HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Annual Review and Proposal for Fees – Financial Year 2015 (Human Medicines, Compliance Activities, Blood, Tissues and Organs Establishments, and Medical Devices)

08 OCTOBER 2014

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1 INTRODUCTION

Since its establishment in 1996, the HPRA (formally the Irish Medicines Board [IMB]), has successfully run its core 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 they arise. This is both a requirement under the IMB 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. In the last 5 years the country has experienced an economic crisis which has created a difficult operating environment for both the HPRA and stakeholders. The HPRA has also experienced a period of considerable increase in its workload arising from both European and new national legislation. In addition the HPRA is faced with managing reduced exchequer funding and managing increased workloads within the context of staffing constraints imposed by the government recruitment moratorium.

The first aim, in respect of fee income for the HPRA must be to match resources from fees with current work volumes and plan for future activity. The second aim must be to provide predictable, stable timelines and costs of the regulatory system that we operate.
To ensure that we manage the business properly we have agreed that we would review our fees on an annual basis to reflect changes to our cost base and service levels. This document summarises the outcome of our 2014 review of fees and it also sets out the current service levels and activities and expected changes in service levels and activities for 2015.

2 REVIEW OF THE 2014 FEES

In 2011 and in 2012 the HPRA substantially reduced the fees across a wide range of fee categories. In 2013 and 2014 the HPRA froze fees across the board and implemented some reductions in certain areas.

3 SUMMARY OF CHANGES PROPOSED FOR 2015

The HPRA, like all its stakeholders, is operating in a different economic environment. The regulatory regime was changed in 2013 and 2014, was the first full year of operations in relation to the implementation of the four new directives (outlined in section 5 below) and national legislation in relation to generic substitution. These changes to the legislative framework significantly increased the workload of the HPRA and necessitated additional resources without a corresponding increase in income.

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

A review of income levels across all categories has shown fluctuation, both increases and decreases in various income categories. It seems however that the fall in income experienced over the last number of years has halted and there are signs of recovery in certain sectors. The HPRA's pricing levels are dependent on volumes and, while we have some capacity to reduce costs, when the volume falls the cost per unit increases and this has been a significant problem for the HPRA over the last number of years. Given the substantive level of fee reductions that the HPRA has delivered since 2011, the Authority is not in a position to further reduce the fees. In addition, given the increased regulatory activity in the longer term, it is possible that fees may need to rise. However, the HPRA is aware of the Government's aim to freeze fees in respect of government agencies in 2015, consistent with the slight recovery in some income categories. Therefore the HPRA are committed to keeping fees to a large extent at 2014 levels. This is despite the substantial increase in HPRA responsibilities arising from new legislation which is outlined below in Section 5. The detail and basis for the changes to this year's fees are outlined in Section 7 of this report.

3.1 Medical devices

A new fee model for medical devices has been developed and is currently being discussed with industry, government and other stakeholders. These new fees (which are proposed for 2015) will be the subject of a separate consultation. It has been recognised for some time that the model whereby the exchequer funds the regulation of medical devices is not sustainable in the longer term. In addition to the new fee model which looks at the totality of the regulation of medical devices, currently, there are also medical device fees in place for certain services. For 2015, it is proposed that these medical devices fees will remain unchanged from 2014.

The new proposed fees for medical devices are in the context of changes to the regulation of medical devices arising, amongst other issues, from a number of high profile issues such as the PIP breast implants and metal-on-metal hip joints enquiries, which have placed a spotlight on the medical device sector. EU Commissioner Dalli has already required that regulatory oversight is increased with a corresponding increase in the resources required by the HPRA. The Medical Devices Directives are to be re-cast in 2015/2016 and there is recognition at a European policy level that fees will need to be levied on the industry, to allow for the level of oversight necessary to ensure safe medical devices on the European market.

3.2 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 8 months of 2014. 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 recession being experienced by both the Irish and worldwide economies means that forecasting is extremely difficult and subject to change.

The HPRA has been able to freeze fees due to the continued management of its cost base. However as noted above, the HPRA are experiencing increased workloads and will have to re-appraise fees in 2015 for the 2016. The HPRA therefore commits to review the proposed fees during the planning cycle in 2015 and further amend the fees and fee structure, if required for 2016.

4 FINANCIAL POSITION IN 2014

While new national applications continue to fall we have seen an increase in new Decentralised Procedure (DCP) and Mutual recognition (MR) incoming applications and also, as part of the HPRA's service offering, an increased the number of outgoing DCP/MRPs. DCP/MR variations continue to fall but national variations have picked up. Overall, while income levels are considerably below 2011 levels, there are some signs of recovery. General costs have stabilised at the 2011 cost base, which reflected the fact that HPRA had negotiated costs downwards to echo the prevailing economic climate. The HPRA's cost base is approximately 70% staff costs. In recognition of the additional responsibilities that the HPRA has undertaken in 2013 and 2014, staff numbers have increased and additional costs have been absorbed, without increasing fee income in 2014 and 2015. It should also be recognised that the salary cost of HPRA has been artificially suppressed with substantive pay cuts across all grades for the last 5 years and with a recovering job market, HPRA is already starting to lose key senior members of staff as salaries are falling below the market place. If HPRA is to continue to deliver the service industry requires it will need to be in a position to recruit staff with the appropriate expertise, at the appropriate salary level. This will impact directly on the HPRA future cost base. Although a surplus is expected at the year-end, the HPRA has entered a period of significant IT expenditure following an IT strategic review of the organisation's needs and existing IT framework. The existing work flow systems are now over 10 years old and cannot be supported in the longer term. Given the importance of IT in the HPRA's service delivery, a three year programme has been initiated to replace all the work flow and stakeholder facing systems to continue providing a "best in class" service. The investment in IT and infrastructure has delivered and will continue to deliver long-term savings and efficiencies.

As noted above HPRA saw a reduction on payroll from the Haddington Road agreement but as stated we believe that without some change to this, the current levels of salaries have the capacity to impact negatively on the ability of the HPRA to retain staff. It should also be noted in relation to payroll costs that the HPRA has a significantly unfunded pension liability and it is proposed that savings arising from salary reductions will be allocated against future pension liabilities.

5 FINANCIAL CHALLENGES IN 2015

The HPRA will face significant financial challenges in 2015. In common with all commercial organisations, the HPRA is facing challenges from the recession. These challenges are compounded by the continued reductions in government funding and increased workloads. In 2015 the regulatory environment will continue to change with the further implementation of the Falsified Medicines Directive[2], the introduction of the Cosmetics Regulations and further development of vigilance under the Pharmacovigilance Directive[3] . These directives significantly increase the regulatory role of the HPRA and require additional resources without a corresponding increase in income. In 2013, the HPRA also became competent authority under the Protection of Animals Used for Scientific Purposes Directive[4] and the Organs Donation and Transplant Directive[5]. While the latter two activities are currently funded by the Department of Health, there is considerable pressure on exchequer funding.

A further challenge for the HPRA in 2015 is managing the requirements under the Health (Pricing and Supply of Medicinal Goods) Act, 2014 where the HPRA is responsible for developing the list of interchangeable medicinal products. While the legislation provides for a fee, much of the preliminary work will be un-funded.

Despite the challenges arising from the recession and the increased regulatory responsibilities, the HPRA must also continue to invest in and deliver services to stakeholders. In 2015 the HPRA must make substantive investments in its IT systems. The HPRA has developed its IT capacity and delivers 'best in class' service across the European regulatory environment. However, an external review of the IT strategy identified that considerable investment in IT systems and people is required if the HPRA are to continue to deliver and develop this service. In particular, the core workflow and medicinal product database system is 10 years old and can no longer support the needs of the organisation into the future. In line with the IT strategy, we will commence the orderly replacement of this system in 2015; given the size and complexity of the system this will represent a very significant investment in IT. In addition the new activities and responsibilities deriving from the legislation will result in further investment in IT systems.

A strategic plan has been completed for the years; 2011 to 2015, which continues to place patient safety at the centre of the HPRA's work, provides a road map for the organisation and

[2] Directive 2011/62/EU

[4] Directive 2010/63/EU

[5] Directive 2010/53/EU

identifies those areas where investment in resources must take place, in order to deliver better regulation to all the stakeholders. The HPRA must continue to invest in the business to ensure that it continues to regulate for a positive benefit risk of medicines to patients and a regulatory environment which supports industry through an effective and predictable regulatory framework.

6 PROPOSED FEES

As outlined above, fees for the year 2015 will be frozen, despite financial pressures on the HPRA finances.

7 DETAILED CHANGES TO FEES

7.1 General changes to fees

It is proposed that there will be **no general** increase applied to any fees.

7.2 Other proposed adjustments to fees human medicines

7.2.1 Annual maintenance fee

It was stated in the 2013 consultation document that HPRA would consider an increase in the Annual Maintenance fee in 2015 to cover additional work generated from the outcome of the PV legislation. Industry has proposed that any increase should only affect active licences and that fees should be maintained at the 2014 level or reduced for non marketed licences.

It was agreed that the Annual Maintenance fee would not be increased in 2015 but an increase would again be considered in 2016 for active licences.

7.2.2 Type IA variations

A proposal was received from industry seeking the removal of the fee for Type IA – C.I.3.A variations. Following consideration of the matter it was agreed to leave this fee in place for 2015 as these variations were not envisaged when the current fee regime was put in place.

It was also discussed whether a fee would be considered for Type IA – C.I.1 applications. It has become evident that there is an increased amount of assessor time spent on processing these applications. However it was agreed not to charge for C.I.1 type IA applications.

It was agreed that both points could be addressed as part of the review of the maintenance fee for 2016.

7.2.3 Interchangeable medicines

A proposal from industry to increase the current fee from €500 to €1,500 was considered.

It was agreed that the HPRA would not increase this fee and the current fee of €500 would remain in place. However, if it transpires that the resource requirements have been underestimated, the HPRA will review this fee in 2016.

7.2.4 Type II changes to the SmPC

It was proposed by industry that there would be a single fee to cover all changes to the MA submitted at the same time. Industry also stated that the caps in place are set too high.

It was agreed that the existing method of charging fees and the level of caps on the fees for multiple variations was appropriate.

7.2.5 Regulatory/scientific advice (pre-submission cases)

It was noted that HPRA staff provide regulatory advice and pre-submission meetings with companies on a regular basis without charge. Where a company submits a dossier/application for a pre-submission review, there is considerable work involved in preparing a file for MRP with work carried out by both assessor and administrators.

It was proposed and agreed that the relevant full new application fee be paid up front for pre-submission applications and if the application is subsequently withdrawn a refund may be considered on a case by case basis according to the level of work completed.

7.2.6 Pre-assessment of product names

The HPRA has been asked to consider introducing a pre-approval process for changes in product names prior to submission of the necessary variation.
This is currently been considered and if implemented a type IB variation fee will be applied and paid in advance.

7.2.7 Work sharing variations

It was noted that the HPRA currently charges the appropriate national or MR/DCP variation fee for national products included in a centralised work sharing procedure. No fee is payable to the EMA for any national marketing authorisations included in a centralised work sharing procedure.

It was agreed that this was the correct way to charge for these procedures.

It was also confirmed that work sharing variations should be charged for different product ranges (per product range and per change).

7.2.8 Complex variations

It was confirmed that a fee should be charged per PA per change – two full fees and reduced fees thereafter. However it was noted that the caps would be applied if the variation cost rose higher than €5,200 per product range and €3,400 per PA.

7.2.9 Ad hoc queries

It was noted that we have received a large number of queries relating to the legal basis under which products are authorised. Accessing this information often requires calling back the dossier from archive and can be labour intensive.

It was agreed that a fee of €73 per hour (fee code 393) would be charged for this and any other ad hoc queries which require a resource input.

7.2.10 Repeat use administrative procedure

In relation to small countries with medicines shortages, the HPRA will act as RMS in a repeat use procedure subject to the CMS accepting an administrative procedure. It was agreed that a fee of €1,489 (code 391) is the appropriate fee and this is to be documented in the Guide to Fees.

7.2.11 Homeopathic Registration variations

It was noted that we can receive variations to the homeopathic master file which can often cover a large number of registrations resulting in a large fee.

It was agreed that a new fee of €2,038 be introduced as a cap for bulk homeopathic variations to the master file.

7.2.12 Herbal medicinal products – Variation fees

Currently HPRA have no fees for herbal variations and currently the normal human medicines fees apply. It was discussed and agreed that the following herbal variation fees be introduced:

National Variations	Fee
Type IB	€375
Type IB reduced	€190
Type II Standard	€400
Type II Standard reduced	€200
Type II Complex	€2,100
Bulk variation for multiple changes	€4,200

MR Variations	Fee
Type IB – Ireland is CMS	€270
Type IB reduced – Ireland is CMS	€140
Type IB – Supplement where Ireland is RMS	€275
Type II Standard – Ireland is CMS	€270
Type II Standard reduced – Ireland is CMS	€140
Type II Standard Supplement - RMS	€270
Type II Complex – Ireland is CMS	€1,435
Type II Complex supplement - RMS	€420

These fees represent a reduction of 20% on the human medicines fees reflecting the HPRA approach to the licensing of herbal medicines in this transition phase.

7.2.13 Designation of Notified Bodies

It was agreed that the designation fee for Notified Bodies would also apply to designation renewals of notified bodies under the new Implementation Regulation 920 of 2013.

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

The most significant projects undertaken by the HPRA in the last three years are driven by the requirement to maintain and further improve patient safety and service levels to industry. These projects include in summary:

- Continued refining of the HPRA's operations to more effectively meet the needs of our stakeholders. Use of lean six sigma processing and capacity based resource allocation has facilitated improved management and increased efficiency of the assessment processes.

  Objectives included:
  - improved efficiency with maintenance of quality,
  - streamlined procedures and processes
  - improved transparency and standardisation of approach
  - ongoing increased productivity, and the continued management and reduction of backlogs

- Continued focus on improving and extending 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, improved utilisation of resource and drive further efficiencies

- Introduction of online reporting for adverse drug reactions and quality defects, accessible to patients, health care professionals and industry

- Continued customer-focused approach

- Development of HPRA's systems to support the generation of a listing of interchangeable medicines to enable the substitution of generic medicines, in line with the Health (Pricing and Supply of Medical Goods) Act 2013. In August 2013, the work on the publication of the interchangeable list commenced. By year end 11 pharmaceutical active substances were published to the interchangeable lists on the HPRA website. The initial approach to development of the list was based on inclusion of a number of priority substances identified by both the Department of Health and HSE as those which would provide the greatest cost saving to the healthcare system and patients. A total of 40 priority substances were identified.

- Focus on the continued provision of guidance and support to industry stakeholders in areas undergoing evolving regulatory development, including:
  - the new requirements under the pharmacovigilance legislation.
  - registration of traditional herbal medicinal products.

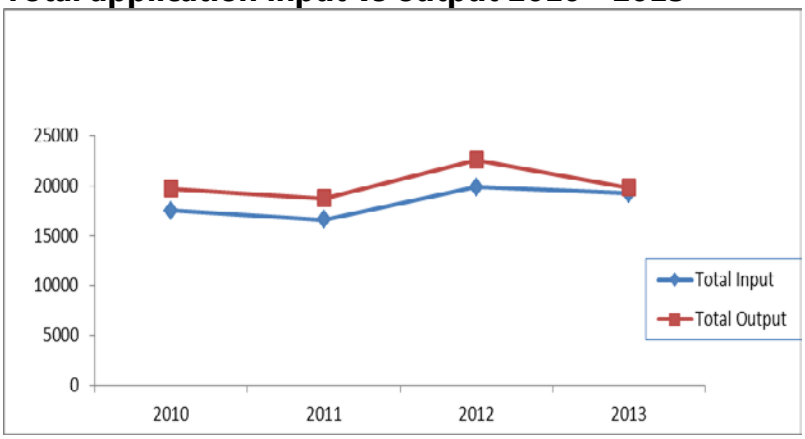
- interchangeable medicines.

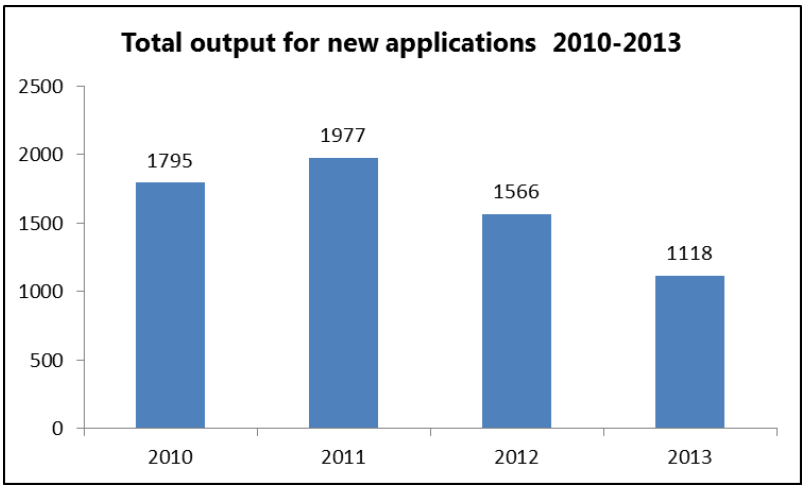
- Continued progression of a public health initiative focused on providing important online information about all medicines licensed by the HPRA. This includes maintaining publication of the summary of product characteristics document and the legal classification status of all human medicines on the HPRA website (www.hpra.ie).

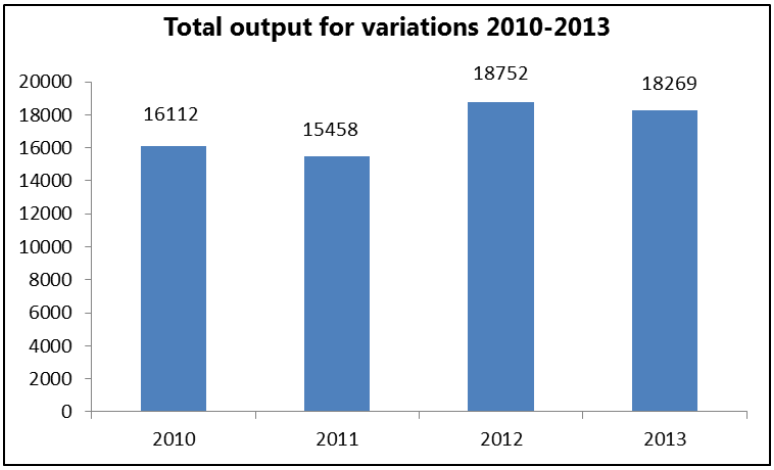
- Raising awareness of the regulation of medicines and important safety considerations via publications and contributions to undergraduate programmes in the medical and paramedical fields

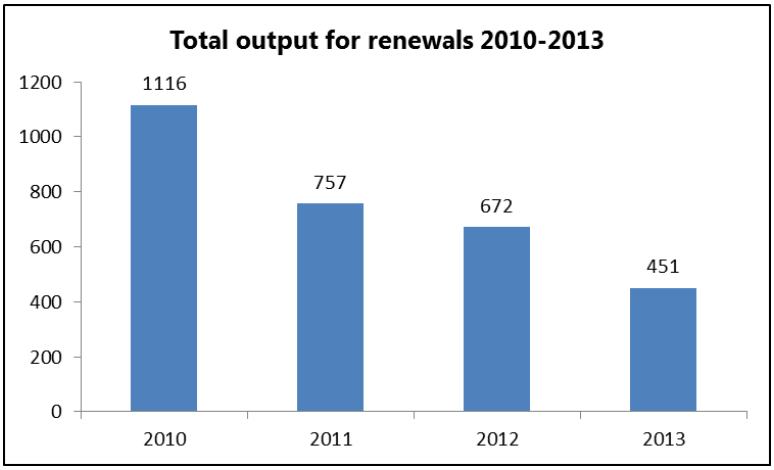
The graphs below outline the output across all application types up to the end of 2013.

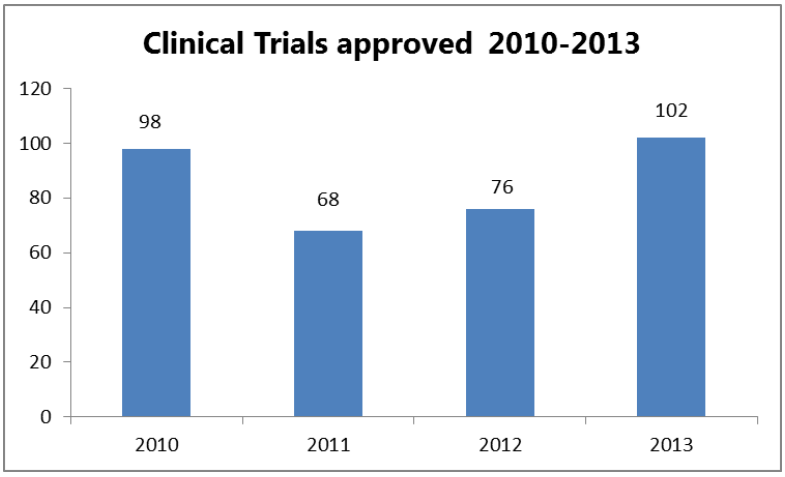
Total application input vs output 2010 - 2013

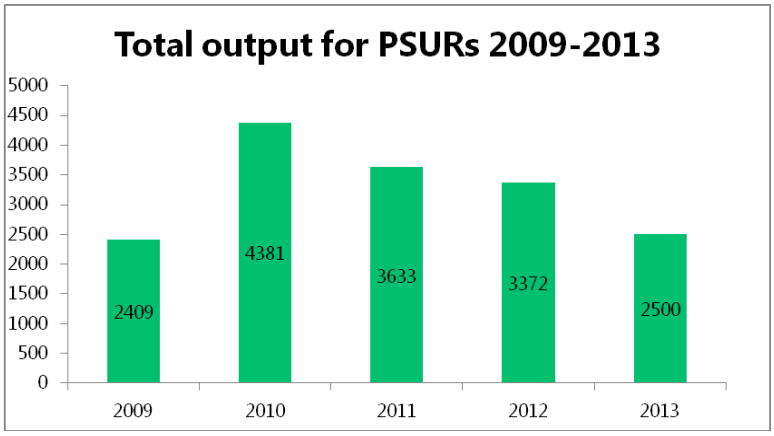


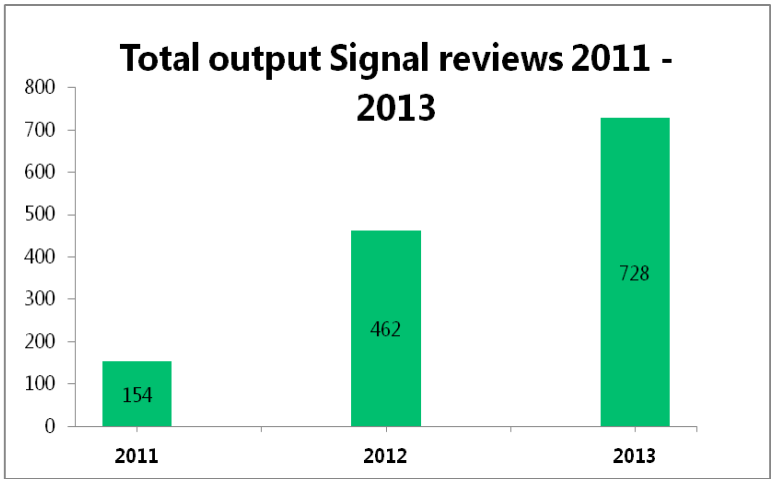



Total output for variations 2010-2013
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
16112
15458
18752
18269
2010
2011
2012
2013


Total output for renewals 2010-2013
1200
1000
800
600
400
200
0
1116
757
672
451
2010
2011
2012
2013


Clinical Trials approved 2010-2013
120
100
80
60
40
20
0
98
68
76
102
2010
2011
2012
2013


Total output for PSURs 2009-2013
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
2409
4381
3633
3372
2500
2009
2010
2011
2012
2013


Total output Signal reviews 2011 - 2013
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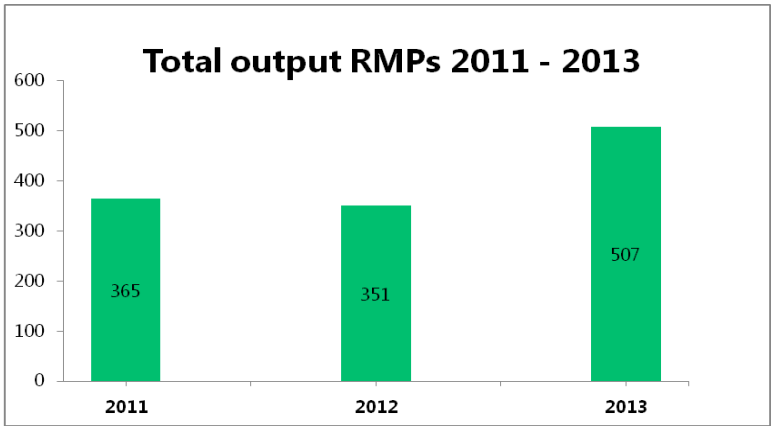
700
600
500
400
300
200
100
0
154
462
728
2011
2012
2013


Total output RMPs 2011 - 2013
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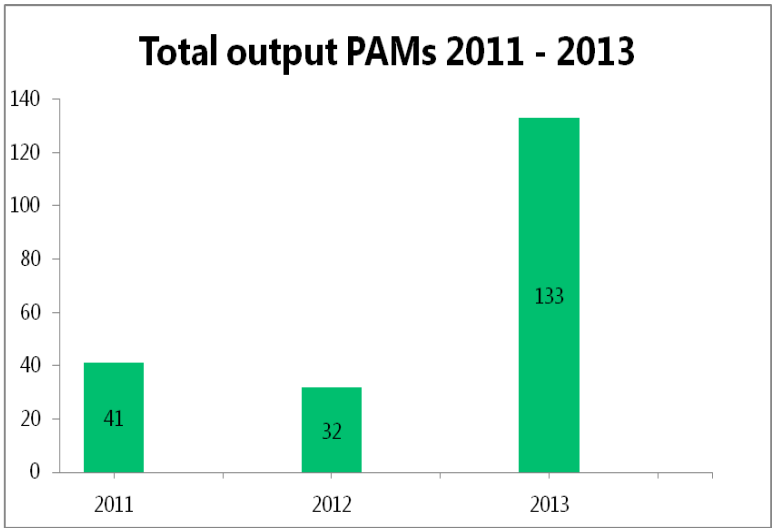
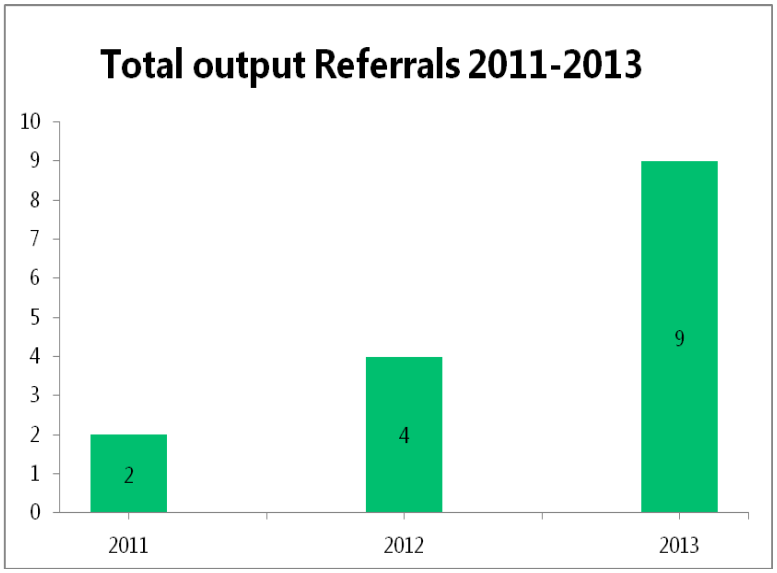
500
400
300
200
100
0
365
351
507
2011
2012
2013


Total output PAMs 2011 - 2013
140
120
100
80
60
40
20
0
41
32
133
2011
2012
2013


Total output Referrals 2011-2013
10
9
8
7
6
5
4
3
2
1
0
2
4
9
2011
2012
2013

APPENDIX II SERVICE LEVELS – COMPLIANCE DEPARTMENT

Compliance Department General Activities

Initiatives undertaken/further developed in 2013/2014 included:

- Further development of a workflow database for compliance case management to improve efficiency in processing authorisations/licences, organisation and follow up of inspections, quality defects and recall management

- Continued provision of support to the Department of Health on the drafting of national legislation aimed at preventing the entry of falsified medicines into the legal supply chain – transposition of Directive 2011/62/EU ('Falsified Medicines Directive' [FMD])

- Under the FMD, provisions were implemented during 2013 relating to registration of manufacturers, importers and distributors of active substances and brokers of medicines for human use. Annual updates to these registrations have been processed during 2014

- Under the FMD, participated in expert group on safety features convened by the European Commission. Updated Irish industry on key decisions and milestones relating to these requirements

- Continued upload of post inspection good distribution practice (GDP) certificates to the EudraGMDP database

- Commenced upload of Wholesale Distribution Authorisations (WDAs) and Manufacturers/Importers Authorisations (MIAs) to the EudraGMDP database

- Worked closely with European Commission, Heads of Medicines Agencies, European Medicines Agency (EMA) and competent authorities of other member states on FMD requirements around importation of active substances from non-EEA countries. Participated in Commission's evaluation of two non-EEA countries that applied for listing as having a regulatory system for active substance manufacture that is equivalent to that of the EEA. While, in the lead up to the 2nd July 2013, there was considerable concern that there would be shortages of imported active substances, these did not materialise. This was primarily due to the considerable work performed by the parties referred to above

- Provision of 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. Evaluation of applications for authorisations from transplant centres continued via inspections and other follow up measures. System for reporting and assessment of serious adverse events/reactions in place. Worked with the National Organ Donation and Transplantation Office (NODTO) of the HSE towards development of a framework for quality and safety or organs for human transplantation

- Liaised with wholesalers on the implementation of revised EU Guidelines on Good Distribution Practice of Medicinal Products for Human Use

- Monitoring, via inspections, of the implementation of Good Manufacturing Practice requirements, Good Distribution Practice, Good Clinical Practice, Good Pharmacovigilance Practice standards, and required controls relating to Controlled Drugs and Precursors

- Monitoring, via inspections, the activities of Marketing Authorisation Holder companies with respect to their obligations under the Medicinal Products (Control of Placing on the Market) Regulations, 2007, as amended

- Active participation in harmonising standards and inspection practices through EMA working groups, the Pharmaceutical Inspection Co-operation Scheme (PIC/S) Committee and its Expert Circle meetings

- Active participation in the work of the Official Medicines Control Laboratories (OMCL) network to promote risk-based approaches to surveillance programmes and effective work-sharing programmes

- Continued development of the advertising compliance monitoring programme which includes regular liaison with the industry to outline HPRA requirements and to clarify the HPRA's 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 products are identified

- Continued development of the role of competent authority for cosmetics. This has included maintenance of effective working relationships with the Department of Health, HSE and the National Consumer Agency and the implementation of a coordinated national approach to market surveillance and testing of cosmetics

- The National Cosmetic Safety Forum was continued by HPRA and 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

- The Cosmetics Regulation, 1223/2009, came into force in July 2013. Accompanying national legislation, the European Union (Cosmetic Products) Regulations, 2013 (S.I. No 440 of 2013) came into force in November 2013. The HPRA continues to work with the HSE and Department of Health on the implementation of these pieces of legislation

Other activities included:

- Continued interaction and communication with stakeholders including industry and other representative groups. These included meetings 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 to support the Quality Defect and Recall programme

- Rapid turnaround of applications for variations for manufacturers' and wholesalers' authorisations, and for export certificates and controlled drugs licences

- Further development of good clinical practice and pharmacovigilance inspections

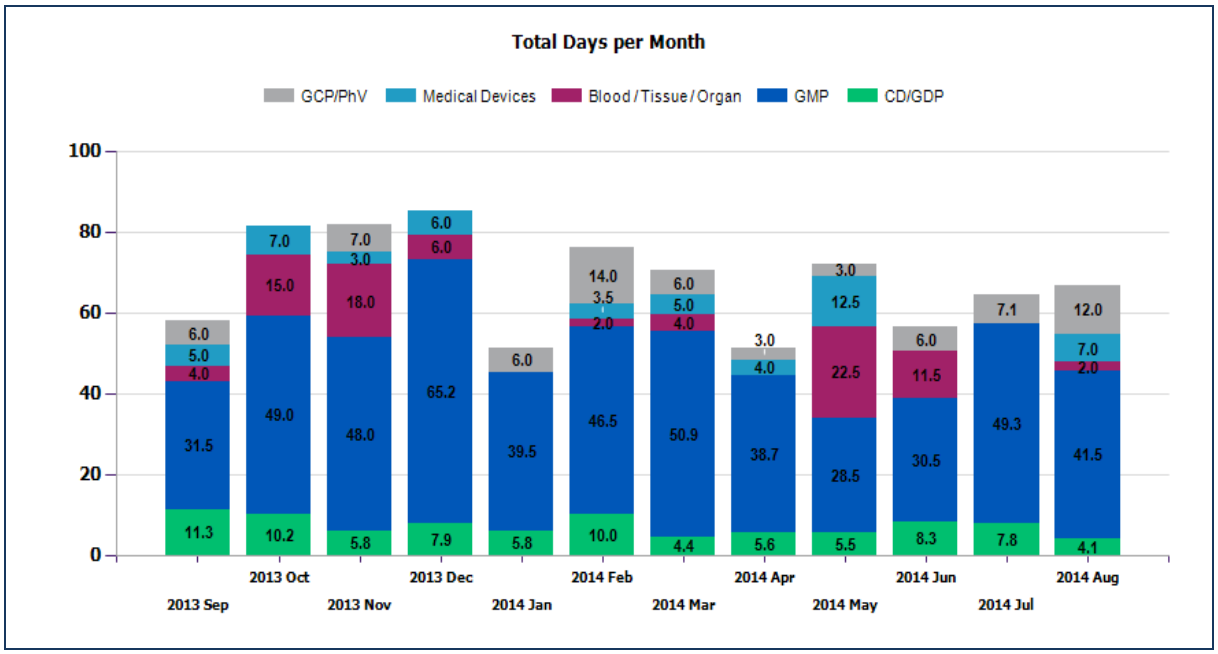
- Full programme of good practice inspections of blood and tissue establishments

- Continued strong focus, through good distribution practice inspections and enforcement activities, on the legitimate supply chain to prevent infiltration of falsified products

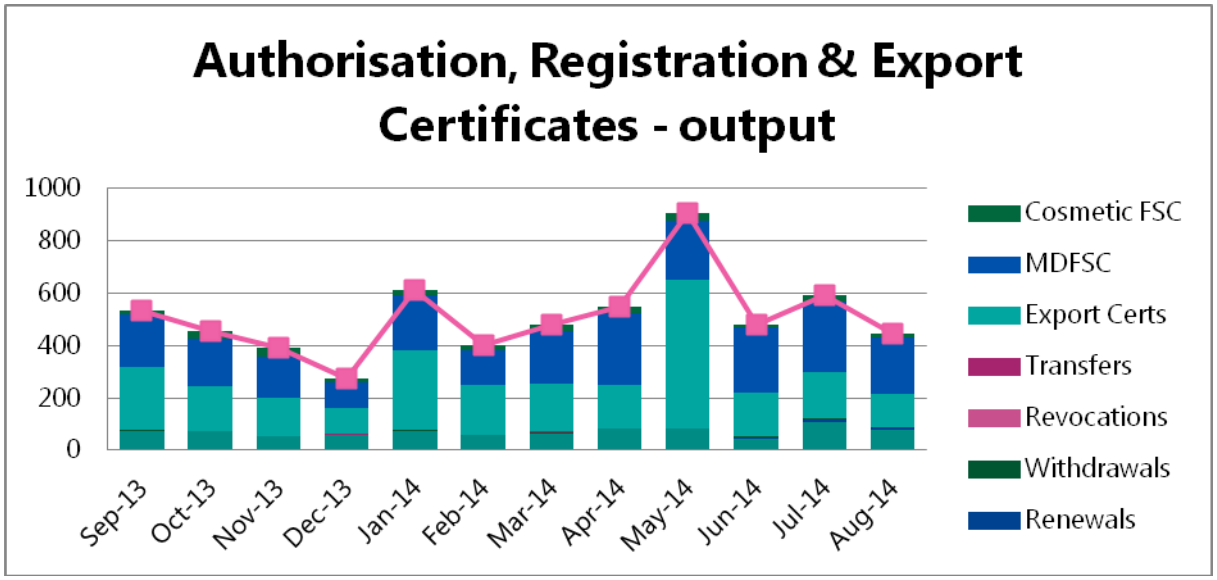
- Continued monitoring of the parallel export of medicines by wholesalers based in Ireland particularly relative to ensuring that the needs of Irish patients are met

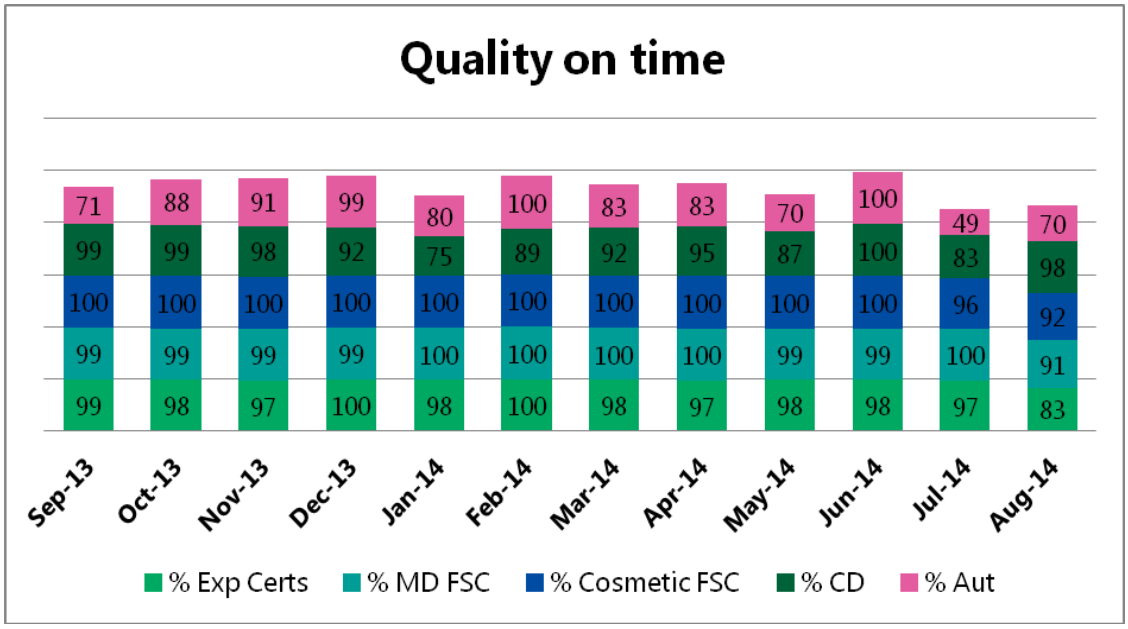
- In co-operation with Revenue's Customs Service, ongoing detection and detention of illegal mail-order importations of prescription-only medicinal products. Co-operation with Customs, An Garda Síochána and enforcement agencies worldwide on Operation Pangea VII, an Interpol - co-ordinated international week of action against illegal supplies of unauthorised prescription medicines via the internet

The graph below shows the level of inspection activity over the period September 2013 to month-end August 2014.

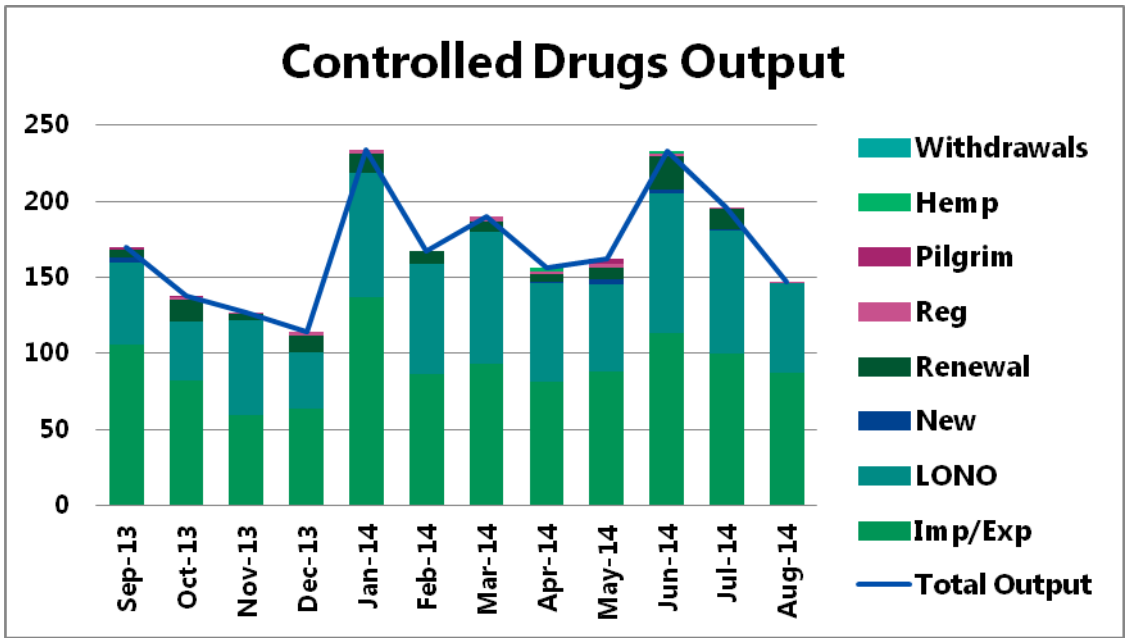


The graphs below shows the numbers issued and the percentages issued on time, for export certificates, controlled drugs licences and GDP, GMP and IMP licences, over the period September 2013 to August 2014 inclusive.

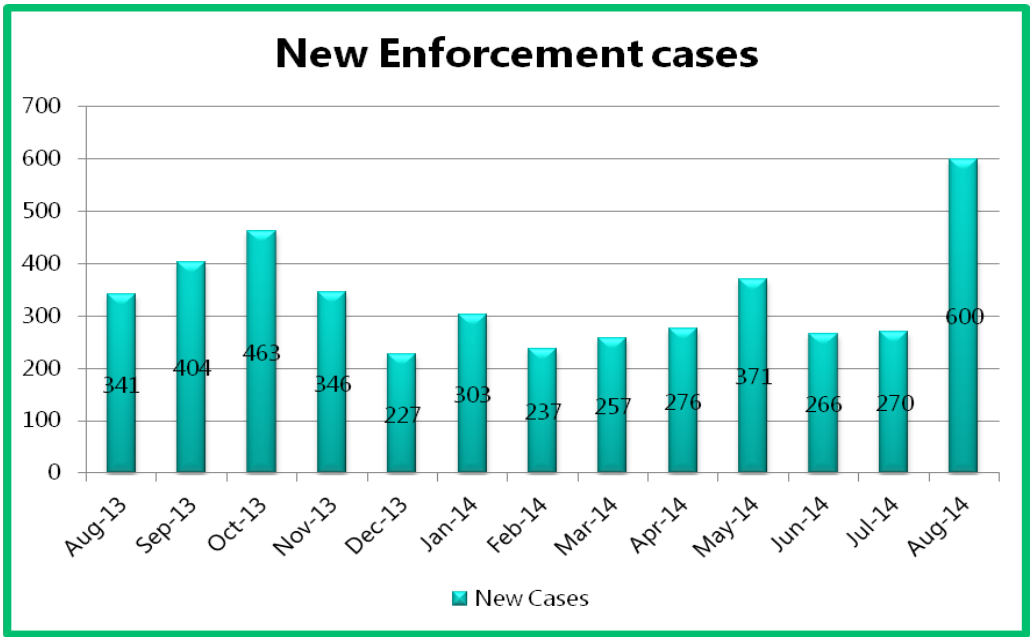




The graph below shows the output of licensing of controlled drugs, by category of licence.



The graph below shows the number of enforcement cases for the period August 2013 – August 2014 inclusive. The majority of these relate to attempts to illegally import prescription-only medicinal products, an amount of which were falsified.



In 2014 - 2015 the regulated sectors will see further benefits, including:

- Continuing focus on the effective management of resources, activities and relationships with interested parties.
- Continuing application of risk-based planning of inspections in some areas and of risk-based approaches to other activities.
- Greater potential for submission of applications electronically.
- Population of the EudraGMDP database with WDAs and MIAs.
- Continued focus on clear communication of requirements and expectations.

Blood and Tissues & Cells Regulation

During 2013 and 2014, 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 tissues and cells legislation requires all sites involved in the procurement, testing, processing, storage and distribution of tissue and cells to be authorised. To date, a full programme of inspections of tissue establishments has been carried out.

Organs for Transplantation

Directive 2010/53/EC was transposed into Irish legislation via Statutory Instrument No. 325 of 2012 on the 27th of August 2012. Under this legislation, the Health Products Regulatory Authority (HPRA) has been appointed as 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 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.

Controlled Drugs

The HPRA continues to be responsible for management of the application and issue processes for all controlled drugs licences, with the Department of Health retaining a signatory role for all official documentation. Inspections related to import, export and holding of controlled drugs and drug precursors have been implemented and continue to be developed.

Exempt Medicinal Products

A significant level of notifications of importation of exempt (unauthorised) products continued through 2013 and 2014, to date. The HPRA use an electronic system for notification and 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

Since the HPRA became the Competent Authority in Ireland for medical devices in 2001 there has been a year-on-year increase in overall activity levels. Caseload volume continued to increase across all of the involved medical device teams during 2013 and 2014 to date. Of particular note is the increase in number of vigilance cases investigated by HPRA. These are increasing in complexity and significance in terms of impact on public health. A number of cases have been high profile including; breast implants and metal on metal hip implants and included cross organisation involvement from all of the medical device staff within HPRA. Another key area of focus during the past year has been the HPRA's contribution to ongoing legislative and other initiatives aimed at developing the regulatory framework. Further details on these issues are outlined below.

Ongoing Regulatory Developments and Initiatives

Several significant medical devices issues, including issues with breast implants, metal on metal hip implants and infusion pumps resulted in a significant workload, from 2012 to 2014. The issue with breast implants resulted in Mr. John Dalli (the then European Commissioner for Health), compiling a joint plan for immediate actions to strengthen the regulatory system for medical devices. This plan requires short and medium term actions from authorities like the HPRA, governments and the European Commission. These relate to enhancing the control and oversight of notified bodies for medical devices, enhancing market surveillance of medical devices, improving coordination, communication and transparency on medical device regulation throughout Europe. Since the plan was published in February 2012 significant additional workload has arisen for the HPRA and this will continue into 2015 and beyond. In addition, analysis of activity indicates a steady increase across all routine activities. Monitoring of critical safety issues on the Irish marketplace and oversight of notified bodies, continue to form the key activities.

Throughout 2013 and 2014, to date, the HPRA contributed significantly at national and European level on the European Commission's development of proposals to revise the medical devices legislation, efforts which have further increased since the recent crises and the formulation of the Commission's joint plan. This required both legislative and technical discussion with the Commission and Member State colleagues and participation in subgroups to develop more detailed technical aspects for the regulatory framework. It was an area of particular focus during the Irish Presidency of the European Council in the first half of 2013. We supported the Department of Health throughout the Presidency to progress the revision of the legislation. The work on this legislation will continue through 2014 and beyond.
The HPRA has been closely supporting and following the drafting of the new implementing regulation for designation of Notified Bodies and has participated in the development and implementation of the Joint Assessment program with the Food and Veterinary Office of the European Commission.

One of the goals of the joint plan is enhancement of market surveillance for medical devices. To more fully contribute to these developments HPRA has set out a re-development proposal for its market surveillance activities to include greater emphasis on proactive and reactive surveillance across the product 'life-cycle'. This revised approach is being implemented in 2014. Another area of focus includes building capability to meet future requirements of the joint plan and Implementing Regulation 920/2013 in the medium term and the new legislative requirements in the longer term.

As a result of this, it has been decided that each HPRA department engaged in medical device regulation will play a role in the different elements of market surveillance. A key focus for HPRA during 2014 and beyond is building resource capability in the area of market surveillance and developing internal coordination of activities. This is to ensure that, in line with the regulatory developments outlined above, the HPRA continues to build on its provision of a robust and effective system of regulation, focussed on public health protection.

The joint plan also highlighted the needs for increased healthcare professional and patient reporting of adverse events. The HPRA has been actively encouraging reporting of vigilance incidents and will continue into 2015. The HPRA has also been lead in relation to the development of the coordinated CA role for vigilance, a topic highlighted in the joint plan and also in the Commission's Proposals. The HPRA during 2014 has taken on the secretariat role for the International Medical Device Regulatory Forum national competent authority reports (IMDRF NCAR) exchange programme. It is foreseen that this role will continue for 3 years. The HPRA also continues to also actively participate in working groups focussed on progression of various initiatives aimed at harmonisation in the areas of regulatory product submission, UDI requirements, Medical Device single audit program.

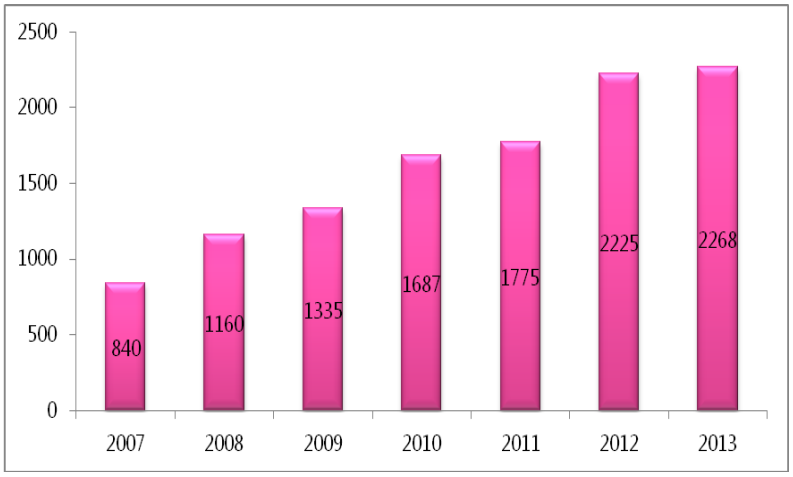
Case Workloads

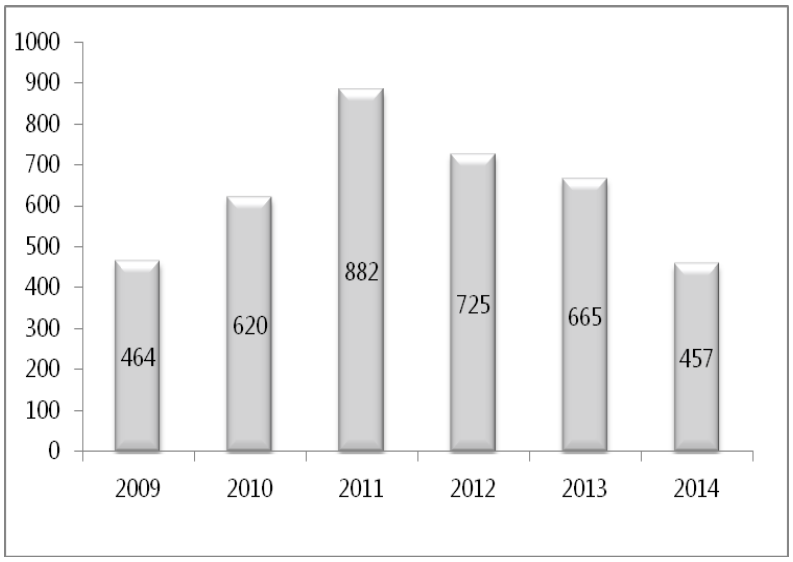
Vigilance & Compliance

To date, 2014 has continued to show an increase in the workload, with an increase in caseload and complexity seen in relation to vigilance cases. Year to date (Jan to August) 1,565 vigilance cases were opened and reviewed. As part of the increased workload, the HPRA has developed a new safety communication strategy, with the issuing of safety notices in a new format. For 2014, to date, 38 safety notices (16 in total for 2013) in relation to key vigilance issues have been issued. In the area of market surveillance 462 compliance files have been opened and reviewed. Significant activities also continued in the audit of manufacturers and the notified body (NSAI). It is expected that these activities will continue to increase and place additional burden on existing resources.

The HPRA continues to be very active at European level in the area of vigilance. It is ranked third in the EU for the total number of NCARs circulated and was joint first in 2012 for the number of NCARs relating to *in vitro* diagnostic medical devices.

See charts showing increased activity levels below.





A full plan for surveillance and observed audits on the Irish notified body is underway. In addition, a programme of audits of class I and custom made manufacturers along with a series of reactive/for cause audits of medical device manufacturers based in Ireland is in progress. In addition, a significant number of queries for advice on regulatory issues have been processed. In 2013, the HPRA conducted 19 audits relating to medical devices. These were comprised of 2 surveillance and 3 observed audits relating to the NSAI; 2 joint assessments with the Food and Veterinary Office of designating authorities; 3 audits of authorised representatives; 3 audits of manufacturers of custom made devices; 3 audits of manufacturers of *in vitro* diagnostics and 3 audits of manufacturers of general medical devices.

Classification Requests

The HPRA received 30 Classification applications for classification of medical devices or products queried as medical devices. The majority of the enquiries received from other medical device competent authorities in Europe or from the European Commission and related to complex classification questions. A quarter of these queries were from external stakeholders relating to IVD or software queries. Two queries were received from notified bodies.

Clinical Investigation Applications

In 2014, to date, the HPRA received 10 new applications for clinical investigations of a medical device to be conducted in Ireland.

There has been a significant increase in these applications over the last 2 years, most from 1 in 2012 to 10 in 2013 and that number will be exceeded in 2014. While there was an increase in the number of applications received, the number of clinical investigations of medical devices ongoing in Ireland remains lower than expected.

Designation and Monitoring of Irish Notified Bodies

During 2014, the HPRA conducted one surveillance assessment of the National Standards Authority of Ireland (NSAI) in the US-based office. In addition, two observed audits are planned of NSAI staff auditing medical device manufacturing sites.

The verification of the notified body, NSAI (as a notified body for devices containing tissues of animal origin) was completed in 2014 and verified to the Commission on 27th February 2014. The HPRA received 76 certification notifications (certificate issuance, modification, withdrawal etc.) during 2014 to date which were then uploaded to the European database EUDAMED as required.

In January 2013, a joint assessment scheme for notified bodies for medical devices was implemented across Europe on a voluntary basis. This joint assessment scheme is now mandatory in accordance with a new Regulation on notified bodies, which was published and came into effect in the last quarter of 2013.

The HPRA participated in 2 mandatory joint assessments in 2014 and 1 voluntary joint assessment.

Technical File Reviews

In 2014, the HPRA increased its focus on review of technical documentation both in the context of market surveillance activities and notified body oversight. A total of 21 technical file reviews were completed to date in 2014.

Product Registrations

The HPRA received 713 notifications of medical devices to the medical device register. These relate to class I, *in vitro* diagnostic and custom made medical devices and to system and procedure packs. Registration of these devices in the Member State in which the manufacturer or their authorised representative is based, is required by legislation as there is a self-declaration of conformity made by the manufacturer.

The Medical Devices regulatory function is currently funded by the Department of Health for the implementation of the medical devices legislation. A small amount of funding is generated from fees for the following activities:

(i) Surveillance audits and observed audits of Notified Bodies
(ii) Issuance of certificates of free sale
(iii) Registration of medical device organisations and their devices
(iv) Review of applications to conduct clinical investigations in Ireland
(v) Review of classification queries from medical device manufacturers
(vi) For cause and reactive audits
(vii) Proactive audits depending on device type and company size