ANNUAL REPORT 2015

MALTA
MEDICINES
AUTHORITY

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Message by the Minister

The Medicines Authority has a vital mission to protect and promote public health in Malta. This is achieved through the regulation of medicinal products and pharmaceutical activities in order to ensure that the quality, safety and efficacy of medicines available on the market are according to the highest European standards.

An independent, science based and effective Medicines Authority is pivotal to the establishment, development and retention of the pharmaceutical sector in Malta. During 2015, the Authority has strengthened its activities whilst making a leap in terms of keeping an eye to the perspective of those who will ultimately use the medicine. I have witnessed the Authority working effectively with its stakeholders, organising its first structured stakeholder meeting, launching a major activity stand at the Medical School Conference, reaching medical practitioners, pharmacists, healthcare professionals and consumers.

The establishment of a Medicines Intelligence and Access Unit within the Medicines Authority is assisting consumers with regards to accessibility to medicines. This is being achieved by supporting the industry and all stakeholders in increasing the access to medicines and empowering all those who use medicines to make informed choices with regards to medicines.

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

The collaboration with the consumer entity, Malta Competition and Consumer Affairs Authority (MCCAA) is an example of the success of joint work which produced a synergistic positive performance in areas and issues of demonstrated benefit to the consumer, such as the numerous price reductions of medicines announced in these last three years.

The Medicines Authority is a prolific example of a public entity which in a relatively short period of time has become a best in class regulator. Such achievements are being witnessed in the record number of applications received practically in all areas. The Authority reached the top five positions in Europe with regards to assessment of generic medicines through the centralised procedure.

In 2015, the Medicines Authority had on its local register over 4800 authorised medicines. This has been achieved through the willingness, trust and efficiency of the Authority which spearheaded decisions by pharmaceutical stakeholders for exploring new marketing initiatives of benefit to the consumers.

These high strength achievements are due to the collaboration between the Authority and the wide, versatile, precious contribution of all stakeholders. Nothing could have been achieved without the high professional and academic attributes of all the staff at the Medicines Authority which places our Medicines Authority in a class of its own.

Message by the Chairperson

This past year has been successful and rewarding for the Medicines Authority. The key values of the Medicines Authority based on people, quality, integrity and innovation as expressed in the Authority's fresh image including its new logo reflect our broader remit and regulatory functions that have grown significantly since the Medicines Authority was first established. The Medicines Authority operates in a fast-paced environment to meet the changes in scientific development, new legislations and stakeholder needs.

The planned outcomes of the Medicines Authority are ambitious but balanced. The Authority is working in closer collaboration with the European Medicines Agency and the European network of medicines regulatory agencies to collaborate and participate in the assessment of medicines. The experience and sharing of knowledge gained from this collaboration has continued to bring a high standard of science on the assessment of medicines. In 2013 the Authority carried out assessment of eight (8) procedures as Reference Member State. This number has tripled to twenty seven (27) procedures in 2015. The Authority also continued to invest to increase the number of bids for assessment for the European Medicines Agency. In 2015 the Authority participated in six (6) procedures as compared to two (2) procedures in 2013. This increased activity in European procedures and the active participation in assessing applications for centrally registered medicines has made the Medicines Authority sustainable while facilitating the registration of medicines in Europe at the most efficient possible way.

The first EU Good Manufacturing Practice (GMP) third-country inspection was carried out in 2013 and in the past two years more than ten (10) inspections of such companies were carried out. These manufacturing sites have all been inspected and awarded a GMP certificate by our highly stringent but equally efficient Medicines Authority inspectors, bringing an income of over two hundred thousand euros (€200,000) from outside of Europe.

The Medicines Authority is well known for promoting continuing education. In 2015, the Authority invested one hundred thousand euros (€100,000) Euros in training, professional development and learning opportunities through international and European exposures. The consumers are the ones ultimately benefiting from this investment in training and development as this will ensure maintaining the high standards of the functions of the Medicines Authority. At the Medicines Authority thirty two per cent (32%) of staff members are furthering their studies both with the University of Malta and other institutions. In addition, ten people are following a traineeship programme which is being offered to postgraduate students of the University of Malta.

Another characteristic of the Medicines Authority is the active listening to and the extended consultation with all stakeholders. We are convinced that listening to stakeholders enriches the quality of the services provided by the Medicines Authority to better meet the needs of the stakeholders.

In view of the relocation of the Medicines Authority to the Malta Life Sciences Centre and in an effort to move towards more electronic records, the Medicines Authority is currently carrying out an exercise to scan all licensing documentation. The estimated cost for this project in 2010 was between six hundred thousand euros (€600,000) and six million euros (€6,000,000). The Authority is using internal resource to carry out this same scanning project at one hundred thousand euro (€100,000) making also use of the support given by the Government Printing Press. I would like to thank all who contributed to this project.

Patients remain at the heart of our work. In 2015 we strengthened the setting up of the Medicines Intelligence and Access Unit to facilitate patient access to medicines and develop opportunities for patient empowerment.

I would like to acknowledge and thank the commitment and competence of all the staff of the Medicines Authority and the staff of the Ministry for Social Dialogue, Consumer Affairs and Civil Liberties without whose active contribution the achievements of 2015 would not have been met.

Professor Anthony Serracino Inglott
Chairperson, Medicines Authority

1. Achieving Results through People, Good Governance and Innovation

1.1 Leadership, Decision Making and Communication

During 2015 the Medicines Authority participated in a strategic review which was carried out in collaboration with the Management Unit (OPM). Meetings with internal and external stakeholders were carried out. Prioritised opportunities for improvements were implemented in line with the Medicines Authority's commitment to protect and enhance public health and the consumer.

Open communication, collaboration and stakeholder engagement were strengthened and the Authority organised its first structured stakeholder meeting to share achievements and better understand the needs and expectations of its clients.

A holistic rebranding exercise was carried out and the four values of the Medicines Authority, quality, integrity, people and innovation were presented in a new logo which reflects the advancements carried out by the Authority.

The Authority participated in the IX Medical School Conference with a stand entitled "Medicines Safety and Access". Through this stand the Authority provided information on its services, objective and unbiased information on medicinal products and carried out research with medical practitioners and health care professionals on safety of medicines.

1.2 Capacity

The number of persons employed by the Medicines Authority at the end of 2015 was forty one (41) (Table 1).

	Female	Male
Management	2	5
Professional	17	9
Administration	6	2
Total	25	16

Table 1: Employees at the Medicines Authority

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 2015 Medicines Authority's employees attended and successfully completed thirty (30) short to medium courses. These courses, which were offered either internally or externally, dealt with a variety of topics, including Good Manufacturing Practice requirements for sterile products, quality management system, inspections and pharmacovigilance.

During 2015 the Medicines Authority also supported its employees to read postgraduate studies through a flexible approach. Four (4) of the Authority's employees are undergoing Doctoral studies and four (4) employees are undergoing studies at Masters Level. Five (5) employees have started a Diploma in Leadership and Management.

Furthermore, the Authority relaunched 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, ten (10) individuals are undergoing Doctoral studies whilst participating in the traineeship programme of the Medicines Authority.

1.4 Quality, Simplification and Better Regulation

The Medicines Authority processed a total of seven (7) policies and thirty (30) standard operating procedures. The process incorporated changes in policies as well as corrective and preventive action identified through implementation of operations, internal audits and Management Review. The Medicines Authority implemented the audit programme for 2015 in line with the three-year audit strategy. A total of three (3) internal audits were performed in 2015 on the internal processes which resulted in a number of quality improvements. A total of thirty eight (38) quality improvements were processed by the Medicines Authority. 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. Thirty two per cent (32%) of the quality improvements identified resulted from internal / external audits. The implementation of all quality improvements is monitored centrally. An annual Management Review was performed, during which the Quality Management System as detailed in the Quality Manual was reviewed. 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.

Five simplification actions were prioritised for 2015. These were identified and prioritised in line with on customer feedback. The first action was the introduction of new guidelines on Pharmacovigilance (safety of Medicines) in order to simplify the industry requirements. The second action was the introduction of new guidelines on fees in order to give clearer information on the fees of the Medicines Authority. The third action was to simplify the submission processes of applications. The Medicines Authority is now accepting applications of centralised procedures and other documents related to post-licensing from the central repository of the European Medicines Agency. The fourth action was to support CPSU (Cental Procurement and Supplies Unit) in the registration of medicinal products in order to simplify the procedures and reduce the list of medicines out-of-stock. The fifth action was to strengthen the support to all relevant stakeholders in order to access the medicines at the lowest possible price. The Medicines Authority in collaboration with the Malta Competition and Consumer Affairs Authority (MCCAA), is providing information to consumers on the prices of available generics compared to the originators or other generic products available on the local market. All five actions are within timelines and budget and has led to simplification for the benefit of stakeholders.

Further enhancement in the receipt of electronic submissions with the reduction in paper submissions was achieved in 2015. During 2015, the Medicines Authority has embarked on a project to start changing all archived paper information to electronic format. Applicants are being encouraged as much as possible to use

the Common European Submission Portal (CESP) and no paper submissions are being requested. During 2015, approximately sixty-seven per cent (67%) of all submissions for European procedures were sent via the portal. Local applicants are being encouraged to register for use of the portal to further reduce the number of submissions on physical media.

1.5 Active Participation at EU and International Level

During 2015, the Medicines Authority has participated actively in European and International fora. Medicines Authority officers participated in one hundred and forty one (141) 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.

In 2015, the Medicines Authority strengthened its participation 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 2015, the Authority followed up data at EU level and actively participated in a project status update. In June 2015, the Medicines Authority hosted the 17th Heads of Medicines Agencies Working Group of Enforcement Officers Meeting. The Working Group of Enforcement Officers (WGEO) was established in 2007 by the HMA to contribute to the protection of human and animal health and welfare. The primary aim of WGEO is promote liaison and co-operation between Member States and agencies with the purpose of sharing information, identify emerging threats to the legal manufacturing and distribution chain, coordinate communications and initiatives, exchanging information with relevant working parties/groups and organisations, provide a valuable network for European counterparts to build trust, share experience, best practice and expertise relating to pharmaceutical crime; and deliver a practical training platform – largely related to the four work-streams: wholesale and distribution, Internet (illegal supply of medicines), falsified medicines and training and education.

1.6 Transparency

The Medicines Authority prioritised measures that encouraged transparency and freedom of information. Meetings were carried out with the Internal Audit and Investigation Directorate within the Office of the Prime Minister and the Authority strengthened its collaboration with this Directorate through the sharing of internal audits carried out by the Authority for the second time, the Authority is publishing an abstract of the audited financial statements to enhance openness and transparency.

2. Safe, Efficacious and High Quality Medicines for the Benefit of Patients

2.1 Scientific Advice

In 2016, Malta will be the Rapporteur evaluating a line extension of an authorised medicinal product for a new significant indication. The Medicines Authority is open to extend its scientific advice function.

2.2 Assessment and Licensing

2.2.1 Malta as Reference Member State and rapporteur in European registration procedures

During 2015 the Medicines Authority continued with activities towards national and European procedures for the registration of new medicinal products. 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 as rapporteur in the Centralised procedure, both for pre- and post-authorisation activities (Figure 1). It is envisaged that these procedures will increase over the next years With planned enhanced capacity and the focus on the competence of its staff, the Medicines Authority will be able to carry out these procedures for a more diverse range of medicinal products. Staff has been recruited for the technical assessment of dossiers for these procedures to ensure adequate capacity to handle more procedures.

For procedures for which Malta is 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, where technical or regulatory decisions are taken or endorsed for a final position for Malta.

There was an increase of forty-two per cent (42%) in the number of new applications received through European procedures with Malta as Reference Member State or rapporteur in 2015. This has also resulted in a higher volume of post-authorisation procedures for these marketing authorisations (Figure 2). It is envisaged that the number of post-authorisation procedures will increase over the next years as the number of new applications finalised increases.

Through the continued collaboration with the Medicines Evaluation Board (Netherlands) signed in 2014, the Medicines Authority has continued to carry out assessment of applications for the Dutch competent authority. This has been a successful cooperation for both entities. It has also helped to enhance the competence of the Medicines Authority assessors, whilst giving some insight into how other competent authorities manage their processes and resources.

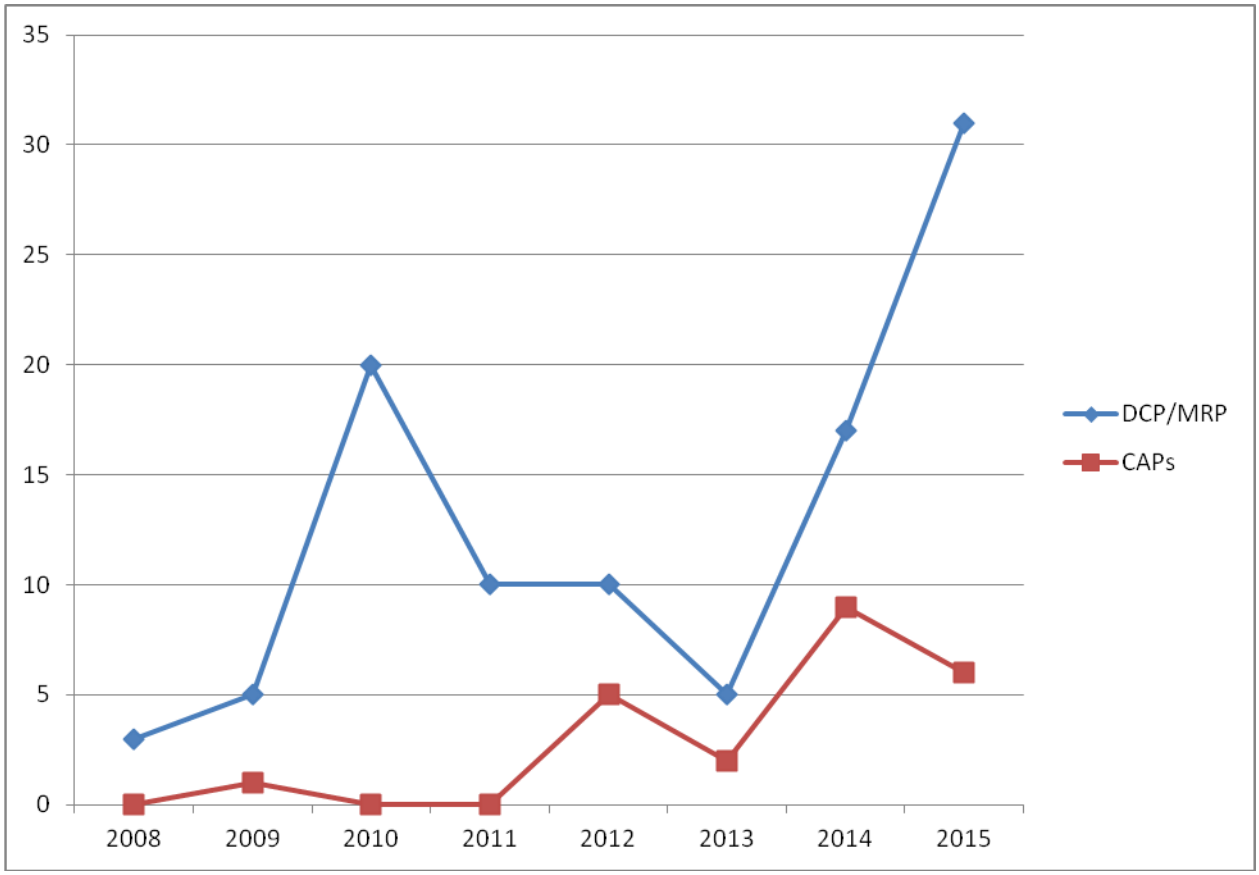

Figure 1: Number of procedures received by the Medicines Authority with Malta as Reference Member State or rapporteur in the period 2008-2015

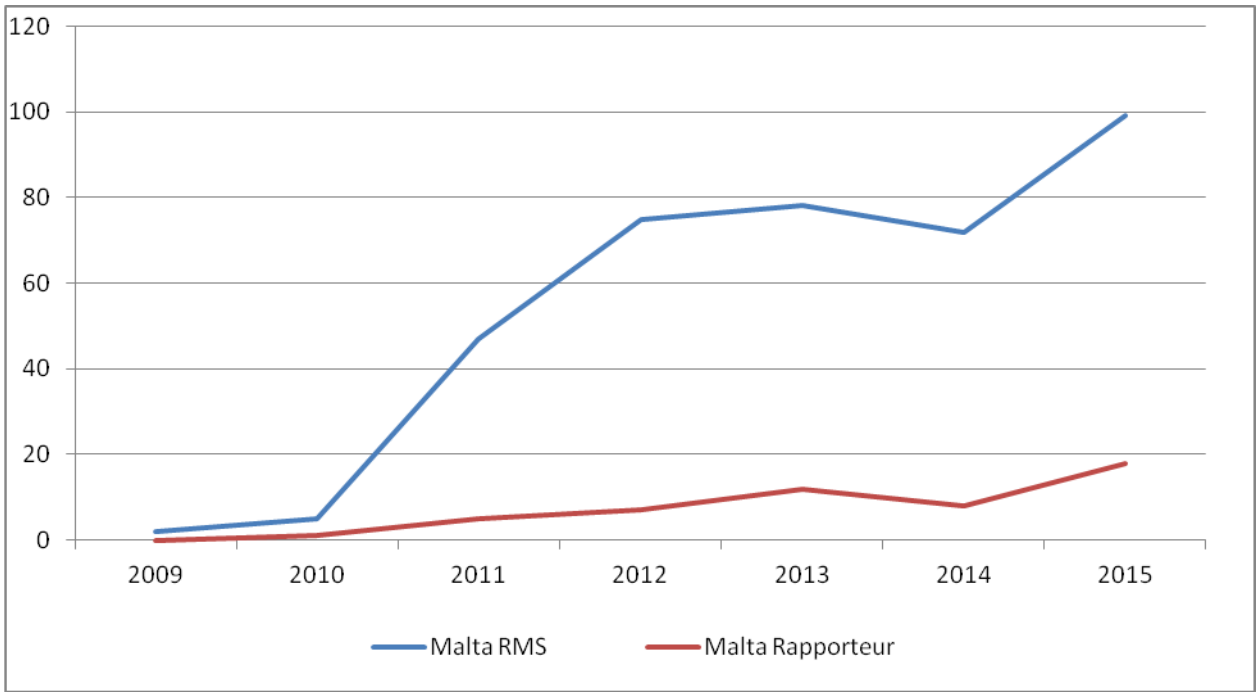

Figure 2: Number of variations received for European procedures with Malta as Reference Member State or rapporteur in the period 2009 – 2015

2.2.2 Applications for new authorisations through various routes resulting in national authorisations

The number of applications for new authorisations for the approval of new products has increased during 2015. The total number of products applied for through all registration routes has increased, resulting in more authorised products to be placed on the Maltese market. Applications received are in Figure 3.

2.2.3 Post authorisation procedures

Nationally authorised products

A number of post-authorisation procedures are received each year including variations, notifications, renewals and withdrawals. The information in Figure 4 refers to nationally authorised products (marketing authorisations (MA), authorisations in accordance with article 126(a) of Directive 2001/83/EC (AA) and parallel imports (PI)) in 2015. The figure also includes information on amendments to clinical trials (CT). National variations and article 61(3) notifications are included in Figure 5.

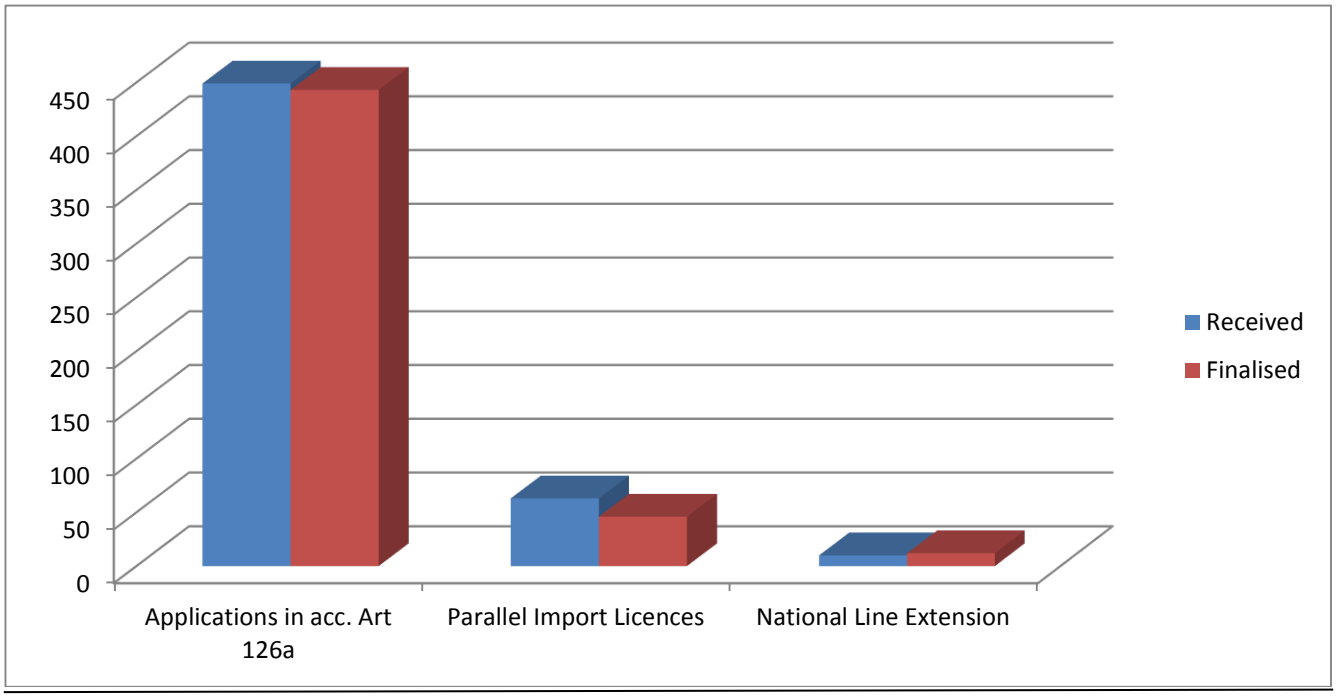

Figure 3: National applications received and finalised in 2015

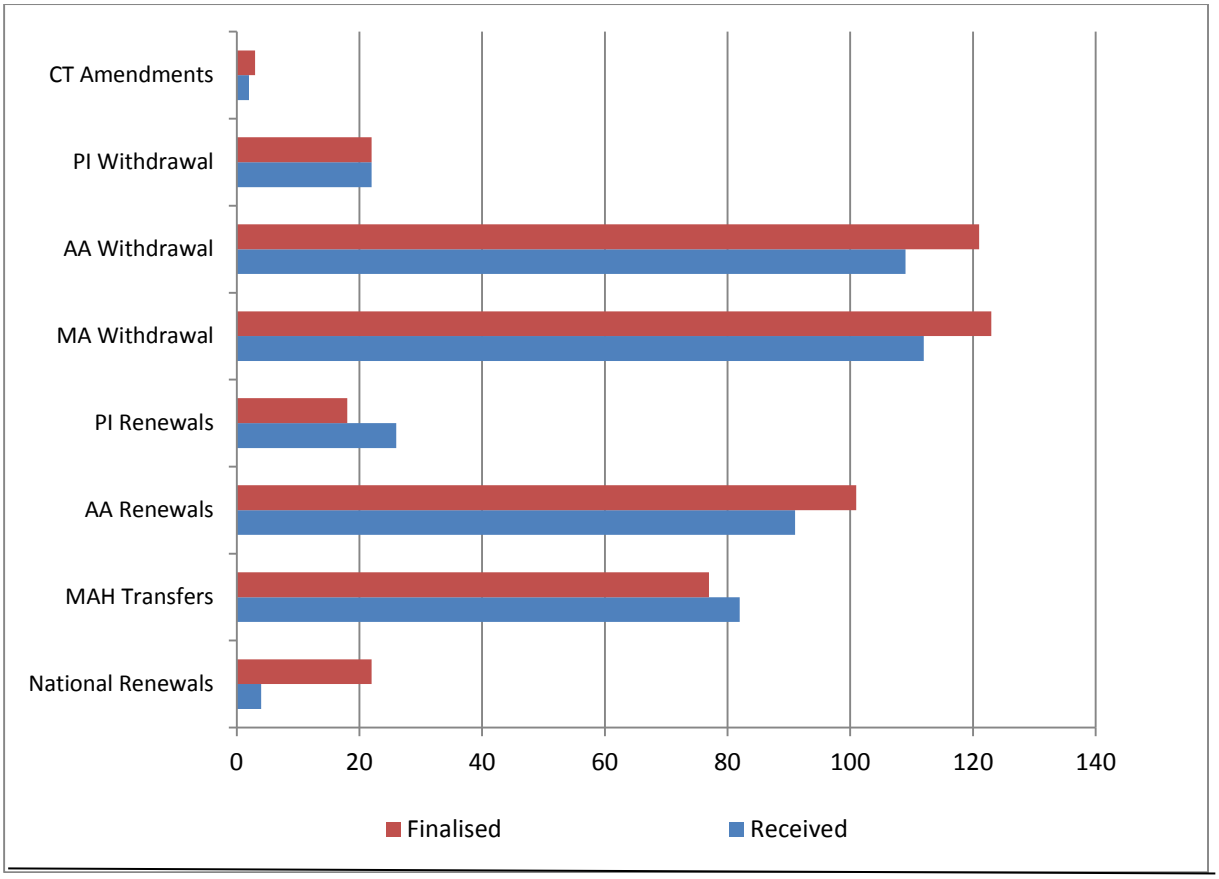

Figure 4: Number of national post-authorisation procedures received in 2015

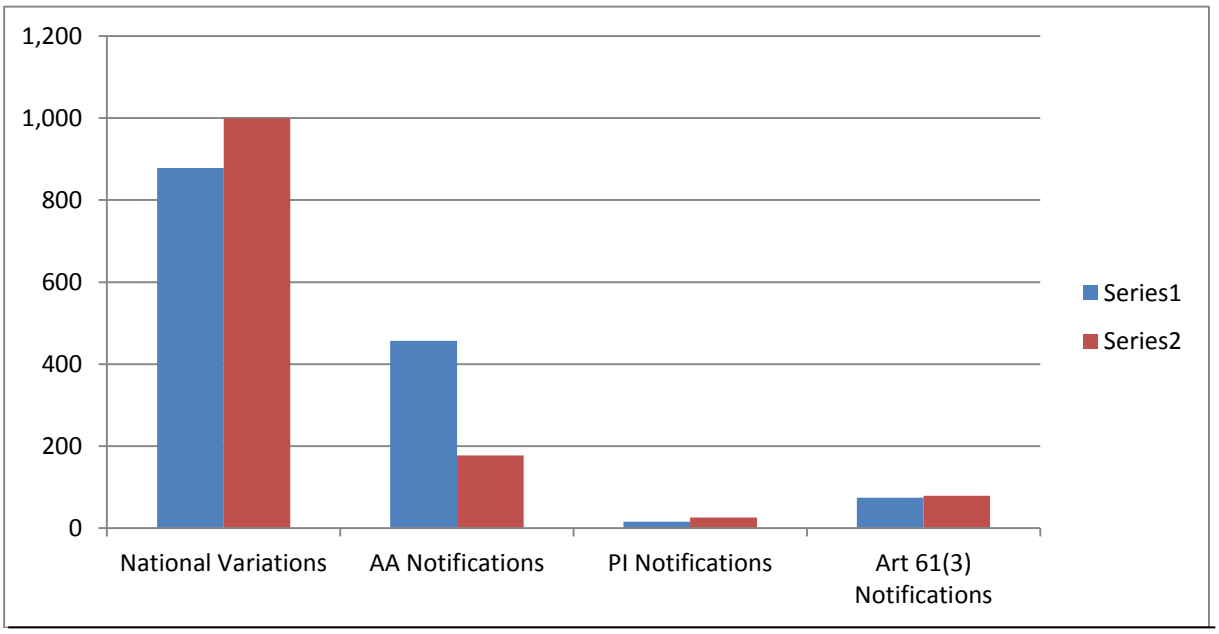

Figure 5: Number of variations and article 61(3) notifications

Products authorised through the Mutual Recognition and Decentralised procedures

Variations, renewals and notifications for procedures received through the European procedure route are shown in Figures 6 and 7.

Paediatric Data Assessment (Article 45 and Article 46 of the Paediatric Regulation

During 2015, Malta was rapporteur for two European work-sharing procedures in accordance with article 45 of European Regulation 1901/2006. This resulted in changes to the information on the products, including the package leaflet of medicines, to enhance safe use in children.

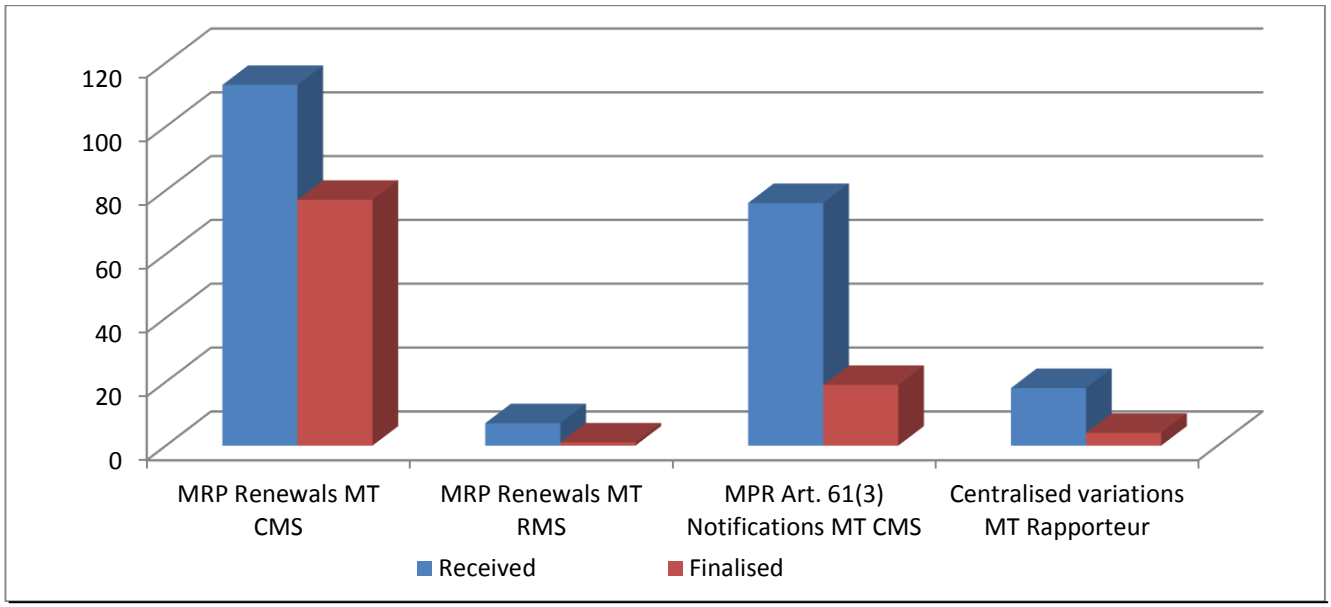

Figure 6: Number of post-authorisation procedures through the MRP received in 2015

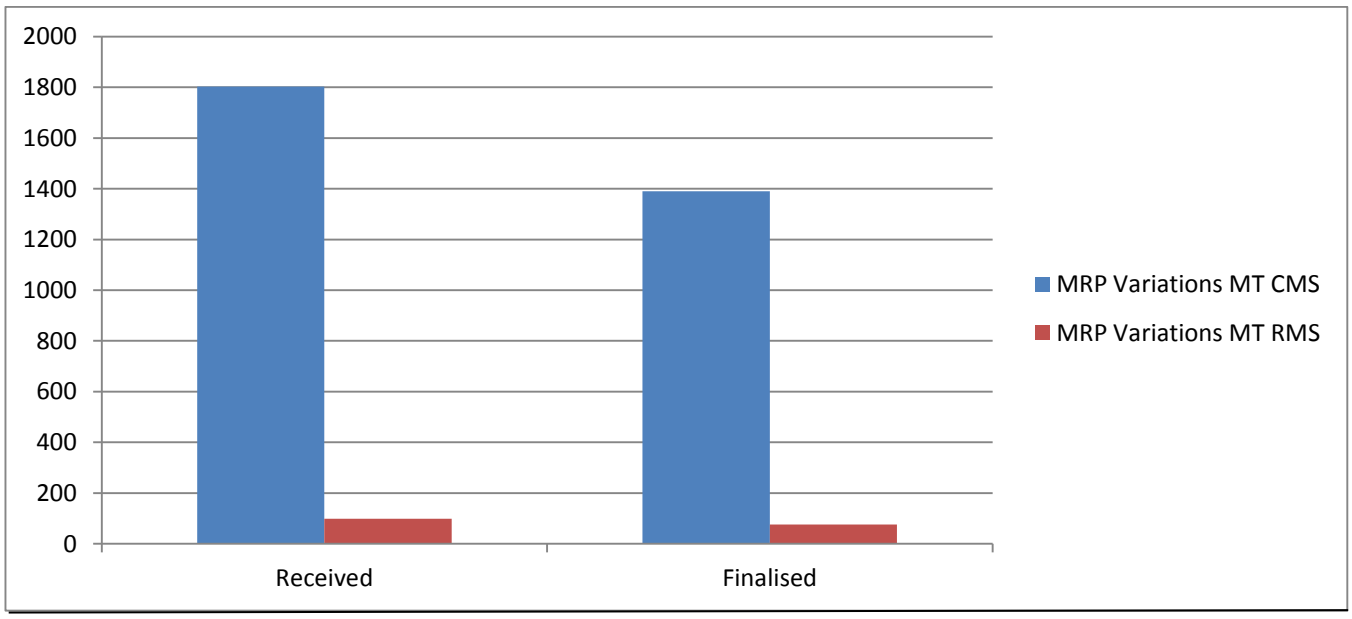

Figure 7: Variation applications received and finalised through European procedures (MT RMS and MT CMS)

2.2.4 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 include feedback from external technical and regulatory meetings attended by members of the Medicines Review Committee and other staff members (e.g. Coordination Group for Mutual Recognition and Decentralised Procedures - Human (CMDh), Pharmacovigilance Risk Assessment Committee (PRAC), Paediatric Committee (PDCO) and Committee for Medicinal Products for Human Use (CHMP) and its working parties) Issues relating to the local market, such as safety issues following on from European referrals are discussed. Meetings are held on a monthly basis.

2.3 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, monitoring and communication of safety related data and, where appropriate, implementation of regulatory action to maximise benefit and minimise risks associated with medicinal products. The Medicines Authority has in the past year, maintained its active role in Pharmacovigilance.

2.3.1 National Pharmacovigilance Activities

The Medicines Authority participates 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 (the 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 as the approval of Direct Healthcare Professional Communications (DHPC) 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 IT applications such as EudraVigiliance (EV) and EV Data Analysis System (EV DAS). In 2015, an additional staff member obtained the necessary E.U. certification to enable input of Adverse Drug Reactions (ADR) within the Eudravigilance database as well as in-house training on ADR assessments.

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 medicines 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. The Medicines Authority hosts the report form for ADRs and medication errors online at www.medicinesauthority.gov.mt/adrportal.

Healthcare professionals are encouraged to use this form to submit ADR reports as per S.L.458.35, 3 (4). In 2015, the Medicines Authority concluded several activities which had been planned within a three (3) year ADR promotion strategy that expired in 2015. The first output was the publication of a new national Guideline for pharmacovigilance obligations specific for Malta. In relation to ADR reporting, in this Guide, Marketing Authorisation Holders were directed to send ADRs directly to the EU database to which the Medicines Authority has direct access for signal detection activities. This has led to a reduced administrative burden of parallel reporting for Marketing Authorisation Holders and the Medicines Authority.

A second output of focus was promotion of the ADR reporting system within the Medical School. Within this event, ADR reporting promotional posters and video material was provided and staff was present to answer questions and receive feedback from stakeholders on the ADR reporting system. In addition, feedback was obtained from stakeholders through a survey on opinions of doctors and pharmacists regarding factors leading to medication errors. This survey was part of an overall attempt to improve the medication error reporting system of the Medicines Authority launched over 2013-2014. The Medicines Authority has also published an article in the Eastern Mediterrean Health Journal journal on the Malta medication error reporting system. This is available in free full text at http://apps.who.int/medicinedocs/documents/s21957en/s21957en.pdf. The Medicines Authority is hopeful that healthcare professionals will realise the value of the medication error reporting system as a learning system to prevent the occurrence of repeat incidents and remain open for questions and suggestions on how to improve the system.

A total of one hundred and twenty two (122) Individual Case Summary Reports (ICSRs) were registered over 2015. Each of these cases detailed at least one adverse drug reaction to the medicinal product concerned thus resulting in a total of six hundred and fifteen (615) individual adverse drug reactions. Figure 8 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 signals

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

Figures 9 and 10 further classify the adverse drug reaction case reports (as received over 2015) 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, concurrently administered 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.

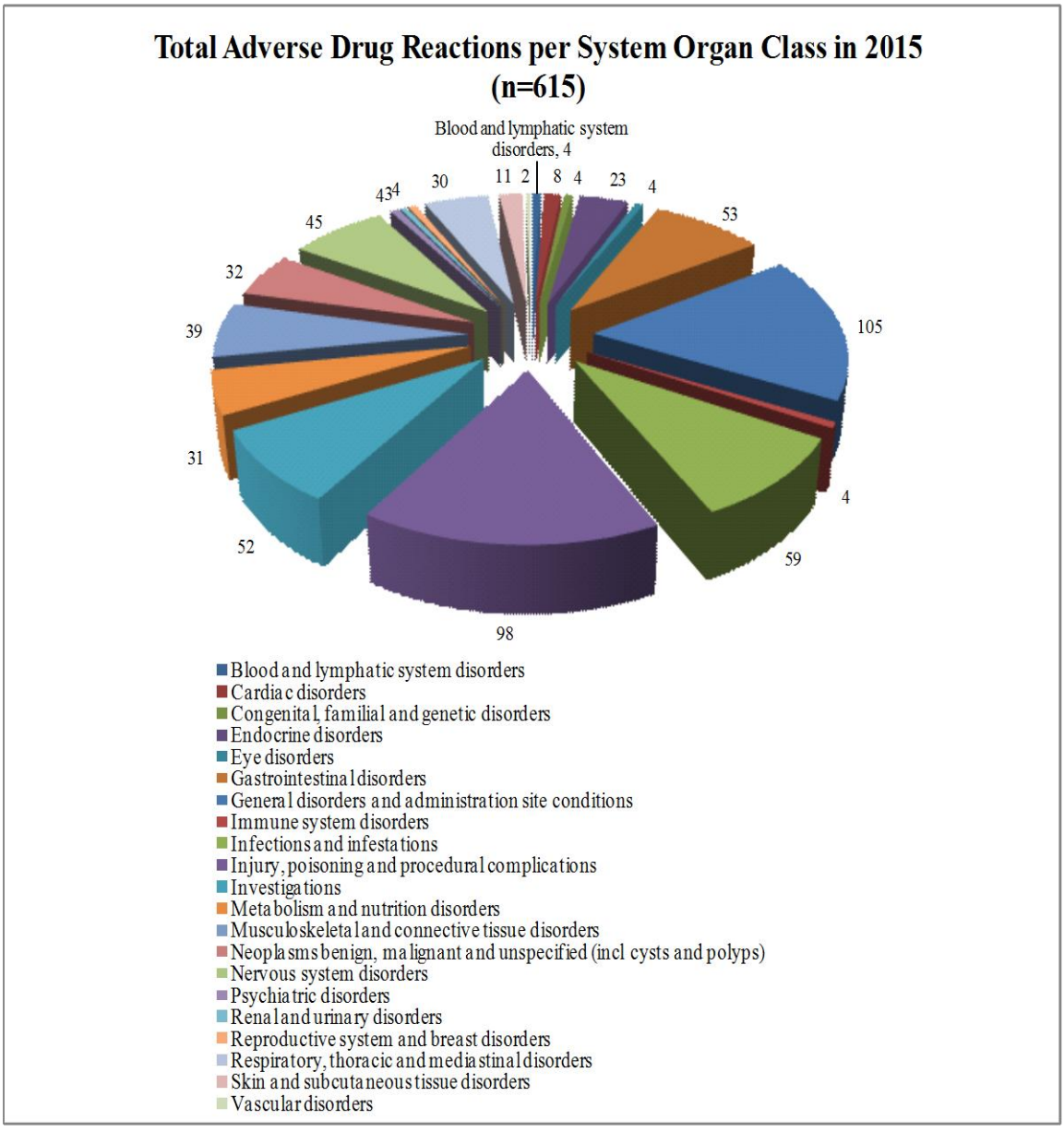

Figure 8: Distribution of Adverse Drug Reactions according to System Organ Classification in 2015

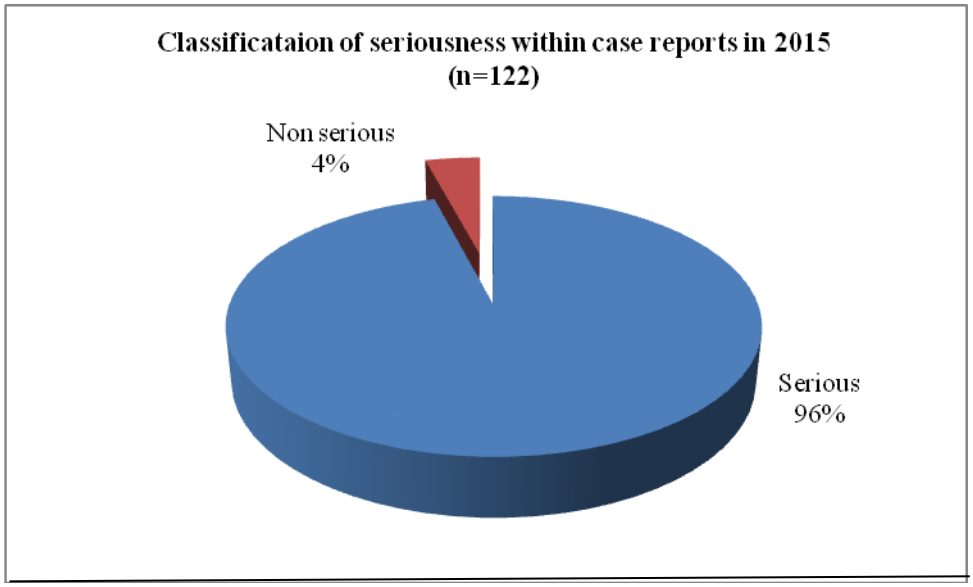

Figure 9: Frequency of ICSRs according to seriousness in 2015 (n=122)

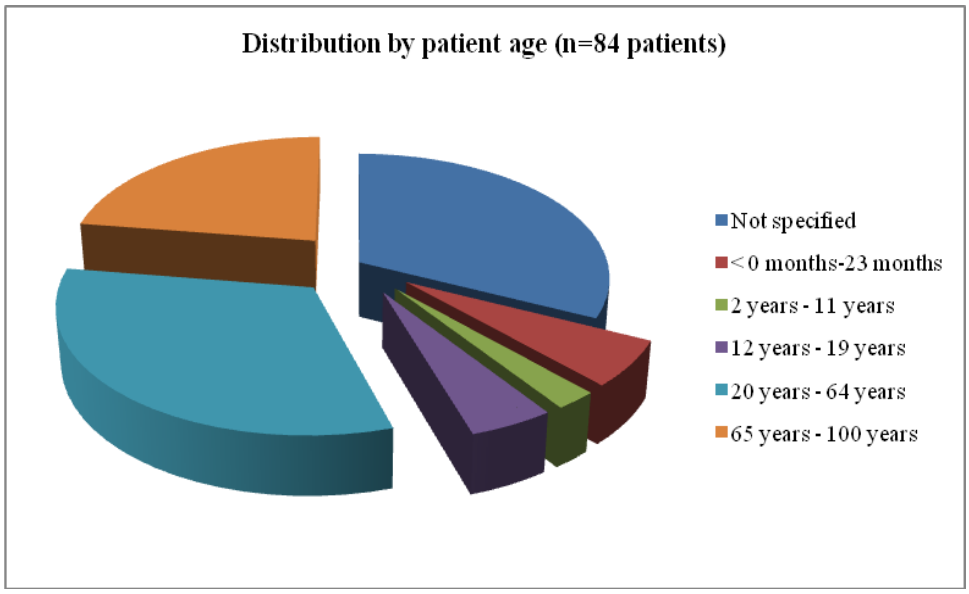

Figure 10: Percentage distribution of case safety reports according to patient age in 2015 (n=84 patients)

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 Medicines Authority may, 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 2015 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), (8) 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), (9) Review of newly emergent data concerning safety evidence of a medicinal product, substance or class upon request, (10) 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 handled over 2015.

The joint DHPC service which was launched in 2014 by the Medicines Authority focussing on initiating a new procedure for a joint DHPC service was maintained in 2015. In this process, when more than one marketing authorisation holder is obliged to circulate the same DHPC or more than 1 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.

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 Periodic Safety Update Reports (PSURs), ADR reporting requirements and Risk Minimisation Measures (RMMs) (Table 3).

In March 2015 the Medicines Authority released a Guidance Notes document following a period of 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 Medicines Authority from 2012 to 2014. The guide can be located at http://www.medicinesauthority.gov.mt/safety in the 'Further Information' section.

At an EU level 2014 saw the start of the centralised PSUSA assessments and over 2015 the Medicines Authority was involved in a number of reconciliation exercises together with the European Medicines Agency. Submissions via the PSUR repository will be mandatory by mid 2016 and at that stage the Medicines Authority will no longer receive PSURs in hardcopy but will access PSURs via the competent authority interface to carry out PSUR assessments.

Documents Received	Number of submissions
PSURs	280
Risk Management Plans	2
SUSAR	0
Annual Reassessments	0
Direct Healthcare Professional Communications	11
Joint DHPCs	2
Safety Circulars	15
Risk Minimisation Measures	83
Rapid Alert	0
Non Urgent Information	14

Table 2: Pharmacovigilance and safety issue reviews and communications - 2015

		Number
1	**PSUR**	15
2	**ADR reporting**	14
3	**RMM**	8
4	**QPPV**	7
5	**Clinical Trial reporting requirements**	4
6	**QRD Text**	4
7	**National PhV legislation and requirements locally**	3
8	**Literature monitoring requirements**	2
9	**Request for ADR related data**	2
10	**Article 57 database**	1
11	**DHPC distribution**	1
12	**Legislation for PhV in Malta**	1
	Total	63

Table 3: Pharmacovigilance related queries in 2015 (n=63)

2.3.2 EU Pharmacovigilance Activities

Following the 2012, Directive 2010/84/EU and commission implementing regulation 520/2012 on Pharmacovigilance which was transposed, and the preparation for the new changes, 2015 saw another year of fulfilling legislative obligations and updating procedures to maintain requirements with the new directive.

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 on the audit outcomes was transmitted to the EU Commission in 2015. No critical or major findings were identified in these audits.

In 2015 Malta started and finalised as lead member state a Period Safety Update Report Single Assessment Procedure (PSUSA).

2.4 Classification of Borderline Products

The Borderline Classification Committee classifies products into medicinal products and non-medicinal products when requests for classification are received from companies and from other sources. The Borderline Classification Committee meets as required and feedback is sought from all Members as well as the herbals expert in line with the updated process. In 2015 thirty-two (32) applications for classification of borderline products were received, out of which eighteen (18), fifty-six per cent (56%), were considered as non-medicinal, eight (8), twenty-five per cent (25%), were considered medicinal and six (6) applications were still being reviewed at the end of the reporting period.

2.5 Advertising of Medicinal Products

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. 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). 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 2015 no advertising complaint was registered with the Medicines Authority.

3. Medicines Intelligence and Access

3.1 Availability of Medicinal Products

Availability Working Group

The main target for the Availability WG for 2015 was to continue working on the harmonisation of the prescription status for some medicinal products which had been authorised during the transitional period. More applications were received by the Medicines Authority 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.

3.2 Rational Use of and Access to Medicinal Products

The Medicines Authority expanded proactively its activities with the setting up of the Medicines Intelligence and Access Unit. This initiative was a very important step to the Medicines Authority, to better communicate the overall objective of safeguarding human health. The Medicines Intelligence and Access Unit is responsible to manage a proactive and targeted approach taking into account the expectations and needs of both patients, health care professionals and other stakeholders.

In collaboration with the Malta Competition and Consumer Affairs Authority (MCCAA), the Medicines Intelligence and Access Unit is on an ongoing process of dialogue with stakeholders in the pharmaceutical sector to ensure that the medicines remain at an affordable price for the patients, and the public will also have access to essential medicines with a reasonable price when compared to other countries. This is leading to a reduction in prices of medicines for the benefit of consumers which in 2015 has led to thirty-nine (39) medicines price reduction. The savings for the consumers was up to forty-eight per cent (48%).

During the ongoing information campaign Mediċini: Għażla Aħjar Għalik', consumers are being informed about the choice of medicines available on the local market and the importance of discussing these choices with healthcare professionals. The Medicines Authority is continuously updating lists of generic medicines which have been recently authorised and is comparing the prices of these medicines with the originators and other generics so that the consumer can use such information to decide the best treatment option. All of these generic medicines have been assessed by the Medicines Authority to ensure that all medicines conform to the established standards of quality, safety and efficacy. In 2015 a list of ninety-two (92) generic medicines has been published for the consumers, including medicines which are up to ninety-two per cent (92%) less expensive than their originator or other generic equivalent.

On the occasion of the World Pharmacist Day, the Medicines Authority in collaboration with the Pharmacy Department at the University of Malta, a press conference was held in order to further raise awareness among the general public about generic medicines. During this day, pharmacy students assisted consumers with their medication queries, provided information about health conditions and lifestyle modifications and carried out point-of-care blood pressure and glucose monitoring.

Pharmacy students performing blood pressure monitoring to consumers during World Pharmacist Day

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 carries 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 2015 the Medicines Authority carried out Good Manufacturing Practice (GMP) inspections for new, renewal or follow up of GMP licences/certificates. These included: one (1) GMP inspection for an active pharmaceutical ingredient; three (3) for non sterile solid dose manufacturers; three (3) inspections for manufacturing authorisation (MAs) for repackaging and re-labelling / partial manufacturing operations; four (4) inspections for MAs of importation activity.

A total of thirty one (31) MAs administrative variation applications were processed in 2015 for manufacturers and importers. One (1) variation with inspection was carried out.

There were four (4) Inspections Review Group meeting held throughout 2015 where seven (7) cases were discussed and decided upon.

During 2015 the Medicines Authority received ninety two (92) 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. Five (5) inspections have been carried out throughout 2015. Another two (2) applications which were processed and prepared for inspection in 2015, were however postponed by the by the applicant for 2016. 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 2015 the Medicines Authority has also fulfilled its Good Distribution Practice (GDP) inspection plan where twenty nine (29) GDP inspections were carried out. During 2015 eight (8) applications for new wholesale dealing licences were submitted, which were all inspected and eventually licensed. Fifteen (15) variation applications for wholesale dealing authorisations were processed in 2014, out of which one (1) required an inspection. Also in 2015 one application for registration of a broker of medicinal products in the distribution chain was received, processed and inspected, with the applicant being registered as a broker.

4.3 Pharmacies

Pharmacies are inspected on a two (2) year cycle. During 2015 the Medicines Authority carried out a total of seventy-six (76) retail

community pharmacy inspections, five (5) Government pharmacies in the National Health Service and one (1) private hospital pharmacy.

There were another eight (8) pharmacy inspections following variation applications for pharmacy premises transfers or alterations which were carried out, whilst forty six (46) administrative variations for pharmacy licences were processed.

4.4 Clinical Trials and Pharmacovigilance Inspections

During 2015 in view that no new Clinical Trials applications were submitted to the Medicines Authority, no inspections for this activity were required.

Three (3) Pharmacovigilance (PhV) inspections were carried out against the national and EU legislation and the Medicines Authority 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 2015 was closed positively.

4.6 Enforcement of legislation

During 2015 the Medicines Authority worked upon four (4) enforcement cases/ investigations which were related to complaints and enforcement. The Enforcement Committee (a specific committee which discusses enforcement cases, chaired by the Licensing Authority) met once in 2015.

In 2015 there were twelve (12) court case sittings concerning pharmacy issues and two ongoing enforcement cases. Medicines Inspectors attended two (2) court sessions regarding enforcement as witnesses.

4.7 Granting of Qualified Persons Status

In 2015 the Medicines Authority received fourteen (14) new applications for the Qualified Person (QP) status. Twelve (12) applicants were interviewed during 2015 and of these eight (8) were approved as eligible for QP status.

4.8 Certificates of Pharmaceutical Products (CPPs)

During 2015 eighty-four (84) Certificate of Pharmaceutical Products applications were received and processed, out of which eighty-one (81) certificates were issued.

Appendix 1:

Extract from Annual Report and Financial Statements for the Year Ended 31 December 2015

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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 17 which comprise the statement of financial position as at 31 December 2015, 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.

Chairperson/CEO's responsibility for the financial statements

As described on page 1, the Chairperson/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 Chairperson/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 Chairperson/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 2015 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.

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Certified Public Accountants
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MAZARS

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

Emphasis of matter

Without qualifying our opinion, we draw attention to note 15 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 2015 the case was still under appeal.

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

12 February 2016

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Medicines Authority

Statement of comprehensive income
For the year ended 31 December 2015

	Notes	2015 EUR	2014 EUR
Income	5	**2,828,519**	1,922,986
Expenditure			
Staff costs	6	**(1,297,743)**	(1,190,207)
Amortisation and depreciation		**(23,733)**	(11,467)
Audit fee		**(2,360)**	(2,360)
Finance costs		**-**	(366)
Other operating expenses		**(507,826)**	(452,819)
Operating surplus for the year before taxation		**996,857**	265,767
Income tax expense	7	**-**	-
Surplus for the year		**996,857**	265,767
Other comprehensive income for the year		**-**	-
Total comprehensive income for the year		**996,857**	265,767

The notes on pages 9 to 17 are an integral part of these financial statements.

Medicines Authority

Statement of financial position
As at 31 December 2015

	Notes	2015 EUR	2014 EUR
ASSETS			
Non-current assets			
Intangible assets	8	13,366	17,595
Tangible assets	9	199,075	10,415
		212,441	28,010
Current assets			
Trade and other receivables	10	754,437	450,836
Cash and cash equivalents		1,153,226	570,108
		1,907,663	1,020,944
Current liabilities			
Trade and other payables	11	751,925	677,632
Net current assets		1,155,738	343,312
Net assets		1,368,179	371,322
RESERVES			
Accumulated fund		1,368,179	371,322

The notes on pages 9 to 17 are an integral part of these financial statements.

The financial statements on pages 5 to 17 were approved by the Chairman / Chief Executive Officer on 12 February 2016;

Anthony Serracino Inglott
Chairman / Chief Executive Officer

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