2010

Annual Report

AWTORITÀ DWAR IL-MEDIĊINI

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Message by the Chief Executive Officer

During 2010, the Medicines Authority continued with all its activities to ensure high quality, safe and efficacious medicinal products on the local market. The number of medicinal products authorised Nationally to be placed on the local market reached 3500. The Medicines Authority continued acting as Reference Member State for generic products with seventeen (17) new applications being started in 2010. The Authority also covered its Pharmacovigilance obligations.

The inspection plan was fully achieved and with over one hundred and forty (140) manufacturers, wholesale dealers, importers, distributors and pharmacies were inspected according to set standards. During 2010, there were thirteen (13) new cases of enforcement.

The Medicines Authority contributed at European level through participation in committees and contribution in assessment for the European Medicines Agency.

During 2010, the Medicines Authority prepared a strategy for communication and information to patients and health care professionals and in a set of initiatives to provide information which included publication of a consolidated medicines list as well as other information material. During 2010, the Medicines Authority achieved three (3) people awards and also managed to be self sustainable through income from fees from activities.

As from 2010, the Medicines Authority was placed under the Office of the Prime Minister as line ministry.

For 2011 the Medicines Authority plans to consolidate and improve on its current operations with enhanced effectiveness in line with available resources. The Medicines Authority will take up the transposition and implementation of current and new legislation and will continue to expand its activities to meet the needs of stakeholders.

Contents

1.0 Organisation

1.1 Leadership and Managamenet

For 2010, the Medicines Authority established ambitious targets both on a technical and management level. The targets for 2010 set in the three year Business Plan (2010 – 2012) were achieved. The Operational Plan was set at the beginning of the year and formal review of achievement and opportunities was held at mid- year. Recommendations from the Benchmarking of European Medicines Agencies (BEMA) were taken on board and it is planned that all the recommendations will be achieved in the next three years. The pro-active leadership started in 2008 continued to consolidate throughout 2010, starting off with an Extraordinary Staff Meeting for team building in January 2010, another such meeting in mid year and a final evaluation meeting with staff which is planned for early 2011. The motto chosen for 2010 was 'Together We Excel'. Excellence should be at that level to translate in all activities and processes. The Medicines Authority's high level of achievement in investment in its employees was confirmed through the attainment of three awards from the Foundation for Human Resources Development (FHRD) for Excellence in Learning and Development, Employee Engagement and Equal Opportunities.

Ten Management Meetings and Four Interface Meetings were held during 2010 and committees functioned as planned. A working group for communications and public relations was set up. The aim of such working groups is to engage staff in operations and to ensure that different aspects and perspectives are taken into consideration.

1.2 Communication with Stakeholders and Customer Satisfaction

The Medicines Authority considers individual meetings with stakeholders as an effective way to understanding customer requirements; communicate with stakeholders and to receive feedback on the service provided. During 2010 the Authority had ninety eight (98) meetings with individual stakeholders within the premises of the Medicines Authority. These were conducted with the industry, unions and chambers, academics and researchers and other European and government entities.

Figure 1 shows the proportion of meetings with stakeholders according to category.

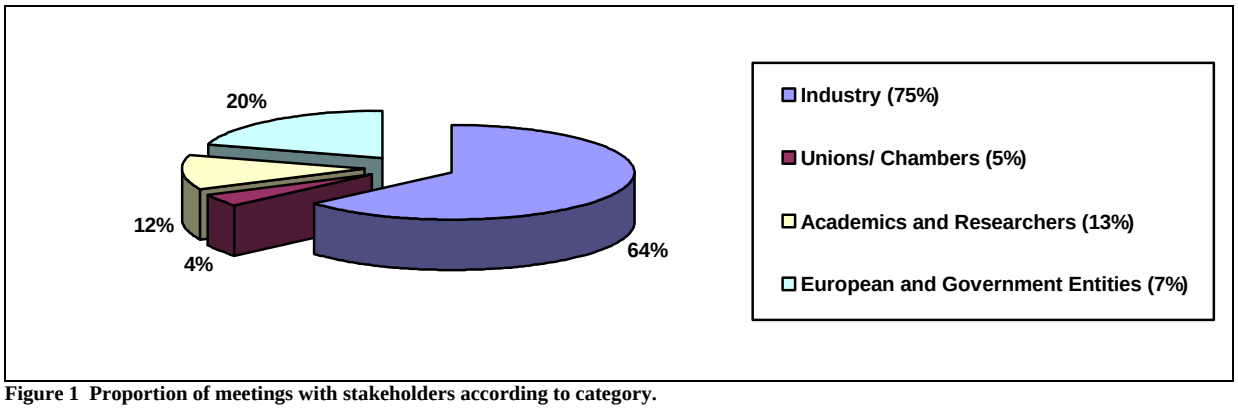

Figure 1 Proportion of meetings with stakeholders according to category.

The Authority regularly communicated with stakeholders through circulars and these were uploaded on the website so as to ensure transparency. The website was regularly updated with relevant information. The lists of licensed manufacturers, importers and wholesale dealers were regularly updated.

During 2010, the Medicines Authority prepared a strategy for communications with health care professionals and consumers. The strategy aims to provide information on medicines, increase awareness of the available resources and promote use of trusted sources (in terms of information). The second aim is to increase awareness, knowledge and trust in the medicines lifecycle and provide information on the regulation of medicines and pharmaceutical activities. The third aim is to inform, educate and empower health care professionals and consumers in choice of medicines. The initiatives taken during 2010 include:

- The publication of the Malta Medicines which aims to provide stakeholders with a comprehensive list of medicinal products which were authorised to be placed on the market. A temporary searchable database was developed until a new website is set up.
- The publication of an information leaflet and posters for patients entitled 'Things you need to know about your medicines' which started being distributed through pharmacies, clinics, hospitals, day care centres and old people's homes.
- The setting up of a helpline (+356 23439111) which is available for health care professionals and the general public from 09:00 to 12:00
- The setting up of a Facebook group (Know Your Medicines) and a Facebook page (www.facebook.co.m/medicinesmalta)
- Participation on interviews and discussions on the local media.

During 2009, nine (9) complaints were dealt with through the standard operating procedure for complaints. These exclude complaints related to enforcement and advertising of Medicinal Products for which there is a separate procedure. All complaint files of 2009 and 2010 were closed by end of 2010.

Two (2) information sessions were organised. One session was for all pharmacy licence holders and managing pharmacists and information was given on the current legislation governing pharmacy practice and regulation, pharmacy standards to be maintained, pharmacy inspections and frequently encountered deficiencies. The same session was repeated in Gozo. Another session was organised for health food shops, pharmacists, managing pharmacists, importers and wholesale dealers of herbal medicines in view of the implementation of legislation on herbal medicinal products.

1.3 Quality Management System

During 2010, over twenty three (23) improvements were registered in the Quality Management Systems, the included reviews of Standard Operating Procedures and amendments to forms and certificates. Relevant Staff members were given training on reviewed procedures as per procedure. In 2010, the Authority focused on addressing the recommendations of the assessors of the Benchmarking of European Medicines Agencies. No audits were held in 2010. An exercise was carried out to transfer official documentation at a central location accessible to staff in a controlled manner. The Medicines Authority prioritised the recruitment of a Quality Manager.

1.4 Finance and Administration

During 2010, the Medicines Authority financed its operating activities through fees generated from the processing of applications as stipulated in Legal Notices supporting the Medicines Act. In fact, in 2010, the Authority did not utilise any Government subvention. The Authority continued showing its commitment towards regular reporting requirements as set out by Government and submitted monthly and quarterly financial information to the Ministry of Finance, Economy and Investment, as necessary and on a timely basis.

1.5 Risk Management

During 2010 an exercise was carried out by management to analyse the risks that the organisation has and to ensure that risk control measures are in place. The seventh version of the risk register was approved by management and risk control measurements relevant to staff were discussed with the employees during a staff meeting. A new procedure for office access and locking of doors was set up with the aim of increasing security if printed data. Measures have been taken to re-organise the stores in way that data is accessible in a controlled manner. With respect to Information Management Systems, the Authority follows procedures and policies of the Malta Information Technology Agency, which is certified in ISO 27001 Information Security Management System (ISMS).

1.6 Human Resources Management

The Medicines Authority worked hard to strengthen and this was mainly done through recruitment of employees, provision of opportunities for learning and development, and development and an organisational climate and culture which is conducive to excellence. During 2010, the Authority recruited three (3) senior pharmacists and one pharmaceutical officer from internal and external calls. One (1) pharmacist was engaged on a contract for services basis. In spite of attempts to recruit, the posts of Clinical Assessors remained vacant. Further attempts for recruitment of staff in approved posts are planned for early 2011. During 2010, four (4) members of staff were on long leave and three (3) employees terminated their work with the Medicines Authority to further their studies or advance in their careers. Figure 2 shows the number of staff according to category as on 31st December 2010.

	Full-time	Part-time/ Reduced Hours
Management	6	0
Technical	19	2
Administration	9	0

Figure 2 - Human Resources at the Medicines Authority as on 31st December 2009

The Authority also has four (4) pharmacists on a contract for service; a professional in the Licensing Directorate for work related to herbal medicinal products, a professional in the Finance and Administration Unit, and individuals who do linguistic checks for the Medicines Authority.

Training and development priorities for 2010 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 priorities and resources of the organisation. Staff members had the opportunity to attend training on bioequivalence, Good Clinical Practice, EudraVigilance, computers and information systems validation, micro and molecular biological aspects for medicinal products and their testing, pharmacovigilance inspections and sterile dosage forms manufacturing inspections in collaboration with the Italian medicines agency (AIFA). 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 'Holding Effective Meetings' and 'Communications and Public Relations', the latter with the support of the Centre for Development, Research and Training (CDRT) within the Office of the Prime Minister. A number of employees attended training on fire fighting and first aid procedures. Employees attended training sessions organised by CDRT. An employee handbook which includes areas for training during the induction period was developed.

1.7 Information Systems Management

The Medicines Authority continued to operate and maintain the existing in-house and European information systems and the ICT infrastructure.

In March all PCs were successfully replaced through the Malta Information technology Agency's Desktop Services. All workstations at the Medicines Authority include an energy-efficient computer and a 19" TFT monitor. As part of a wider strategy to move to reduce the use of paper, quality assessors were provided with a second TFT screen. This initiative proved to be very successful as the Authority reduced the overall use of paper by twenty six per cent (26%).

The European Pharmacovigilance Issues Tracking Tool (EPITT), provided by the European Medicines Agency, was installed at the Authority and access was provided to staff members who handle pharmacovigilance issues. EPITT is an online system which allows specialists within the EU to track product-related pharmacovigilance safety issues.

Discussions were held with the Malta Information Technology Agency (MITA) on a Licensing System for the Medicines Authority. It was concluded that a Request for Information will be issued by the Medicines Authority and MITA in 2011.

A new domain name was registered, namely www.knowyourmedicines.gov.mt to host a new microsite aimed at informing the consumer about medicinal products. A searchable database for the Malta Medicines List was developed in-house. Preparations for a new website planned to be launched in 2011 were done.

The implementation of the Freedom of Information Act (FOI) was completed. Members of the public can find information about the FOI at http://www.medicinesauthority.gov.mt/aboutus.htm.

1.8 Collaboration with other Entities

During 2010, the Authority discussed a Technical Protocol of collaboration with the Italian Medicines Agency (AIFA). The Protocol aimed at streamlining exchange of experience to promote the exchange of information on pharmaceutical products and inspection procedures, to facilitate joint Good Manufacturing Practices (GMP) and Good Clinical Practices (GCP) inspection activities, and to promote training activities for assessment of medicinal products. The areas of cooperation will also include the exchange of experience regarding Quality Management Systems, including audits, and the sharing of information on the development of integrated ICT systems to support regulatory activities.
The Technical Protocol, that shall remain effective for a period of five years, falls under the activities foreseen by the Memorandum of Understanding between the Ministry of Health of the Italian Republic and the Ministry for Social Policy of Malta, signed in Malta (Valletta) on December 23rd, 2009. It is planned that the Technical Protocol will be signed in February 2011.

2.0 Assessment and Authorisation of Medicinal Products

During 2010, the Medicines Authority continued with activities towards national and European procedures whilst consolidating its operations as Reference Member State in the Decentralised Procedure.

2.1 The Medicines Review Committee

The Medicines Review Committee within the Medicines Authority continued to meet to discuss regulatory and technical issues relating to ongoing applications related to medicinal products, both national and European. These include applications for all pre- (e.g. scientific advice) and marketing authorisation applications 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 are held monthly.

2.2 European Procedures

2.2.1 Marketing Authorisation Procedures

Malta as rapporteur in the Centralised Procedure

No new applications were received with Malta as rapporteur in 2010 in the centralised procedure, as the planned number of assessment procedures to be handled had been filled by decentralised procedures. An application started in 2009 was concluded positively allowing the authorisation of fourteen (14) centrally authorised medicinal products EU/1/10/635/001-14. Furthermore, two (2) Follow up Measures procedures were positively concluded. These procedures were the first medicinal product benefit/risk assessment carried out by the Medicines Authority at the level of the Committee Human Medicinal Products.

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

During 2010, seventeen (17) Decentralised procedures with Malta as Reference Member State were started (excluding parallel procedures). The total number of products (all strengths and forms) involved was sixty six (66). By the end of 2010, two procedures were successfully finalised. The other procedures are currently ongoing. Until the end of 2010, only applications for generic oral products have been assessed, in the form of tablets and oral solutions. Specialised training provided in 2010 by assessors from other competent authorities and through the European Medicines Agency will enable the Medicines Authority to accept applications for injectable and other sterile preparations as Reference Member State in the last quarter of 2011.

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. In fact, apart from the regular monthly meetings, the Medicines Review Committee can be convened *ad hoc* should a decision need to be taken in between meetings.

There were seven (7) cancellations for procedures scheduled to start in 2010, for some of which replacement with other procedures was not possible, as the Medicines Authority was informed of cancellation towards the planned date of submission.

The number of procedures planned for the year is in line with the Medicines Authority's three year business plan which takes into account both capacity in terms of human resources and also expertise available, both in-house and locally. Cancellations have a considerable negative impact, due to the small size of the agency and on the resources allocated for the procedures.

Malta as Concerned Member State

Two hundred and twenty two (222) European marketing authorisation applications were received in 2010 for Malta as Concerned Member State. Sixty one (61) were received through the Mutual Recognition Procedure and one hundred and sixty one (161) through the Decentralised Procedures. The number of marketing authorisations granted for the two types of procedures for the same period was forty two (42) and ninety nine (99) respectively.

European post-authorisation procedures

One thousand and fifty two (1052) Mutual Recognition Procedure variation applications were received in 2010 and seven hundred fifty (750) were finalised Sixty four (64) renewal applications were received and thirty nine (39) were finalised. Twenty five (25) article 61(3) notifications were received and seven (7) finalised during 2010.

Application type	Received	Finalised
Centralised Procedure - MT rapporteur	0	1
MA DCP - MT RMS	26	2
MA MRP - MT CMS	61	42
MA DCP - MT CMS	161	99
Variations DCP - MT RMS	16	11
Variations MRP - MT CMS	1052	750
Notifications MRP - MT CMS	25	7
Renewals MRP - MT CMS	64	39
Paediatric Data Assessment WS MT rapporteur	3	1

Figure 3 - Summary of Marketing Authorisation applications received and finalised in 2010. A number of procedures have been carried forward from previous years.

2.2.2 Work-sharing Procedures

Throughout 2010, the Medicines Authority participated in EU procedures at the level of the European Medicines Agency. This shows the Authority's continuous effort to support the European medicines network — a partnership of more than forty (40) medicines regulatory authorities in the European Union (EU) and the European Economic Area (EEA) — coordinated by the European Medicines Agency. The Medicines Authority participated in EU procedures as active members of the EMA's scientific committees, working parties and related groups.

Medicines for Children

Malta has been a rapporteur for three (3) paediatric data assessment 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. One procedure was ongoing as at 31 December 2010. During 2010, the Medicines Authority representatives at the Paediatric Committee at the European Agency in London were involved as rapporteurs or peer reviewers for thirteen (14) different procedures (fourteen (14) products). As at end 2010, twelve (7) of these procedures were concluded, 4 were at sign-off stage at the European Medicines Agency and 3 were ongoing.

2.3 National Procedures

National marketing authorisation applications

A total of nine (9) national marketing authorisation applications were received in 2010. These were line extensions to already authorised products. Six procedures (6) were finalised in the same period.

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 2010 was two hundred and twenty one (221) and two hundred ninety seven (297) authorisations were issued in the same period.

National variation applications

One thousand one hundred and fifty one (1151) national variation applications were received in 2010. One thousand and fifteen (1015) procedures were finalised.

National notification 61(3) applications

Two hundred and sixty four (264) (367 products) national article 61(3) notifications were received one hundred and sixty eight (168) (240 products) procedures finalised.

National renewals

Seventy eight (78) national renewal applications were received and thirty (30) finalised in 2010.

Transfer of marketing authorisations

Forty four (44) applications for the transfer of a marketing authorisation holder were received and thirty eight (38) processed.

Parallel import applications

Forty two (42) parallel import licences applications were received and twenty seven (27) finalised by the end of 2010. There has been a marked increase of parallel import applications during this year.

Withdrawals of authorisations/licences

Application for the withdrawal of marketing authorisations, authorisations in accordance with article 126a and parallel import licences numbered 63, 34 and 3 respectively. A summary of the procedures received and finalised in 2010 is given in Figure 3.

Application type	Received	Finalised
Marketing Authorisations national	9	6
Authorisations article 126a	221	297
Licences Parallel Import	42	27
Variations national	1151	1050
Notifications national	264	168
Renewals national	78	30
Transfers of MAH	44	38
Withdrawal MA	63	76
Withdrawal PI	3	0
Withdrawal 126a authorisation	34	21

Figure 4 - Summary of national procedures received and finalised in 2010. Some procedures were continued from previous years.

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

In 2010 the Medicines Authority continued to coordinate procedures for linguistic review of product information in Maltese for products authorised through the centralised procedure were processed.

2.5 Scientific Advice

Since 2009, the Medicines Authority has implemented a system to process 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. The website of the Medicines Authority has been updated with the process of how applicants can apply for scientific advice. In 2010, no scientific advice requests have been submitted to the Medicines Authority.

3.0 Clinical Trials

During 2010, two (2) new Clinical Trials applications were submitted to the Medicines Authority. Three (3) in total were approved but one (1) is currently undergoing pending responses to issues raised during the procedure from the applicant. Fifteen (15) amendments to trials which are being conducted in Malta were also received. Fourteen (14) amendments were approved in total in 2010. All information has been inputted in the European Database for Clinical Trials. Compared to 2009, there have not been an increase in Clinical Trial applications submitted to the Medicines Authority over 2010. It is expected that an increased number of substantial amendments will be submitted in 2011 as compared to 2010. Throughout 2010, the quality system for Clinical Trials has been improved with the publication of the Guidance notes on Good Clinical Practice (GC1.10).

4.0 Pharmacovigilance

Safety of medicines has been and will continue to be a priority area for the Medicines Authority and the Authority will continue to strengthen its efforts to ensure the safe use of medicinal products authorised. 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 through the ways described in this report.

The Medicines Authority endeavours in a number of activities to ensure that only safe medicinal products are kept on the Maltese market and within hospitals. 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 may also request modifications to be implemented to medicinal product information following safety signal detection by foreign 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-wide 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 ninety four (194) adverse drug reaction case reports (ICSRs) were registered over 2010. Each of these cases detailed at least one adverse drug reaction to the medicinal product concerned thus resulting in a total of four hundred and 3 (403) individual adverse drug reactions. The receipt distribution over 2010 is documented in Figure 4 while Figure 5 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 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 6 and 7 further classify the adverse drug reaction case reports (as received over 2010) 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 2010, 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.

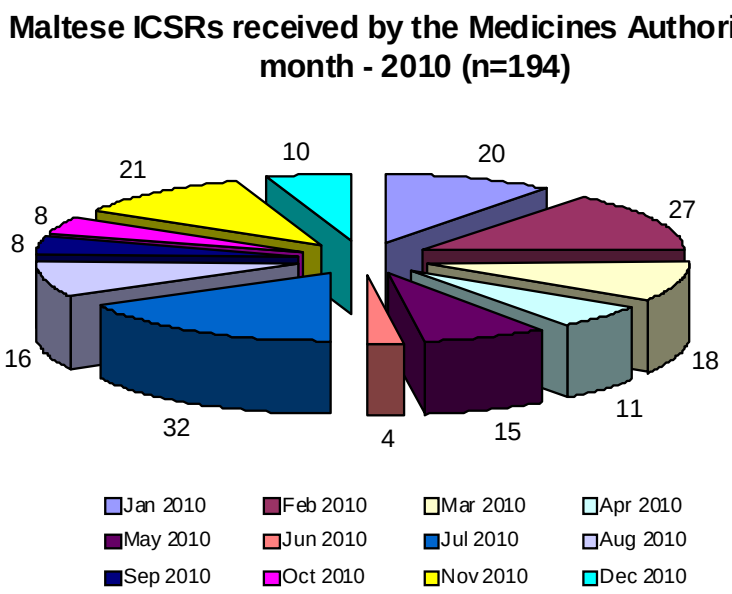

Figure 5: Distribution of ICSRs received per month over 2010

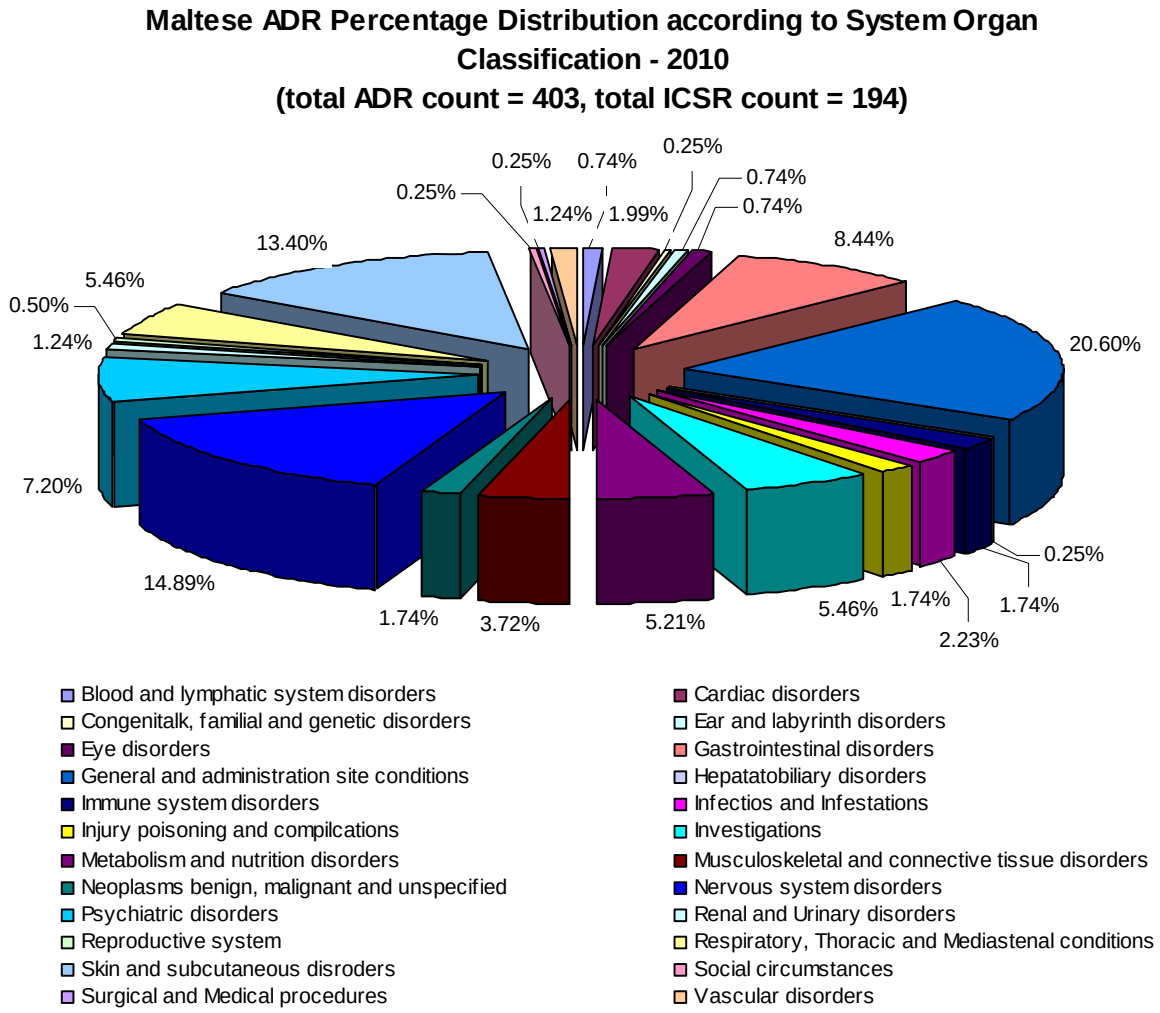

Figure 6: Distribution of adverse drug reactions according to System Organ Classification – 2010

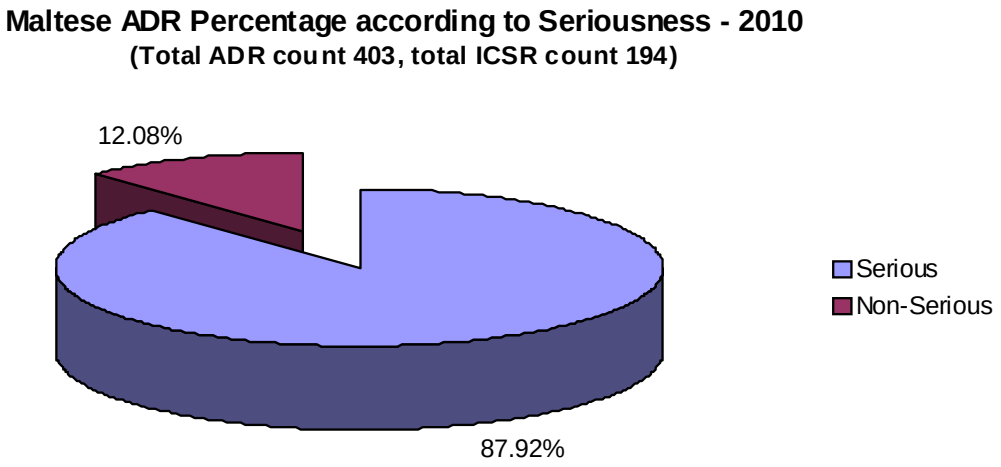

Figure 7: Percentage distribution of adverse drug reactions according to seriousness - 2010

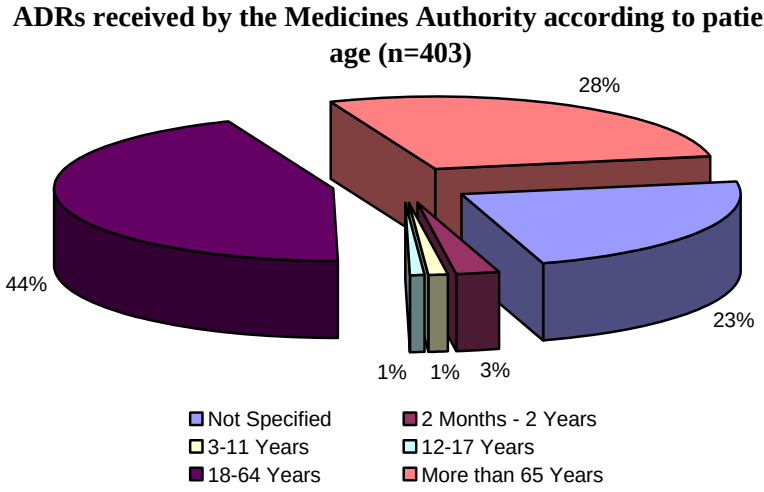

Figure 8: Percentage distribution of case safety reports according to patient age - 2010

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:

- Issue of Direct Healthcare Professional Communications (DHPCs) detailing safety/risk changes to scientific information and recommendations on product administration methods;
- Investigation of newly identified safety signals with immediate product suspension and/or recall as relevant (Safety Signal Investigations, Rapid Alerts and Product Safety Recalls);
- Approval and monitoring of Pregnancy Prevention Programmes as proposed in relation to potentially teratogenic medicinal products;;
- Monitoring of risk minimisation programmes relating to high risk medicinal products and provision of the relevant regulatory information in order to establish such programmes;
- Issue of Safety Circulars and Media Statements addressed to healthcare professionals and the general public respectively. These documents normally detail novel recommendations on medicinal product use and applicable cautionary and precautionary measures;
- Communication as relevant with the Department of Healthcare Services Standards on toxicological risks identified in relation to blood products (Haemovigilance);
- Initiation and subsequent approval of variations to scientific medicinal product information relating to identified novel or increased risk (Urgent Safety Restrictions);
- 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).
- Review of newly emergent data concerning safety evidence of a medicinal product, substance or class upon request.
- Review of queries that may be related to a possible safety issues with a medicinal product, substance or class.

Figure 8 below gives the distribution of reviews and communications which the Medicines Authority handled over 2010 in respect of the previously mentioned safety monitoring measures. Any queries

related to pharmacovigilance activities are attended to by the post-licensing department. 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. The latter communications are denoted by the abbreviations: ADRs/SUSARs/PSURs.

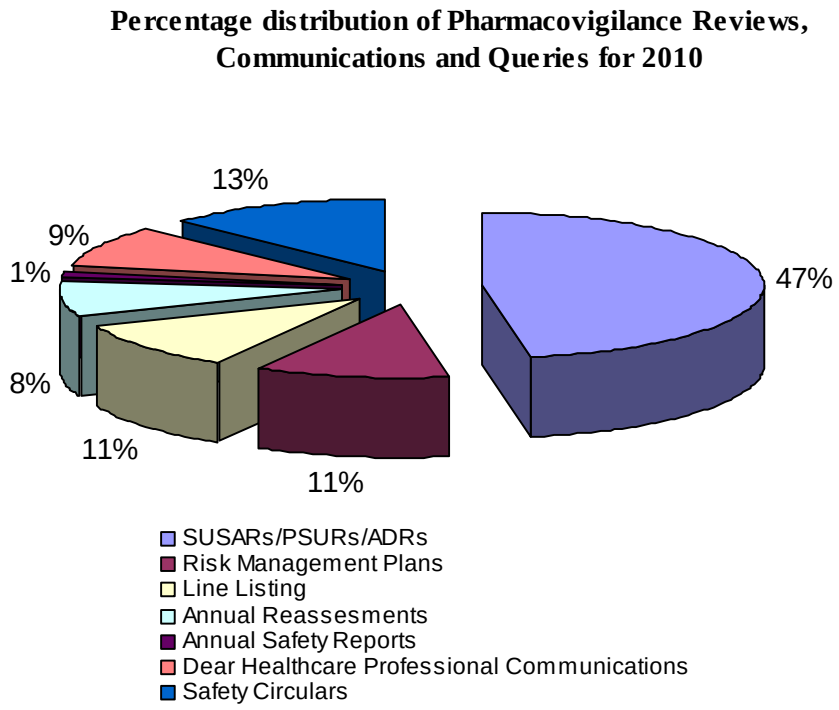

Figure 9: Distribution of Pharmacovigilance and safety issue reviews and communications – 2010

5.0 Inspection and Licensing of Pharmaceutical Activities

The Medicines Authority is responsible for inspecting and recommending issuance of licences for manufacturers and wholesale dealers according to national legislation and EU Good Manufacturing Practice and EU Good Distribution Practice respectively, whilst pharmacies are inspected against national legislation and standards.

For the time being, inspections are not carried out on a risk based approach (except for GCP inspections), but all 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 entities 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.

For the second consecutive year the Medicines Authority continued with the inspections of clinical trials for Good Clinical Practice (GCP). Two GCP inspections were identified based on a risk based approach, carried out and successfully concluded in 2010.

5.1 Inspection Review Group and Inspectors Meeting

The Inspectors Review Group (IRG) is fulfilling its functions. Four meetings were held during 2010 whereby eleven cases were discussed and decided upon, whilst follow up of previous pending cases was also carried out. Four (4) inspectors meetings were held whereby technical issues were discussed within the group of inspectors and agreements reached for improvement of work and better standardisation and streamlining of work to be carried out by the Inspectorate and Enforcement Directorate. All inspectors meetings are minuted and endorsed.

5.2 Good Manufacturing Practice

During 2010 the Medicines Authority directorate continued to get itself involved in the international Good Manufacturing Practice (GMP) arena through its participation in PIC/S meetings as described in

section six (6) of this report. The directorate continued to also give a very proactive role by one of its member of staff working actively in the PIC/S expert working circle on QRM which expert working circle was concluded satisfactorily in 2010.

During 2010 the Medicines Authority fulfilled its GMP inspection plan where nineteen (19) GMP inspections were carried out and concluded as follows:

- Five (5) Manufacturing Authorisations (MAs) were renewed for non sterile solid dose manufacturers;
- Five (5) renewals of MAs for repackaging and re-labelling operations and one new MAs for repackaging and re-labelling operations;
- Four (5) renewals of MAs for importation activity from countries which have Mutual Recognition Agreements (MRAs) with the EU for GMP and two (2) new MAs for importation activity from countries which have Mutual Recognition Agreements. One inspection was carried out for renewal of an MA for importation from third countries with chemical and microbiological laboratory analysis.
- One (1) inspection was carried out to renew the GMP certificate of a local laboratory providing microbiological testing services to the pharmaceutical industry.
- A total of seventeen (17) manufacturing authorisation variation applications were processed in 2010 out of which four (4) required an inspection prior to the variation.

5.3 Good Distribution Practice

During 2010 the Medicines Authority has also fulfilled its Good Distribution Practice inspection plan where forty four (44) Good Distribution Practice inspections were carried out of which two were for new Good Distribution Practice licences. Fifteen (15) variations for wholesale dealing authorisations were processed in 2010.

5.4 Good Distribution Practice

During 2010 the Medicines Authority has also fulfilled its Good Distribution Practice (GDP) inspection plan where 29 GDP inspections were carried out of which 4 were for new GDP licences. Eighteen (18)

variations for wholesale dealing authorisations were processed in 2010 out of which seven (7) required an inspection prior to the variation.

5.5 Good Clinical Practice

During 2010 the Medicines Authority continued to carry out clinical trails inspections against Good Clinical Practice (GCP) guidelines. During 2010 there were thirteen (13) approved clinical trials. Since according to present legislation not all clinical trials need to be inspected, a risk based approach was taken. All the twelve (12) clinical trials were evaluated for the presence of these identified risk factors and a score given to each trial according to the number and type of risk factors associated with it. The aim of the Medicines Authority was to carry out GCP inspections of around 20% of the clinical trials. Therefore the two clinical trials that got the highest score in our risk-score exercise were targeted for inspection. The inspections were communicated with the respective investigators, planned and executed as planned. Deficiencies and issues arising from the inspections were followed up and both clinical trials inspections were eventually successfully closed out. In 2011 it is planned that a similar evaluation exercise is carried out and around 20% of the clinical trials are identified using our risk factor weightings for GCP inspection.

5.6 Pharmacies Standards

The Medicines Authority took over the responsibility for pharmacies from Public Health in August 2005. During 2010 the Medicines Authority started again the second round of the two-year cycle inspection for pharmacies. The first two-year cycle for pharmacy inspections was initiated in 2008 and was concluded in 2009. In 2010 a total of seventy three (73) retail pharmacies were inspected. Eighteen (18) variation applications were received out of which three (3) needed an inspection prior to varying their licence. Apart from these inspections, another six (6) inspections were carried out in connection with new applications which are being currently considered for new pharmacy licences in line with LN 279 of 2007 and out of which two new licences were issued in 2010. Also there were three inspections for new in-patients pharmacies in private hospitals.

5.7 Granting of Qualified Person Status

In 2010 the Medicines Authority received eight (8) applications for the Qualified Person (QP) status. One applicant did not fulfil the Directive criteria to be considered for the QP status and was hence his application was rejected. The other seven (7) applicants were interviewed in two (2) separate QP interview sessions. Six (6) were accepted as being eligible for QP status whilst one interviewee failed the interview.

5.8 Certificates of Pharmaceutical Products (CPPs)

During 2010, one hundred and sixty seven (167) Certificates of Pharmaceutical Products (CPPs) applications were received by the Medicines Authority. Eventually one hundred and sixty six (166) CPPs were issued. One (1) CPP application was not processed as it was not in line with the WHO requirements for CPPs.

6.0 Implementation of regulation on the local market

6.1 Borderline Classification Committee

The Borderline Classification Committee (BCC) met three (3) times in 2010. No formal appeals to the BCC Appeals Board were made on decisions taken by the Committee in 2010. During the past year 54 requests for classification were received. Forty three originated from other regulatory bodies (in particular the Malta Standards Authority), six (6) directly from importers or manufacturers, four (4) from Mater Dei Hospital and one (1) from the Environmental Health Directorate. Sixteen (16) products were classified as medicinal products (4 of which were herbal products) and thirty two (32) as non-medicinal. Some cases are still pending as the Medicines Authority is waiting for more information. Some others have been included in the traditional herbal medicinal products registration scheme. One request was withdrawn by the applicant.

6.2 Traditional Herbal Medicinal Products

During 2010, the Medicines Authority has discussed at length how to implement the Traditional Herbal Medicinal Products Directive (Directive 2004/24/EC). Following several internal meetings and also with the Licensing Authority, the Malta Standards Authority and the Food Safety Commission, a plan was set up. This was communicated to stakeholders in a seminar held in April 2010. During the seminar general information for the industry on how the Medicines Authority would be implementing the directive was given. The aim is to carry out the implementation as required by the European legislation without having a substantial negative impact on the importers of herbal medicinal products and on patients and consumers.

The importers were requested to fill in an Herbal Products Sheet, in which they were required to list all their products (medicinal and non-medicinal) containing herbal preparations and substances and send the list to the Medicines Authority. The purpose of the list is to enable the Medicines Authority to classify which products are medicinal and those which can fall in other non-medicinal categories (e.g. food supplements, cosmetics). As a first outcome, the importers and wholesale dealers will be informed which products are definitely medicinal and those which are not. The products classified as medicinal products would have to be sold only from pharmacies and would require registration to continue to be placed on the market. Companies are being requested to submit applications for authorisations or through the simplified registration scheme (for traditional herbal medicinal products) by the end of the year 2011.

The Medicines Authority is currently reviewing the extensive information given by the local stakeholders to classify products into medicinal and non-medicinal. Further to this the products classified as medicinal products have to be further classified into those that fall within the scope of the traditional herbal medicinal products directive (simplified procedure) and those that need full registration as medicinal products. From the information given, it is not possible to classify a large number of the products and further information will be requested from companies. The classification form with which more information can be gathered will enable a classification of these products and therefore registration requirements will then be clearer for the Medicines Authority (with regards human and other resources that would be needed) and the applicants.

New herbal medicinal products not placed on the market before 1 October 2010 must be registered before being placed on the market in Malta as per the requirements of Directive 2004/24/EC.

Only those products for which an application is received, and subsequently authorised, may be placed on the market after 31 March 2012.

6.3 Advertising of Medicinal Products and Promotional Material

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 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).

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 2010, five (4) advertising complaints were registered with the MA. Following assessment, breaches to the legislation were identified in relation to four (4) reports.

6.4 Product Information

Since patients are increasingly interested in decisions about their health and want to take part in them, the Medicines Authority provides information on medicinal products on human use contributing to the promotion of public health in Malta. This is of major importance in particular in the era of Internet where citizens are able to reach information from all over the world. During 2010, the Authority Published an Information leaflet about medicines and published the Malta Medicines List as highlighted in other sections of this report.

6.5 Rational use of medicines

The Medicines Authority has a national public health remit with respect to pharmaceutical activity, information and use of medicinal products on the local market. Thus appropriate rational use of medicines is a goal that needs to be achieved so that medicines are prescribed, dispensed or sold appropriately, as well as taken correctly by patients, since the overuse, underuse or misuse of medicines results in wastage of scarce resources and widespread health hazards. The continuously updated Medicines Authority website is used as source of independent information on medicines contributing to public 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 Public Health Regulation Division

7.0 Enforcement and surveillance of the local market

7.1 Enforcement

During 2010 the Medicines Authority received thirteen (13) enforcement reports compared to twenty seven (27) in the precedent year. All enforcement issues reported to the Medicines Authority were investigated.

In 2010 four (4) Enforcement Committee meetings were held. The Enforcement Committee was set up as a special committee dedicated solely to discussion of enforcement cases thus leaving the Inspectorate Review Group solely dedicated to discussion and decisions which need to be taken on inspection issues. During these Enforcement Committee meetings held in 2010, three cases of breaches made to the advertising regulations were also discussed and acted upon.

The Medicines Authority is also contributing to the Working Group of Enforcement Officers (HMA-WGEO) through the leadership of work-stream I within the HMA/WGEO whereby differences between member states in WDL/Enforcement legislation and inspection/enforcement procedures are being studied. Work-stream I to date had three aims/objectives out of which were all conclude and have now drafted two (2) new objectives to pursue in 2011. The concluded objectives to date were:

- The drawing up of a concept paper on Good Distribution Practice (GDP) Guidelines after conducting a survey amongst member states, with the aim of proposing improvements for the EU GDP Guidelines. This was achieved and forwarded to the EMEA GMDP working group in 2008.
- To identify the gaps in EU legislation with regards to wholesale dealing from an enforcement perspective, suggest principles for due diligence to wholesalers and identify amendments which need to be proposed to the current legislation. Gaps were identified, principles for due diligence were drawn up and recommendations for amendments made and forwarded to the heads of medicines agencies in 2009.
- To explore the difference between member states in relation to their application of and understanding with respect to ‘control reports’ mentioned in Directive EC 2001/83 and ‘medicines for compassionate use’, and how these are regulated, if any. A survey was devised to address and tackle these issues and circulated amongst member states. This objective was tackled and closed off / finalised in 2010.

The Inspectorate and Enforcement Director attended seven (7) court sittings during 2010 to provide court witness services, all concerned with pharmacy issues. Medicines Inspectors had eight (8) calls for court witness between them during 2010 regarding enforcement cases three (3) enforcement cases are currently pending court jurisdiction). During 2010 one (1) new enforcement case was referred to courts for hearing. It is envisaged that the court hearing for this new enforcement case will start in 2011.

7.2 Batch defect Reports

In this reporting period the Medicines Authority received eighty two (82) rapid alerts which were investigated and out of which nine (9) resulted in recalls from the local market. Another one (1) rapid alert ended in a caution-in-use notification.

7.3 Sampling of Medicines on the market

All results from the sampling plan of 2009 have been received and there were no out of specification results. The sampling plan for 2010 has been accomplished, i.e. twenty four (24) samples as originally planned have been collected and sent for analysis. Three products were also sampled under the European Market Surveillance for centralised products.

8.0 Regulatory Affairs

8.1 Participation at meetings at EU level

The Medicines Authority actively participated in over one hundred (100) meetings and conferences where various aspects of regulation (policy, legislation, administrative and scientific) were discussed and decided.

Amongst the meetings of the European Medicines Agencies and Heads of Medicines Agencies attended in 2010, there are the Committee for Medicinal Products for Human Use (9 meetings), the Paediatric Committee (6 meetings), the Committee for Orphan Medicinal Products (6 meetings), the Committee on Herbal Medicinal Products (6 meetings), the Committee for Advanced Therapies (9 meetings), the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (8 meetings), the Biologics Working Party (6 meetings), Joint CHMP-CVMP Quality Working Party (4 meetings), the Working Group on Quality Review of Documents (1 meetings), the Clinical Trials Facilitation Group, the Pharmacovigilance Working Party (3 meetings), the Pharmacogenetics Working Party (1 meeting), the GCP Inspectors Working Group (3 meetings), the GMP-GDP Inspectors Working Group (4 meetings), the Pharmacovigilance Inspectors Working Group (5 meetings), the European Medicines Agencies Group on the Cooperation on Legal and Legislative Issues (EMACOLEX) (2 meetings) and the Working Group of Enforcement Officers (2 meetings), Working group for Communications Professionals (2 meetings), Patients' and Consumers' Working Party(2 meetings), Working group for the Quality of Documents (4 meetings) . The Medicines Authority was also active in the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme Committee (1 meeting).

At the level of the European Commission and Council, members of staff of the Medicines Authority participated at the council meetings on Pharmaceuticals and Medical Devices (10 meetings) to discuss legislation included in the Pharma Package.

Conferences organised by the European Generics Association and European Federation of Pharmaceutical industries and Associations amongst others were also attended.

8.2 Participation in drafting new legislation

The Medicines Authority continued to participate on behalf of the Ministry at meetings of the Pharmaceuticals and Medicinal Devices Working Party proposed by the Commission. Meetings were regularly attended; reports and instruction notes for these meetings were drawn up.

8.3 Update and Implementation of new legislation

During 2010 the Medicines Authority issued the following legal notices (LN):

- Legal Notice 198 of 2010 - Pharmacy licence (Amendment) regulations, 2010 - amending regulation 4 of the principal regulations (LN 279 of 2007).
- Legal Notice 252 of 2010: Medicines (Marketing Authorisation) (Amendment) Regulations 2010
- Legal Notice 253 of 2010: Medicinal Products (Package Leaflets and Labelling) (Transitional Arrangements) (Amendment) Regulations, 2010
- Legal Notice 476 of 2010 - Pharmacies (Opening Hours) Rules – repealing Opening Hours of Dispensaries Order: Legal Notice 364 of 2002

Advanced Therapies Regulation

Transposition of Directive 2009/120/EC dealing with the implementation of the Advanced Therapies Regulation (Regulation 1394/2007/EC), has been carried out by the publication of LN 252 of 2010. The transposition of this directive further consolidates the administrative measures at a national level to further implement the advanced therapies regulation.

The Regulation and Directive on Pharmacovigilance

On 31 December 2010, amendments to the European Pharmacovigilance legislative framework are expected to come into force in 2011 through Regulation (EU) No 1235/2010 and Directive 2010/84/EU, following the adoption of the proposed amendments to Directive 2001/83/EC on the Community code relating to medicinal products for human use and to Regulation (EC) No 726/2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency. The Regulation shall apply 18 months after publication in the official journal of the EU. The amendments to the Directive and the Regulation will induce changes in the European Union in terms of evaluation of risk associated with medicinal products as well as the framework on how the Union takes harmonised regulatory action on drug safety.

Work in 2011, will focus in transposing and implementing the new provisions of the Directive and Regulation in the area of pharmacovigilance.

Variations

Regulation 1234/2008/EC on the examination of variations to marketing authorisations came into force in January 2010. During 2010 the Medicines Authority implemented the regulation for variations coming in through European procedures, as required by the legislation in force. The deadline for applying the requirements of the regulation to national procedures is January 20, 2011, as per Directive 2010/53/EC. During 2010, to allow for a transitional phase where applicants get used to the new regulation and where submissions were already being handled in line with the new regulations in other Member States, the Medicines Authority was accepting applications for national procedures in accordance with both the previous and the current legislation. It is envisaged that variation fees be revised to reflect the new definitions and classifications of variations. Consultation meetings are planned for early 2011.