2009

Annual Report

AWTORITÀ DWAR IL-MEDIĊINI

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Highlights of 2009

- Consolidation of the procedures of the Medicines Authority

- Benchmarking of European Medicines Agencies

- Strengthening of Decision-Making

- Formal Adoption of Risk-Based Approach

- First Centralised Procedure

- First Periodic Safety Update Report Assessment

- First Good Clinical Practice Inspection

- Participation in EU fora

- Attainment of Human Resources Award

The Medicines Authority invites you to read the 2008 Annual Report and send any enquiry and comment to info.medicinesauthority@gov.mt

Message by the Chief Executive Officer

2009 was a year of consolidation of operations for the Medicines Authority. Following the Twinning light project of 2008 whereby there was a high level of training and capacity building in preparation for the performance of new high level activities, in 2009 there was the actual implementation of the targeted new activities. At the same time there was an overview and revision of the standard operating procedures for all the established processes of the Medicines Authority. There was increased streamlining of roles and duties in support of operations.

In 2009 the Medicines Authority continued to invest in its employees. The active leadership which had started in 2008 accelerated. Moreover recruitment continued and in the second half of the year, for the first time full recruitment of the originally proposed management team and the planned staff complement was achieved. The Medicines Authority's high level of achievement in investment in its employees was confirmed through the attainment of an award from the Foundation for Human Resources Development (FHRD) for Excellent Training and Development Initiative.

The level of activity and requirements of national operations is continually increasing, particularly in the area of licensing of national pharmaceutical activity and requirements for enforcement. The Medicines Authority achieved its objective of being able to meet the requirements of the local stakeholders. Licensing procedures for medicinal products with Malta as a Reference Member State became an ongoing activity, with Malta also taking up its first application as rapprorteur for a centralised procedure. The number of Reference Member State applications accepted was in line with the available capacity. The first inspections for clinical trials were held. Malta did its first Periodic Safety Update Report (PSUR) assessment as rapporteur in the work-sharing procedure.

The Medicines Authority contributed at European level through the European Medicines Regulatory network both by participation at committees and through

Medicines Authority Mission

The mission of the Medicines Authority is the protection of public health in Malta through the regulation of medicinal products and pharmaceutical activities.

Medicines Authority Objectives

The Medicines Authority achieves its mission through performance of the duties delegated to it by the Licensing Authority through the Medicines Act:

- The regulation of the safety, quality and efficacy of medicinal products for sale or supply on the Maltese market and the EU market

- The authority is committed to providing high quality licensing, monitoring and inspection service for pharmaceutical activities, to enforce the relevant legislation

- The Authority is responsible for post licensing safety monitoring through pharmacovigilance and adverse drug reporting

- Monitoring of advertising of medicinal products

- The Medicines Authority has a national public health remit with respect with respect to pharmaceutical activity, information and use of medicinal products on the local market

assessment for the European Medicines Agency and also at the level of Heads of Medicines Agencies (HMA). The Medicines Authority supported and contributed in line with its capacity and limited availability of resources.

In November 2009 the Medicines Authority had its exercise on Benchmarking of European Medicines Agencies. The whole Authority had prepared well through self- assessments for this exercise with final assessments being held at end 2008 and finally in June 2009. The indicators of this exercise were used as the key performance targets for 2009 with gap analysis leading to stressing on bridging of operations and strengthening of decision making particularly in areas concerning more than one directorate. The final evaluation by the external assessors was done over three days from the 23rd to the 25th of November and was a very positive and fruitful exercise.

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 health and in support of economic activity in Malta.

Dr. Patricia Vella Bonanno
Chief Executive Officer
Medicines Authority

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1.0 Organisation

1.1 Leadership and Managamenet

In 2009 the Medicines Authority fully achieved the targets set in its corporate calendar with minimal delays from the established datelines. These targets included the setting 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 2010-2012, Management Review in Quarter 3 and performance appraisals of employees at mid-year and at end of year. Over and above these annual targets, in 2009 the Medicines Authority continued with self-assessment using the Key Performance Indicators for the Benchmarking of European Medicines Agencies (BEMA) at end 2008 and a final assessment as at the end of June 2009. The BEMA Key Performance Indicators (KPIs) and the gap analysis from the questionnaire served as the main objectives for improvement for 2009. These were included as an integral part of the Operational Plan for 2009. The pro-active leadership started in 2008 continued to consolidate throughout 2009, starting off with an Extraordinary Staff Meeting for team building in January 2009, another such meeting in mid year and a final evaluation meeting with staff in December. Leadership is increasingly becoming an integral part of the corporate calendar. Organisational restructuring took place mainly to close gaps identified through the BEMA process and to streamline operations in order to support operations, strengthen decision making and enable monitoring of performance. The roles and responsibilities were clearly defined at management level and also cascaded to individual performance plans. This definition was also reflected in standard operating procedures.

Decision making was consolidated at committee level to ensure that it is done by all the designated partners and it is documented. At a management level there was separation between the Management Meetings (which were aimed to remain specific for management decisions) and a newly set Interface committee meetings- which were aimed for technical decisions and discussions particularly for areas relevant to more than one directorate. Eight Management Meetings and two Interface Meetings were held during 2009. On a technical level the Medicines Review Committee, established in 2008, was consolidated to incorporate all decisions regarding licensing of medicinal products, clinical trials and pharmacovigilance. The Inspection Review Group was streamlined to cover decisions relating to inspections and licensing of pharmaceutical activities while enforcement decisions to cover all activity were to be taken in a separate committee- the Enforcement Committee. A number of initiatives were taken in order to strengthen the enforcement function and activity, in line with the increasing demands emanating from the local market.

The Medicines Authority adopted a structured and formal system for risk based approach in the prioritisation of its operations in line with the availability of its resources. Clear criteria for prioritisation were set at the planning phase. This approach was utilised for the inspection plan for 2009, for targeting clinical trials for Good Clinical Practice inspections and in the assessment of medicinal products at pre- and post- authorisation stages. For work which was not under national obligation prudence was exercised whereby the number of procedures planned did not exceed the capacity available to perform this work.

1.2 Customer Satisfaction and Communication with Stakeholders

As from inception the Medicines Authority has maintained good communication with stakeholders. 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 2009 the Authority had seventy six (76) 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. Most of the meetings were held on request and were related to specific issues in compliance with regulatory requirements. Figure 1A shows the proportion of meetings with stakeholders according to category.

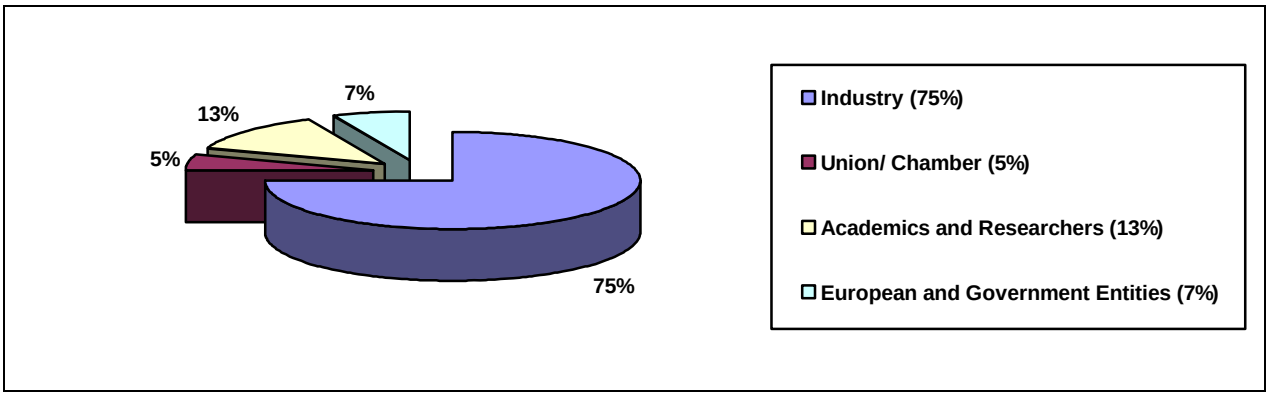

Figure 1A Proportion of meetings with stakeholders according to category.

The Authority regularly communicated with stakeholders through circulars and these were uploaded on the website so as to ensure transparency. The website was updated with relevant information. The list of Authorised Medicinal products (together with the summary of product characteristics and the package leaflets) and the list of licensed wholesale dealer on the website were regularly updated. In 2009, it was decided that a structured approach would be adopted for understanding the needs of stakeholders.

During 2009, five (5) complaint files were dealt with through the standard operating procedure. These exclude complaints related to enforcement and advertising of Medicinal Products for which there is a separate procedure. Three (3) files were closed or referred by end December 2009. One thousand and ninety seven (1097) enquiries were logged. These are separate from queries about particular products or procedures, which are the responsibility of the technical directorates.

1.3 Quality Management System

During 2009 there was a full review of the established standard operating procedures, most of which were at the stage of the second three- year review. This general review addressed the gaps and targets originating from the Benchmarking of European Medicines Agencies (BEMA) self assessment as well as the changes in functions and in responsibilities at the level of the Authority. Moreover the review incorporated changes in policies as well as corrective and preventive action identified through implementation of operations, internal audits and Management Review.

During 2009 the Medicines Authority adopted the BEMA indicators as the main targets for quality improvement. Moreover the pending internal audits from the previous years were closed and recommended corrective and preventive actions were implemented and considered as an integral part of the overall quality management review. The whole exercise reflected an improved level of maturity in terms of consolidation of quality management across the Authority.

1.4 Risk Management

During 2009 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 sixth 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. An internal policy which amongst other issues tackles specific risks of the organisation was circulated.

1.5 Human Resources Management

1.5.1 Recruitment and Retention

The work of Human Resources is guided by the Medicines Authority mission and objectives identified in the quality manual and in the strategic path identified in the business plan. The Medicines Authority continued strengthening its human resources by increasing staff with 35% over 2008. The organisation had external recruitment of an Operations and Regulatory Affairs Manager, a Quality Assessor, an Inspector, a Pharmacist and four Finance and Administration Assistants. There were also internal promotions for the posts of two Quality Assessors and a Finance and Administration Executive. In spite of attempts to recruit, the post of Medical Assessor remained vacant. During 2009, two members of staff were on long leave and the Medicines Authority also entered into Contract for Services with five Pharmacists, three of which are still in force. Figure 1B shows the number of staff according to category as on 31st December 2009.

	Full-time	Part-time/ Reduced Hours	Contract for Service
Management	6	0	1
Technical	19	2	4
Support Staff	10	0	0

Figure 1B - Human Resources at the Medicines Authority as on 31st December 2009

1.5.2 Training and Development

Further to the twinning light project of 2008, and the achievement of all the key learning indicators, training and development continued being a priority for the Medicines Authority and initiatives were organised to ensure the development of the whole spectrum of activities by the Medicines Authority, both current and future. In 2009, staff had the opportunity to attend training and development initiatives both in Malta and in other European Countries.

The Medicines Authority highly values on the job training. Thus, new staff members were trained through peer review, shadowing and observation and junior pharmacists were invited to attend assessment team meetings for training purposes. Since in 2009 most of the Standard Operational Procedures were

revised and new procedures were written, there was extensive training on the new/ revised procedures. In-house training was also valued, and training was organised on diverse subjects in regulatory affairs and scientific research. Three members of management continued attending the Continuing Professional Development sessions for Level II Management organised by the Health Division training centre.

Assessors were mainly trained on quality assessment of sterile medicinal products since these will be taken up for assessment during the next three years. Assessment training is continuous as during all procedures with Malta as rapporteur or Reference Member State, shadow assessors are being actively involved. Initial training on the assessment of sterile products was delivered over a one week period in August by a trainer assessor from the Medicines Products Healthcare Agency (MHRA). Training on the assessment of oral solutions was given by an in-house assessor in December. In-house training on analytical methods was also given by a quality assessor with experience in this area of expertise. Furthermore, three quality assessors attended training organised by the European Medicines Agency on writing assessment report. For training purposes, a visit to a local Good Manufacturing Practice (GMP) facility in June was organised to enable technical staff within the licensing directorate to get a better insight into this area, in particular in relation to manufacturing processes and equipment.

Pharmacovigilance staff attended training in Eudravigilance and assessment of bioequivalence studies at the European Medicines Agency and on medication errors at the World Health Organisation annual meeting for National Competent Authorities.

Medicines Inspectors attended training on Good Clinical Practice (this type of inspections where initiated for the first time in 2009); on Pharmacovigilance Inspections (this type of inspections are planned for next year) and especially on sterile manufacturing (this type of inspections are planned for 2011). Two observed inspections consisting of two visits in sterile dosage forms manufacturing in Latina- Rome with the collaboration of AIFA, Italy were carried out. There was a training seminar held on sterile manufacturing and Good Manufacturing Practice issues organised by the World Health Organisation in Geneva and another seminar organised by PIC/S in Uppsala, Sweden on sterile manufacturing. Furthermore, medicines inspectors attended the EMA training camps in Good Clinical Practice, Rome and another one on Pharmacovigilance inspections held in Paris.

1.5.3 Performance Management, Working Conditions and Staff Satisfaction

During 2009 the Medicines Authority continued to implement the Collective Agreement with the Union Ħaddiema Magħqudin.

Monitoring of output and support to employees was enhanced through the implementation of performance review meetings with line managers twice a year, rather than once every year. Other measures used by the Medicines Authority to manage performance are peer review and team meetings where output was openly discussed.

In 2009, a staff satisfaction survey was sent to all staff on-line and the response rate was of 71.43%. It was found that 93.3% of the respondents are very satisfied or satisfied with their job at the Medicines Authority. The results and feedback were discussed in a staff meeting and relevant opportunities for improvement were included in the 2010 Operational Plans.

1.5.4 Health, Safety and Well being

Occupational Health and Safety was prioritised in 2009. A new health and safety officer and two fire safety officers were nominated. An occupational health and safety risk assessment was conducted with the collaboration of the Environmental Health Directorate and the Nursing Services Directorate and implementation of recommendation started in 2009 and will be finalised in 2010. A new health and safety committee was established in December 2009 and one meeting was organised. Waste separation was prioritised as the green initiative of 2009. A green focal point was appointed and waste separation bins were introduced and promoted. As from 2009 all shredded paper is sent for recycling.

1.5.5 FHRD - HR Award - Excellent Training and Development Initiative

In 2009 the Medicines Authority joined the Foundation for Human Resources Development as a member. In November 2009 the Authority received the HR Award for Excellent Training and Development Initiative. The initiative is the Twinning Light Project entitled 'Further Capacity Building at the Medicines Authority' which was organised in a partnership with The Netherlands Ministry of Health, Welfare and Sport - National Institute for Public Health and the Environment (RIVM) in collaboration

with the Medicines Evaluation Board (MEB) of the Netherlands and the Health Care Inspectorate. The project was aimed to train technical staff of the Medicines Authority to carry out advanced assessment work and inspections to enable Malta to act as Reference Member State for the Mutual Recognition and Decentralised procedures.

The Award acknowledged the standard of good practice of the initiative which went beyond the overall purpose of the project. The project has led to the involvement of people from the different departments within the organisation, further motivated and empowered the staff of the Medicines Authority and has led to an increase in performance and quality of the operations.

1.6 Information Systems Management

During 2009 the IS Unit continued to operate and maintain the existing in-house and European information systems and the ICT infrastructure. A process to change all computers to faster, more powerful and energy efficient PCs started through a central government vote. 37% of PCs have been changed in until end 2009 and the rest are scheduled for 2010.

Regular Information Systems meetings were held by the Information Systems manager to inform management about new developments and discuss business requirements presented by the departments. Improvements have been done on the server setup and the Link Library intranet with the benefit of streamlining operations and maximising uptime. In January of 2009 the Authority submitted a letter of intent to the Medicines Evaluation Board (MEB) to commission a report to analyse the business requirements of the Authority and map the requirements to the ICI System. The report and contract were received by the Authority.

Data Protection requirements are being proposed to all directorates and units. Upon approval by management, the legislation will be implemented across all departments. The implementation of the Freedom of Information Act (FOI) has commenced and a FOI Officer and Alternate have been nominated to co-ordinate the implementation of legislation.

1.7 Collaboration with other Entities

During 2009, the Medicines Authority has reviewed and renewed the established Memorandum of Understanding (MoU) with the Directorate General for Public Health Regulation and also signed a MoU with the Directorate for Environmental Health for prosecution services. Another MoU was signed with the Strategy and Sustainability Division within the Ministry for Social Policy, Health**,** the Elderly and Community Care to formalise existing collaborations. The Medicines Authority also reviewed and renewed the contract agreements for analysis services with Belgian lab and with MHRA, the latter covering also both sterile and non-sterile dosage forms.

2.0 Assessment and Authorisation of Medicinal Products

The Medicines Authority is responsible for assessing information as regards the safety, quality and efficacy of medicinal products to be placed on the market in Malta. During the last three years, through the Medicines Authority, Malta built the capability to act as Reference Member State in decentralised procedures and in 2009 the Authority started participating as rapporteurs in the centralised procedure (for generic products). Assessment of Medicinal Products is conducted according to national and EU legislation. Decision-making is done in committees. Standard Operating Procedures are followed.

2.1 The Medicines Review Committee

The Medicines Review Committee within the Medicines Authority meets 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, pharmacovigilance issues) as well as clinical trial applications and European work-sharing procedures. The main objective is to reach an integrated opinion and support decision making on positions to be taken by the Medicines Authority in all ongoing technical procedures, at different levels. The technical decisions taken at the meeting are then put forward as recommendations to the Licensing Authority for a final overall decision. 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. The committee was set up in 2008 and the mandate and rules of procedure were finalised in 2009. Thirteen (13) meetings were held in 2009.

2.2 European Procedures

2.2.1 Marketing Authorisation Procedures

Malta as rapporteur in the Centralised Procedure

In early 2009, the decision was taken by management to start participating as co-/rapporteurs in the centralised procedure for generic products. As per the business plan, two procedures were bid for. One started in 2009 and is ongoing. The other one was cancelled by the applicant.

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

Following a management decision taken in 2005 to participate more actively in the European procedures, the Medicines Authority accepted its first application as Reference Member State in a Decentralised Procedure in December 2007. This procedure was finalised in October 2009. Up to that point in time, it had been decided that for the purposes of Reference Member State assessment, the Medicines Authority would only accept applications for oral solid dosage forms for which extensive training was carried out in 2008 during a Twinning Light programme with another competent authority. Therefore all applications received in 2009 were for this type of pharmaceutical form. In 2009, management decided to extend its remit to injectable products. Training provided in 2009 will enable the Medicines Authority to start taking up oral solutions in the current year and injectable (sterile) preparations are planned for 2011.

In 2009, four (4) procedures (equivalent to a total of 25 marketing authorisations – different strengths or parallel procedures) with Malta as Reference Member State in a Decentralised Procedure were started. Two (2) procedures (6 marketing authorisations) have been finalised successfully and four are ongoing. An additional six (6) procedures which were meant to start in Q4 2009 have now been transferred to a start date in 2010 (at the request of applicants) pushing up the total of procedures planned for 2010 to twenty three (23). With the current resources this is the maximum number of procedures that can be taken up. Bookings are being accepted for 2011 and some procedures are on the waiting list for possible cancellations in 2010. The number of procedures to be accepted are in line with the Medicines Authority three year business plan which takes into account both capacity in terms of human resources and also expertise available, both in-house and locally.

Six (6) variations (type 1B) were received for products authorised by the decentralised procedure with Malta as Reference Member State.

The experience with these procedures so far has been very positive. A team is set up for each procedure, consisting of a product coordinator, and quality, clinical, pre-clinical, pharmacovigilance assessors. Other team members also include 'shadow' assessors or peer reviewers and line managers. Technical staff in other posts may be invited to attend team meetings for training purposes. Before scheduling of procedures it is made sure that there are no conflicts of interest of any of the team members.

A total of twenty two (22) case team meetings were organised. Team meetings are organised regularly to discuss the progress of the procedure 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 at several stages during the procedure, 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.

Malta as Concerned Member State

One hundred and seventy nine (179) European marketing authorisation applications were received in 2009 for Malta as Concerned Member State. Sixty five (65) were through the Mutual Recognition Procedure and one hundred and fourteen (114) were through the Decentralised Procedures. The number of marketing authorisations granted for the two types of procedures for the same period was sixty five (65) and one hundred and twenty one (121) respectively.

European post-authorisation procedures

Nine hundred seventy six (976) new Mutual Recognition Procedure variation applications were received and four hundred forty three (443) procedures were finalised. Eighty (80) renewal applications were received and 10 were finalised. Fifteen (15) article 61(3) notifications were received and eight (8) finalised during 2009.

The low fees generated through the Concerned Member State Procedures and through variations result in low levels of resources available and afforded for these procedures.
A risk-based approach is taken for Concerned Member State procedures This is based on the experience gained so far in processing these applications but also in line with the approach taken by many other Member States. This requires enhanced trust between competent authorities and fulfils the real spirit of mutual recognition. No full parallel assessment of procedures where Malta is Concerned Member State is done and our decision is largely based on the assessment of the Reference Member State. Criteria for requirement of more in-depth assessment are outlined in a policy document and in some cases described therein some assessment is carried out, in particular where there are issues related to public health or the local scenario.

Application type	Received	Finalised
Centralised Procedure - MT rapporteur	10 (1)*	0
MA DCP - MT RMS	25 (4)*	6 (2)*
MA MRP - MT CMS	65	65
MA DCP - MT CMS	114	121
Variations MRP - MT RMS	6	0
Variations MRP - MT CMS	1917 (976)	767 (443)
Notifications MRP - MT CMS	29 (15)	19(8)
Renewals MRP - MT CMS	80	10
Paediatric Data Assessment WS MT rapporteur	1	0

* Number in parenthesis is the number of procedures. Other numbers are equal to number of actual marketing authorisations

Table 2A - Summary of Marketing Authorisation applications received and finalised in 2009

2.2.2 Work-sharing Procedures

Throughout 2009, 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.

Committee for Medicinal Products for Human Use

During 2009, Medicines Authority representatives at the Committee for Medicinal Products for Human Use were involved as a rapporteur for one (1) re-examination procedure for an Article 31 referral for Dextropoxyphene EMEA/H/A-31/968 that has been concluded and one (1) centralised marketing authorisation application for a generic medicinal product that is still ongoing (December 2009. 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.

Medicines for Children

Malta has been a rapporteur for 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. During 2009, the Medicines Authority representatives at the Paediatric Committee at the European Agency in London were involved as rapporteurs or peer reviewers for thirteen (13) different procedures (nineteen (19) products). As at end 2009, twelve (12) of these procedures were concluded, one (1) was ongoing and almost concluded.

PSUR Assessment in the European Work-sharing Procedure

As described under Directive 2001/83/EC, marketing authorisation holders are legally required to systematically collect and evaluate information on safety data related to their marketed medicinal products and to transmit this information to the competent authorities. Under the auspices of the 'Heads of Medicines Agencies' an initiative has been undertaken to ensure that medicinal products with the same active substance follow the same safety report submission scheme in all EU countries, thereby avoiding unnecessary duplication of work both for pharmaceutical companies and even for National Competent Authorities since a single Reference Member State is selected to perform the safety assessment of a specific active substance. The initiative thereby allows for improved evaluation of safety within the collated EU data for the active substance under investigation and for the establishment of harmonised safety texts across the EU.

During 2009, the Medicines Authority performed the first medicinal product safety/risk assessment, specifically in regard to product formulations containing the active ingredient ursodeoxycholic acid. This assessment was conducted within the context of the above-mentioned European Work-sharing Scheme and for which Malta was the assigned reference member state. Safety assessment of ursodeoxycholic acid preparations with Malta as Reference Member State comprised a novel and challenging endeavour in that it entailed the application of EudraVigilance and the European Pharmacovigilance Information Tracking Tools for purposes of scientific and statistical risk evaluation within the context of the prevailing regulatory controls. The task also necessitated multiple communications with all relevant Marketing Authorisation Holders in order to allow for collation of all safety data pertinent to the review.

Discussions and decisions on the final proposed safety texts were also undertaken within European *fora*. The assessment was finalised successfully in September 2009.

2.3 National Procedures

National marketing authorisation applications

A total of 3 national marketing authorisation applications were received in 2009. These were line extensions to already authorised products. Three procedures (3) 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 2009 was three hundred twenty eight (328) and two hundred fifty six (256) authorisations were issued in 2009.

National variation applications

One thousand nine hundred and seventy one (1971) national variation applications were received in 2009. One thousand two hundred and twenty seven (1227) procedures were finalised. There has been a marked improvement in the number of variation applications processed this last year compared to the number of national variations processed between 2005 and 2008, which had totalled one thousand three hundred sixty three (1363) over 4 years. 47% of all the finalised variations were processed in 2009. This resulted from having more focussed resources allocated to these procedures.

National notification 61(3) applications

Two hundred and sixty (260) (200 products) national article 61(3) notifications were received one hundred and eighty one (181) (141 products) procedures finalised.

National renewals

Four (4) out of the twenty five (25) national renewal applications were processed in 2009.

Transfer of marketing authorisations

Thirty six (36) applications for the transfer of a marketing authorisation holder were received and twenty (20) processed.

Parallel import applications

Twelve (12) parallel import licences applications were received and eight (8) finalised by the end of 2009.

Withdrawals of authorisations/licences

Application for the withdrawal of marketing authorisations, authorisations in accordance with article 126a and parallel import licences numbered 83, 12 and 4 respectively.

A summary of the procedures received and finalised in 2009 is given in table 2B.

Application type	Received	Finalised
Marketing Authorisations national	3	3
Authorisations article 126a	328	239
Licences Parallel Import	12	8
Variations national	1971 (1281)	2024 (1227)
Notifications national	260 (200)	181 (141)
Renewals national	25	4
Transfers of MAH	36	20
Withdrawal MA	83	42
Withdrawal PI	4	1
Withdrawal 126a authorisation	12	2

*Number in parenthesis is the number of procedures. Other numbers are equal to number of actual marketing authorisations

Table 2B - Summary of national procedures received and finalised in 2009

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

In 2009 six hundred and one (601) procedures for linguistic review of product information in Maltese for products authorised through the centralised procedure were processed. The number of procedures by category is outlined in table 2C.

Procedure Type	
New products	78
Variations	403
Notifications article 61(3)	8
Annual re-assessments	8
Referrals	21
Renewals	59
Line extensions	24

Table 2C - Product information linguistic review (2009)

2.5 Scientific Advice

Since the second quarter of 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 2009, no scientific advice requests have been submitted to the Medicines Authority.

3.0 Clinical Trials

During 2009, eight (8) new Clinical Trials applications were submitted to the Medicines Authority. Six (6) in total were approved but two (2) are currently undergoing validation (31st December 2009). Sixteen (16) amendments to trials which are being conducted in Malta were also received. Sixteen (16) amendments were approved in total in 2009. All information has been inputted in the European Database for Clinical Trials. Compared to 2008, there has been a 60% increase in Clinical Trial applications submitted to the Medicines Authority over 2009. It is expected that an increased number of substantial amendments will be submitted in 2010 as compared to 2009. Throughout 2009, the quality system for Clinical Trials has been reviewed where both the standard operating procedure as well as the Guidance notes on Good Clinical Practice (GC1.07) issued by the Medicines Authority were reviewed.

4.0 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 authorised.

4.1 National Pharmacovigilance Activities

The Medicines Authority endeavours in a number of activities to ensure medicinal product safety 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. Lastly but not least, 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. As previously mentioned, the collection of safety information from local healthcare professionals comprises the major and most basic pharmacovigilance activity. 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

A total of one hundred and eighty four (184) adverse drug reaction case reports were registered over 2009. Each of these cases detailed at least one adverse drug reaction to the medicinal product concerned thus resulting in a total of four hundred twenty seven (427) individual adverse drug reactions. Figure 4a overleaf 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 4b and 4c further classify the adverse drug reaction case reports (as received over 2009) 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 MA 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 2009, 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.

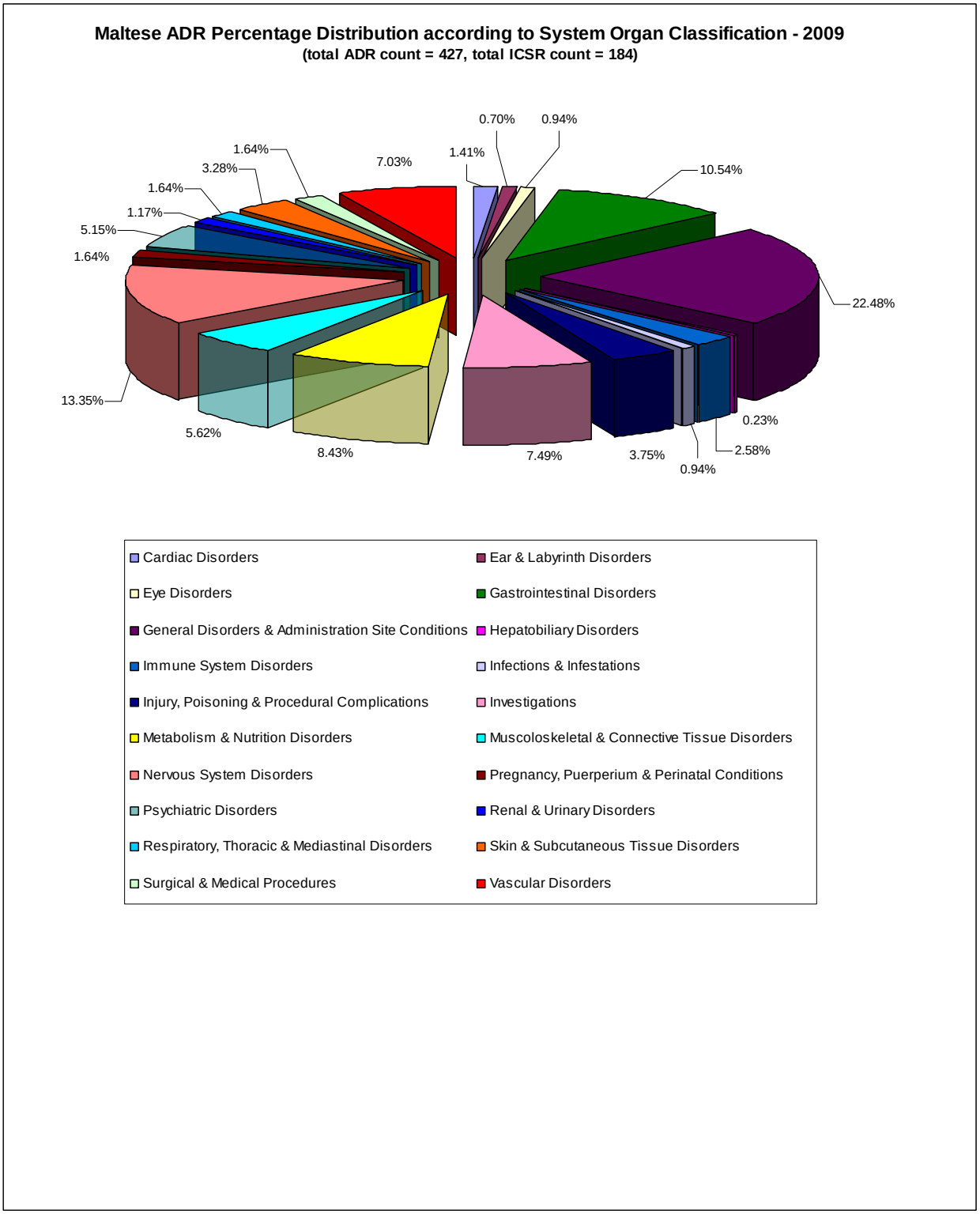

Figure 4a Distribution of adverse drug reactions according to System Organ Classification - 2009

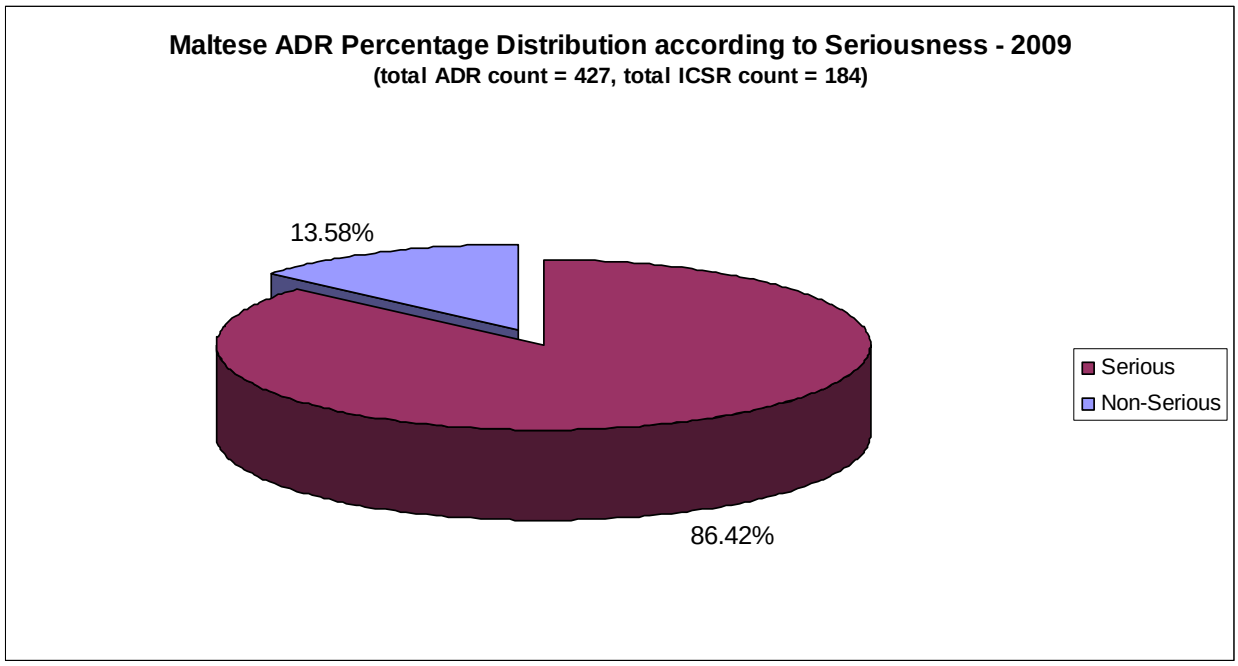

Figure 4B Percentage distribution of adverse drug reactions according to seriousness - 2009

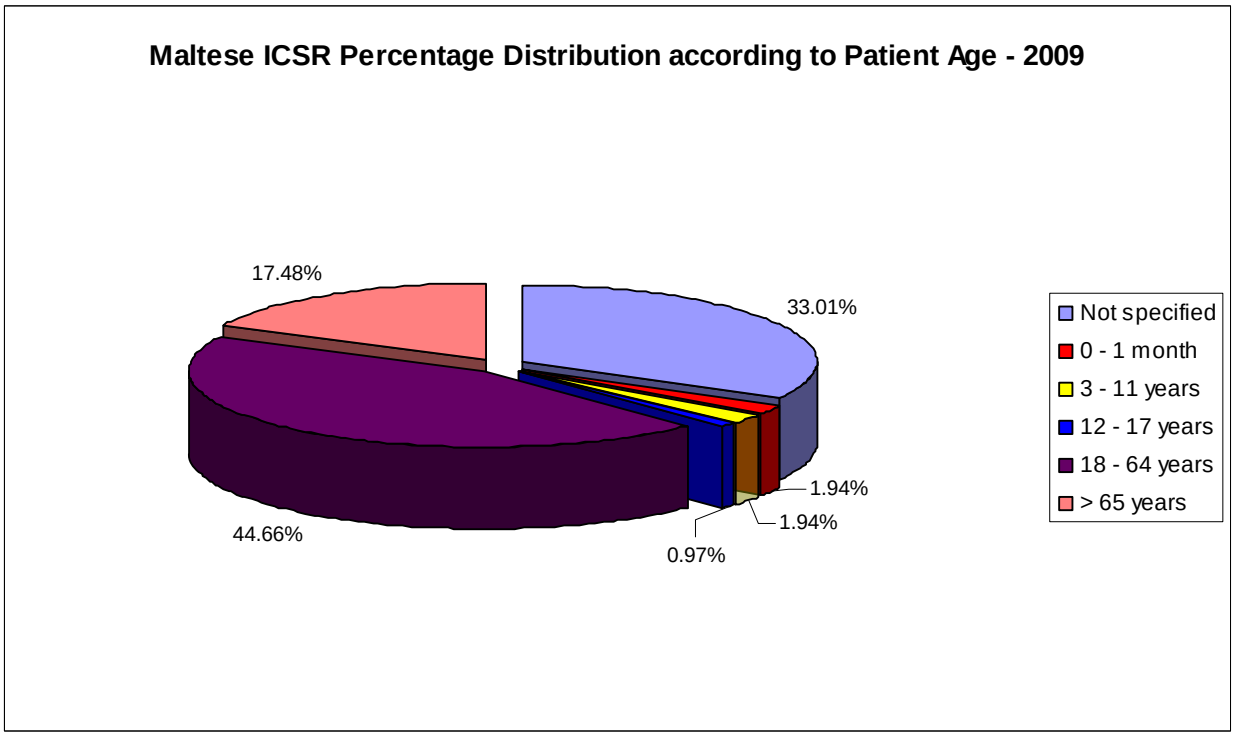

Figure 4C Percentage distribution of case safety reports according to patient age - 2009

As mentioned earlier, 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).

Figure 4d below gives the distribution of queries and communications which the Medicines Authority handled over 2009 in respect of the previously mentioned safety monitoring measures together with 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/EudraVigilance.

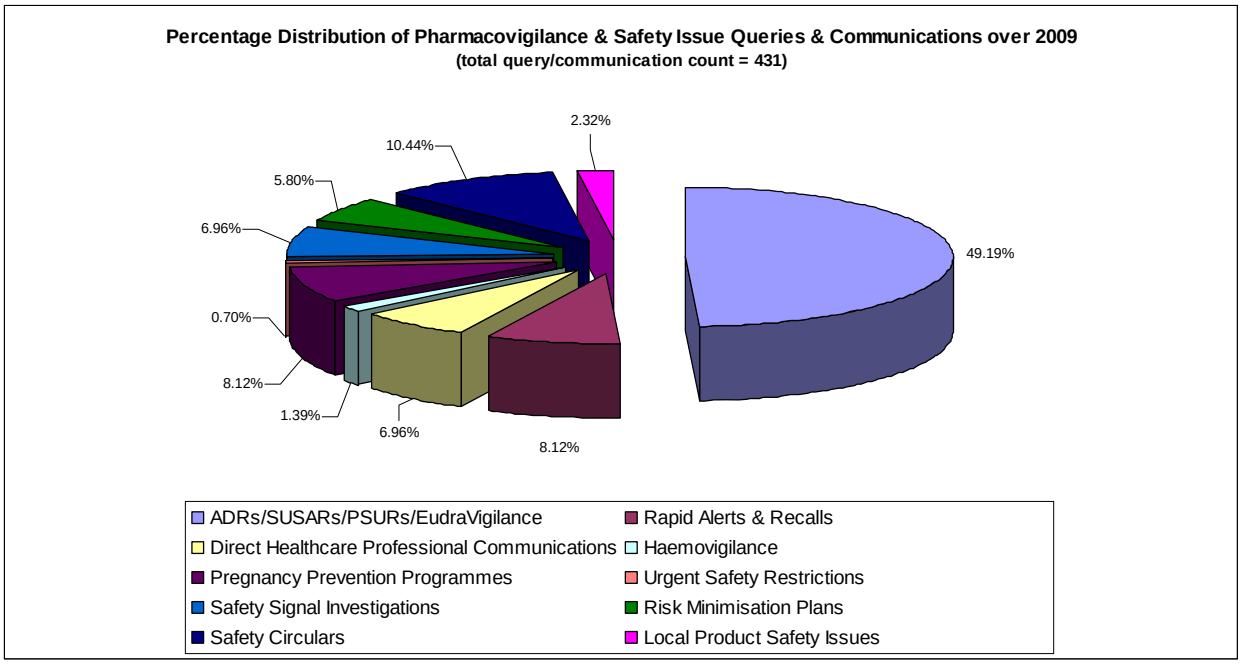

Figure 4D Distribution of Pharmacovigilance and safety issue queries and communications - 2009

4.2 Upgrades to the Medicines Authority's Pharmacovigilance Procedures

Over 2009, 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 and EU legislative requirements particularly in respect of management of adverse drug reaction reports, pharmacovigilance queries, rapid alerts and safety information.

5.0 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 EU Good Distribution Practice respectively, whilst pharmacies are inspected against national legislation and standards.

Good Clinical Practice Inspections are carried out on a risk based approach and all other 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 Good Manufacturing Practice 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 Good Manufacturing Practice certificate (this is still permissible with the current EU and local legislation). Therefore these two facilities are issued with only a Good Manufacturing Practice certificate and are inspected once every three years.

For the first time ever the Medicines Authority initiated inspections of clinical trials for Good Clinical Practice. Two Good Clinical Practice inspections were identified based on a risk based approach, carried out and successfully concluded in 2009.
During 2009, there were seven (7) meetings of the Inspectors Review Group (IRG) whereby twelve new cases were discussed and decided upon, whilst follow up of previous pending cases were also carried out.

5.1 Good Manufacturing Practice

During 2009 the Medicines Authority fulfilled its Good Manufacturing Practice inspection plan where seventeen (17) Good Manufacturing Practice inspections were carried out and concluded as follows:

- Four Manufacturing Authorisations were renewed for non sterile solid dose manufacturers;
- One Manufacturing Authorisation renewed for a medicinal gas manufacturer;
- Five renewals of Manufacturing Authorisations for repackaging and re-labelling operations;
- Five renewals of Manufacturing Authorisations for importation activity from countries which have Mutual Recognition Agreements (MRAs) with the EU for Good Manufacturing Practice.

- One inspection was carried out to include in the Manufacturing Authorisation Investigational Medicinal Products (IMPs).

An inspection of the Mobile Blood Donation unit was also carried out in 2009, after which the first time ever inspection of the National Blood Establishment initiated in 2008 was able to be successfully closed and the Blood Establishment issued with a licence for blood collection, storage, processing and distribution.

A total of thirteen (13) manufacturing authorisation variation applications were processed in 2009.

During 2009 the Medicines Authority continued to get itself involved in the international Good Manufacturing Practice arena through its participation in PIC/S meetings and seminars described in section 1.5.2 of this report. The Authority 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.

5.2 Good Distribution Practice

During 2009 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 2009.

5.3 Good Clinical Practice

During 2009 the Medicines Authority started off for the first time inspections of clinical trails against EU Good Clinical Practice guidelines. During 2009 there were twelve (12) approved clinical trials. Since this was the first time clinical trails were going to be subjected to inspections, an informative meeting was set up with all investigators supervising and carrying out these clinical trails. Since according to present legislation not all clinical trials need to be inspected, a risk based approach was taken. A series of risk factors were devised assigning to each factor a particular numerical value as a 'weight' number. 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 Good Clinical Practice inspections of around twenty per cent (20%) of the clinical trials. This percentage is a rule of the thumb used by many agencies to allocate resources to clinical trials inspections and was disclosed to the Authority by the Dutch Inspectorate during the Twinning Light Project of 2008. 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 2010 it is planned that a similar evaluation exercise is carried out and two other clinical trials are identified for Good Clinical Practice inspection.

5.4 Pharmacies Standards

The Medicines Authority took over the responsibility for pharmacies from Public Health in August 2005. During 2009 the Medicines Authority carried out the remaining pharmacy inspections rolled over from 2008, totalling to one hundred and forty one (141) retail pharmacy inspections. One new retail pharmacy licence was issued and one new licence for a national hospital pharmacy (Zammit Clapp Hospital Pharmacy) was issued as well. Therefore, between 2008 and 2009 all the retail pharmacies were inspected for the first time on a two year cycle. In 2010 the two year cycle of inspections for pharmacies will start again, inspecting those pharmacies which were inspected in 2008.

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

In 2009 the pharmacy licences were issued for the first time with a new set of dispensary/pharmacy licence conditions which had been drafted and agreed upon with stakeholders and the Licensing Authority in 2008.

5.5 Qualified Person

In 2009 the Medicines Authority received two (2) applications for the Qualified Person status. One (1) applicant did not fulfil the Directive criteria to be considered for the Qualified Person status and was rejected. The other applicant was interviewed and accepted as eligible for Qualified Person status.

6.0 Participation at Meetings at an EU level

The Medicines Authority is actively involved in a number of EU committees and working parties. Over the year 2009, members of staff of the Medicines Authority and other professionals nominated by the Medicines Authority actively participated in one hundred thirty five (135) meetings and conferences where various aspects of regulation (policy, legislation, administrative and scientific) were discussed and decided.

The CEO participated at the meetings of the Heads of Medicines Agencies and also participated as a member of the European Medicines Agency Management Board. The Quality Manager participated at meetings of the Working Party of Quality Managers and meetings regarding the Benchmarking of European Medicines Agencies II. The Operations and Regulatory Affairs Manager started participating in the Communications Professionals Working Group and the Information Systems Manager attended meetings related to Eudra services.

Amongst the meetings of the European Medicines Agencies and Heads of Medicines Agencies attended in 2009, there are the Committee for Medicinal Products for Human Use (11 meetings), the Paediatric Committee (7 meetings), the Committee for Orphan Medicinal Products (8 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 (10 meetings), the Biologics Working Party (4 meetings), Efficacy Working Party (3 meetings), Joint CHMP-CVMP Quality Working Party (4 meetings), the Safety Working Party - Human Medicine (3 meetings), the Working Group on Quality Review of Documents (4 meetings), the Clinical Trials Facilitation Group, the Pharmacovigilance Working Party (3 meetings), the Pharmacogenetics Working Party (2 meetings), the GCP Inspectors Working Group (2 meetings), the GMP-GDP Inspectors Working Group (2 meetings), the Pharmacovigilance Inspectors Working Group (3 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). 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).

7.0 Implementation of regulation on the local market

7.1 Borderline Classification Committee

In 2009, the remit and rules of procedure of the Borderline Classification Committee were revised to make the process more transparent and efficient. Five (5) meetings were held in 2009 for determination whether products were medicinal products or not. Fifty one (51) applications for classification were received. Most requests forty two (42) were from Malta Standards Authority, two (2) from Mater Dei Hospital and the rest from local importers. Seven (7) products were classified as medicinal products. No marketing authorisation applications for these products were received as a result. One (1) product was considered as fulfilling the requirements of the traditional herbal medicinal products (THMP) directive. Four (4) cases received in 2009 are still pending a decision. No formal appeals to the BCC Appeals Board were made on decisions taken by the Committee.

7.2 Traditional Herbal Medicinal Products

During 2009, three (3) meetings regarding the implementation of the Traditional Herbal Medicinal Product Directive (THMP) (Directive 2004/24/EC amending Directive 2001/83/EC) were held with the Licensing Authority and with other authorities and bodies, including with Malta Standards Authority, Department for Environmental Health and Port Health. These meetings were held to discuss the current scenario of herbal product regulation and the implementation of the directive by 2011, the deadline for the derogation allowed by the European directive. The impact on the stakeholders, in particular the importers and the patients and on the Medicines Authority was the focus of the discussions.

Since October 2005, all new herbal products falling under this directive have to be authorised as medicinal products before being placed on the market. Products that were already on the market before October 2005 have until 2011 to come in line and be granted a marketing authorisation by the Medicines Authority, if they are to be kept on the local market.

No applications for the registration of traditional herbal medicinal products have been received. It is expected that applications will start coming in during 2010. The capacity, in terms of human resources

required for their assessment will be known once the approximate number of products falling under the Traditional Herbal Medicinal Products directive is established.

It is envisaged that some problems may be encountered in the implementation of this regulation. Products currently placed on the market as food supplements may require registration and have to be eventually only sold from pharmacies (as all other medicinal products) once they are authorised as medicinal products. This is being discussed with the Licensing Authority and feedback from stakeholders will also be discussed during the planned information session in 2010.

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. 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 2009, five (5) advertising complaints were registered with the MA. Following assessment, breaches to the legislation were identified in relation to four (4) reports.

To a lesser degree, control of advertising material is also implemented via the ad hoc selection and investigation of local advertisements as presented within the major media formats. This activity principally aims at ensuring public health protection via the affirmation that the applicable legislation is consistently being upheld and rigorously adhered to. Over 2009, two (2) advertisements were assessed via this monitoring procedure.

7.4 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. The Medicines Authority provides information about medicines by publishing the patient leaflet (PL) as well as the summary of product characteristics (SmPCs) for medicinal products for human use. As of 31 December 2009, the total number of PLs and SmPCs published on the Medicines Authority's website were four thousand one hundred thirty one (4,131). Furthermore, twelve (12) safety circulars were published and sent to healthcare professionals and made available to the general public in 2009. Since November 2009, staff from the Medicines Authority have been working on the compilation of version one of the Malta Medicines List. The Malta Medicines List is a list comprising of all medicinal products authorised in Malta through a Marketing Authorisation (central or national) and in accordance with article 126(a) of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community Code relating to medicinal products for human use, as amended by Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004. The Malta Medicines List will contain information on the ATC code of the medicinal products authorised. In addition, staff of the Medicines Authority throughout 2009, have compiled a list of medicinal products that have a risk management plan and pregnancy prevention plan to be implemented by marketing authorisation holders in Malta.

7.5 Rational use of medicines

The Medicines Authority has a national public health remit with respect 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. Through its activity in setting up the Malta Medicines List by ATC code, the Authority is developing a national essential medicines list. Furthermore, 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

8.0 Enforcement and surveillance of the local market

8.1 Enforcement

During 2009 the Medicines Authority had twenty six (26) complaint & enforcement investigations compared to eighteen (18) in the preceding year (almost a 40 % increase in enforcement activity) and a 160% increase when compared to the ten (10) cases of 2007.

The Inspectorate and Enforcement Director is also the group leader for 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 two (2) have been concluded and one (1) is currently being addressed. These are:

- To draw up 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 in 2009. The aim of this objective will be fully achieved and finalised in 2010.

The Director attended six (6) court sittings during 2009 to provide court witness services. Five (5) cases concerned pharmacy issues and one concerning a wholesale dealing case. Cases related to pharmacy issues are on the increase and a number of cases are pending court jurisdiction.

Medicines Inspectors had nine (9) calls for court witness between them during 2009 regarding enforcement cases (two enforcement cases are currently pending court jurisdiction). During 2009 two (2)

other new enforcement cases where referred to courts for hearing. It is envisaged that the court hearings for these two new enforcement cases will start in 2010.

8.2 Batch defect Reports

In this reporting period the Directorate received 88 rapid alerts which were investigated and out of which 3 resulted in recalls from the local market (two recalls at pharmacy level and one recall at patient level). Another one (1) rapid alert ended in a caution-in-use notification.

8.3 Sampling of Medicines on the market

All results from the sampling plan of 2008 have been received and there were no out of specification results. The sampling plan for 2009 has been accomplished, i.e. twenty one (21) samples from eight (8) different products originally planned have been collected and sent for analysis.

9.0 Regulatory Affairs

9.1 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.

9.2 Update and Implementation of new legislation

Paediatric

In February 2009, staff of the Medicines Authority compiled the Malta list of medicines used in paediatrics. The target to transmit this list to the European Union by February 2009 as stipulated by Regulation 1901/2006/EC was therefore met.

Advanced Therapies Regulation

Transposition of article 28 of the Advanced Therapies Regulation (Regulation 1394/2007/EC), has been carried out by the publication of LN 231 of 2008. Administrative measures at the national level are being worked upon in order to further implement the provisions of article 28 of the advanced therapies regulation.

Variations

Regulation 1234/2008/EC on the examination of variations to marketing authorisations came into force in January 2010. This regulation changes the process for the assessment of variations of products authorised through the European procedures (MRP, DCP and centralised procedure). This new regulation allows for grouping of variations (same variations can be grouped for different products falling under the same 'global' marketing authorisation and different variations effecting one marketing authorisation can also be grouped together in one application form), enhanced work-sharing between Member States and also for submission of fewer type 1A variations (except for those that require immediate notification) as they can be grouped in an annual report. These are a few of the main changes to the regulatory requirements for variations. These should bring a positive outcome to the resources required from both the industry and competent authorities. All variations submitted from 1 January 2010 have to be submitted in accordance

with the regulation. Directive 53/2009/EC is based on the same requirements of the regulation but will impact national variations. The same grouping is allowed and work-sharing between Member States even for national products will reduce parallel assessment of the same variation applications in the different Member States, with improved approval times and the need for fewer resources.

This directive has come into force in June 2009. Member States have to implement this directive by 20 January 2011. Some Member States will start implementing this directive at the same time as the regulation i.e. January 2010. Some Member States will implement during 2010 whilst others will do so in January 2011.

It is planned to hold an information session in 2010 on the main changes that this directive will bring to the submission and processing of variations. As soon as the Directive is transposed, it would be reasonable to start implementing. It would be easier for all stakeholders to have only one set of rules for both European and national procedures. However, being a small Member State, the Medicines Authority may decide to accept both types of applications in this transitional year to allow for applicants to come in line with both pieces of legislation.

New Legal Notices

In 2009 four (4) new legal notices (LN) were issued, LN 29 of 2009 entitled 'Health Ethics Committee (Fees) Regulations', LN 58 of 2009 entitled Availability of Medicinal Products within the Government Health Services Regulations, LN 188 of 2009 entitled 'Rules of 2009 on the Provision of Medicinal Products through the GenitoUrinary Clinic within the Government Health Services', LN 252 of 2009 entitled 'Manufacture and Importation of Medicinal Products for Human Use (Amendment) Regulations, 2009'.

An exercise was carried out whereby articles of the Medicines Act were reviewed and amendments suggested bringing the legislation in line with the norm of practice. Also suggestions were made to change article 98 'Adulteration of medicines' to make reference to counterfeit products, whilst article 99 'Offences and Penalties' was reviewed in association with penalties imposed and articles referred-to for these penalties.

9.3 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, or legal quality of regulations and the administrative procedures, tariffs and fees derived therefrom. Following the initiatives carried in previous years, during 2009, further training was delivered in better regulation.