2011

Annual Report

AWTORITÀ DWAR IL-MEDIĊINI

Review by the Chief Exe

Dr. Patricia Vella Bonanno

Medicines Authority
203,Level 3,
Rue D'Argens,
Gzira,GZR 1363
Tel: (+356) 2343 9000
Fax: (+356) 2343 9161
Email: info.medicinesauthority@gov.mt

Protecting and Enhancing Public Health

During 2011, the Medicines Authority continued making a contribution to protect and enhance public health both in Malta and the EU. Four hundred and ninety one (491) medicinal products were authorised through European and National Procedures. There were eleven (11) procedures where Malta was Reference Member State. The Medicines Authority collaborated with the Medicines and Healthcare Regulatory Agency (UK) and the Irish Medicines Board (Netherlands) to increase the inclusion of Malta as a Concerned Member State. The total amount of authorised products (excluding centrally authorised products) amounted to three thousand nine hundred and forty seven (3947). The Authority continued monitoring medicinal products on the market after authorisation. The total amount of inspections (GCP, GMP, GDP, Pharmacy and Pharmacovigilance inspections) amounted to two hundred and twenty one (221). Pharmacovigilance Inspections were done for the first time.

A paper[1] on the Seven years of EU pharmaceutical regulation in Malta was published to give an overview of the developments in the pharmaceutical regulation since accession in the EU in 2004 and the outcome of regulation in terms of public health and the development in the sector.

Leadership, Opportunities, Innovation and Sustainability

During 2011, the Medicines Authority focused on four main areas: Leadership, Opportunities, Innovation and Sustainability.

Leadership: The Medicines Authority's milestones set by the corporate calendar were followed and achieved. These included corporate staff meetings at the beginning, mid and end of the year, management review at mid year and performance appraisals for all staff. The Medicines Authority implemented new assignments through focused working groups and through projects.

[1] Vella Bonanno, P. and Flores, G. (2011) ***Seven Years of EU Pharmaceutical Regulation in Malta.*** WHO Drug Information. vol. 25, no. 4, pp. 343-353.

Opportunities: The Authority continued seeking opportunities for contributing towards the protection of public health. The Authority strengthened its capacity for evaluation of medicinal products through extending the range of pharmaceutical dosage forms considered as Reference Member State. The Authority extended its contribution at European level by contributing in the evaluation of medicinal products through participation in paediatric work sharing and through active participation at meetings of the European Medicines Agency, the European Commission and meetings of the Council Working Parties. Preparations for a tender for an Integrated Information Management System started in 2011 and the tender is planned to be issued in 2012. A tender was also issued for new website which is planned to be launched in 2012. The Medicines Authority carried out its first Stakeholder Satisfaction Survey and the results, which are summarised in this report, were encouraging. Opportunities for improvement were considered through management cycles.

Innovation: In 2011, the Medicines Authority focused its priorities to inform and empower patients and health care professionals in line with its communication strategy. The 'Know Your Medicines' initiative was officially launched and a leaflet with information on innovator and generic medicines and on the risks of falsified medicines was distributed to all households in Malta and Gozo. The initiatives were aimed to support and empower patients and healthcare professionals in the choice and use of medicines. A new service of sms notifications for healthcare professionals was also launched. The service aims to enhance the dissemination of updates on quality and safety of medicinal products. The Medicines Authority was awarded two People Awards in the areas of Employee Engagement and People Management Impact on Business Success. Following participation at EU level, particularly at the Council Working Party, in drafting of new legislation on Pharmacovigilance and falsified medicines, the Authority supported the process for the transposition process of Directive 2010/84/EU and Directive 2011/84/EU. Moreover, a process to assign a risk rating to all Manufacturers, Importers and Wholesale dealers based on the Pharmaceutical Inspection Co-operation Scheme started and it is planned that the exercise is finalised by end 2012 to enable risk based inspections in 2013.

Sustainability: During 2011, the Medicines Authority continued focusing on its core business whilst diversifying into new areas of operations. A process to map operations and increase streamlining, efficiency and effectiveness was carried out. The Medicines Authority had a number of cancellations of slots booked by companies for Reference Member State activities. The cancellations were mainly at a short notice and affected the Authority's budget. The Authority continued diversifying its operations and increased the number of bids for rapporteurships for centralised procedures. Although the income decreased, during 2011 the Medicines Authority did not require government subvention. The Medicines Authority proposed a new fee structure to the Line Ministry for consideration.

CONTENTS

1.0 Organisation

1.1 Leadership and Management

In 2011, the Medicines Authority fully achieved the main activities of its corporate management cycle. These activities included the compilation of an Operational Plan at the beginning of the year and formal review of its achievement at mid-year, a business plan for the period 2011-2013, Management Review at mid-year and performance appraisals for employees which are performed twice a year. Five (5) Management and six (6) Interface meetings were held.

1.2 Customer Satisfaction and Communication with Stakeholders

During 2011, the Medicines Authority engaged into a proactive exercise to listen to stakeholders' feedback so as to: (1) assess its performance as perceived by different stakeholders; (2) measure stakeholders' satisfaction with the Medicines Authority's services; (3) increase the Medicines Authority's awareness of stakeholders' needs and expectations to add-value to public health and to pharmaceutical operations; (4) act on relevant opportunities for improvement in line with the objectives, priorities and resources of the Medicines Authority. Consumers and the general public were not within the scope of the exercise as a separate exercise was carried out in 2010.

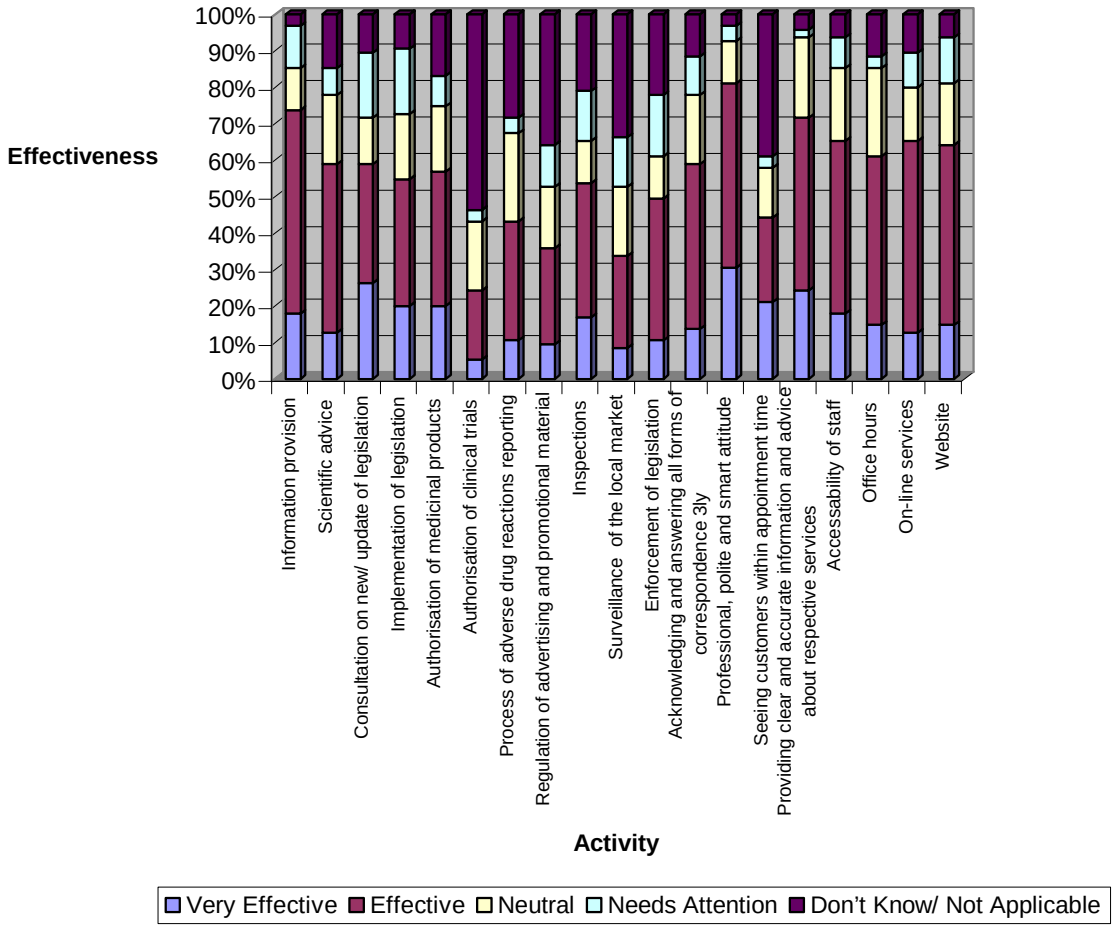
The survey was widely circulated to all stakeholder groups and to stakeholders registered in the Authority's stakeholders list. There were 95 (ninety five) replies out of a total of 750 customers. Thus, the response rate was of 12.7%. The classification of respondents is Healthcare Professionals (26%), Marketing Authorisation Holders (20%), Pharmacy Owners (16%), Wholesale Dealers (13%), Manufacturers (9%), Importers (6%), National/ EU Institutions (4%), Chamber / Union (2%), Researcher/ Academics (1%), Patient / Consumers (1%), Other (1%).

The great majority of respondents were fully satisfied or satisfied with the quality of service of the Medicines Authority (76%), the level of experience and knowledge of staff members of the Medicines Authority (77%), the responsiveness of the Medicines Authority to their needs (71%), the provision of an effective yet supportive regulatory environment (71%), the approach and attitude of the Medicines Authority to its customers (71%) and the Integrity of the Medicines Authority (76%). The other

respondents were neutral, not satisfied or replied 'don't know/ not applicable'. With regards to serving customers and the community and honouring commitments, an average of 45% said that they are fully satisfied or satisfied, 25% answered neutral, 7% not satisfied and 23% answered 'don't know/ not applicable'. The majority of respondents said that they are fully satisfied or satisfied in relation to how the Medicines Authority prevents and solves problems (54%). A quarter said that they are neutral (22%), 12% said that they are unsatisfied and 13% answered 'don't know/ not applicable'. The majority (57%) were fully satisfied or satisfied with the equity of service of the Medicines Authority, 23% were neutral and 16% answered 'don't know/ not applicable', 4% of respondents were unsatisfied.

Customers were also requested to share their perceived effectiveness on the Medicines Authority's activities and a summary of stakeholders' replies is found in Figure 1.

Figure 1: Percieved Effectiveness of the Medicines Authority's Activities



Feedback from customers was mainly positive and a number of suggestions and opportunities for improvement were highlighted. The Medicines Authority evaluated the responses and is following up a number of recommendations.

The Authority regularly communicated with stakeholders through circulars and these were uploaded on the website so as to ensure transparency. The website was updated with relevant information and continuous update of the list of Authorised Medicinal products (together with the summary of product characteristics and the package leaflets) and the list of licensed wholesale dealer.

During 2011, seven (7) complaints files regarding pharmaceutical activities in Malta, medicinal products and activities of the Medicines Authority were opened (excluding complaints related to enforcement and advertising of Medicinal Products for which there is a separate procedure). All complaints were closed by end of the year.

1.3 Quality Management

During 2011, twenty eight (28) quality improvements were registered in the Quality Management Systems. These include reviews of Standard Operating Procedures and amendments to standard documentation. Staff members were given training on reviewed standard operating procedures. In 2011, the Authority continued focusing on addressing the recommendations of the assessors of the Benchmarking of European Medicines Agencies which took place in November 2009. The Medicines Authority conducted a process for the recruitment of a Quality Manager.

1.4 Human Resources Management

The Medicines Authority achieves its objectives through its people and it is committed towards the development of competent work force and development of an organisational climate and culture which is conducive to excellence. During 2011, the Authority recruited two (2) clinical assessors, four (4) pharmacists, and two (2) senior pharmacists through internal and external calls. During 2011, two (2) members of staff were on long leave and five (5) employees terminated their work with the Medicines Authority. Table 1 shows the human resources capacity at the Medicines Authority as on 31st December 2011.

	Full-time	Part-time/ Reduced Hours
Management	6	0
Technical	26	4
Administration	10	0

Table 1 - Human Resources at the Medicines Authority as on 31st December 2011

Training and development priorities for 2011 were set at the beginning of the year and staff had the opportunity to attend training and development initiatives both in Malta and in European Countries in line with training needs and resources of the organisation. Areas for training for 2011 included efficient and effective quality assessment, technical validation, evaluation of quality, safety and efficacy of blood products, bioanalysis guideline, herbal medicinal products, Pharmacovigilance legislation audit-inspections, Pharmacovigilance Systems with the Collaboration of AIFA, Italy, observed inspection on sterile dosage forms manufacturing facility in India with the collaboration of MHRA, UK, inspection techniques and inspection processes held by PIC/S at Cape Town, South Africa and Good Clinical Practice Inspectors basic training course.

Induction training was delivered to all new staff members, internal training sessions for the propagation of knowledge attained through external training sessions were developed and implemented in a structured approach.. Training sessions were organised for all staff on Equality and Sexual Harassment at the Place of Work with the support of the National Commission for the Promotion of Equality. Staff members also participated in a number of webinars organised by the European Medicines Agency. A number of employees attended training on better regulation and the standard cost model. Employees attended training sessions organised by the Centre for Development, Research and Training (CDRT) within the Office of the Prime Minister.

Five staff meetings were held during 2011. During the staff meetings, important decisions were communicated, initiatives were taken to motivate staff and employees had the opportunity to discuss and share their opinion on the way forward of the Medicines Authority.

In 2011 the Medicines Authority obtained two People Awards from the Foundations from human Resources Management. The Awards were given for Employee Engagement and People Management Impact on Business Success.

1.5 Information Systems Management

During 2011 the Information System Unit continued to operate and maintain the existing in-house and European information systems and the ICT infrastructure. Two Requests for Information were issued to obtain information on an Integrated Licensing Management System and on Digitalisation of Scientific Dossiers respectively. The network switches and the router to connect to the Malta Government network were changed. A process was started to implement EURS is Yours (EiY) review tool for assessors. The Medicines Authority is working on a tender for a Licensing System and the process to develop the tender document started with the support of the Malta Information Technology Agency. The Medicines Authority has also issued and adjudicated a tender for the development of a new corporate website.

1.6 Collaboration with other Entities

During 2011, the Medicines Authority continued to collaborate with other entities, mainly the Superintendence for Public Health, the European Medicines Agency, the European Commission and other competent authorities and departments in Malta and the European Union.

2.0 Regulatory Affairs

2.1 Participation in drafting new legislation

The Medicines Authority continued to participate on behalf of the Ministry on the 'Pharmapackage' proposed by the Commission, by attending meetings held under the Council and drawing up reports and instruction notes for these meetings on the Proposal for a Directive of the European Parliament and of the Council amending Directive 2001/83/EC as regards the prevention of the entry into the legal supply chain of medicinal products which are falsified in relation to their identity, history or source. The Authority also participated in the discussions on a Commission proposal for a Directive of the European Parliament and of the Council amending, as regards pharmacovigilance, Directive 2001/83/EC.

2.2 Update and Implementation of legislation

In 2011, the Medicines Authority supported the Licensing Authority in the transposition process of Directive 2010/84/EU on Pharmacovigilance and Directive 2011/84/EU on Falsified Medicines. An information session to stakeholders on these dossiers was carried out in collaboration with MEUSEC.

2.3 Better Regulation

The Medicines Authority is actively participating in the government better regulation strategy which aims at improving the quality of legislation, by enhancing the performance, cost-effectiveness, and legal quality of regulations and the administrative procedures, tariffs and fees derived thereof. Staff from the Medicines Authority attended training on better regulation organised by the Better Regulation Unit. An exercise was carried out to cost the simplification initiatives implemented by the Medicines Authority between 2008 and May 2011. The results showed that simplification measures adopted by the Medicines Authority resulted in a saving of approximately 200,000 euro to the industry.

3.0 Assessment and Authorisation of Medicinal Products

During 2011, the Medicines Authority continued with activities towards national and European procedures whilst consolidating its operations as Reference Member State in the Decentralised Procedure. The number of authorised medicinal products in Malta (excluding products authorised through the centralised procedure) as on 31st December 2011 was above 3947 (see Figure 2). Internal training of the technical staff in regulatory and assessment of applications continued to be organised.

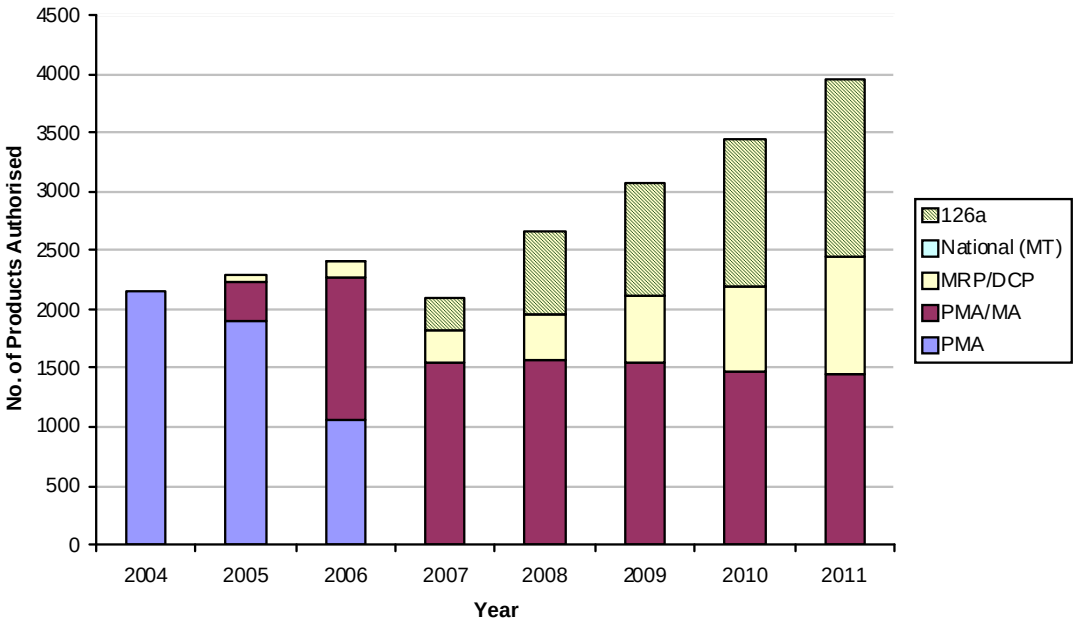


Figure 2 – Cumulative Number of Authorised Medicinal Products in Malta (excluding products authorised through the centralised procedure) as on 31st December 2011

3.1 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, where relevant and discussion on any guidelines that have an impact on the procedures discussed in the Committee. Meetings were held on a monthly basis.

3.2 European Procedures

3.2.1 Marketing Authorisation Procedures

Malta as rapporteur in the Centralised Procedure

Malta assessed variations for the product for which Malta was rapporteur through the centralised procedure. During 2011, Malta was also the rapporteur for a re-examination procedure. During 2011, Malta was awarded bids for the year 2012 for centralised procedures with Malta as Rapporteur..

Malta as Reference Member State (RMS) in the Decentralised Procedure (DCP)

Out of the twenty nine booked slots for 2011, eleven (11) Decentralised procedures with Malta as Reference Member State were actually started (excluding parallel procedures). There were nineteen (19) slot cancellations for procedures scheduled to start in 2011. For some of these cancellations, replacement with other procedures was not possible, as the Medicines Authority was informed of the cancellation close to the planned date of submission. At that point it was more difficult to fill the slots with other procedures.

The total number of procedures received was eleven (11). Some of the procedures started in 2011 are currently still ongoing. Until the end of 2011, applications for generic oral products have been assessed, in the form of tablets and oral solutions. An application for the pharmaceutical form eye drops solution was received in 2011. Specialised training provided in 2010 by experts from other competent authorities, mainly the UK MHRA and through the European Medicines Agency enabled the Medicines Authority to accept applications for injectable and other sterile preparations as Reference Member State in the last quarter of 2011 and to include them in the plan for 2012. Internal training is also ongoing on other pharmaceutical forms to be taken up in the near future in procedures with Malta as Reference Member State or as rapporteur.

For Reference Member State procedures, team meetings are organised regularly 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 discussed in the Medicines Review Committee, in particular where technical or regulatory decisions have to be taken or endorsed for a final Malta position.

Due to the small size of the Authority cancellations have a considerable negative impact. The Medicines Authority continues to strive to continue to participate actively in European procedures as a Reference Member State/ Rapporteur.

Malta as Concerned Member State

Two hundred and eighty five (285) European marketing authorisation product applications were received in 2011 with Malta as Concerned Member State. Sixty eight (68) were received through the Mutual Recognition Procedure and two hundred and seventeen (217) through the Decentralised Procedures. The number of marketing authorisations granted for the two types of procedures for the same period was eighty five (85) and one hundred thirty five (135) respectively. Figure 3 summarises the above. Compared to 2010, the number of de-centralised and Mutual Recognition procedures with Malta as Concerned Member State increased by 22% and this is a positive advancement in increasing the number of authorised products on the market in Malta. This was achieved thanks to the initiative taken with the collaboration of the Medicines and Healthcare Regulatory Agency (UK) and the Irish Medicines Board (Ireland) to invite Marketing Authorisation Holders to also include Malta as a Concerned Member State when UK and Ireland are the Reference Member State in a European procedure.

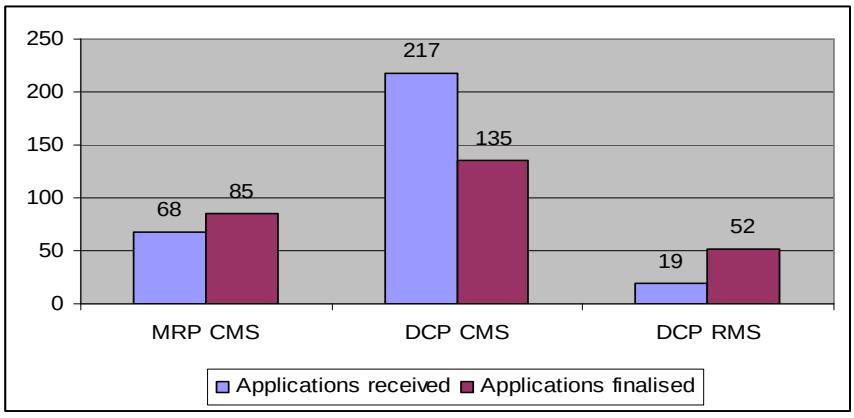


Figure 3 - Summary of marketing authorisation applications received through European Procedures (MRP and DCP) in 2011 – MT CMS and RMS (by product)

European post-authorisation procedures

One thousand four hundred twenty six (1426) Mutual Recognition Procedure variation applications were received in 2011 and one thousand one hundred and seventy four (1174) were finalised. Ninety one (91) renewal applications were received and sixty four (64) were finalised. Forty four (44) article 61(3) notifications were received and twenty six (26) were finalised during 2011 (Figure 4).

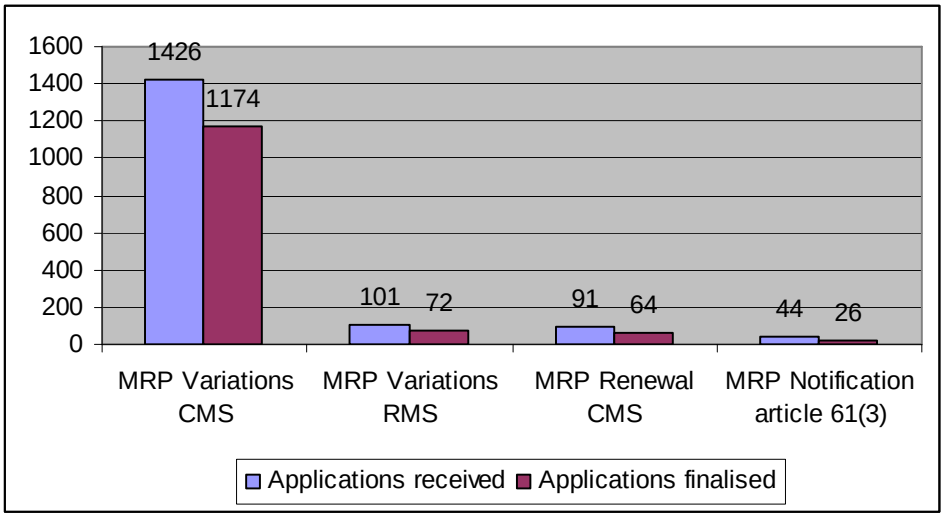


Figure 4 - Summary of post-authorisation procedures received through the European Procedures (MRP) in 2011 – MT CMS and RMS

3.2.2 Work-sharing Procedures

Throughout 2011, the Medicines Authority participated in EU procedures at the level of the European Medicines Agency, in particular in paediatric work sharing. Malta has been a rapporteur for two (2) paediatric data assessments in the European work-sharing procedure in accordance with article 45 of the Paediatric Regulation 1901/2006/EC. This procedure consists of the assessment of all data in relation to the effective and safe use of a medicinal active substance in children. The Summary of Product Characteristics and package leaflet are then updated to reflect the conclusions of this assessment. Both procedures were ongoing as at 31 December 2011. During 2011, the Medicines Authority representatives at the Paediatric Committee at the European Medicines Agency in London were involved as rapporteurs or peer reviewers for eleven (11) different procedures. As at end 2011, seven (7) of these procedures were concluded and four (4) were ongoing.

3.3 National Procedures

National marketing authorisation applications

A total of nine (9) national marketing authorisation applications were received in 2011, mainly line extensions to nationally authorised products. Ten procedures (10) were finalised in the same period.

Parallel import applications

Thirty eight (38) parallel import licence applications were received and forty (40) finalised by the end of 2011. There has been a marked increase of parallel import applications during the last couple of years as compared to previous years.

Authorisations in accordance with article 126a of Directive 2001/83/EC, as amended

The number of applications for authorisations in accordance with article 126a of the directive 2001/83/EC as amended received during 2011 was two hundred and forty nine (249) and two hundred fifty (250) authorisations were issued in the same period. The number of applications received is comparable to that of 2010. A summary of the national authorisation procedures received and finalised in 2011 is given in Figure 5.

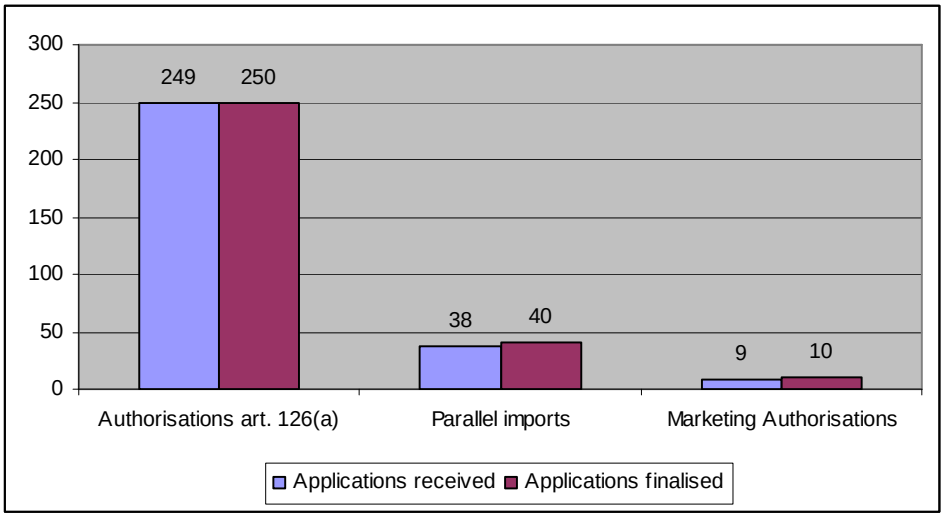


Figure 5 - Summary of national procedures received and finalised in 2011. Some procedures were continued from previous years.

National variation applications

One thousand three hundred and eighty three (1383) national variation applications were received in 2011. Two thousand five hundred and ninety two (2592) procedures were finalised. Some backlogs from previous years are being dealt with and this explains the numbers of procedures finalised being higher than those received. Some of the provisions of the new variations regulations came into force in 2011 for nationally authorised products.

National notification 61(3) applications

One hundred forty (140) national article 61(3) notifications were received. Two hundred and seventy one (271) procedures for 377 products were finalised. These had an impact on the package leaflets of two hundred and nine (209) products.

National renewals

One hundred forty three (143) national renewal applications were received and one hundred and two (102) were finalised in 2011.

Transfer of marketing authorisations

Sixty seven (67) applications for the transfer of a marketing authorisation holder were received and one hundred and one (101) processed.

Withdrawals of authorisations licences

Requests for the withdrawal of marketing authorisations were seventy seven (77), forty eight (48) authorisations in accordance with article 126a and seven (7) parallel import licences.

Summary

A summary of the procedures received and finalised in 2011 is given in Figure 6.

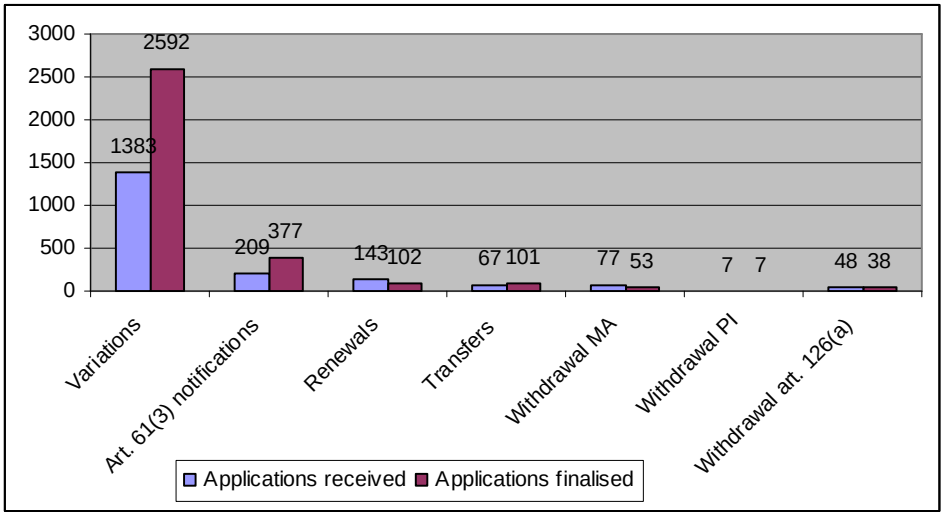


Figure 6 – Summary of national post-authorisation procedures received and finalised in 2011

3.4 Linguistic Checks of product information of products authorised through the Centralised Procedure

In 2011 the Medicines Authority continued to coordinate procedures for linguistic review of product information in Maltese. This activity is carried out for products authorised through the centralised procedure. This information is published on the EMA and Commission websites.

3.5 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 2011, no scientific advice requests were submitted to the Medicines Authority.

4.0 Clinical Trials

During 2011, no new Clinical Trials applications were submitted to the Medicines Authority. One (1) clinical trial application was approved; none (0) are currently ongoing. Seven (7) amendments to trials which are being conducted in Malta were received. Twelve (12) amendments were approved in 2011, while one (1) was closed due to an end of Trial Notification. All information has been inputted in the European Database for Clinical Trials. Compared to 2010, there has been a decrease in Clinical Trial applications submitted to the Medicines Authority over 2011.

5.0 Pharmacovigilance

Safety of medicines is a priority area for the Medicines Authority and the Authority will continue 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 early identification of potential safety hazards, evaluation, monitoring 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.

5.1 National Pharmacovigilance Activities

The Medicines Authority endeavours in a number of activities to ensure that the medicinal products on the Maltese market are safe. The collection, investigation and reporting of drug safety information in accordance with European requirements comprises one such major Pharmacovigilance activity carried out by the Medicines Authority. The Medicines Authority also requests modifications to be implemented to medicinal product information following safety signal detection by medicines authorities, the European Medicines Agency and/or international health organisations such as the World Health Organisation. 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 on 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). 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.

A total of one hundred and fifty (150) Individual Case Summary Reports (ICSRs) were registered over 2011. Each of these cases detailed at least one adverse drug reaction to the medicinal product concerned thus resulting in a total of two hundred and seventy three (273) individual adverse drug reactions. Figure 7 gives a breakdown of these adverse drug reactions according to system organ classification. Each case report was assessed by the Medicines Authority 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 8 and 9 further classify the adverse drug reaction case reports (as received over 2011) 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. Over 2011, 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.

Figure 7 Distribution of Adverse Drug Reactions according to System Organ Classification in 2011

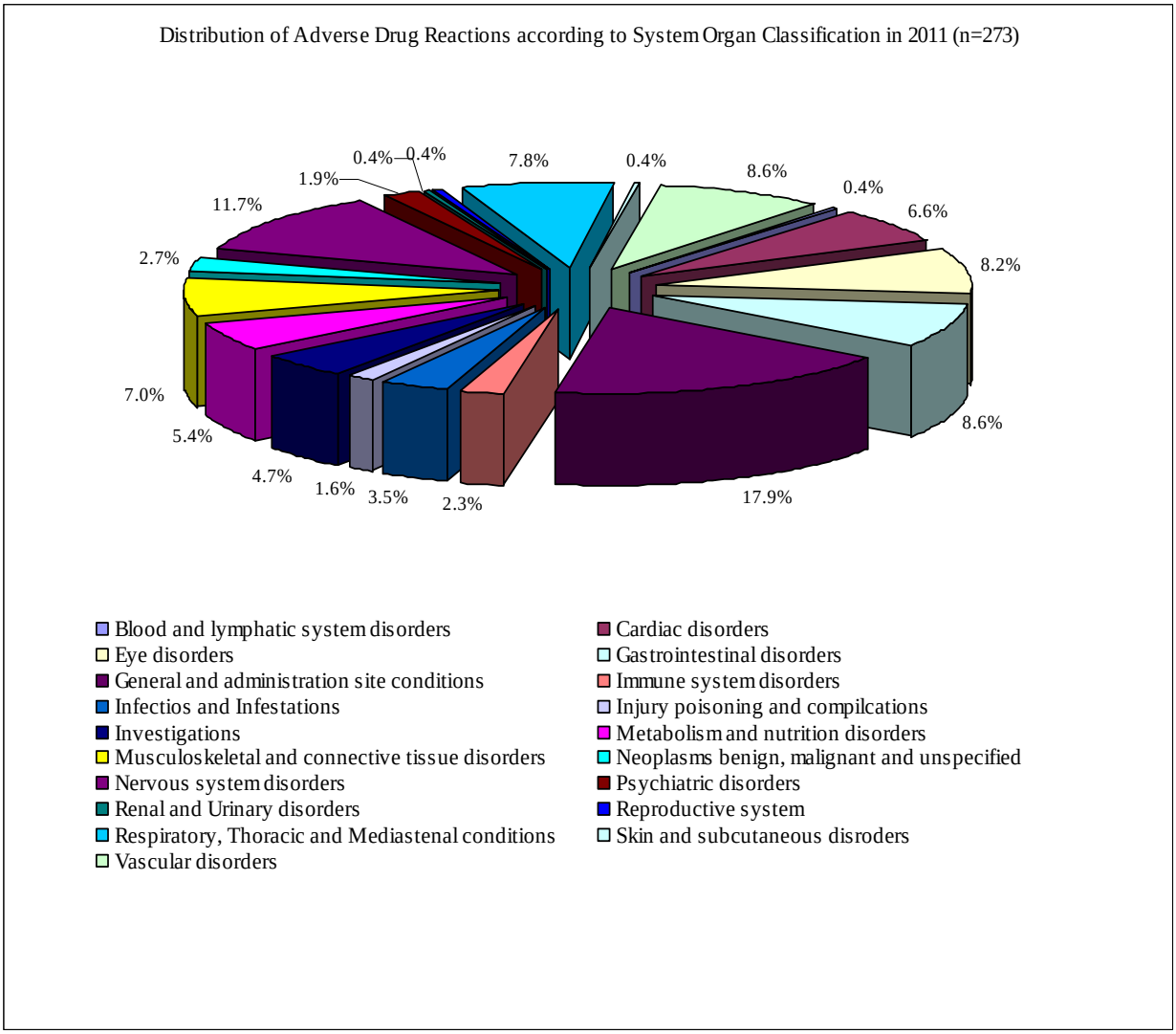


Figure 8 Frequency of ICSRs according to seriousness in 2011 (n=150)

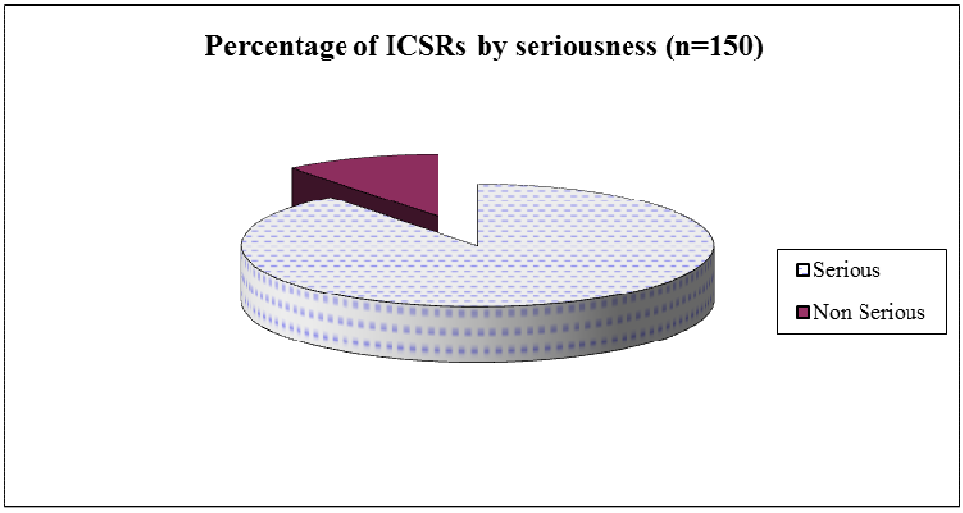
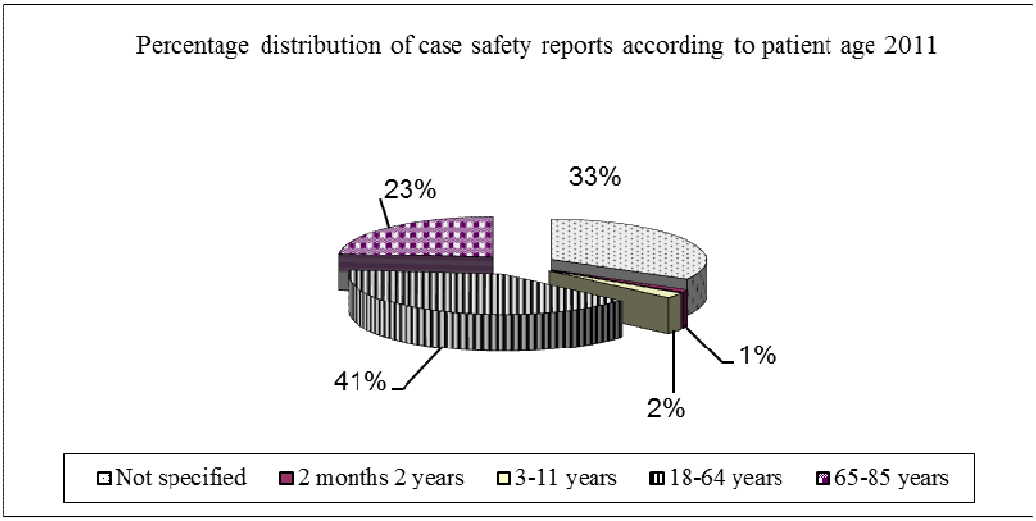


Figure 9 Percentage distribution of case safety reports according to patient age 2011



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, 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. This year the Medicines Authority has introduced an 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) Detailed assessment and 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 2011.

Table 2: Pharmacovigilance and safety issue reviews and communications – 2011 (n=297)

Pharmacovigilance content submitted for review	Number of submissions
Periodic Safety Update Reports	145
Risk Management Plans	47
Line Listing/SUSAR/DSURs	11
Annual Reassesments	11
Direct Healthcare Professional Communications	26
Safety Circulars	21
Additional risk minimisation measures	36
TOTAL	297

Coupled with this, any queries related to Pharmacovigilance activities are attended to by the post-licensing directorate. The main area of queries were those relating to the collection, assessment and reporting of local adverse drug reactions by healthcare professionals and Marketing Authorisation Holder representatives (Table 3).

Table 3: Pharmacovigilance related queries in 2011 (n=105)

ADRs	Query	Number
	Testing requirements	18
	Request for acknowledgments (3rd country and EU)	6
	Request for ADR forms	2
	Literature report requirements	3
	Request for more information on an ADR	2
	DPPM follow ups	1
	Clarification on populating ICSRs in E2B (R2)	3
	TOTAL 1	35
PSURs	Format; NeeS or eCTD/Eudralink/email or cd	5
	Renewals and PSURs	2
	Requirements for 126a products and centralised	7
	PSUR cycles (HBD,DLP & SBR)	7
	TOTAL 2	22
Clinical Trials	SUSARs	5
	ASRs	1
	Line-listings format	1
	TOTAL 3	7
Other	Review and approval of educational material for RMPs	6
	EU-QPPV or Drug safety responsible requirements	6
	Student projects related to PL	3
	Confirmation of MA details	2

During 2011, the following medicinal products were suspended: Avandia, Avandamet and Avaglim due to the association of rosiglitazone and increased cardiovascular risk.

5.2 New Pharmacovigilance Procedures by the Medicines Authority

Malta initiated its (2nd) second PSUR-assessment under the European work-sharing procedure in 2011. The first two (2) Pharmacovigilance inspections were performed as collaboration with inspectorate Directorate. These inspections are done on marketing authorisation holders who have their Pharmacovigilance headquarters in Malta (refer to Section 6.5). In 2011, Directive 2010/84/EU on Pharmacovigilance was published and there was a preparation for these changes, involving the interpretation of the directive and the local transposition of the Pharmacovigilance regulation as well as the review and planning for the widened definition of ADRs. This involved the redesign of the national ADR report form in order to improve the collection of data on ADRs and to enable the capture of medication errors. These activities will be carried over to 2012.

Over 2011, a number of discussions were held among various directorates within the Medicines Authority with the specific purpose of upgrading and streamlining quality systems in respect of currently applied Pharmacovigilance methods and processes. Standard Operating Procedures were drawn up in line with adopted practices particularly in respect of safety circular compilation, the assessment and approval of additional risk minimisation measures as well as the assessment and approval of Direct Healthcare Professional Communications (DHPCs).

6.0 Inspection and Licensing of 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 also started for the first time in 2011 to carry out Pharmacovigilance inspections. Table 4 shows the number of authorised pharmaceutical activities in Malta.

	2004	2005	2006	2007	2008	2009	2010	2011
GMP authorised sites	5	6	11	18	21	24	28	32
Wholesale Dealers	82	74	66	69	74	72	71	71
Community Pharmacies	208	206	207	207	208	209	211	215

Table 4: Authorised Pharmaceutical Activities in Malta (Cumulative) as on 31st December 2011

In 2011, the Medicines Authority started to assign a risk rating according to a Quality Risk Management (QRM) tool developed at PICS and adopted by the Medicines Authority. When the current two yearly cycle of inspections is over by end of 2012, the Medicines Authority would have assigned a risk rating to all GMP & GDP operators and hence would be able to devise inspections plans based on a risk based approach also for GMP & GDP inspections. All currently licensed activities are regularly inspected on a two year cycle. These include all pharmacies, all wholesale dealers, all importers, all full line manufacturers and re-packagers. The only exception to this is those which are issued with only a GMP certificate (valid for three years) but not with a license. These are: one laboratory carrying out analyses on contract for the manufacturing industry and one API manufacturer who opted not to have a licence but only a GMP certificate (this is still permissible with the current EU and local legislation). Therefore these two facilities are issued with only a GMP certificate and are inspected once every three years.

Two Good Clinical Practice (GCP) inspections were identified based on a risk based approach, carried out and successfully concluded in 2011. For the first time Inspectorate and Enforcement Directorate also carried out two Pharmacovigilance inspections for the two national marketing authorisations of medicinal oxygen.

6.1 Participation of Inspectors in international fora

During 2011 the Medicines Authority continued to get itself involved in the international GMP arena through its participation in PIC/S meetings and seminars. The Authority also participates proactively through one of its member of staff working as in the PIC/S expert working circle on QRM where the QRM tool was finally finalised at PICS level and adopted by the Medicines Authority.

The Inspectorate and Enforcement Director is also the group leader for work-stream within the Heads of Medicines Agencies Working group for Enforcement Officers whereby differences between member states in WDL/Enforcement legislation and inspection/enforcement procedures are studied. The current objective being pursued by the work stream is a Question and Answer for due diligence to be conducted by wholesalers when sourcing products for the first time from new sources.

6.2 Manufacturing and Importation Authorisations (MIAs)

During 2011 the Medicines Authority fulfilled its GMP inspection plan where seventeen (17) GMP inspections were carried out and concluded, out of which two were new applications for partial manufacturing and two were new applications for importers [total of four (4) new GMP applications and inspections]:

Six (6) Manufacturing Authorisations (MAs) inspections were carried out, two for medicinal gases, one for an active pharmaceutical ingredient and three for non sterile solid dose manufacturers; Six (6) inspections for MAs for repackaging and re-labelling / partial manufacturing operations; Five (5) inspections for MAs of importation activity: three from countries which have Mutual Recognition Agreements (MRAs) with the EU for GMP and two (2) from countries which do not have an MRA.

A total of twenty six (26) MAs variation applications were processed in 2011 for manufacturers and importers, out of which four (4) required an inspection. Cumulative number of EU GMP authorised activities is shown is Figure 10.

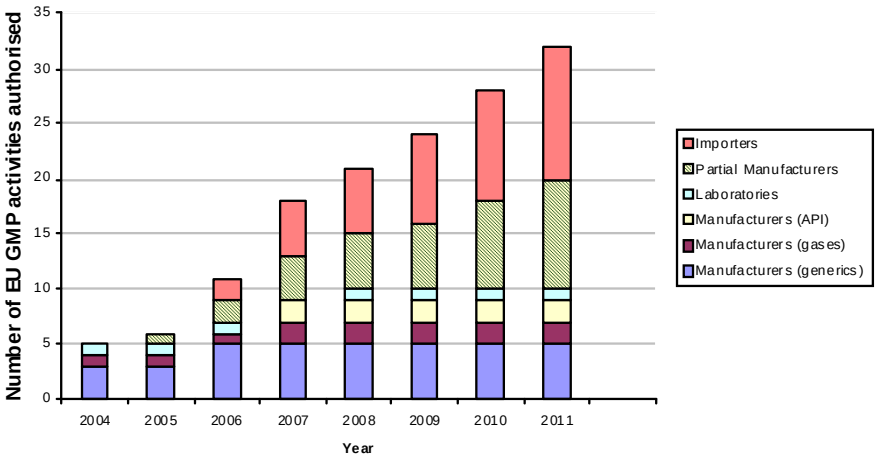


Figure 10: Cumulative Number of EU GMP activities authorised

6.3 Authorisations for wholesale dealing

During 2011 the Medicines Authority has also fulfilled its GDP inspection plan where fifty one (51) GDP inspections were carried out of which three (3) were for new GDP applications and inspections. Twenty one (21) variations for wholesale dealing authorisations were processed in 2011 out of which one (1) required an inspection.

6.4 Clinical trials

During 2011 the Medicines Authority continued to carry out inspections of clinical trails against EU GCP guidelines, which type of inspections, were started off for the first time in 2009. Two (2) GCP inspections were conducted in 2011 from the twelve (12) approved clinical trials in 2011, based on a risk based approach as specified in a dedicated SOP for clinical trials inspections.

6.5 Pharmacovigilance Inspections

Pharmacovigilance inspections started to be conducted for the first time in 2011. Two inspections were carried out for the national marketing authorisations for medicinal oxygen (which are the only two national marketing authorisations). The Pharmacovigilance inspections were carried out against the national and EU legislation and the MA Pharmacovigilance obligations.

The inspection team was composed of one medicines inspector who acted as the lead inspector and one Pharmacovigilance assessor as a technical expert. These were carried out successfully and henceforth Pharmacovigilance inspections will continue to be included in the annual inspection plan of the Medicines Authority and carried out as agreed. Identification of which Marketing Authorisation Holders should be subjected to Pharmacovigilance inspections should be based on a risk based approach which system for these types of inspections should still be developed. It is intended to be developed and approved by end of first half of 2012.

6.6 Pharmacies

Pharmacies are inspected on a two year cycle. During 2011 the Inspectorate and Enforcement Directorate carried out the remaining pharmacy inspections of the 2010-2011 cycle, totalling to one hundred forty nine (149) retail pharmacy inspections. Therefore between 2010 and 2011 all the community retail pharmacies were inspected for the second time on a two year cycle started off in 2008. In 2012 the two year cycle of inspections for pharmacies will start again, inspecting those pharmacies which were inspected in 2010.

Another eight (8) inspections were carried out in relation to new licences. Six (6) inspections following variation applications for pharmacy premises transfers or alterations were carried out whilst four (4) administrative variations for pharmacy licences were processed.

In 2011 six (6) new applications for a community retail pharmacy licence were submitted and three (3) new applications for hospital pharmacies were also received.

6.7 Granting of Qualified Person Status

In 2011 the Medicines Authority received ten (10) applications for the Qualified Person (QP) status. Five new QPs were approved in 2011.

6.8 Certificates of Pharmaceutical Products (CPPs)

During 2011, one hundred and forty six (146) CPPs were issued.

7.0 Regulation of medicinal products on the market and their use

7.1 Borderline Classification Committee

In 2011, thirty (30) requests were received for the classification of 'borderline' products. By the end of the year decisions were made for twenty one (21) products.

7.2 Traditional Herbal Medicinal Products and Homeopathic Products

During 2011, ten (10) internal meetings regarding the implementation of the Traditional Herbal Medicinal Product Directive (THMP) (Directive 2004/24/EC amending Directive 2001/83/EC) were held. These followed on from meetings in previous years with the Licensing Authority and with other authorities and bodies, including with Malta Competition and Consumer Affairs Authority, Environmental Health Directorate and Port Health regarding the way forward on implementation of this legislation.

The focus of the meetings held during 2011 was the classification of products from the information received from stakeholders. Following on from 2010, classification of more than 1000 requests was made. Of the products received, more than 85% have been classified as non-medicinal and the companies have been informed. One hundred thirty seven products are still pending a decision because the Medicines Authority is still waiting for further information from the companies to enable classification. Twenty eight (28) products have been discontinued since. Applications for classification continue to be received. No applications for the registration of traditional herbal medicinal products have been received

Homeopathic products

No applications for the registration of homeopathic medicinal products have been received to date. The information session on herbal medicinal products will also focus on the need for registration of homeopathic medicinal products.

7.3 Advertising of Medicinal Products and Promotional Material

The Medicines Authority (MA) 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 the major media formats, namely local newspapers and/or 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).

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 2011 eight (8) advertising complaints were registered with the Medicines Authority. Following assessment, breaches to the legislation were identified in relation to three (3) cases.

7.4 Rational use of medicines

The rational use of medicines is supported through the continuous update of the Medicines Authority website which is used by stakeholders as a source of independent information on medicines contributing to information and education about medicines. The Medicines Authority gave input into the National Guidelines for the use of Medicines and other relevant guidelines being prepared by the Superintendence of Public Health.

7.5 Product Information

The Medicines Authority provides information on medicinal products on human use In 2011, the Medicines Authority focused its priorities to inform and empower patients and health care professionals in line with its communication strategy. The ‘Know Your Medicines’ initiatives were officially launched and a leaflet with information on innovator and generic medicines and the risks of falsified medicines was distributed to all households in Malta and Gozo. The initiatives were aimed to support and empower patients and healthcare professionals on the choice and use of medicines. A new service for healthcare

professionals to start receiving sms notification was also launched. The service aims to enhance the dissemination of updates on quality and safety issues of medicinal products.

8.0 Surveillance of the local market

8.1 Rapid Alerts, GMP Non Compliance Notifications and Batch Defect Report

In this reporting period the Medicines Authority received one hundred and nine (109) rapid alerts and fourteen (14) GMP non compliance notifications, which were investigated and out of which 10 resulted in recall of medicinal products from the local market. One of the rapid alerts ended in a caution-in-use notification.

8.2 Sampling of Medicines

The sampling plan for 2010 was closed positively and testing certificates issued by MHRA lab were received for all samples. The sampling plan for 2011 was executed and all samples were sent abroad for analysis. The sampling plan included twenty five (25) National products market surveillance, one (1) defective product investigation and three (3) EU Centrally Authorised Products surveillance.

9.0 Enforcement of Legislation

During 2011 the Medicines Authority carried out ten (10) investigations related to complaints and enforcement. The Enforcement Committee (a specific committee which discusses enforcement cases, chaired by the Licensing Authority) met two times during 2011.

The Inspectorate and Enforcement Director attended eight (8) court sittings during 2011 to provide court witness services. Seven (7) cases concerned pharmacy issues and one concerned an enforcement case. Medicines Inspectors attended six (6) court sittings regarded enforcement as witnesses.

10.0 Conclusion

During 2011, the Medicines Authority continued making a contribution to protect and enhance public health both in Malta and the EU. Almost five hundred medicinal products were authorised, and Malta acted as a Reference Member State for eleven (11) procedures. The Authority strengthened its capacity for evaluation of medicinal products through extending the range of pharmaceutical dosage forms considered as Reference Member State. The Medicines Authority conducted two hundred and twenty one (221) inspections with Pharmacovigilance inspections being held for the first time. The milestones set by the corporate calendar were followed and achieved. These included corporate staff meetings at the beginning, mid and end of the year, management review at mid-year and performance appraisals for all staff. The Medicines Authority was awarded two People Awards in the areas of Employee Engagement and People Management Impact on Business Success. The first Stakeholder Satisfaction Survey was carried out and the Know Your Medicines Initiatives were launched to provide objective and unbiased information to empower healthcare professionals and patients on the choice and use of medicines. A new sms notification service was also launched.

During 2011, the Medicines Authority started preparations for a tender for an Integrated Information Management System and for a new corporate website. Following participation at EU level, particularly at the Council Working Party, in drafting of new legislation on Pharmacovigilance and falsified medicines, the Authority started the process for the transposition process of Directive 2010/84/EU and Directive 2011/84/EU. The Medicines Authority looks forward to continue to consolidate its functions and responsibilities as the National Competent Authority for the regulation of medicinal product and pharmaceutical activities in Malta and at Europe level through the transparent and consistent execution of its regulatory role, this to the benefit of public.