Malta Medicines Authority

Annual Report 2014

Mission

We Protect and Enhance Public Health through the Regulation of Medicinal Products and Pharmaceutical Activities

CONTENTS

Message by the Minister

Our vision for regulators is that they take a consumer-centred approach, create an environment which fosters innovation and competition and work in a sustainable manner.

The Medicines Authority, whose role is to protect and enhance public health, has a very important task to perform in our society. It is its responsibility to ensure that medicinal products released and pharmaceutical activities taking place in Malta adhere to the high standards pertaining to a modern European country.

In the last two years we offered a new and different direction to the Authority, and as a result, the Medicines Authority has undergone important changes that allow it to fulfil its role in a more efficient and effective manner whilst achieving sustainability.

New activities, such as inspections in third countries commenced, and activities which showed potential for growth, such as assessment for the European Medicines Agency, were strengthened. In line with the Government's commitment to invest in people, we can point to the Medicines Authority as exemplary in successfully engaging staff members in further training and development.

The Authority collaborated effectively with MCCAA to ensure that the prices of a number of medicines were reduced to the benefit of consumers. It also supported the administration in enhancing the service given to patients and consumers and to achieve this in a more cost-effective manner.

These achievements would not have been possible without the dedication of the employees of the Authority, who are the key players behind such important changes. The outcomes achieved are the result of a motivated and competent leadership and staff.

I look forward to a sustained effort from the Medicines Authority and I trust that the work carried out will continue having an impact on consumers and all stakeholders.

Dr Helena Dalli
Minister for Social Dialogue, Consumer Affairs and Civil Liberties

Message by the Chairperson

The Medicines Authority has set two important objectives for 2014:

- Regulating effectively and proportionally through a skilled workforce, good governance and an approach which listens and supports innovation,
- Improving the Medicines Authority sustainability through the introduction of cost-saving initiatives, revision of the fee structure and generation of new revenue.

This annual report is an opportunity to reflect on the work we carried out, celebrate achievement and identify opportunities for improvements.

During 2014, the number of applications for medicinal products to be placed on the market surpassed six hundred and fifty (650). This is one of the highest numbers of applications and authorisations in the history of the Medicines Authority and is fostering a more competitive environment for the benefit of consumers. The Authority invested heavily in attracting stakeholders to choose Malta as a Reference Member State and in increasing the number of bids for assessment for the European Medicines Agency. Despite a very competitive scenario, the Authority managed to set a new record for assessment of procedures.

The Authority has signed important cooperation agreements with two National Competent Authorities. The first agreement was reached with the Health Products Regulatory Agency (Ireland) for collaboration with regards to an IT system, through which we saved over 200,000 Euro. The second with the Medicines Evaluation Board (Netherlands) through which MEB started outsourcing part of its quality assessment work to Malta. For the first time Malta collaborated on joint scientific advice, whereby staff from the Medicines Authority collaborated with their counterparts in Austria to deliver a consistent and scientifically sound advice to industry. We are proud that stakeholders are choosing Malta and the Medicines Authority for their scientific and regulatory work.

For the first time, the Inspectorate team started performing inspections in third countries, and we believe that this is an opportunity to enhance Malta's positioning as a centre of excellence for pharmaceutical regulation.

We are investing heavily in the knowledge and capacity building of staff as we believe that the Medicines Authority can only reach its objectives if it has a competent workforce. Currently 22% of our staff is reading for post-graduate studies.

A traineeship program for students who are undergoing doctoral studies was also launched and four students started a traineeship with the Medicines Authority.

We strengthened our governance and management structures and the Authority was certified by the International Standard Organisation as ISO 9001 compliant.

The Medicines Authority cannot achieve its objectives without a sustainable financial model. With the support of our stakeholders, we have revised our revenue and expenditure and the results as highlighted in Appendix 1 are self-explanatory. We aim to continue investing to strengthen the pharmaceutical sector in Malta.

During 2015, we target to continue building on our achievements to strengthen the Medicines Authority. We will focus on enhancing accessibility of medicinal products, and empower patients, consumers and prescribers to take more informed choices with regards to medicines. We aim to continue working with all stakeholders and enhance the status of the Authority to create a best in class regulator.

I take the opportunity to thank all our staff, for their effort, beyond their call of duty, for adopting a patient and consumer centric approach whilst developing a regulatory framework which supports innovation. All this would not have been possible were it not for the cooperation of all the stakeholders in the field.

Professor Anthony Serracino Inglott
Chairperson, Medicines Authority

1. Achieving Results through People, Good Governance and Innovation

1.1 Leadership, Decision Making and Communication

Leadership and decision making were strengthened during 2014. A Director and a Manager were recruited with a view to strengthen strategy, finance, operations and regulatory affairs. Existing Directorates were also strengthened through expansion of capacity. This was mainly achieved through a traineeship programme. A number of important strategic decisions affecting the future of the Medicines Authority were taken, including the introduction of a new financial model leading to growth and sustainability, relocation of the premises, signing of a Memorandum of Understanding for the introduction of a new Information System, expansion of capacity and raising the qualifications and competencies of staff, starting new initiatives such as third country inspections and expansion of initiatives such as Rapporteurships for Centralised Procedures. Internal technical decision making committees were also supported through the provision of resources.

An approach based on open communication, collaboration and stakeholder engagement was adopted and the Medicines Authority supported other entities such as those responsible for pricing and procurement of medicinal products to ensure that patients and consumers are protected.

New internal policies for internal and external communication and customer satisfaction were launched and these included aspects related to stakeholder consultation. Staff meetings were held throughout the year to inform, motivate and engage staff to achieve objectives.

1.2 Capacity

The number of persons employed by the Medicines Authority at the end of 2014 was forty (40) (Table 1).

	Female	Male
Management	2	5
Technical	16	8
Administration	7	2
Total	25	15

Table 1: Employees at the Medicines Authority

In an effort to introduce an innovative organisational model based on both internal and external expertise, an Expression of Interest for evaluators, inspectors and experts was published on a European level. This was carried out following extensive consultation with the Public Administration Collective Bargaining Unit (within OPM) and the Ministry. It is envisaged that through this initiative, the Medicines Authority can further expand its technical capacity and train existing staff whilst maintaining a sustainable approach which takes into consideration risks associated with fluctuation in demand.

During 2014, the Medicines Authority team was nominated for the Premju Ħaddiem tas-Sena 2014. It was of great satisfaction to the Medicines Authority team to be placed as runner up for the Team of the Year Award.

1.3 Learning and Development

The Medicines Authority understands that the fulfilling of its mission requires a knowledge-based approach. The accomplishment of the Authority's role is achievable only if its employees are motivated and have the necessary skills and competences to perform their duties. The Medicines Authority therefore ensures that its employees are offered the possibility to develop their skills and competences through ongoing training and professional development.

In 2014 Medicines Authority's employees attended and successfully completed nineteen (19) short to medium courses. These courses, which were offered either internally or externally, dealt with a variety of topics, including quality management system, internal auditing and clinical statistics.

During 2014 the Medicines Authority also supported its employees to read postgraduate studies through a flexible approach. Three (3) of the Authority's employees started Doctoral studies and six (6) employees are undergoing studies at Masters Level. This translates into 22% of all staff who are benefitting from such initiative.

Furthermore, the Authority launched a traineeship programme to support individuals undergoing level eight studies (doctoral) in an effort to build a new generation of pharmaceutical leaders. Through this initiative four (4) individuals are undergoing doctoral studies whilst participating in the traineeship programme of the Medicines Authority.

1.4 Quality, Simplification and Better Regulation

Award Ceremony for ISO 9001:2008 Certificate

During 2014, for the first time, the Medicines Authority was certified in ISO 9001:2008, a certificate showing its commitment towards meeting the needs and expectations of its stakeholders and to ensure quality in its processes and output. Training was delivered to all staff regarding quality management and a new set of internal auditors were trained to be in a position to strengthen quality management at the Medicines Authority.

The Quality Management Unit processed a total of seven (7) policies three (3) of which were new policies). Thirty one (31) standard operating procedures, most of which were at the stage of the second or third issue, were reviewed. The review incorporated changes in policies as well as corrective and preventive action identified through implementation of operations, internal audits and Management Review.

The Quality Management Unit implemented the audit programme for 2014 in line with the three-year audit strategy. A total of twelve (12) internal audits were performed in 2014 on the internal processes which resulted in a number of corrective and preventive actions. A total of fifty one (51) corrective actions and seventy one (71) quality improvements were processed by the Quality Management Unit. These relate to internal operations and resulted in the setting up / review of policies, standard operating procedures and amendments to standard documentation with the aim of continuously improving the internal operations towards increasing effectiveness and efficiency of its internal operations. 55% of the quality improvements identified resulted from internal / external audits. The implementation of all corrective and preventive actions is monitored centrally. An annual Management Review was performed, during which the Quality Management System as detailed in the Quality Manual was reviewed. Also, this involved review of the operations of each Unit and Directorate within the Medicines Authority, evaluation of results of stakeholder (internal and external) feedback, including complaints; evaluation of results of previous audits (internal and external); and analysis of quality improvements. This resulted in a number of action points. This aims to ensure continuous improvement and the continued suitability, adequacy, and effectiveness of the Quality Management System.

Four simplification actions were prioritised for 2014 based on customer feedback.

The first action was the introduction of a fast track licensing procedure for article 126a of Directive 2001/83/EC as amended.

The second action was the introduction of a user-friendly system to search for nationally and centrally authorised products. In addition, certain important product details, such as registration status, the active ingredients, the prescription status and the marketing authorisation holder can be seen at a glance through the advanced search option. A new feature has been included to offer the possibility to download all products - nationally and centrally authorised - in one worksheet, useful in particular for the community of pharmacists.

The third action was to promote electronic submissions. Enhancement in the receipt of electronic submissions with the reduction in paper submissions was achieved in 2014 through the creation of a new platform. Following an improvement from the previous years, where paper application forms were not being requested any longer for any type of application, a large number of applications are now being received fully electronically through the Common European Submission Portal (CESP). Malta was part of the pilot project where Member States were involved in trying out the system together with the pharmaceutical industry. This has eliminated the need for the submission of application by CD or DVD and therefore makes the submission of applications safe and fast, reducing the burden to both stakeholders and the Medicines Authority. Although it is not yet mandatory for Malta, this is being considered, at least for some types of applications. During 2014 more than half of applications were received through CESP. In 2014, the common repository for centralised procedures has been implemented with full functionality to be able to move towards a complete paperless submission of centrally authorised marketing authorisations.

The fourth action was the introduction of an Information management system for the Medicines Authority. A Memorandum of Understanding was signed with the Health Products Regulatory Agency of Ireland in this regard.

All four actions are within timelines and budget and has led to simplification for the benefit of stakeholders.

1.5 Active Participation at EU and International Level

During 2014, the Medicines Authority has participated actively in European and International fora. Medicines Authority officers participated in one hundred and forty five (145) meetings/ training sessions at EU and International Level. These initiatives were primarily funded by the EU and resulted in increased public health impact, participation in revenue generating procedures, active participation in policy development at European level and the possibility of sharing work and best practices with other agencies, resulting in increased efficiency and maximisation of resources.

A main achievement with regards to impact at European level is the signing of a cooperation agreement between the Medicines Authoruty and the Medicines Evaluation Board, the National Competent Authority of the Netherlands, so that part of the quality assessment is 'outsourced' to the Medicines Authority. Through this initiative, assessors from the Medicines Authority were trained in the processes of the Medicines Evaluation Board, gained exposure to the workings of another National Competent Authority and provided an opportunity to enhance the cooperation between the two entities.

In 2014, the Medicines Authority participated in an EU Funded Project. The Project entitled Strengthening Collaboration for Operating Pharmacovigilance in Europe (Scope) Joint Action aims to support medicines regulators to operate pharmacovigilance systems in line with the EU legislative requirements. The Authority is collaborating with other agencies within the EU to improve skills and capability which will help in safeguarding public health. During 2014, the Authority presented data at EU level with regards to four (4) streams of the project and further participation is planned for 2015.

1.6 Work-Place Environment

In 2014 a decision was taken to relocate the Medicines Authority to new premises. After negotiations with the Malta Enterprise, a new location was identified and an agreement was reached to transfer the Medicines Authority to the Life Science Park. The relocation is planned to take place in 2015. The relocation decision was based on both strategic and financial considerations.

1.7 Transperancy

The Medicines Authority prioritised measures that encouraged transparency and freedom of information. An officer from the Medicines Authority drafted guidelines for the EU Medicines Regulatory Network on the management of conflict of interest. To enhance openness and transparency, management decided to publish an abstract of the audited financial statements as part of this annual report.

2. Ensuring that Medicines Marketed are Safe, of Good Quality and Effective

2.1 Scientific Advice

Since 2009, the Medicines Authority has set a process for scientific advice and protocol assistance requests. The applications accepted are for generic medicinal products in line with the Medicines Authority's Reference Member State activity. In 2014, one (1) scientific advice request has been submitted to the Medicines Authority. To facilitate the process for industry and ensure consistency at European Level, the advice was given jointly with the Austrian Medicines Agency (AGES). Officers from the Medicines Authority participated and delivered their scientific evaluations in Vienna to an applicant developing a medicinal product in the area of Duchenne's Muscular Dystrophy an orphan disease.

2.2 Assessment and Licensing

2.2.1 Malta as Reference Member State and Rapporteur in European Procedures

During 2014 the Medicines Authority continued with activities towards National and European procedures. It has enhanced its activities within the European network by increasing the number of procedures where Malta acts as Reference Member State in the Mutual Recognition and Decentralised Procedures (MRP/DCP) and rapporteur in the Centralised procedure (Figure 1). To ensure that the Medicines Authority meets the demands, the Authority is planning to enhance capacity and competence to carry out these procedures for a more diverse range of medicinal products.

For procedures for which Malta is a Reference Member State or rapporteur, team meetings are organised for each procedure to discuss the progress of the procedures and for a consolidated and fact-based decision to be taken at each step of the procedure. Each procedure is also presented at the Medicines Review Committee, in particular where technical or regulatory decisions have to be taken or endorsed for a final position for Malta.

This has also resulted in a higher volume of post-authorisation procedures for these marketing authorisations (Figure 2). It is envisaged that the number will increase over the next years as the number of new applications finalised increases.

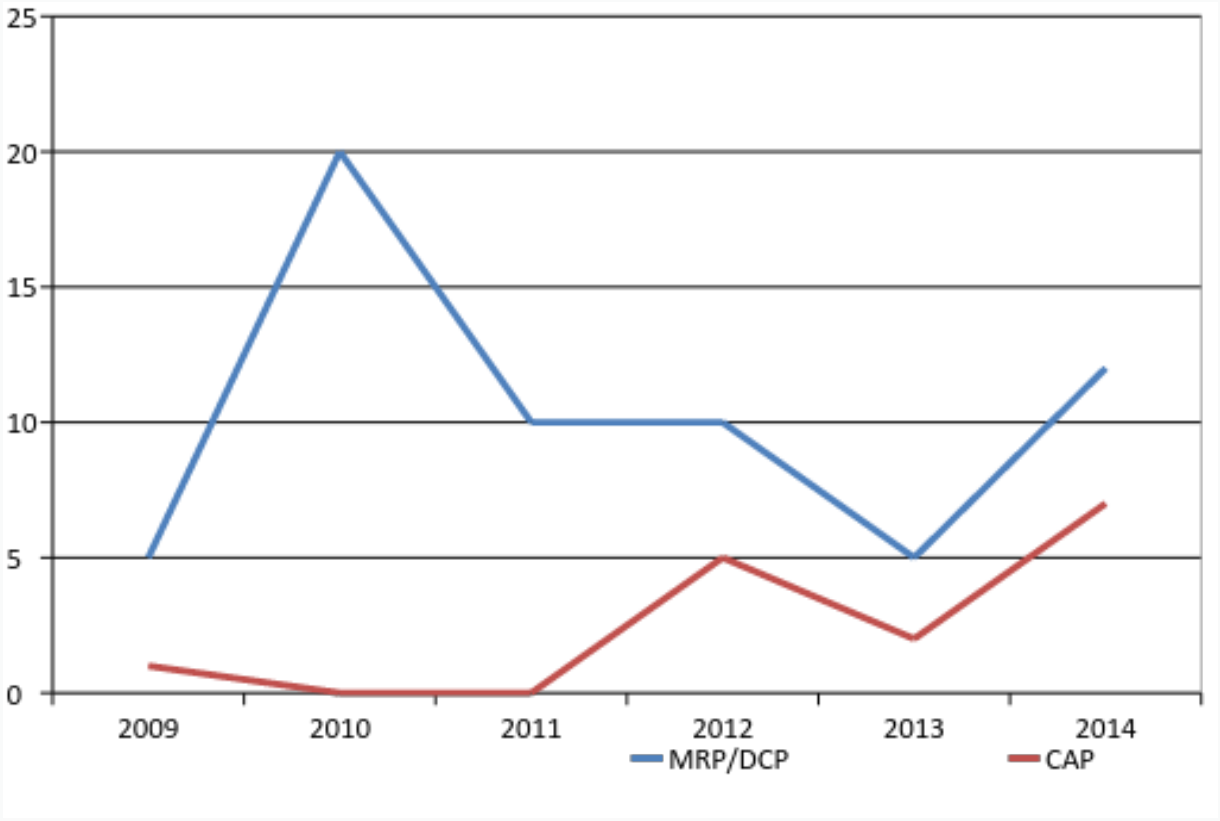

Figure 1: Number of procedures received by the Medicines Authority with Malta as Reference Member State or rapporteur started in the period 2008-2014

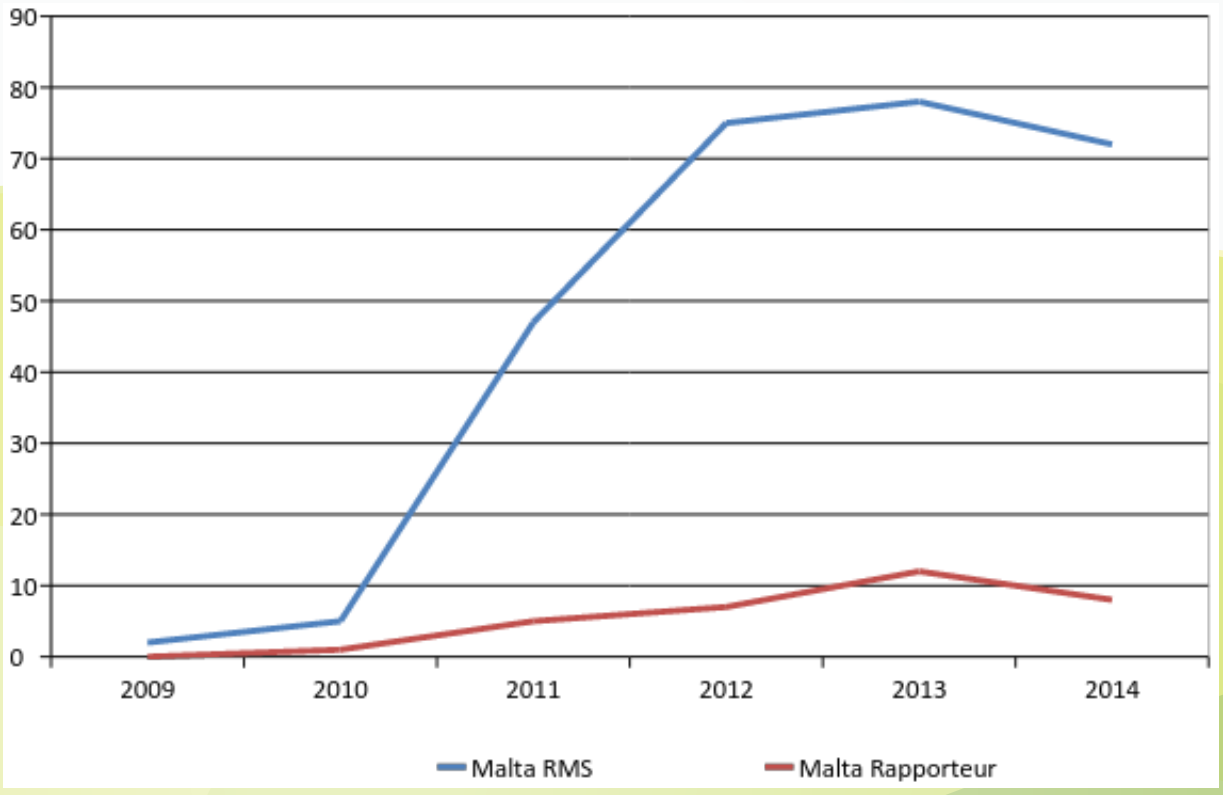

Figure 2: Number of variations received for European Procedures with Malta as Reference Member State or rapporteur in the period 2009 - 2014

2.2.2 Applications for National Authorisations

The number of applications received for new authorisations for the approval of new products received in the period 2004 and 2014 (Figure 3) through all authorisation routes has fluctuated over the years. In general, the number of applications through European procedures (MRP and DCP) has fluctuated but has seen a steady increase since 2012. The number of applications received through legal basis article 126a of Directive 2001/83/EC has also increased steadily but peaked in 2007 (Figure 3). The total number of applications over the years has increased as a total number of products applied for through all routes, resulting in more authorised products to be placed on the Maltese market.

Attention supplier: Change MRP/DCP to Mutual Recognition Procedure/ Decentralised Procedure in graph

2.2.3 The Medicines Review Committee

The Medicines Review Committee within the Medicines Authority continued to meet regularly to discuss regulatory and technical issues relating to ongoing applications for marketing authorisations for medicinal products, both National and European. These include applications for marketing authorisation and post-authorisation activities (e.g. variations, renewals, pharmacovigilance issues) as well as clinical trial applications and European work-sharing procedures. Other items presented to the

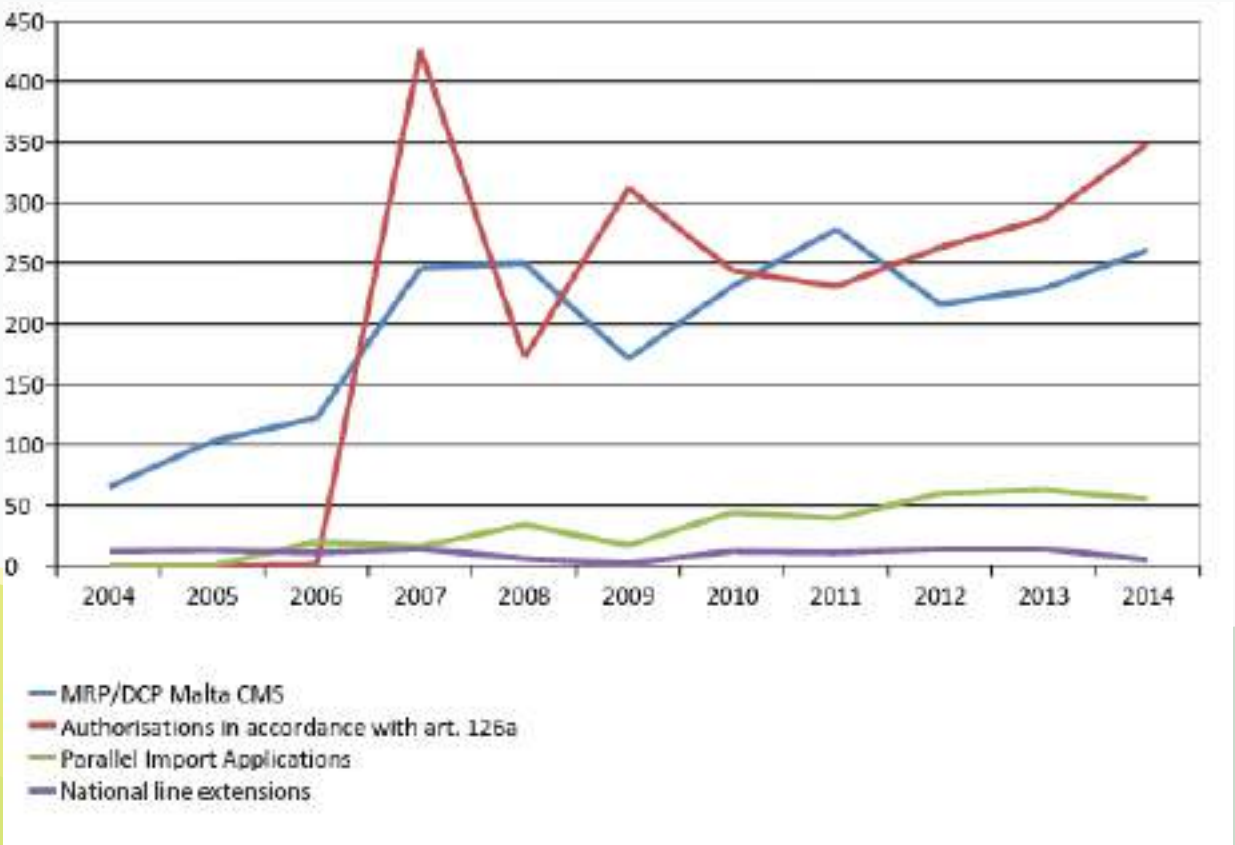

Figure 3: Applications for new products resulting in national authorisations

committee include feedback from external technical and regulatory meetings attended by members of the MRC and other staff members (e.g. Committee for Human Medicinal Products, Coordination Group for Mutual recognition and Decentralised procedure (Human), Pharmacovigilance Risk Assessment Committee and working parties). Issues relating to the local market, such as safety issues following on from European referrals are discussed within the Committee.

2.3 Post-Authorisation Procedures

A number of post-authorisation procedures are received each year including variations, notifications, renewals and withdrawals. The number of post-authorisation procedures received is shown in Figure 4.

During 2014, the timeliness of applications continued to improve for a considerable number of application types, both at National and European level. This was possible through redeployment of resources to make sure that statutory timelines are met. A 500% improvement in timelines for national variations has been achieved over the last five (5) years. This is a result of streamlining of the processes, more dedicated resources as well as more staff motivation to achieve the desired results.

The average time for the finalisation of National variations has gone down from five hundred seventy one (571) days in 2011 to an average timeline of seventy (70) days in 2014. The same can be said of authorisations in accordance with article 126a of Directive 2001/83 as amended, where timelines achieved have improved with a resulting average time of twenty three (23) days in 2014.

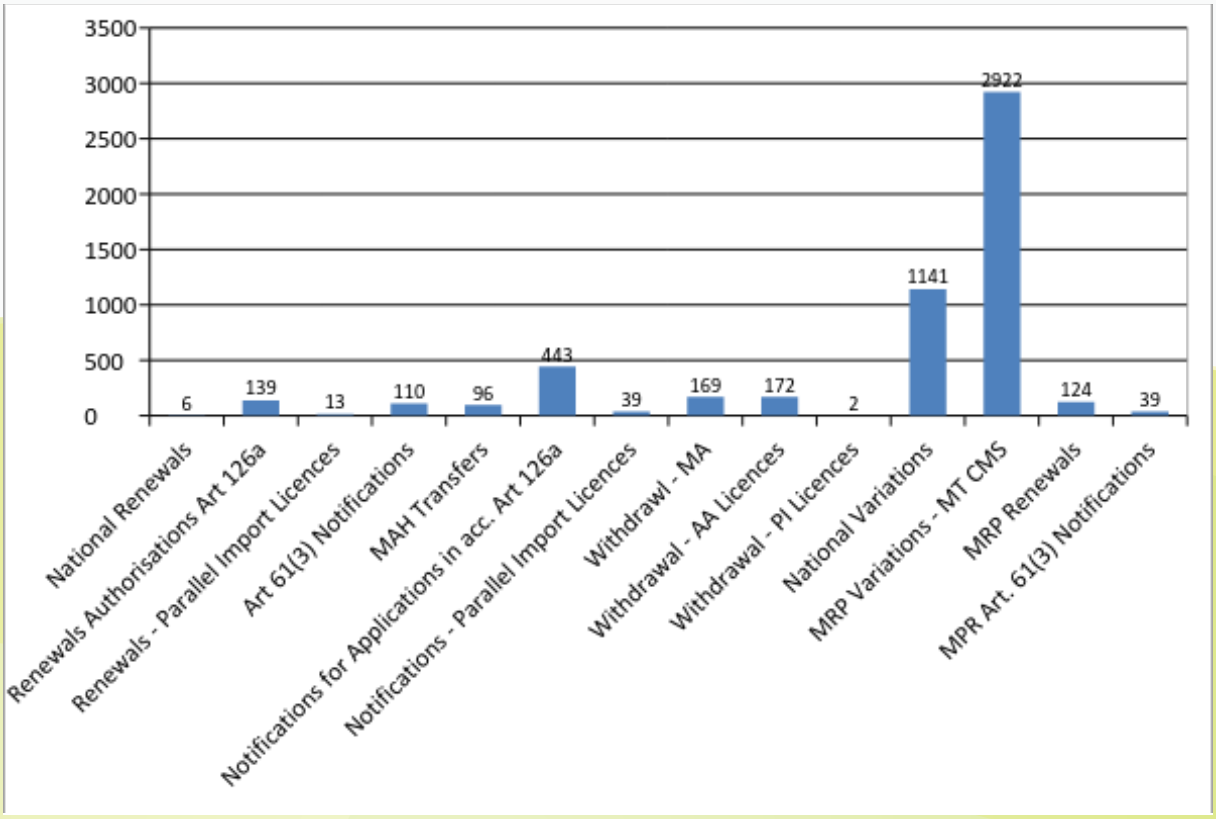

Figure 4: Post-authorisation procedures received through all routes in 2014

The national step at the end of European procedures, which by legislation should be thirty (30) days to issue the marketing authorisation from the positive end of the procedure, has also been prioritised and an improvement has been registered over the years. In 2014, this timeline has been achieved for all procedures where the information to finalise the process has been received from the applicant within the required timelines. The average time for completion of MRP (Mutual Recognition Procedure) and DCP (Decentralised Procedure) applications has gone down from one thousand and nine (1009) days in 2010 to one hundred and thirty five (135) days in 2014. A sustained improvement was attained over the last five (5) years as more resources were put in place and processes were streamlined in line with an agreed risk-based approach.

2.4 Pharmacovigilance

Safety of medicines is a priority area for the Medicines Authority and the Authority continues to strengthen its efforts to ensure the safe use of medicinal products on the local market. The main objectives of the Pharmacovigilance role of the Medicines Authority includes the evaluation and monitoring of safety data and, where appropriate, implementation of regulatory action to maximise benefits and minimise risks associated with medicinal products. The Medicines Authority has in the past year, maintained its active role in Pharmacovigilance.

2.4.1 National Pharmacovigilance Activities

The Medicines Authority endeavours in a number of activities to help ensure that only safe medicinal products are kept on the Maltese market. The collection, investigation and reporting of drug safety information (Spontaneous Reporting System) in accordance with European requirements comprises one such major Pharmacovigilance activity carried out by the Medicines Authority. The Medicines Authority requests the implementation of risk minimisation measures that are conditions of marketing authorisations from marketing authorisation holders as well the approval of Direct Healthcare Professional Communications informing of key messages to prescribers and suppliers of medicinal products for human use. The Medicines Authority also requests modifications to be implemented to medicinal product information following safety signal detection activities by the European Medicines Agency and the opinions adopted by its Committees. Safety information updates as supplied by the medicinal products' Marketing Authorisation Holders are also assessed and followed up at a local level. These may sometimes also result in the implementation of product safety recalls in an effort to ensure public safety. The Medicines Authority assesses and monitors risk management programmes as proposed by Marketing Authorisation Holders or as recommended at a European level. The Authority also participates in discussions related to safety of medicinal products at European level.

The Medicines Authority utilises a number of European information technology application systems and networks for the implementation of the above mentioned activities. The collection of safety information from local healthcare professionals comprises the major and most basic Pharmacovigilance activity and this is furthered by the collation of these reports using these European information technology applications such as EudraVigiliance (EV) and EV Data Analysis System (EV DAS). During 2014, a new version of the EV DAS software was released and one staff member trained. One staff member within the post-licensing directorate was also certified with Eudravigilance after passing the DIA's compliance exam.

Reports detailing occurrence of adverse drug reactions to medicinal products available on the market or at hospital are regularly submitted to the Medicines Authority for review and assessment. Such adverse drug reaction reports are mainly

compiled and reported by healthcare professionals or the local Marketing Authorisation Holder representatives for the medicinal product.

Wherever medicinal products are being used, there should be a readiness to observe and report unwanted and unexpected medical events. The Medicines Authority strives to foster an attitude of participation by promoting the need for drug safety monitoring in all its collaborations with marketing authorisation holders as well as healthcare professionals. In 2014, pharmacies received a set of the Medicines Authority's new ADR-medication error forms to facilitate the reporting of Adverse Drug Reactions and medication errors. Reporting can also be done online on the Medicines Authority website.

A total of one hundred and sixty nine (169) Individual Case Summary Reports (ICSRs) were registered over 2014. Each of these cases detailed at least one adverse drug reaction to the medicinal product concerned thus resulting in a total of seven hundred and forty-one (741) individual adverse drug reactions. Figure 5 gives a breakdown of these adverse drug reactions according to system organ classification. Each case report received at the Medicines Authority was assessed and reported electronically to the European Medicines Agency and the World Health Organisation as the central adverse drug reaction repositories. Adverse drug reaction databases maintained at these organisations typically comprise essential medicinal product safety monitoring tools which allow for the identification of potential/novel safety

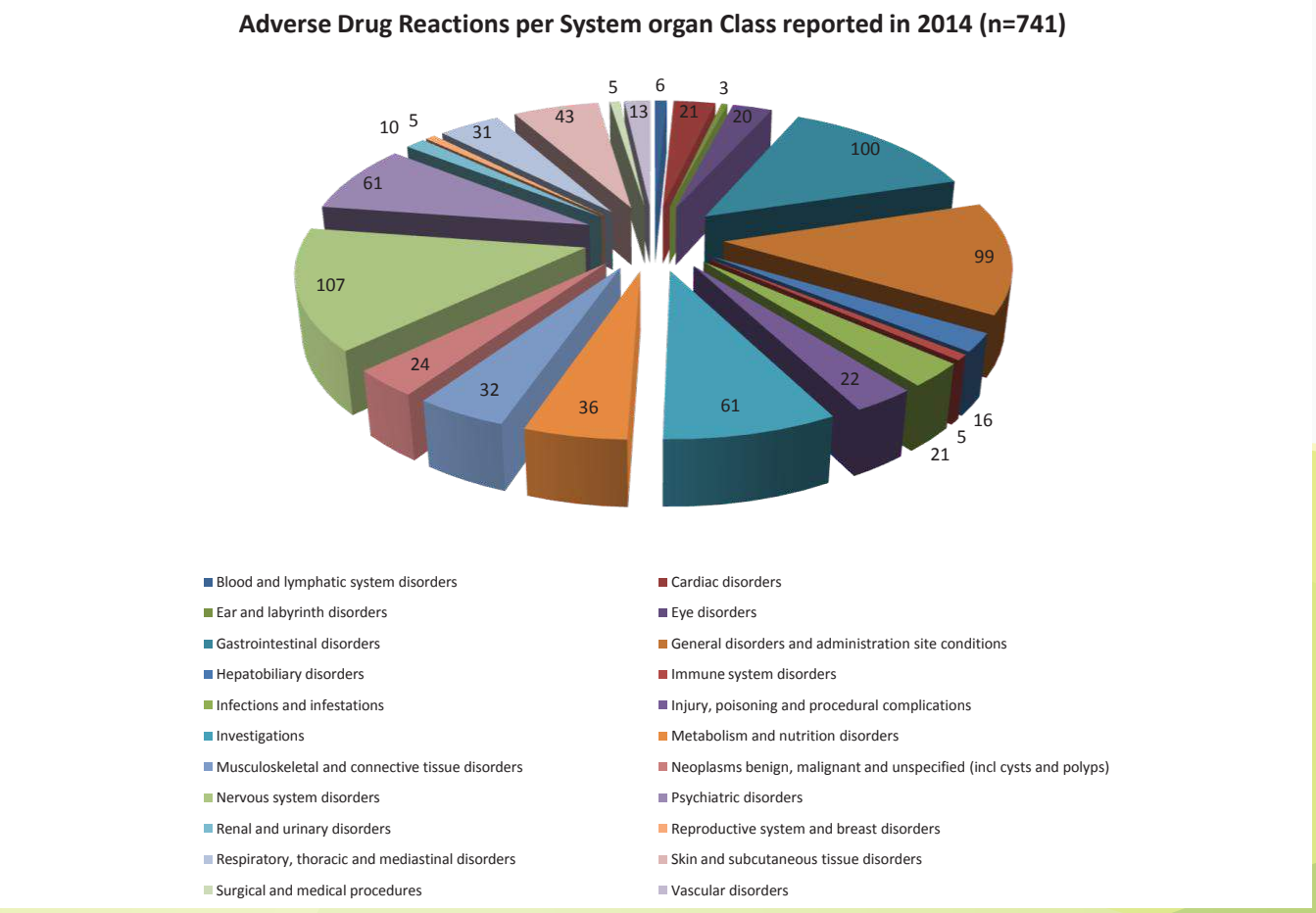

Figure 5: Breakdown of adverse drug reactions according to system organ classification.

signals associated with the use of specific drugs particularly when these are administered at certain doses and/or to distinct patient categories.

Figures 6 and 7 further classify the adverse drug reaction case reports (as received over 2014) according to seriousness and patient age respectively. The severity of the adverse drug reaction reports is normally assigned by the reporting healthcare professional or by the Medicines Authority following careful assessment and consideration of applicable factors such as dose of the medicinal product, indication for use, concurrent administration of drugs and underlying patient disease.

The establishment and maintenance of a viable electronic reporting system with the European Medicines Agency and the World Health Organisation has comprised a major Pharmacovigilance endeavour necessary for the reporting of adverse drug reactions according to European legislative requirements. Over 2014, the use of the European electronic reporting systems (specifically the use of the EudraVigilance network) was sustained and further validated by the Medicines Authority for purposes of determining proper case reporting by the Marketing Authorisation Holders at a local level and subsequent case collation within a centralised European database. This task helped ensure population of the European database with all adverse drug reaction reports originating in Malta, and thereby allowed for European wide safety risk assessments to be performed whenever necessary and on any of the currently authorised medicinal products. In 2014, a new staff member obtained certification on the use of the Eudravigilance software to carry out ADR data inputting tasks.

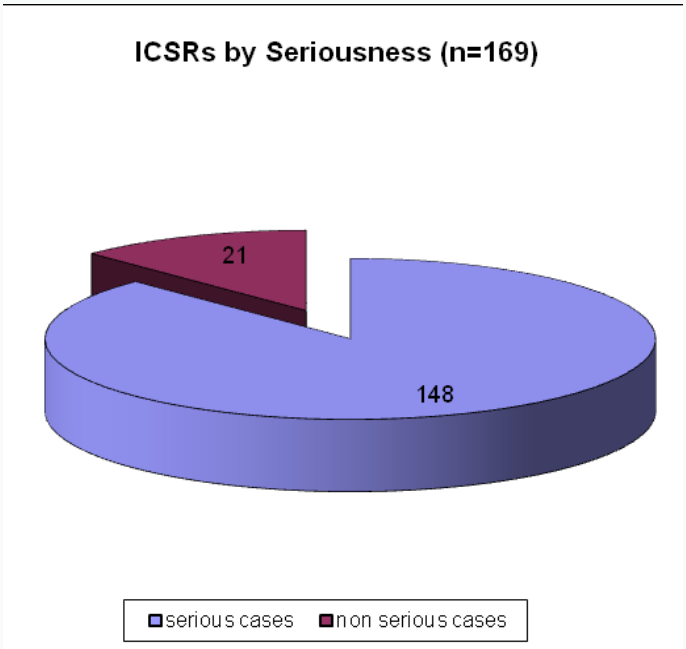

Figure 6: Frequency of ICSRs according to seriousness in 2014 (n=169)

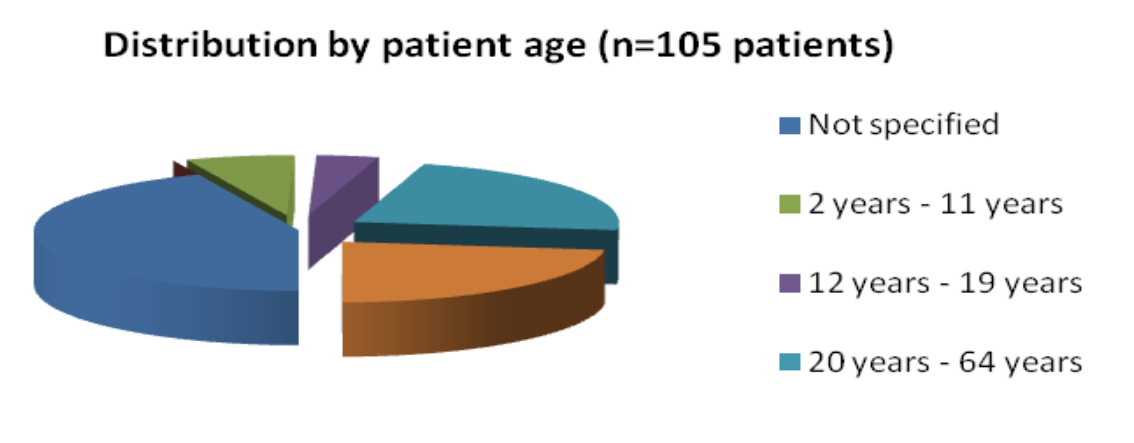

Figure 7: Percentage distribution of case safety reports according to patient age 2014 (105 patients)

The Medicines Authority is also responsible for ensuring medicinal product safety via the assessment and approval of circulars detailing proposals for safety updates to scientific product information. Approval of such information is normally requested by the concerned product's Marketing Authorisation Holders or its local representative. The Authority may, on the other hand, initiate such requests for product safety updates following toxicological signal identification and expert working party or committee decisions taken at European Medicines Agency or World Health Organisation level. Requests may also entail product suspension or recall.

Several activities are undertaken by the Medicines Authority for purposes of attaining effective product safety surveillance, amongst which are the (1) approval of Direct Healthcare Professional Communications (DHPCs) detailing safety/risk changes to scientific information and recommendations on product administration methods; (2) investigation of newly identified safety signals with immediate product suspension and/or recall as relevant (Safety Signal Investigations, Rapid Alerts and Product Safety Recalls); (3) approval and monitoring of Pregnancy Prevention Programmes as proposed in relation to potentially teratogenic medicinal products; (4) monitoring of risk minimisation programmes relating to high risk medicinal products and provision of the relevant regulatory information in order to establish such programmes; (5) issue of Safety Circulars and Media Statements addressed to healthcare professionals and the general public respectively. These documents normally give recommendations on medicinal product use and applicable cautionary and precautionary measures. Throughout 2014, the Medicines Authority continued implementing the SMS notification service whereby subscribed medical and healthcare professionals can receive alerts and links to the safety circulars as soon as they are published on the website. (6) Communication as relevant with the Department of Healthcare Services Standards on toxicological risks identified in relation to blood products (Haemovigilance); (7) Initiation and subsequent approval of variations to scientific medicinal product information relating to identified novel or increased risk (Urgent Safety Restrictions); (9) Investigation into locally reported incidences of severe unexpected medicinal product toxicity or any anomalous lack of efficacy following medicinal product administration (Local Product Safety Issues). (10) Review of newly emergent data concerning safety evidence of a medicinal product, substance or class upon request. (11) Review of queries that may be related to a possible safety issues with a medicinal product, substance or class. Table 2 below gives the distribution of reviews, communications and approvals which the Medicines Authority post-licensing directorate handled over 2014.

During 2014 the Post-Licensing Directorate focused on initiating a new procedure for a joint DHPC service as this was being requested by stakeholders. In this process, when more than one marketing authorisation holder is obliged to circulate the same DHPC or more than one product is the subject of a DHPC, then license holders may request the service of the Medicines Authority to circulate the letter on their behalf. While it is not obligatory to partake in a joint DHPC licence holders must still send the letter to the stakeholders unilaterally as the provision of new emerging safety information to doctors and other healthcare professionals by pharmaceutical companies is an obligation set by the EU's directive on pharmacovigilance, 2001/83/EC.

Table 2: Pharmacovigilance and safety issue reviews and communications – 2014

Documents Received	Number of submissions
PSURs	1219
Risk Management Plans	27
SUSAR	2
Annual Reassessments	26
Direct Healthcare Professional Communications	20
Joint DHPCs	6
Safety Circulars	19
Risk minimisation measures	80
Rapid Alert	2
Non Urgent Information	13

An additional stakeholder service performed by the Medicines Authority is that of responding to any queries related to Pharmacovigilance activities in a timely manner. The main area of queries were those relating to the collection, assessment and reporting of local adverse drug reactions, and submission requirements for PSURs/RMPs and RMMs (Table 3).

Table 3: Pharmacovigilance related queries in 2014 (n=92)

		Number	Percent
1	ADR reporting	17	20
2	Additional monitoring and black triangle	1	1
3	Advertising	6	7
4	Clinical Trial reporting requirements (SUSARs/ DSURs)	8	9
5	DHPC distribution requirements	3	3
6	Literature Monitoring	8	9
7	Local QPPV	10	12
8	Medical device classification	4	5
9	Pharmacovigilance ADR reporting text	4	5
10	PSMF	2	2
11	PSUR/RMP/RMM submission requirements	16	19
12	Others	7	8
	TOTAL	**86**	**100**

In late December 2014, the Medicines Authority released a draft Guidance Notes document for consultation with the pharmaceutical industry. The basis of the updates in the guidance notes were a compilation of hundreds of pharmacovigilance related queries received by the directorate from 2012 to 2014.

At an EU level 2014 saw the start of the centralised PSUSA assessments and the Medicines Authority was involved in a number of reconciliation exercises together with the European Medicines Agency.

2.4.2 New Pharmacovigilance Procedures by the Medicines Authority

In early 2014, the last of a series of pharmacovigilance systems audits were carried out successfully. A second report to the European Commission declaring compliance with EU directive 2001/83/EC and Regulation 726/2004/EC as well commission implementing regulation will be transmitted to the EU Commission in September 2015.

During 2014, work on implementation of Directive 2010/84/EC and Directive 2012/26/EU as well as Regulations (EU) no 1027/2012 of the European Parliament and of the Council of 25 October 2012 amending Regulation (EC) no. 726/2004 was prioritised. The new Commission implementing Regulation 520/2012 implementation phase was finalised in 2014.

2.5 Classification of Borderline Products

The borderline classification committee classifies products into medicinal and non-medicinal products when requests for classification are received from companies and from other sources. The Borderline Classification Committee meets in line with exigencies and feedback is sought from all members as well as the herbals expert in line with the updated process. During 2014, the Committee received forty nine (49) applications, fifteen (15) were classified as medicinal and thirty two (32) were classified as non-medicinals and two (2) applications could not be finalised in view that the applicant failed to submit the requested information.

2.6 Clinical Trials

During 2014, no new Clinical Trials applications were submitted to the Medicines Authority. Six (6) amendments to trials which are being conducted in Malta were received. Two (2) amendments were approved in 2014. All information has been inputted

in the European Database for Clinical Trials. Since 2010, there has been a decrease in Clinical Trial applications submitted to the Medicines Authority, a trend which has been recorded from 2010 to 2014.

2.7 Advertising of Medicinal Procedures

The Medicines Authority monitors the advertising of medicinal products and the issue of any promotional material related to such products and as being presented either to the public or to healthcare professionals. There is self-regulation in this area. Monitoring and assessment of medicinal product advertising typically extends over major media formats, namely local newspapers and journals, local electronic medical journals and local television or radio broadcasts. Control of promotional material such as the provision of medicinal product samples to healthcare professionals and the sponsoring of promotional activities or scientific congresses is also regularly undertaken. Advertising and promotional material regulatory control is implemented according to the criteria set out within the Medicinal Products (Advertising) Regulations (L.N. 380 of 2005).

To a lesser degree, control of advertising material is also implemented via the ad hoc selection and investigation of local advertisements as presented within the major media formats. This activity principally aims at ensuring public health protection via the affirmation that the applicable legislation is constantly being upheld and rigorously adhered to.

Monitoring is mainly implemented via the application (in accordance with European legislation) of a self-regulatory approach whereby medicinal product advertising complaints as reported by external stakeholders are assessed and investigated in detail for purposes of verifying claims of breaches to the Advertising Regulations. Over 2014 one (1) advertising complaint was registered with the Medicines Authority. All advertising complaints were dealt with within 2014.

3. Availability, Rational Use and Access to Medicines

3.1 Availability of Medicinal Products

The Medicines Authority has set a Working Group for Availability of Medicinal Products. The main target for the Working Group for 2014 was to start working on the harmonisation of the prescription status for some medicinal products which had been authorised during the transitional period. A new 'switching' guideline (Prescription Only Medicine to Over The Counter) was drafted and following discussions and agreement was published on the Medicines Authority website. A stakeholder information meeting was held to inform local contact points on the process for the application for switching legal status of applicable medicinal products. As a result, a number of applications were received by the directorate for a switch in legal status. The assessment has been finalised for a number of products. Outcomes are communicated through circulars to pharmacists and also through the Medicines Authority website.

The Working Group also worked on the identification of therapeutic gaps in availability. It is planned to discuss these gaps with the Licensing Authority to establish any required actions for enhanced access and availability of medicines for Maltese patients.

Hon Minister Helena Dalli announcing reduction of prices of a number of medicines

3.2 Rational Use of and Access to Medicinal Products

During 2014, the Medicines Authority prioritised access and rational use of medicines. Collaboration between the Medicines Authority and the Malta Competition and Consumer Affairs Authority (MCCAA) led to the notification of reduction of prices for forty (40) medicinal products.

A campaign entitled 'Il-Mediċini: Għażla Aħjar Għalik' was launched with the Malta Competition and Consumer Affairs Authority (MCCAA) with the support of the Malta EU Steering and Action Committee (MEUSAC). The Authority collaborated with the University of Malta to promote and educate consumers on generic and reference medicines. Officers from the Medicines Authority participated in media programmes to inform, educate and empower consumers. A new database for medicinal products was launched to provide real time information to consumers on authorised medicines.

4. Ensuring High Standards for Pharmaceutical Activities

The Medicines Authority is responsible for inspecting and recommending the issue of licences for manufacturers and wholesale dealers according to national legislation and EU Good Manufacturing Practice (GMP) and EU Good Distribution Practice (GDP) respectively, whilst pharmacies are inspected against national legislation and standards. The Medicines Authority also carried out Good Clinical Practice inspections of clinical trials on a risk based approach and Pharmacovigilance inspections.

4.1 Manufacturing and Importation

All medicinal products for human use manufactured or imported into Malta and the EU, including medicinal products intended for export, are to be manufactured in accordance with the principles and guidelines of Good Manufacturing Practice (GMP).

During 2014 the Medicines Authority carried out Good Manufacturing Practice (GMP) inspections for new, renewal or follow up of GMP licences/certificates. These included: two (2) GMP inpsections for an active pharmaceutical ingredient; fifteen (15) for non sterile solid dose manufacturers; one (1) contract laboratory inspection for its GMP certificate renewal; three (3) inspections for Manufacturing authorisation (MAs) for repackaging and re-labelling / partial manufacturing operations; eight (8) inspections for MAs of importation activity.

A total of thirty seven (37) MAs administrative variation applications were processed in 2014 for manufacturers and importers. One (1) variation with inspection was carried out. Cumulative number of EU GMP authorised activities is shown is Figure 10.

There was one (1) Inspections Review Group meeting held throughout 2014 where one (1) case related to GDP issues was discussed and decided upon.

During 2014, the Medicines Authority received One hundred and forty one (141) rapid alerts and GMP non compliance notifications, which were investigated and out of which seven (7) resulted in recall of medicinal products from the local market and one in a cautionary use letter.

During the year under review, the Medicines Authority started to carry out Good Manufacturing Inspections in countries outside the European Union. Six (6) inspections have been carried out throughout 2014. Through this process, the Medicines Authority is facilitating the possibility that more companies would be in a better position to import medicinal products within the European Union. Additionally, these procedures attract new revenue to the Medicines Authority and provide exposure to different manufacturing facilities to the inspectors of the Medicines Authority.

4.2 Distribution

A distributor of medicinal products sources the products one distributes from within the EU/EEA. Distributors are required to follow good practice guidelines known as Good Distribution Practice (GDP) in order to ensure that the quality of

the medicinal products is not compromised in the supply chain and in order to be in a position to carry out a recall of any defective product.

During 2014 the Medicines Authority has also fulfilled its Good Distribution Practice (GDP) inspection plan where thirty one (31) GDP inspections were carried out. During 2014, nine (9) applications for new wholesale dealing licences were submitted. Eight (8) applications were inspected and eventually seven (7) licensed, whilst the other application is still being processed. Twenty one (21) variation applications for wholesale dealing authorisations were processed in 2014, out of which two (2) required an inspection.

4.3 Pharmacies

Pharmacies are inspected on a two (2) year cycle. During 2014, the Medicines Authority carried out a total of ninety eight (98) retail community pharmacy inspections.

There were another three (3) pharmacy inspections following variation applications for pharmacy premises transfers or alterations which were carried out, whilst fifty six (56) administrative variations for pharmacy licences were processed.

4.4 Clinical Trials and Pharmacovigilance Inspections

During 2014, in view that no new Clinical Trials applications were submitted to the Medicines Authority, no inspections for this activity were required.

Four (4) Pharmacovigilance (PhV) inspections were carried out against the national and EU legislation and the MA Pharmacovigilance obligations.

4.5 Surveillance of the Local Market

The Medicines Authority collaborates with the Medicines and Healthcare Regulatory Agencies (UK) so that the latter carried out testing in an Official Medicines Control Laboratory for the Medicines Authority. In this regard, the Local Market Surveillance Plan for 2014 was closed positively.

4.6 Enforcement of Legislation

During 2014, the Medicines Authority worked upon six (6) enforcement cases / investigations out of which five (5) new cases opened in 2014 were related to complaints and enforcement. There was no need for the Enforcement Committee (a specific committee which discusses enforcement cases, chaired by the Licensing Authority) to meet during 2014.

In 2014 there were two (2) court case sittings concerning pharmacy issues and two sitting sessions concerned an enforcement case. Medicines Inspectors attended one (1) court session regarding enforcement as witnesses.

4.7 Granting of Qualified Person Status

In 2014 the Medicines Authority received nine (9) new applications for the Qualified Person (QP) status. Nine (9) applicants were interviewed during 2014 and of these eight (8) were approved as eligible for QP status.

4.8 Certificates of Pharmaceutical Products (CPPs)

During 2014, one hundred and forty eight (148) Certificate of Pharmaceutical Products applications were processed and issued.

Appendix 1:
Extract of the Annual Report and Financial Statements for the Year Ended 31 December 2014

MAZARS

Independent auditors' report to the Ministry for Social Dialogue, Consumer Affairs and Civil Liberties

Report on the financial statements

We have audited the accompanying financial statements of the Medicines Authority ("Authority") set out on pages 5 to 18 which comprise the statement of financial position as at 31 December 2014, and the statement of comprehensive income, statement of changes in equity and statement of cash flows for the year then ended and a summary of significant accounting policies and other explanatory notes.

CEO's responsibility for the financial statements

As described on page 1, the Chief Executive Officer ("CEO") is responsible, for the preparation and fair presentation of the financial statements in accordance with the Medicines Act, 2003 (Cap 458) and International Financial Reporting Standards as adopted by the EU, and for such internal control as the CEO determines to be necessary to enable the preparation of financial statements that are free from material misstatements, whether due to fraud or error.

Auditors' responsibility

Our responsibility is to express an opinion on these financial statements based on our audit. We conducted our audit in accordance with International Standards on Auditing. Those standards require that we comply with ethical requirements and plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement.

An audit involves performing procedures to obtain audit evidence about the amounts and disclosures in the financial statements. The procedures selected depend on the auditor's judgement, including the assessment of the risks of material misstatement of the financial statements, whether due to fraud or error. In making those risk assessments, the auditor considers internal controls relevant to the Authority's preparation and fair presentation of the financial statements in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Authority's internal control. An audit also includes evaluating the appropriateness of accounting policies used and the reasonableness of accounting estimates made by the CEO, as well as evaluating the overall presentation of the financial statements. We believe that the audit evidence obtained is sufficient and appropriate to provide a basis for our audit opinion.

Opinion

In our opinion, the financial statements give a true and fair view of the financial position of the Authority as at 31 December 2014 and of its financial performance and its cash flows for the year then ended in accordance with International Financial Reporting Standards as adopted by the EU.

Emphasis of matter

Without qualifying our opinion, we draw attention to note 16 to the financial statements whereby in January 2010 the Courts of Malta condemned an officer who had occupied the position of Director Corporate Services within the Authority in 2006 of misappropriation of funds totalling EUR 165,000. The latter was ordered to reimburse the funds to the Authority, however as at 31 December 2014 the case was still under appeal.

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Mazars Malta
Certified Public Accountants
VAT Reg No. MT15296002

MAZARS

Independent auditors' report to the Ministry for Social Dialogue, Consumer Affairs and Civil Liberties (continued)

Report on other legal and regulatory requirements

In our opinion, the financial statements have been properly prepared in accordance with the provisions of the Medicines Act, 2003 (Cap 458).

This copy of the audit report has been signed by
Anthony Attard (Partner) for and on behalf of

Mazars Malta
Certified Public Accountants
Attard

11 February 2015

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Medicines Authority

Statement of comprehensive income
For the year ended 31 December 2014

	Notes	2014 EUR	2013 EUR
Income	5	**1,922,986**	1,483,368
Expenditure			
Staff costs	6	**(1,190,207)**	(1,083,902)
Amortisation and depreciation		**(11,467)**	(9,124)
Audit fee		**(2,360)**	(2,360)
Finance costs		**(366)**	-
Other operating expenses		**(452,819)**	(428,541)
Operating surplus/(deficit) for the year before taxation		**265,767**	(40,559)
Income tax expense	7	**-**	-
Surplus/(deficit) for the year		**265,767**	(40,559)
Other comprehensive income for the year		**-**	-
Total comprehensive income for the year		**265,767**	(40,559)

Medicines Authority

Statement of financial position
As at 31 December 2014

	Notes	2014 EUR	2013 EUR
ASSETS			
Non-current assets			
Intangible assets	8	**17,595**	15,591
Tangible assets	9	**10,415**	9,454
		28,010	25,045
Current assets			
Trade and other receivables	10	**450,836**	222,192
Cash and cash equivalents		**570,108**	358,737
		1,020,944	580,929
Current liabilities			
Trade and other payables	11	**677,632**	500,419
Net current assets		**343,312**	80,510
Net assets		**371,322**	105,555
RESERVES			
Accumulated fund		**371,322**	105,555

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