-2019
16
14
12
10
8
6
4
2
0
15
5
6
6
8
5
2014
2015
2016
2017
2018
2019


Number of adverse reaction reports received by the HPRA
2018 - 2020
1200
1000
800
600
400
200
0
763
664
834
551
1001
777
785
605
808
741
894
695
762
708
853
691
808
663
884
681
681
526
821
584
750
509
683
467
810
510
773
531
878
740
792
597
775
617
669
611
688
533
681
538
634
603
Aug-18
Sep-18
Oct-18
Nov-18
Dec-18
Jan-19
Feb-19
Mar-19
Apr-19
May-19
Jun-19
Jul-19
Aug-19
Sep-19
Oct-19
Nov-19
Dec-19
Jan-20
Feb-20
Mar-20
Apr-20
May-20
Jun-20
Jul-20
New Reports
Follow-up reports

APPENDIX II SERVICE LEVELS – COMPLIANCE DEPARTMENT

Compliance Department General Activities

Initiatives undertaken/further developed in 2019/2020 included:

- Preparations for Brexit, in conjunction with other departments across the organisation, have included:
  - Continued engagement with stakeholders with the primary purpose of maintaining supplies of health products through and beyond Brexit.
  - 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.
  - 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.
  - Meetings with industry representative bodies, and attendance at workshops organised by some of those bodies, in order 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 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.
  - Liaison with other agencies, including the Health Service Executive and Revenue's Customs Service, on issues of mutual interest.
- In the year 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. In this capacity we chair teleconferences and produce inspection procedures and aides memoire.
  We also participate in a National Implementation Group, convened by the Department of Health, 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 envisaged that this transition will be resumed in the latter part of 2020
- 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 transposition and implementation of national legislation on quality and safety of human tissues and cells regarding the single European code (Commission Directive (EU) 2015/565 amending Directive 2006/86/EC) and importation requirements (Commission Directive (EU) 2015/566 implementing Directive 2004/23/EC as regards the procedures for verifying the equivalent standards of quality and safety of imported tissues and cells)
- 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 was scheduled to become fully operational in September 2020.
- 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 53 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.

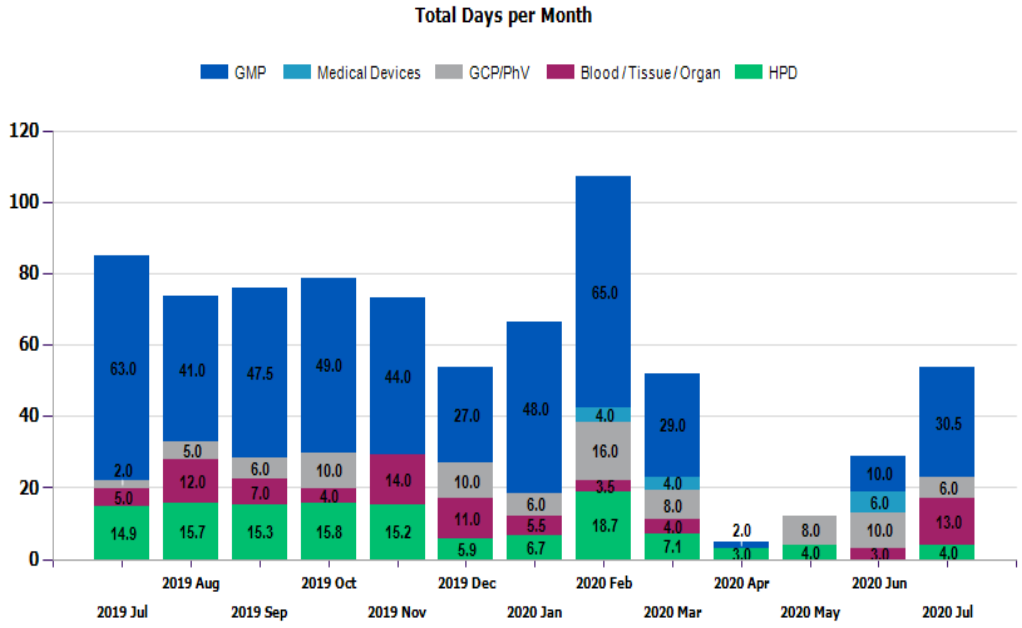
Other activities included:

- Continued interaction and communication with stakeholders, including industry and other representative groups. These included meetings (some 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

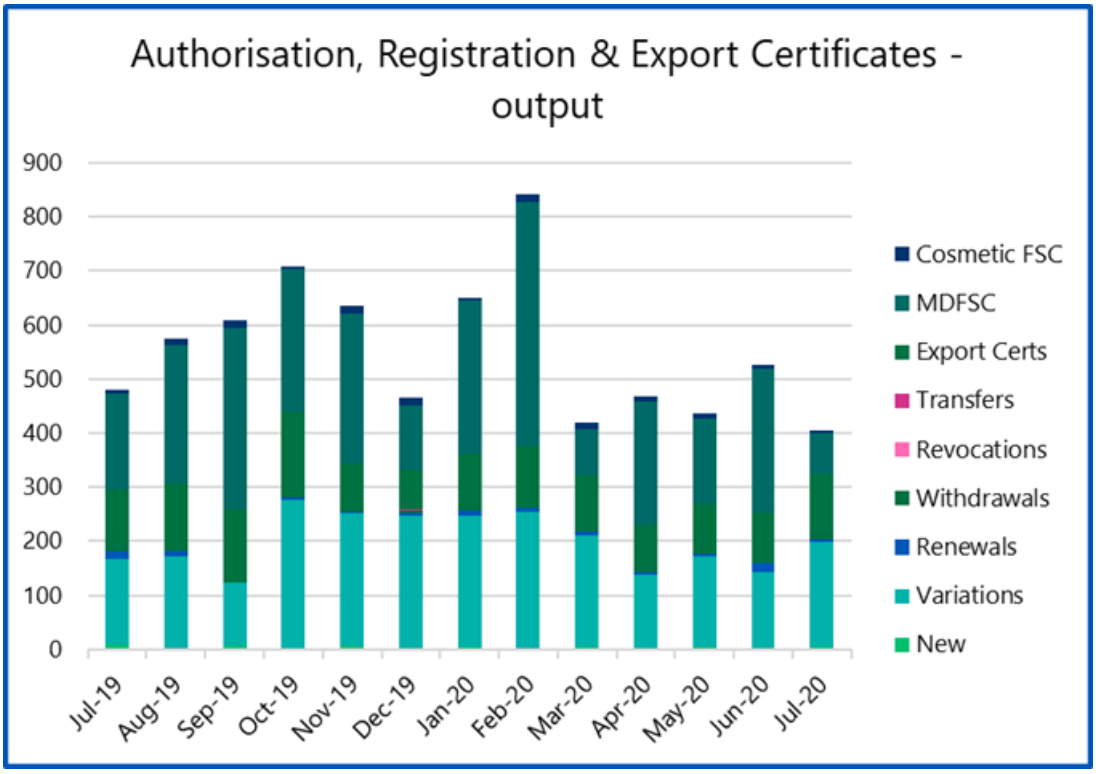
continue to serve as a source of relevant information for the Quality Defect and Recalls programme.

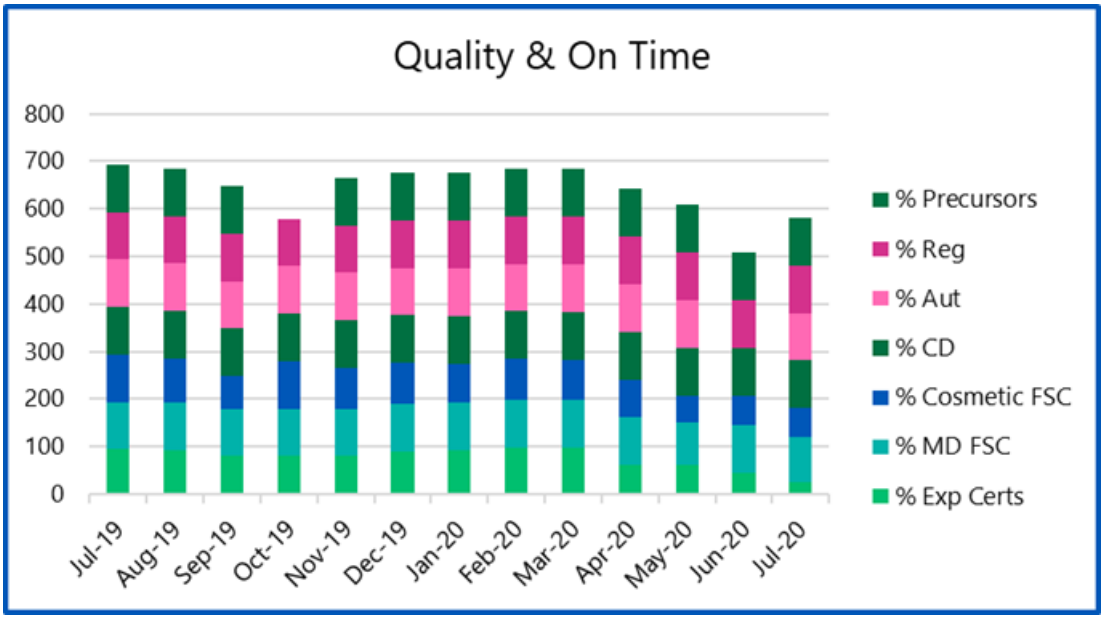
- Efficient turnaround of applications for variations to manufacturers' and wholesalers' authorisations, and for export certificates (medicines, medical devices and cosmetics) and controlled drugs licences.
- Further development of good clinical practice, bioequivalence and pharmacovigilance inspections.
- 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 2019 to month-end July 2020.

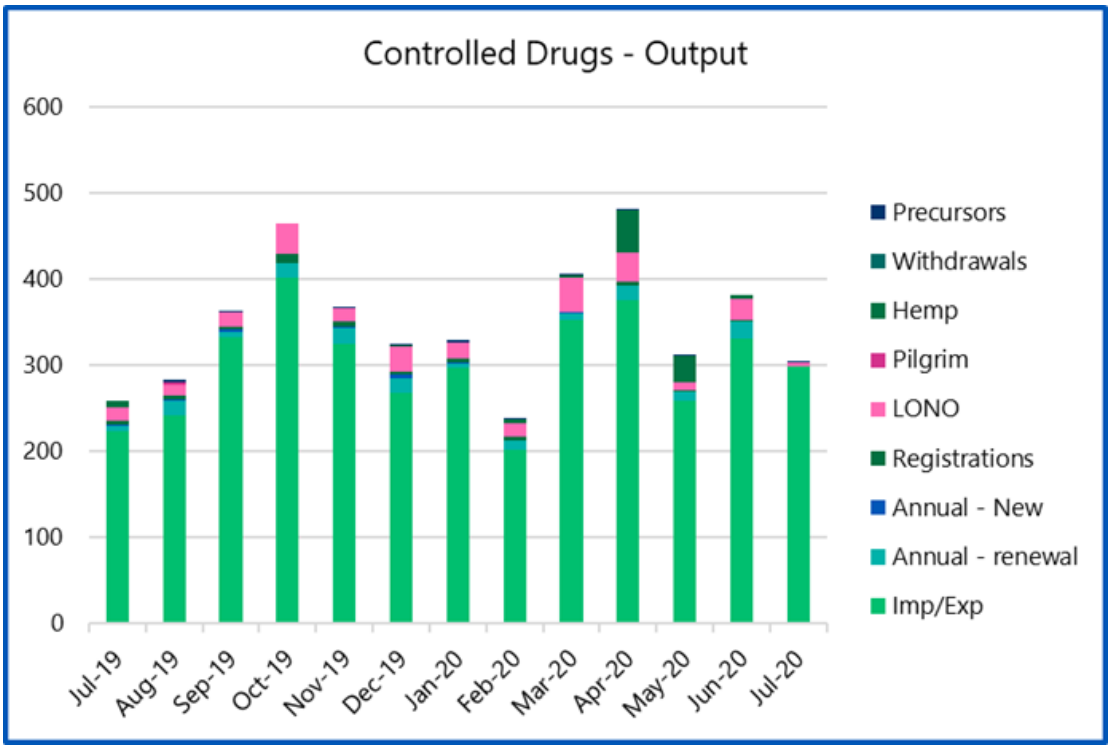


The following graphs show the numbers issued and the percentages issued on time, for export certificates, controlled drugs licences and GDP, GMP and IMP licences, over the period July 2019 to July 2020, inclusive.

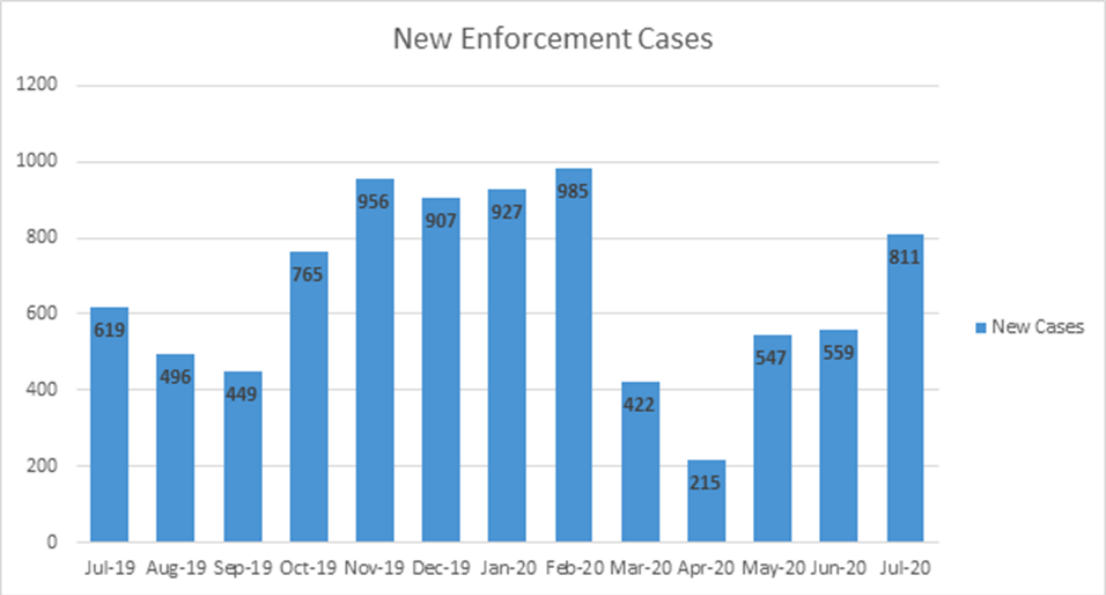




The graph below shows the output of licensing of controlled drugs, by category of licence.



The graph below shows the number of enforcement cases for the period July 2019 – July 2020 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 2019 and 2020 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.