European Medicines Agency

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Second Status Report on the Implementation of the EMEA Road Map

I Introduction

The EMEA Road Map to 2010 provides the Agency's long-term vision on the further evolution of the pharmaceutical arena within the European Union (EU). It describes the initiatives to be undertaken that will contribute to better protection and promotion of public and animal health, that will improve the regulatory environment for medicinal products and will help to stimulate innovation, research and development in the EU.

In March 2006 a first Status Report on the Implementation of the EMEA Road Map (Doc. Ref. EMEA/171321/2006) was published. Progress made in 2006 and the first half of 2007 have been described in the current document. As was the case with the first Status Report, high-level information is given on the progress made over the past 18 months. It should be noted that important achievements made in 2006 have also been included in the 2006 EMEA Annual Report.

The Agency's Management Board noted at its 4 October 2007 meeting the Second Status Report on the Implementation of the EMEA Road Map and agreed on its publication.

II Current Status of the EMEA Road Map Implementation

Very good progress could be observed over the past 18 months on the further implementation of the EMEA Road Map. In few areas, however, progress has not been as originally planned. Although the large majority of activities undertaken during this reporting period relate to actions listed in the 2005 EMEA Road Map Implementation Plan, important new areas of activities have emerged (such as paediatric and biosimilar medicines) which need to be taken into account during the EMEA Road Map implementation. It should be emphasised that in various fields (e.g. strengthening the operation of the EU Regulatory System, but also in more specific areas such as improving the safety of medicines or addressing specific needs for veterinary medicines), progress has been facilitated through a close cooperation between the EMEA and Heads of Medicines Agencies (HMA) in the context of the joint EMEA/HMA initiatives. Through such excellent collaboration it has been possible to reinforce the networking model.

A summary of the achievements over the past 18 months as well as information on delayed activities is provided below. More details on the progress made can be found in Annex 1.

II.1 Summary of Achievements (Reporting Period January 2006-June 2007)

Looking at the priority areas for the EMEA for 2006 and 2007, important achievements in the frame of the EMEA Road Map implementation during the reporting period are the following:

Improving the safety of medicines

Progress was achieved with respect to both the European Risk Management Strategy (medicines for human use) and the European Surveillance Strategy (medicines for

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veterinary use), in close collaboration with the National Competent Authorities (NCAs) at HMA level.

In the field of medicines for human use efforts were directed to establishing a more intensive drug monitoring system through initiatives such as further implementing and developing the EudraVigilance system. Activities to complement knowledge derived from spontaneous reporting focussed on the introduction of the European Network of Centres for Pharmacovigilance and Pharmacoepidemiology (ENCePP) project, and the provision of input to the European Commission on research projects in the context of the Health Theme of the 7th Framework Programme.

With respect to medicines for veterinary use activities also focussed on further improving the spontaneous reporting scheme through EudraVigilance Veterinary (EV Vet). Other initiatives related to improving and facilitating reporting by veterinarians and streamlining the assessment of pharmacovigilance data by NCAs.

Stimulating research and innovation

The Innovative Medicines Initiative (IMI) and the 7th Framework Programme have been important opportunities for the EMEA to support the European Commission in its efforts to stimulate research and innovation in the EU. In addition to such support, the EMEA undertook complementary initiatives, such as work in the context of the EMEA/Committee for Human Medicinal Products (CHMP) Think-Tank group on innovative drug development, meetings with academia and pharmaceutical industry to identify expertise, expectations and bottlenecks in the area of advanced therapies, as well as the establishment of an EMEA Small and Medium-sized Enterprise (SME) Office to provide administrative and financial support to SMEs, both in the field of human and veterinary medicines.

Efforts in the veterinary field were directed to discussions on the Strategic Research Agenda in the context of the European Technology Platform on Global Animal Health, hence providing an important contribution to promoting access for innovative medicines for veterinary use, including those for limited markets.

Improving access to medicines

A revised and more efficient scientific advice procedure, initiatives to facilitate the integration of pharmacogenomics in drug development, and the implementation of new legal tools (such as conditional marketing authorisation, accelerated assessment and compassionate use) are examples of the initiatives undertaken by the Agency to improve access to medicines for human use.

In addition, 2006 and 2007 saw the implementation of the new paediatric legislation which should provide an important contribution to the availability of medicines to the paediatric population. Furthermore, as a follow-up to the TGN 1412 clinical trial report, the European Commission, the EMEA and HMA jointly undertook work to address the findings of the report, resulting in the availability of a dedicated guideline providing guidance to sponsors in the transition from non-clinical to early clinical development.

The availability issue in the area of medicines for veterinary use was progressed by adapting data requirements for products for minor uses and minor species, by promoting the authorisation through the centralised licensing route of vaccines against epizootic diseases, and by carefully balancing the requirements for a thorough environmental risk assessment against the possible impact on the availability of veterinary medicines. In addition, the pilot scheme for free scientific advice for veterinary medicines for minor uses and minor species was extended.

Strengthening the provision of information and the interaction with the Agency's stakeholders

Efforts were undertaken to facilitate public information about medicines and to improve transparency of regulatory activity. Achievements over the past 18 months relate to the

launch of EudraPharm, the introduction of new and more targeted tools (such as European Public Assessment Report (EPAR) summaries for the public and Question and Answer (Q&A) documents) to improve communication to the general public. Information is now systematically provided on withdrawals and refusals of both marketing authorisation applications and new indications for approved medicines.

Transparency in opinion-making has been enhanced through the implementation of revised rules on access to EMEA documents in line with EU legislation in this field.

Interaction with all stakeholders further developed during the reporting period. In the field of interaction with patients this development was more outspoken (creation of a new Working Party and participation of patients' and consumers' organisations in such Working Party on the basis of eligibility criteria, more active involvement of these organisations in various EMEA activities). In other areas, such as the interaction with healthcare professionals, academia and learned societies, the already existing collaboration has been more formalised. Interaction with pharmaceutical industry saw a shift in emphasis from the preparation for implementation of new Community legislation to monitoring such implementation, hereby taking due account of pharmaceutical industry's initial experience with the new legislative provisions.

Reinforcing international collaboration

The preparation for further enlargement of the EU focussed in 2006 and 2007 on various initiatives to facilitate the involvement of Accession Countries in the Agency's activities. This enabled a smooth integration of Bulgaria and Romania in the Agency's work, whilst activities involving Croatia and Turkey are in a more preparatory phase.

Interaction with non-EU Regulatory Authorities resulted in a strengthening of the collaboration with the Food and Drug Administration (FDA) through a broadening of the scope of the activities contained in the Confidentiality Arrangements Implementation Plan, and an agreement on Confidentiality Arrangements between the EU and the Japanese Health Authorities in the field of medicines for human use. Collaboration with the World Health Organisation (WHO) was further diversified through the undertaking of new activities in the context of Article 58 scientific evaluations for medicines intended for non-EU markets and pandemic influenza preparedness.

Strengthening the European Union Regulatory System

The functioning of the EU Regulatory System networking model was further improved through various initiatives, such as strengthening the quality assurance of the activities undertaken in the network, enhancing competence development, providing for better planning of workload and resources, introducing the concept of worksharing. Of particular note are several operational improvements introduced in the EU Pharmacovigilance System for both medicines for human and veterinary use.

In the field of the EU Information Technology (IT) Strategy major deliverables related to the launch of databases (EudraPharm and EudraGMP) and the further development of existing databases (EudraVigilance). Such efforts should support and facilitate the operation of procedures established by Community legislation, and should ultimately result in an increased efficiency and an enhanced transparency.

II.2 Delayed Activities

In a number of areas progress with the implementation of the EMEA Road Map has encountered delays. This relates to domains such as:

- Strengthening the EU Regulatory System networking model: some initiatives to enhance the availability at EU level of top quality scientific expertise, and to strengthen the competence development at EU level (in particular through the

involvement of academia and learned societies in the provision of high-quality specialist training).

- Enhancing the interaction with the Agency's stakeholders: improving the interaction between the EMEA Secretariat/EMEA Scientific Committees and the pharmaceutical industry by developing a Best Practice Guide.
- Improving transparency and communication: initiatives to arrive at an EU Transparency and Communication Strategy, and to increase openness on opinion-making in the field of non-product related issues (in terms of publication of meeting agendas and minutes).
- Improving the safety of medicines for veterinary use: further developing EV Vet through the introduction of additional functionalities, in particular the Datawarehouse.

It should be noted that any originally planned initiatives (as listed in the 2005 EMEA Road Map Implementation Plan) which have not yet been completed will be taken up in the next implementation phase of the EMEA Road Map (period 2008-2009). This should allow to address the aforementioned delays. The 2008-2009 EMEA Road Map Implementation Plan is currently being developed.

European Medicines Agency

Annex 1

Details on the Progress Made in 2006 and the first half of 2007 on the EMEA Road Map Implementation

As stated in Section II, the EMEA Road Map implementation progressed very well since the first Status Report, published in May 2006. Further details on the current status of implementation of the EMEA Road Map in the various areas are described below.

I Organisation of the EU Regulatory System

The EMEA networking model

- Several aspects in relation to the (future) organisation of the EU Regulatory System were subject of in-depth discussions at HMA level, resulting in the development of the document "HMA Strategy for the European Medicines Regulatory Network", and contributing to a further strengthening of the existing networking model.
- Initiatives undertaken since 2006 in order to further strengthen the EU Regulatory System included formal preparatory steps to establish an EU-wide up-to-date inventory of the available scientific expertise. It needs, however, to be emphasised, irrespective of such formal approach, that the EMEA experts database is updated on an ongoing basis with additional high-quality scientific expertise as need arises.
- HMA in close collaboration with the EMEA progressed the development of an EU Competence Development Strategy. A joint Training Project Team was established in 2007 with the objective to formalising a common system of training and continuous education of scientific and regulatory staff of both the NCAs and the EMEA. In the meantime the EMEA continued to organise conferences, workshops and training sessions for assessors and inspectors, designed to share competences and strengthen cooperation among the network of experts in the EU.
- Efforts relating to reinforcing quality assurance of the activities undertaken within the EU Regulatory System focussed on the follow-up to the first Benchmarking of European Medicines Agencies (BEMA) cycle. Experience with the first benchmarking cycle was reviewed at HMA level and proposals for improvement including on the methodology were prepared and agreed upon ahead of the second BEMA cycle. In addition, NCAs shared experiences on best practices. At the level of the EMEA Scientific Committees existing peer review systems were reviewed and further improvements, where necessary, were introduced.
- Discussions on workload and resources planning are systematically held at HMA level, taking into account input on forecast of activities provided by the EMEA. The objective is to present a report on workload and resources planning for discussion by HMA in 2008. In addition, a new procedure on (Co)-Rapporteur appointment for activities at the level of the CHMP was finalised in July 2006.

The EMEA Secretariat

- In relation to the functioning of the EMEA Secretariat and its support to the Agency's Scientific Committees and their Working Parties, work progressed over the past 18 months on providing a better clarification of such functioning in the light of the 2005 legislative provisions. This resulted in the drafting of an Explanatory Paper which will be

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discussed with all EMEA Scientific Committees. This should allow in a next phase to more clearly specify the roles and the responsibilities of all involved parties in the regulatory process.

- In order to consolidate the increased scientific role of the EMEA Secretariat and to contribute to the consistency and predictability of the Agency's opinion-making, the position of Senior Medical Officer was created at the EMEA.
- In parallel with discussions on the functioning of the EMEA Secretariat, the EMEA has launched in 2006 an Agency wide Process Improvement Exercise. Looking at various key processes managed at the level of the EMEA, the aim of the exercise is to increase efficiency in operation, avoid duplication of efforts and improve teamwork. Results are expected towards the end of 2007.

The EU IT Strategy

- Important progress could be noted in the field of implementation of the EU Telematics Master Plan. EudraPharm was launched on 6 December 2006, but is currently limited to information about medicines authorised through the centralised procedure. In the field of EudraVigilance, the focus in 2007 has been on the validation of the EudraVigilance Datawarehouse and Analysis System (EVDAS), resulting in the roll-out of EVDAS to the Member States in July 2007. As a result, progress on the introduction of additional functionalities for EudraVigilance and the development of the Eudra Datawarehouse has not been as initially planned. In the field of Good Manufacturing Practices (GMP), version 1 of the EudraGMP database was launched on 27 April 2007.

The funding of the EMEA networking model

- In relation to the funding of the EMEA networking model discussions continued over the past 18 months at the level of the EMEA Management Board. Although, on the basis of a report prepared by the Management Board group on long-term financing, a decision in principle was taken to revise the scale of fees system, it was also agreed that this matter needed further consideration. Given the impact of any change to a new system on both the EMEA and the NCAs, the need to have a thorough analysis of any new option was emphasised. It was decided as a next step to first agree on generally accepted international costing methods.

II The EMEA Processes

Innovative medicines

- The EMEA contributed to the IMI through a continuous dialogue with the responsible European Commission Services. Input provided related to the Agency's proposals for inclusion of topics of public health interest in the project, such as pharmacovigilance.
- In the context of the Health Theme of the 7th Framework Programme, input by the EMEA included collaboration on the definition of project objectives in the field of rare diseases and on calls in the field of paediatric medicines. In addition, proposals were made for further research on safety related aspects for Non-Steroidal Anti-Inflammatory Drugs (NSAIDs).
- Complementary actions undertaken by the EMEA relate to the activities in the frame of the Think-Tank group on innovative drug development which resulted in the finalisation of a report in March 2007. Implementation of the various recommendations made in the report is now underway.

- In the veterinary field, the EMEA efforts focussed on active involvement in the European Technology Platform on Global Animal Health. In this respect, the Agency assisted in finalising the Strategic Research Agenda, of which the aim is to promote access to the market for innovative products for animal health, including those for limited markets.

Specific needs for new technologies

- Aspects in relation to advanced therapies and emerging treatments have been considered in the context of the EMEA/CHMP Think-Tank group on innovative drug development. As stated in the Section "Innovative Medicines", the focus is now on the implementation of the recommendations made.
- Further initiatives undertaken by the Agency relate to the need to promote early dialogue with sponsors on potential applications for advanced therapies, and emerging products and technologies. Procedures to facilitate such early dialogue have been set up and meetings with sponsors to address scientific and regulatory matters arising from these products and approaches are being organised. In addition, meetings with academia and pharmaceutical industry are taking place to identify expertise, expectations and bottle-necks related to this field.

Specific needs for veterinary medicines

- Considerable efforts were undertaken during the reporting period to stimulate the availability of veterinary medicines for minor uses and minor species by publishing guidelines on the specific data requirements for these medicines and by extending the pilot scheme for free scientific advice. In order to facilitate use of these guidelines and to allow for a harmonised implementation across the EU, reflection papers have been produced to better define limited markets, including minor uses and minor species, and to outline a procedure whereby the Committee for Veterinary Medicinal Products (CVMP) can classify medicinal products as indicated for this type of market. Proposals for measures to assist pharmaceutical companies with the submission applications relating to limited markets are well advanced.
- Important work also continued to limit the impact on public and animal health of the development of antimicrobial resistance resulting from the use of veterinary medicines. A new longer-term strategy on antimicrobials was adopted. Furthermore, progress was made as regards the use of quinolones and fluoroquinolones in the EU through the adoption of a reflection paper addressing the potential impact on human and animal health, and by proposing risk management actions.
- Since the publication of the EMEA Road Map, the animal health situation within the EU has evolved such that a greater priority has been given to measures to promote the authorisation through the centralised licensing route of vaccines against epizootic diseases such as avian influenza, bluetongue and foot-and-mouth disease. In addition to measures such as drafting guidelines for authorisation under exceptional circumstances, considerable progress has been made with developing proposals to amend the regulatory framework to make it more able to cope with vaccines against such antigenically variable viruses.
- In the field of environmental risk assessment, guidance was published by the CVMP in support of V-ICH requirements. In addition, and taking into account the need to carefully balance the requirements for a thorough environmental risk assessment against the possible impact on the availability of veterinary medicines, advice was given by the CVMP to the European Commission on the practical implementation of the legislative provisions.
- Work in the field of the European Surveillance Strategy continued through the finalisation of an Action Plan addressing issues such as the reporting of pharmacovigilance data into EudraVigilance, and co-operation and harmonisation

between the NCAs in the assessment of these data, as well as on risk management. Furthermore, the annual bulletin on veterinary pharmacovigilance in the EU for 2006 was published early 2007. A guide directed to veterinarians to improve and facilitate reporting, finalised and published in 2006, is now being made available by the NCAs in their local language(s).

Generic, biosimilar and non-prescription medicines

- Further to the receipt in 2005 of the first generic application for a veterinary medicinal product, 2006 saw the submission of the first applications for generics of Centrally Authorised Products (CAPs) for human use. Positive Opinions for these generic applications were issued in 2007, hence providing an important contribution to public health in the EU.
- An important milestone related to the first positive Opinions for biosimilar medicines adopted in 2006. Important preparatory work undertaken by the EMEA focussed on the publication of the necessary guidance documents for pharmaceutical industry.
- Building on the successful interaction with innovative and generic pharmaceutical industry, the EMEA took initiatives to strengthen its interactions with self-medication industry which will result in the establishment of a more formal discussion platform before the end of 2007. Discussions in 2006 with such industry primarily focussed on the need for special criteria to be applied for invented names for non-prescription medicines.

Herbal medicines

- Work to increase the efficiency of operation of the Herbal Medicinal Products Committee (HMPC) and to allow for a full implementation of Community legislation in the area of herbal medicines continued over the past 18 months. To this end the process for producing Community monographs and the Community list entries was reviewed in 2007. Furthermore, the HMPC developed a procedure for the publication of calls for scientific data for use in the assessment work carried out by the Committee, as well as for the assessment of clinical safety and efficacy.
- Efforts were also undertaken to assist NCAs in their implementation of the simplified registration scheme, and to help pharmaceutical industry in their preparation of marketing authorisation or traditional use registration applications.
- A report on the Committee's activities and achievements since its establishment in September 2004 was prepared and provided to the European Commission as a contribution for the preparation by the European Commission of its report to the European Parliament and the Council concerning the application of the relevant legislative provisions relating to traditional herbal medicines.

Paediatric medicines

- Considerable work has been undertaken by the EMEA in 2006 and the first half of 2007 to allow for an adequate implementation of the Paediatric legislation which entered into force in January 2007. Activities focussed on the establishment of the new Scientific Committee, the Paediatric Committee (PDCO), including the necessary procedures and processes to allow the PDCO to fulfil its legal tasks, as well as the preparation of the necessary guidance documents for pharmaceutical industry, e.g. in relation to the Paediatric Investigation Plans (PIPs).
- As part of the other initiatives deployed by the Agency in the field of paediatric medicines, work started to prepare a strategy for establishing a pan-European paediatric research network. The EMEA also contributed to establishing recommendations on the ethics of clinical trials in children and to a workshop on medicines for neonates.

III Provision of Incentives for Small and Medium-sized Enterprises

- Further to the establishment of a dedicated EMEA SME Office in December 2005, the first 18 months of operation of the SME Office saw increasing interest from SME pharmaceutical industry in the support provided by the Agency, resulting in some 211 companies which have been granted SME status, including 7 companies developing exclusively veterinary medicines.
- Support provided by the EMEA to SMEs related to a variety of services, such as the provision of regulatory assistance and scientific advice, granting SME fee reductions or SME fee deferrals, assisting in the translation of product information for centrally processed applications. In addition, the first SME workshop providing training on specific topics for SMEs was held in February 2007, and the first News Bulletin for SMEs was launched in May 2007.

IV Interaction with the Agency's Stakeholders

Interaction with pharmaceutical industry

- In the field of medicines for human use, regular contacts with the European Industry Associations continued during the reporting period. Emphasis now has shifted from preparation for the implementation of new Community legislation to monitoring such implementation. Feedback from pharmaceutical industry in this respect has been very useful for the Agency's considerations on the need for process improvements. Such implementation of new Community legislation not only focussed on the 2005 legislative package, but more recently on the implementation of the paediatric legislation. In addition, a workshop on biomarkers with the participation of pharmaceutical industry was held in December 2006.
- Pharmaceutical industry representatives also formally participated in discussion fora on specific topics relating to medicinal products for human use, such as the Think-Tank group on innovation, and the EudraVigilance Expert Working Group. In addition, some EMEA Working Parties continued to hold regular meetings with industry representatives.
- In the veterinary sphere an Info Day was held with IFAH-Europe in November 2006 whereby discussions focussed on topics such as risk-benefit assessment, user-safety guidelines and environmental risk assessment.

Interaction with patients

- Interaction with patients has been further improved. A new Working Party, the EMEA Human Scientific Committees' Working Party with Patients' and Consumers' Organisations (PCWP) was established. The PCWP will build on the work already undertaken by the former EMEA/CHMP Working Group. Its objective is to provide recommendations to the EMEA, including its Scientific Committees, on all matters of interest to patients.
- Further to the development of a dedicated framework for interaction with patients' and consumers' organisations, the EMEA launched a call for expression of interest for involvement in EMEA activities. Following assessment taking into account established eligibility criteria, 18 organisations so far have met the criteria.
- Further to the publication in June 2006 of rules for the involvement of patients' and consumers' organisations in the activities of the EMEA, including its Scientific Committees, such involvement has started in 2007 in the context of the review of Package Leaflets (PLs) at the time of renewal, and the preparation of EPAR Summaries. On a case by case basis participation from patients' organisations has been requested in the review of Q&A documents, e.g. on emerging safety issues.

Interaction with healthcare professionals

- The EMEA has also started to formalise its interaction with healthcare professionals. The EMEA/CHMP Working Group with Healthcare Professionals' Organisations was created in December 2006 following a workshop held in March of the same year. Its aim is to make recommendations and proposals in view of the development of a framework for interaction with healthcare professionals' organisations. Preparatory work on the development of such framework has started.

Interaction with academia and learned societies

- Although the Agency's interaction with academia and learned societies has been less formalised as with other stakeholders, several initiatives have been undertaken over the past 18 months. The EMEA has started to develop interactions in all therapeutic fields of the mandatory scope of the centralised procedure, with focus on the areas of oncology, diabetes, neurodegenerative diseases and paediatrics. Of particular note is that the Agency established collaboration with leading European professional societies and cancer-research institutions to increase communication and broaden the network of experts.
- In the context of the Agency's activities on innovative drug development, academia contributed through participation in the Think-Tank group on innovation. Academia also play an important role in the development of the ENCePP project, hence contributing to the establishment of a more intensive drug monitoring system in the EU.
- In addition, academia and learned societies participated in various workshops organised by the EMEA, e.g. in the fields of biomarkers, neonates, disease progression for neurodegenerative diseases. In the field of paediatrics, collaboration has started with the Paediatrics Academic group and existing paediatric clinical research networks in view of future EMEA responsibilities relating to a strategy for the European paediatric research network.

V International Collaboration

- Several initiatives were taken to facilitate the accession of Bulgaria and Romania. Exchange of information under the terms of the (n) Collaboration Agreement of Drug Regulatory Authorities in European Union Associated Countries (CADREAC) simplified procedure, as well as participation by representatives of Bulgaria and Romania as observers in the work of the Management Board, the EMEA Scientific Committees and their Working Parties allowed for a smooth transition to EU membership in the field of medicines regulation. In addition, a Pre-Accession Linguistic-Check process ((PALC) II) was set up to ensure a good standard of quality for Bulgarian and Romanian translations of product information for CAPs.
- Preparation for the accession of other countries to the EU focussed on the launch in 2006 of a multi-beneficiary programme on participation of Croatia and Turkey in EMEA activities. A conference was held in Croatia in April 2007 on the pharmaceuticals' Regulation and Croatia's road to EU membership. Both countries have also been encouraged to send representatives as passive observers at EMEA meetings.
- The interaction between the EMEA and the FDA in the context of the EU/FDA Confidentiality Arrangements has been further strengthened over the past 18 months. Activities in 2006 related to various areas, and in addition to routine exchange of information and the development of guidelines, the focus has been on scientific advice, applications for marketing authorisation (with the introduction of monthly teleconferences to intensify cooperation on oncology matters), emerging safety issues, vaccines (particularly pandemic influenza vaccines), paediatric medicines, as well as GMP and Good Clinical Practices (GCP) inspections. Following a review of the

regulatory cooperation in 2006 and 2007, an agreement was reached in June 2007 to expand current cooperative activities in several important areas for medicines for human use. Interactions will be intensified in the areas of paediatrics and orphan medicines. In addition, the scientific dialogue has been widened to include extensions of indications and risk management plans. A "Principle of Interactions" document was published to facilitate the timely exchange of information on scientific and ethical issues for paediatric medicines.

- In February 2007, the EMEA, the European Commission and the Japanese Health Authorities (Ministry of Health, Labour and Welfare (MHLW) and Pharmaceuticals and Medicines Devices Agency (PMDA)) agreed on Confidentiality Arrangements in the field of medicines for human use, allowing for exchange of confidential information about the authorisation and safety of medicines. Since February 2007, interaction mainly has taken place on safety related aspects.
- The Visiting Experts programme continued over the past 18 months with experts from various non-EU Regulatory Authorities (Canada, Japan, Taiwan) visiting the EMEA.
- Collaboration with WHO continued to address a number of areas such as pharmacovigilance, international non-proprietary names, GMP and quality issues, GCP, etc. Particular attention was given on the further elaboration of various aspects in relation to Article 58 scientific evaluations for medicinal products intended for markets outside the EU. Furthermore, there has been extensive collaboration in the frame of the pandemic influenza preparedness. Such discussion also involved EU Institutions such as the European Centre for Disease Prevention and Control (ECDC).

VI The EMEA Areas of Activity

Area of scientific advice

- In July 2006 a new framework for the provision of scientific advice was implemented for medicines for human use. Characteristics of such new framework include a broader scope for requesting scientific advice and for follow-up requests, an extension of Scientific Advice Working Party (SAWP) meetings to 3 days meetings each month, and a streamlining of the procedure resulting in a shortening of the time to provide scientific advice. In addition, coordinators and their assessors/experts are now systematically involved in the pre-submission phase of all scientific advice procedures, and transparency and communication with the stakeholders has been increased. Experience following the implementation in 2006 of the revised procedure is currently being reviewed with a view to introducing further improvements.
- Experience gained with the parallel scientific advice procedure for medicines for human use introduced in 2004 both at the level of the EMEA and the FDA has been reviewed, resulting in an extension in March 2006 of the pilot programme. Further experience gained was discussed at the June 2007 EU/FDA bilateral meeting and the need to improve the process was recognised.
- In relation to medicines for veterinary use, the pilot scheme for free scientific advice for veterinary medicines for minor uses and minor species was extended. This should improve the availability of such medicines.
- It is important for Regulatory Authorities to become familiar with issues stemming from the integration of pharmacogenomics in drug development and to ensure that the pharmaceutical industry is informed on the regulators' scientific perspectives. Therefore the EMEA, the European Commission and the FDA agreed in May 2006 on a procedure for joint EMEA-FDA briefing meetings with sponsors following voluntary submission of genomic data. Such procedure will allow to have more in-depth scientific discussions on various aspects related to pharmacogenomics.

Area of scientific assessment

- The pilot phase introduced in 2005 at CHMP level to improve the quality of the scientific assessment carried out by the Committee in the frame of initial marketing authorisation applications was strengthened in 2006. CHMP Members assigned as peer reviewers, reviewed, together with the EMEA Secretariat, the proposed questions in the light of the scientific justifications and argumentation presented by the (Co)-Rapporteurs in their initial assessment report. Aspects related to the concept of risk management plans have been included in such peer review process.
- Further to the implementation in November 2005 of various legal tools to facilitate early access to market (conditional marketing authorisation, accelerated assessment, compassionate use), the EMEA Secretariat is currently reviewing experience gained so far. Where necessary, improvements will be introduced.
- The EMEA continued its efforts to provide the CHMP with specialised expertise. In addition to ad-hoc experts called in to assist the Committee on discussions on specific matters (e.g. in the context of Article 58 scientific evaluations) and co-opted pharmacovigilance experts providing systematic input through the Pharmacovigilance Working Party (PhVWP), the Agency's focus has been on the establishment of additional Scientific Advisory Groups (SAGs). A total of 7 SAGs has now been established, covering all therapeutic areas in the mandatory scope of the centralised procedure, and on cardiovascular issues, hence providing a high-quality specialist input into the CHMP scientific assessment process.
- Specialised expertise was also provided at the level of the Committee for Orphan Medicinal Products (COMP) in the frame of the initial assessment of orphan drug designation and the assessment of the confirmation of the significant benefit before the granting of the marketing authorisation (for orphan drugs designated under such criteria).
- Following the publication of the TGN1412 clinical trial report, initiatives were undertaken jointly by the EMEA, the European Commission and HMA to address the findings of the report. The CHMP was asked to develop a guideline relating to first-in-human clinical trials for high risk products. Following an external consultation with its stakeholders, including discussion at a workshop held at the EMEA in June 2007, the CHMP finalised the guideline which addresses strategies to identify and mitigate risks for first-in-human clinical trials with investigational medicines. The guideline, which has been published in July 2007, will provide guidance to sponsors in the transition from non-clinical to early clinical development.

Area of monitoring of medicinal products

- Efforts to implement 2005 Community legislation focussed on various aspects, including the novel concept of risk management plans. Updated guidance was made available through a complete revision of Volume 9A of "The Rules Governing Medicinal Products in the European Union – Guidelines on Pharmacovigilance for Medicinal Products for Human Use", which was subject to an extensive public consultation. The emphasis is now on the monitoring of the implementation of the new legal tools, e.g. the Review and Learning project in the field of risk management plans.
- Additional work was also undertaken to achieve a more intensive drug monitoring system for medicines for human use. Improvements in the area of spontaneous reporting of adverse drug reactions focussed on the further implementation of EudraVigilance (resulting in an increasing number of NCAs and pharmaceutical industry reporting electronically) and the introduction of additional functionalities for EudraVigilance. An EudraVigilance Action Plan was finalised to address a number of implementation issues, particularly in the fields of the quality of the submitted data and the legal reporting deadlines.

- In order to complement knowledge obtained through the spontaneous reporting scheme, the ENCePP project was introduced, aiming to facilitate the conduct of multi-centre post-authorisation safety issues. Various centres across the EU have been identified, and the focus is now on the organisational and operational aspects of the network.
- Important input was provided to the European Commission on research in the context of the Health Theme of the 7th Framework Programme, leading to a first concrete result in the field of NSAIDs with proposals made on various aspects to be covered in further research with this class of medicines.
- The operation of the EU Pharmacovigilance System was strengthened through various initiatives within the context of the European Risk Management Strategy such as the introduction of the aforementioned formal peer review system at CHMP level, a reinforcement of the scientific expertise at the level of the PhVWP, a strengthening of the interaction between the PhVWP and the Coordination Group for Mutual Recognition and Decentralised Procedures (human) (CMD(h)), and the introduction of the work-sharing concept in the field of assessment of Periodic Safety Update Reports (PSURs). Important work was also undertaken in the frame of the pandemic influenza preparedness through the availability of a crisis management plan for the evaluation and maintenance of pandemic influenza vaccines and antivirals.
- In the field of medicines for veterinary use, EV Vet has become the main reporting tool for NCAs with respect to CAPs, and also the pharmaceutical industry has started to report electronically. In order to encourage electronic reporting a simplified electronic reporting tool was made available, primarily for use by SMEs. The adoption of an EV Vet Action Plan has given the necessary predictability to the future development of EV Vet to allow NCAs' confidence in allocating commensurate resources.
- In the context of the European Surveillance Strategy for veterinary medicines, initiatives undertaken relate to the development of an Action Plan for better harmonisation and work-sharing between NCAs (including the initiation of a pilot PSUR work-sharing scheme), a revision of the PhVWP mandate, and the preparation of guidance for regulators, pharmaceutical industry and veterinarians to strengthen the EU Pharmacovigilance System for veterinary medicinal products.

Area of transparency and communication

- Adherence to the EMEA Transparency Policy measures adopted by the Management Board in October 2003 continued over the past 18 months. In addition, further improvements were introduced, relating to areas such as the publication of Press Releases and Q&A documents. Efforts were undertaken to increase the use of these communication tools to allow for more comprehensive information (through Press Releases) in areas such as new types of applications, new technological advances and the approval of pandemic flu vaccines or to help with communication (through Q&A documents) on subjects such as compassionate use or biosimilar/generic medicines. Q&A documents are now also systematically published at the time of withdrawal or refusal of applications.
- Furthermore, new initiatives, complementing the 2005 legislative provisions were taken, such as the publication of information on the withdrawal by a company of the marketing authorisation application between the CHMP Opinion and the European Commission Decision. Information is now also published on withdrawals by companies and on refusals of applications concerning new indications for approved medicines. In addition, the EMEA publishes regular information about its activities in support of SMEs (e.g. the names of companies that have been assigned SME status by the Agency).
- In an additional step forward for transparency in opinion-making, the EMEA implemented revised rules on access to EMEA documents in order to better reflect EU legislation on access to documents. Characteristics of the revised procedure are clarification on the types of documents that can be released and introduction of the

possibility for the EMEA to give partial access when exceptions to release apply to some parts of the document.

- Info Days with the EMEA Scientific Committees continued to be held, allowing for a platform for discussion with Interested Parties on non-product related issues. In addition, meeting summaries of discussions on non-product related topics for some Scientific Committees (e.g. the HMPC) and other fora (e.g. the PCWP and the EMEA/CHMP Working Group with Healthcare Professionals' Organisations) were made publicly available.

Area of provision of information on human medicines to patients

- Since major work on the follow-up to the recommendations from the former EMEA/CHMP Working Group with Patients' and Consumers' Organisations was already undertaken in 2005, the focus has now been on the provision of support to the Pharmaceutical Forum activities in this field. Based on the contribution from the Working Group the EMEA prepared and published the report "Statutory Information on Medicines" which has also been taken into account in the context of the European Commission's report to the European Parliament and the Council.

Area of GXP

- In the field of GMP, good progress was made in establishing the EudraGMP database. The first phase of the EudraGMP database on manufacturing authorisations and GMP certificates was launched on 27 April 2007.
- Progress was made in the field of Process Analytical Technologies (PAT), with work undertaken to ensure that the EU Regulatory System can conduct thorough and effective evaluations of PAT-based submissions. A Q&A document, aiming at clarifying certain dossier provisions, has been published on the EMEA website, and a meeting focussing on the application of PAT to biological products was held at the EMEA in March 2007.
- The European Joint Audit Programme for GMP inspectorates was optimised in 2006, resulting in a revision of the documentation and procedures for such programme. Furthermore, activities to ensure consistent quality standards and harmonised approaches were coordinated by the EMEA.
- In the field of the International Conference on Harmonisation (ICH), important progress could be noted on the implementation of guidelines in quality risk management and the publication of a draft guideline on quality systems.
- Finally, a wide range of support was provided by the EMEA to the implementation of the clinical trials legislation through initiatives such as progressing work on harmonised procedures for GCP inspections, organising training and establishing collaboration with the CMD(h) on issues related to bioequivalence trials. In addition, the European Commission and the EMEA will host a Conference in October 2007 on the operation of the Clinical Trials Directive and perspectives for the future. The further development of the EudraCT database was also supported.