The European Agency for the Evaluation of Medicinal Products

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Discussion Paper
The European Medicines Agency Road Map to 2010:
Preparing the Ground for the Future

Executive Summary

The European Medicines Agency Road Map provides the Agency's viewpoint on how it should prepare for the challenges the European Medicines Agency will face over the next several years, by specifying the initiatives that need to be undertaken in close cooperation with the Agency's partners (i.e. the European Commission and the National Competent Authorities) and its stakeholders (patients/users of medicines, health care professionals and the pharmaceutical industry). These challenges will result from a changing regulatory environment in terms of legislative, institutional and scientific developments.

The key aspect of the Agency's vision for the coming years is to further strengthen the protection and promotion of public and animal health in the European Union (EU), whilst encouraging and facilitating innovation and research in an enlarged EU. In order to implement such vision it will be paramount to further strengthen the current Agency networking model and to reinforce the firm partnership between all EU Regulatory Authorities, resulting in the establishment of a network of excellence at EU level.

The EMEA Road Map will address

(1) the positioning of the European Medicines Agency over the coming years in a changing regulatory environment,

(2) the consequent development of the European Medicines Agency in such an environment, including the objectives to be achieved,

(3) the prerequisites that need to be fulfilled in order to allow the Agency to successfully achieve the objectives, and

(4) the finalisation of the European Medicines Agency Road Map.

In addition, particular emphasis has been paid to six areas for the implementation of the Agency's vision. Such areas relate to scientific advice, scientific assessment, post-authorisation activities, transparency and communication, provision of information to patients and Good Manufacturing Practices/Good Clinical Practices. For each area proposals for the implementation of the Agency's vision have been made.

Taking into account the characteristics of the EU Regulatory System, it is of utmost importance for the European Medicines Agency Road Map to be debated over the coming months with all partners and stakeholders in order to achieve the broadest possible consensus on how to provide for better protected and informed patients and users of medicines and to reinforce the competitiveness of EU based pharmaceutical industry.

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Chapter 1
Introduction

The European Medicines Agency[1] was established in 1995.

The Agency's Mission Statement is to contribute to the protection and promotion of public and animal health by

(1) mobilising scientific resources from throughout the EU to provide high quality evaluation of medicinal products, to advise on research and development programmes and to provide useful and clear information to users and health care professionals,

(2) developing efficient and transparent procedures to allow timely access by users to innovative medicines through a single European marketing authorisation, and

(3) controlling the safety of medicines for humans and animals, in particular through a pharmacovigilance network and the establishment of safe limits for residues in food-producing animals.

The European Medicines Agency works as a network, bringing together the scientific resources of the Member States to ensure the highest level of evaluation and supervision of medicines in the EU. The Agency cooperates closely with international partners, reinforcing the EU contribution to global harmonisation.

[1] It should be noted that the new name for the Agency, as stated in new Community legislation, has been applied throughout the document.

Chapter 2
A Changing Regulatory Environment

2.1 The Current Regulatory Environment

The current EU Regulatory System is unique in the international regulatory environment in so far that Community legislation has provided for a network between all national regulatory bodies, coordinated by the European Medicines Agency.

The benefits of such networking model are numerous. It has allowed for the best scientific expertise available in the National Competent Authorities (NCAs) to be brought together at the level of the European Medicines Agency in order to assess innovative medicines using common standards and to subsequently provide for rapid access to such medicines for EU patients/users of medicines. It has also contributed to the harmonisation process between all Member States by further standardising the requirements for the evaluation and monitoring of medicines irrespective of the licensing route and, as a result, has led to coordinated approaches in several fields.

However, it needs to be recognised that there exist areas where the overall successful networking model could still benefit from further strengthening, particularly in the light of the challenges the EU Regulatory System is facing in the coming years. Best use of the available limited resources, hence avoiding duplication of work, and increasing the efficiency of operation of the system is to be encouraged, together with the need for further coordination to ensure a harmonised approach in fields such as scientific advice, transparency, communication and outcome measurement. All such initiatives should be undertaken in concert with the application of good regulatory practice.

2.2 The New Regulatory Environment

The EU Regulatory System will be confronted over the next few years with significant changes of a legislative (impact of new Community legislation) and institutional (impact of the 2004 enlargement of the EU) nature.

In addition to these significant challenges having an immediate impact on the overall system, other developing factors which are nonetheless important will have to be taken into account. Amongst them are political factors such as the continuation of the EU enlargement after 2004 with Romania and Bulgaria joining in 2007/2008 and other countries such as Turkey also seeking membership.

In addition, one of the key issues to be addressed by the international regulatory environment will be its ability to prepare adequately for the introduction of new technologies, from a scientific, legal and regulatory perspective. Appropriate measures will have to be taken in order to ensure that pharmaceutical industry can take advantage of new pharmaceutical technologies in the manufacturing and analytical areas, and anticipate the implications of gene and cell therapies.

Other factors to be considered are the impact of an ageing population, increased demands for medicines in areas of unmet medical need, the possible unavailability of medicines both in the human and veterinary field, the ever increasing concerns about the development of antimicrobial resistance, etc.

In the veterinary sector the safety of medicines in food producing animals will be underpinned by the Agency's continued role in the establishment of Maximum Residue Limits as a reference in the Community and worldwide for trade in meat products and other food commodities.

These changes are not to be regarded as pure challenges, but rather as new opportunities, which, through adequate proactive initiatives should lead to an enhanced protection and promotion of public and animal health in an enlarged EU.

Chapter 3
The European Medicines Agency in the Changing Regulatory Environment

3.1 Impact Analysis

The impact of the changing environment on the European Medicines Agency will be considerable. The Agency with its network of 42 NCAs in the European Economic Area (EEA), through which scientific resources are made available to the European Medicines Agency, will become one of the world's foremost Regulatory Authorities for medicinal products. The European Medicines Agency will have to demonstrate that, after enlargement, the networking Agency model is still able to perform competently in the different fields of medicines regulation, with no negative consequences for the quality of the work which is undertaken, in close collaboration with 42 and possibly more NCAs.

The impact of the European Medicines Agency's scientific opinions will become increasingly important, both from a public/animal health perspective and an economical viewpoint. Moreover, the influence of the European Medicines Agency in both the EU and the international regulatory environment will continue to increase due to a further strengthening of its role and responsibilities, hence leading to a higher visibility towards the outside world. In addition, its role and responsibilities will also change.

One of the major tasks of the Agency will continue to be the coordination of the scientific resources provided by the Member States and such task will be further extended, e.g. in the field of Good Manufacturing Practices (GMP), where inspections of the manufacturers of active ingredients will soon need to commence, and in pharmacovigilance. Another example of increased responsibilities for the Agency is the imminent implementation of Community legislation on herbal medicines and the establishment of a new Scientific Committee.

The European paediatric initiative will also have important consequences for the European Medicines Agency. New Community legislation would aim to increase the development of medicines for children (both new and existing medicines) and improve the availability of information on the use of medicines in children. A new Scientific Committee, the Paediatric Board, will be established at the Agency and the European Medicines Agency will be requested to coordinate a European paediatric network for performing paediatric studies.

The scientific component of the Agency's activities will also become more important. Provision of scientific opinions to the World Health Organisation (WHO) is one such an example of increased scientific input. In addition, the European Medicines Agency's tasks will become more public health orientated and its international role will be further developed.

3.2 Challenges Ahead

The main challenge for the European Medicines Agency over the next few years will be its ability to meet the increasing expectations of its stakeholders. The European Medicines Agency will particularly focus on the needs and expectations of patients and users of medicines. Special attention will also be given to Small and Medium Sized enterprises. New legislation will provide for specific measures aiming at reducing the cost for such enterprises. Where possible, additional incentives could be provided, building on the positive experience obtained in the fields of orphan drugs and EudraVigilance. The European Medicines Agency will have to find the right balance in terms of expectations such as applying high scientific knowledge for the timely delivery of science based opinions, increased involvement in the protection and promotion of public and animal health, regulatory and scientific consistency, predictability, greater transparency, better information and earlier communication.

As the European Medicines Agency becomes more accountable for its actions, maximising the overall quality and efficiency of operation should be the key objective, resulting in a regulatory public body which provides for a modern, high standard civil service.

The continuation and adaptation of the Agency's networking model will also require that Member States are able to adequately respond to the changing regulatory environment, which will result from the legislative and institutional changes. In order for the EU Regulatory System to position itself successfully in the international environment as one of the world's foremost regulatory systems, NCAs should carefully examine how they can best contribute to the future system since this will be key for the overall success. It should be emphasised that the network between the European Medicines Agency and NCAs can only be optimised if there is a stronger cohesion between all parties concerned, looking at complementing the achievements already obtained by introducing further actions aiming at reinforcing the networking model. In order to achieve such aims a common understanding on the architecture of the future EU Regulatory System is paramount. Once such common understanding has been obtained, in a next step important issues such as roles and responsibilities (in different fields such as regulatory, scientific, organisational and technical) of all involved parties need to be addressed in order to reach complete transparency on the accountability for the different activities to be undertaken in the context of the EU Regulatory System.

Chapter 4
The Future Development of the European Medicines Agency

4.1 European Medicines Agency Vision

The European Medicines Agency should strive to maintain and further develop its position as one of the leading regulatory authorities, which is science-driven, and transparent in the way it operates. Its aim should be to provide for better protected and informed patients and users of medicines, whilst encouraging and facilitating innovation and research in an enlarged EU.

The Agency should be supported by high quality scientific resources made available by the NCAs and a high standard IT infrastructure which provides an adequate and secure network between all European Regulatory Agencies in order to meet such a target.

A further strengthening of the current networking model and a reinforcement of the firm partnership which has already been established between all European Regulatory Authorities, hence leading to a network of excellence at EU level, will be vital in order to implement this vision.

4.2 Objectives to be Achieved

In order to enable the European Medicines Agency, as a networking Agency model, to reach such aspirations before the end of the decade, a number of objectives should be achieved:

Top Quality Scientific Assessment

With more complex global development programmes and increasing Research and Development (R&D) costs for a new active substance, predictability of outcome is becoming key in development programmes. A reinforced scientific advice process as well as the introduction of Scientific Advisory Groups as stated in new Community legislation will contribute to the resolution of pharmaceutical industry's concerns in this field, but should be underpinned by a robust Quality Assurance System, managed by the European Medicines Agency. A strengthening of the peer review system to which the Agency should actively contribute both in terms of regulatory and scientific memory, hence reinforcing the consistency of the outcome of the scientific assessment, should be key in such a Quality Assurance System.

In addition, globalisation of development programmes will drive the need for an enhanced collaboration with other non-EU Regulatory Authorities, in particular the FDA/USDA, ideally leading to parallel reviews in the key areas of the scientific assessment process. As the impact of the European Medicines Agency review will become more influential due to the consequences of enlargement and legislative changes, the public scrutiny of the review process is expected to increase. Benchmarking with other non-EU Regulatory Authorities, whilst acknowledging the different regulatory environments such authorities are operating in, will become more critical as to differential outcomes, hence leading to the need for a robust EU assessment standard.

One of the strengths of the EU system is the ability to source expertise from whatever location in the EU. One needs, however, to emphasise that the system will be confronted with particular challenges, such as in the field of new therapies, due to the scarcity of experts in these areas and their possible involvement in pharmaceutical industry. Transparent and robust conflict of interest mechanisms will need to be available to reassure the public. Whereas in some fields one might face a scarcity of scientific expertise, in other areas one might be confronted with an overcapacity of such expertise, due to a shift in workload. The introduction of the new Agencies could add to this overcapacity issue and could also lead to potential quality problems of the

EU scientific review system. In order not to endanger the quality of such system, adequate measures need to be taken to ensure the existing pool of scientific experts at the highest level of expertise.

Timely Access to Innovative Medicines

The current centralised procedure has shown to be very stable with respect to timing and has demonstrated to be capable of delivering fast reviews. New Community legislation will, despite the absence of a real rolling review concept, provide several new legislative tools, which will allow a more rapid access to innovative medicines. In addition, the Agency will strive for a further gain in efficiency of the operation of the centralised procedure (e.g. in relation to the number of review cycles and the duration of clock stops) without compromising the quality of the assessment process, hence complementing the legislative initiatives.

Continuous Monitoring of Medicinal Products

This is probably the most challenging area with the greatest potential of vulnerability for the Agency. A proactive approach in pharmacovigilance and the introduction of risk management strategies should be further strengthened. In addition, a further reinforcement of the close collaboration with Member States is of paramount importance.

Although new legislative tools will be made available in order to strengthen the conduct of pharmacovigilance, regulators will have to make sure that the overall system is equipped to deal in an efficient and timely way with crisis situations in terms of robust scientific assessment, sound regulatory action, adequate transparency, appropriate communication and monitoring of impact. In this respect, it needs to be recognised that the area of impact of regulatory action and its effectiveness in public health terms is currently a rather untouched field. Links with other relevant institutions/organisations such as the EU Centre for Disease Prevention and Control should be established.

New therapies will constitute once again a particular challenge with respect to the adequacy of the legal tools, since their exposure within a population of ~ 450 million remains an unknown factor. A strengthening of the collaboration with other non-EU Regulatory Authorities and especially the FDA/USDA will be particularly important in this innovative field.

Access to Information and Transparency

Several initiatives, either through legislative changes or as a follow-up to the G10 Recommendations[2] and the Resolution of the Council of Health Ministers[3] will be taken to improve access to information.

The European Medicines Agency should take advantage of this situation by increasing its profile with the outside world as an “approachable” informative and transparent organisation. Information needs to be presented in a more accessible way, i.e. disease category driven, in order to provide the public with comprehensive information on products available in a given area. Systematic feedback from health care professionals, patients and users of medicines should be obtained in order to continuously improve the information released by the European Medicines Agency and to provide customised information to the Agency’s stakeholders. This should include the concept of user testing in order to allow for information that is easy to read and be understood by patients and users of medicines. Adequate electronic systems will have to be available in order to allow the European Medicines Agency to build up a unique resource of data regarding pharmaceuticals. EuroPharm and EudraVigilance will be key channels in order to provide the general public with high-quality information on medicines.

[2] G10 Recommendations of the High Level Group on Innovation and the Provision of Medicines.
[3] Resolution of the Council of Health Ministers of 1 and 2 December 2003.

Specific Needs for Veterinary Medicines

There are specific issues which relate to veterinary medicines and need adequate consideration. In addition, one needs to bear in mind that veterinary medicines are not only essential in protecting animal health and welfare. There is also a significant impact on public health that needs to be considered. Specific needs for veterinary medicines are discussed in detail in attachment 1.

4.3 Prerequisites to be Fulfilled

In order to allow the European Medicines Agency to successfully achieve the above objectives, the following prerequisites should be fulfilled:

Provision of high-quality scientific resources by the National Competent Authorities

The continuation and even strengthening of the provision of high-quality scientific resources by NCAs to the European Medicines Agency activities is key for the success of the EU Regulatory System. The pitfalls in relation to this prerequisite, e.g. in terms of availability of a critical mass of highly specialised experts, have already been addressed above. Important choices will have to be made also at national level on how to best contribute to the overall regulatory system. The EU should move into a direction whereby centres of assessment are established in the EU. To achieve the highest possible quality output should be the main driver for selecting such centres of assessment. Clear and transparent procedures need to be put in place in relation to the selection process for the provision of the best scientific expertise to the European Medicines Agency, whilst recognising the Member States' responsibilities and accountability as regards the medicinal products available in their territory. Contractual arrangements should include adequate and sufficiently detailed indicators in order to measure the quality of the work undertaken by the selected providers of scientific expertise to the Agency.

Availability of an adequate Quality Assurance System

The overall quality and efficiency of operation will be key for the Agency to position itself successfully in the regulatory environment and to meet its stakeholders' expectations. This necessitates an even stronger Integrated Quality Management System at the European Medicines Agency (e.g. strengthening of the audit system, introduction of more sophisticated performance indicators, further implementation of the risk management concept) in order to achieve an adequate level of scientific and regulatory consistency in the outcome of the scientific evaluation processes.

However, the requirements for good governance, good regulatory practices and integrated quality management should extend from the European Medicines Agency Secretariat towards its Scientific Committees, their Working Parties, and also to the NCAs who act in the network as scientific resource providers. The benchmarking with Accession Countries will be complemented by a similar exercise with the current Member States. This should result in a regular cycle of benchmarking in order to achieve a strengthening of the Quality Assurance Systems in place at the level of all European Regulatory Authorities.

Availability of a high-quality IT infrastructure

The quality of the overall IT infrastructure, underpinning the EU Regulatory System, will be vital for the success of such system. Taking into account the Agency's new role as the coordinator and hub in the harmonised collection, validation, evaluation and dissemination of authorative information on medicinal products, the European Medicines Agency will host, operate and support a family of European information systems to make regulatory procedures more efficient and more transparent. In order to achieve such objective the Agency should gradually replace the fragmented administrative and operational information systems by an integrated form of information

repositories and electronic workflow tools. This should enable the introduction of near-real time electronic business reporting.

Availability of a high-quality European Medicines Agency professional workforce

The changing role of the Agency necessitating an increased scientific input has already been addressed above. The proposed role and functioning of the European Medicines Agency Secretariat is provided as attachment 2. Such a changing role should be underpinned by a higher scientific profile of its Staff Members. It will be critical to identify the areas of scientific competence where the European Medicines Agency needs to strengthen its resources. Subsequently, a full training and competence development programme should be put together and implemented.

In view of its new and extended tasks, the organisational structure of the European Medicines Agency should also be looked at and changes introduced, where relevant. Taking into account the Agency's increasing competence which go far beyond the primary evaluation role, a reappraisal of the establishment plan is necessary in order to allow the European Medicines Agency to meet its stakeholders' expectations. Considering the European Medicines Agency's increasing role in the regulation of human and veterinary medicines, the current funding model should be critically reviewed and a long-term financing plan should be developed. In relation to the financing of the Agency, particular emphasis should be put on the funding of collateral activities in the areas of orphan drugs (and similarly in the veterinary sector), paediatric initiatives, consumer information, safety monitoring, etc.

Finally, the Agency's changing role will also have important consequences in terms of logistical and administrative support. The European Medicines Agency should critically examine and, where appropriate, re-engineer existing business processes to maximise efficiency and suitability for the new environment. The Agency should also improve internal procedures by replacing paper trails with electronic workflows, by consolidating and integrating existing systems and by introducing new systems. This would include electronic management of documents, automated electronic publishing, web-based self-service systems for information requests and integrated administrative and business systems with electronic workflows.

Chapter 5
Finalisation of the European Medicines Agency Road Map

The Action Plan to improve the Agency's processes in relation to medicinal products for human use reflected the Agency's 2003 stocktaking of its performance in relation to the processes for human medicines. Such Action Plan addressed the findings further to three initiatives taken (i.e. the CPMP[4] audit, an internal review of the Agency's processes and feedback from pharmaceutical industry) and the proposed improvements (it should be noted that a similar initiative with the CVMP[5] will begin in the 4th quarter of 2004). Building on the proposals made in this Action Plan and in order to implement its vision, particular attention has been paid to six areas. In the areas of scientific advice, scientific assessment, post-authorisation activities, transparency and communication, provision of information to patients, and GXP[6], further initiatives that should be undertaken have been identified. Such proposals are provided in annex (attachments 3-8). It should be emphasised that the European Medicines Agency will develop additional proposals in relation to other activities that are currently undertaken or will be performed by the Agency in accordance with new Community legislation.

As was already stated before, it is the European Medicines Agency's aim to achieve the highest possible consensus at EU level in order to meet twin objectives: the promotion and protection of public and animal health and the competitiveness of EU based pharmaceutical industry. To this effect a consultation with all the Agency's partners and stakeholders needs to be undertaken with a view to finalising the European Medicines Agency Road Map in the 3rd quarter of this year. The Agency's Action Plan for the finalisation of its Road Map is provided in annex (attachment 9).

For such consultation exercise to be successful it is imperative for all consulted parties not only to comment on the European Medicines Agency's proposals on its contribution to the future EU Regulatory System, but also to complement, where relevant, these proposals by elaborating on own initiatives that will be undertaken in order to reinforce the global networking model.

4 CPMP: Committee for Proprietary Medicinal Products.
5 CVMP: Committee for Veterinary Medicinal Products.
6 GXP covers both GMP and Good Clinical Practices (GCP).

Attachments

The European Medicines Agency Road Map to 2010: Preparing the Ground for the Future

Attachment 1

Specific Needs for Veterinary Medicines

Specific needs for veterinary medicines relate to the provision of sufficient veterinary medicines to minor species. While these species may not be significant in terms of animal numbers in comparison to major species, they represent a significant livestock sector in the Member States concerned.

Bioterrorism in the livestock animal sector is a real and present danger and has yet to be adequately addressed in the EU. In addition, the threat of newer epizootic diseases such as the Blue Tongue Fever and the West Nile Virus Fever, already prevalent in some Member States, will require urgent provisions for the control of such threats, in which the Agency will have a role to play in the authorisation of suitable vaccines in a timely and efficient manner.

Both in the veterinary and the human field, there are increasing concerns about developments such as the growth in antimicrobial resistance in man and animals and a CVMP Scientific Advisory Group on Antimicrobial Resistance will be established to address the regulatory challenges ahead in the animal sector. This is entirely in line with the recommendations made by the European Parliament during the review of pharmaceutical legislation that the CVMP should provide scientific advice on the use of antibiotics in food producing animals in order to minimise the occurrence of bacterial resistence in the Community. In addition, the adequacy of systems in place to ensure the environmental safety of human and veterinary medicines will come under sharp focus.

As regards the monitoring of veterinary medicines it needs to be recognised that the application of pharmacovigilance in the veterinary sector is somewhat heterogeneous throughout the EU. However, the European Medicines Agency will continue its commitment to optimise Good Pharmacovigilance Practice for veterinary medicines, building on the initiatives that are currently underway in partnership with the Member States.

Recognition must be given to the importance of animal health and welfare and its direct impact on public health in the Community, and such considerations of consumer safety will prove an incentive at the policy and resource level to further progress the development of much-needed new veterinary medicines within the EU.

Attachment 2

Proposed Role and Functioning of the European Medicines Agency Secretariat

One of the main responsibilities of the Agency through its Scientific Committees is to deliver scientific opinions on any aspects related to medicinal products.

The role of the Agency is to coordinate within the EU Regulatory System networking model the European scientific resources made available by the NCAs, as well as any additional expertise necessary for the fulfilment of its responsibilities.

Such role will be extended in accordance with the legal provisions of new Community legislation since the Agency's Secretariat "shall provide technical, scientific and administrative support for the Committees". It should be emphasised that the enhancement of the European Medicines Agency's scientific role not only relates to the Agency's Staff Members, but also to its Committees, which are an integral part of the Agency and composed of scientific resources made available by the NCAs.

To adequately complete the task of coordinating the European scientific resources, and to further strengthen the Agency networking model, the European Medicines Agency will, as required in the new legislation, expand the scientific role of the Secretariat. The European Medicines Agency Secretariat will have a complementary role to the role of the experts from the National Agencies or academia.

Such coordination, with a greater input from the Secretariat, should lead to an overall improvement of the quality of the EU regulatory environment. This will allow adequate, high quality management of a more complex regulatory system in an enlarged EU. The current concept of product leaders throughout the lifecycle of medicinal products will be further strengthened in order to allow enhanced coordination during the assessment of such products.

Science driven and consistent regulatory opinions and actions are prime objectives.

Aspects where the Secretariat will provide complementary input relate to a contribution to different steps of the procedure from scientific advice to marketing authorisation and post-authorisation, at the levels of the different Scientific Committees. This support will concentrate on the quality assurance of the scientific components of the assessment during the various phases of the review process, especially with regards to the consistency of the assessments across applications, through the Agency scientific memory of CXMP deliveries. The Secretariat should also facilitate and complement the assessment performed by the assessors through the provision of the necessary documents regarding scientific memory information on previous procedures, and regulatory advice or guidance given.

The Secretariat will also contribute to the peer review of applications during the assessment phase. Being responsible for the finalisation of the CXMP assessment report, it will ensure that all necessary justification on the opinions or views expressed will be sufficiently substantiated and it will contribute both in terms of regulatory and scientific memory. It will also contribute to the finalisation of the product information.

Assistance to the CXMP will include aspects related to the identification of the needs for additional expertise, in particular through the secretarial role for the Scientific Advisory Groups and the specialised experts in the framework of the handling of safety concerns for centrally processed applications.

With regards to the preparation of the CXMP notes for guidance, the Secretariat should ensure an identical level of support to the Working Parties of the Committees as provided during the assessment phase. It should particularly ensure that recommendations are

scientifically substantiated and in compliance with legal requirements, that the feasibility aspect has been taken into account and that the consultation process had been as wide as possible before new standards are set up.

The Secretariat should also become involved in the area of outcome research, whereby the impact of regulatory decisions on public health should be looked at.

The internal scientific expertise will continue to contribute to the high level of information required for communication aspects to stakeholders in particular through the European Public Assessment Reports (EPARs). Understanding of disease and product specific issues, as well as stakeholders' related concerns, is key for a successful communication to patients/users of medicines and to health care professionals.

Finally, the Secretariat's role in the coordination of the activities of its different Committees is becoming increasingly important due to the establishment of new Committees in the future.

The successful involvement of the European Medicines Agency in each of these domains is directly dependent on the availability of scientifically competent staff. The ability to easily identify and exploit scientific and regulatory experience is essential for the Agency's possibilities to successfully address the new responsibilities and the increased expectations.

Attachment 3

Proposals for the Implementation of the European Medicines Agency Road Map

Area of Scientific Advice

Scientific advice to be provided by the Scientific Committees of the Agency facilitates access of medicinal products to patients and users of medicines in optimising R&D, reducing uncertainties in regulatory outcomes and accelerating time for approval.

The European Medicines Agency will establish the best possible environment for the provision of scientific advice on medicinal products by its Scientific Committees, in particular for new therapies.

Such provision of scientific advice will allow open discussions and proactive identification of difficulties and will lead to proposals to be made to sponsors.

All future users of the centralised procedure will be encouraged to engage, as early as possible, in an ongoing dialogue with the Agency on the development of their product. This will include regulatory advice allowing the European Medicines Agency to develop a secure landing zone for all sponsors.

In addition, specific efforts will be made to support Small & Medium Sized enterprises and to develop protocol assistance for Orphan Medicinal Products. Further developments of similar initiatives in the veterinary sector will be pursued, dependent on the outcome of the pilot project allowing free advise for medicines intended for Minor Uses/Minor Species.

All scientific advice procedures will include possibilities for face-to-face meetings between sponsors and regulators at the different stages of the development of medicinal products, as well as the involvement of specific and complementary expertise on an individual basis or through panels of experts. In addition, consultation of patient's representatives will be developed particularly for rare diseases. Opportunities for parallel advice with the FDA will be proposed on a voluntary basis, in particular for "global" development programmes.

Priorities will take into account the new and extended scope of the centralised procedure. This will lead progressively to the development of a certain degree of specialisation within the CPMP Scientific Advice Working Group, according to disease or product specificities while maintaining overall consistency.

The processes for scientific advice will develop towards differential procedures depending on the scope of the requests, the type of products and their stage of development. Early interactions with sponsors and pre-filing advice should complete the possibilities offered to sponsors for advice during development. Such opportunities as well as the possibility for pre-validation of the scientific data to be submitted in the context of a marketing authorisation application will provide a necessary continuity from the R&D phase to the licensing phase. The scope of the scientific advice procedure will also be extended to include post-authorisation, pharmacovigilance and risk management/minimisation aspects.

Although the possibility for pharmaceutical industry to obtain scientific advice at national level is recognised, there is a need for enhanced transparency as regards the provision of scientific advice at EU and national level. This could be facilitated by appropriate communication between the Agency and NCAs on the scientific advice given and the development of a best practice guide for pharmaceutical industry on how to obtain scientific advice.

Attachment 4

Proposals for the Implementation of the European Medicines Agency Road Map

Area of Scientific Assessment

The European Medicines Agency has, in accordance with Community legislation, to provide science-based opinions.

The assessment process is characterised by three pillars: a scientific, a regulatory and a procedural pillar.

Scientific opinions have to be based on sound and robust scientific assessment. This should ensure that the Public Health objectives of the scientific assessment performed by the Scientific Committees are met, in particular in case of centrally processed applications and referral /arbitration procedures, or other scientific aspects for which the Committees have responsibilities.

The European Medicines Agency Secretariat will, in accordance with new Community legislation, develop a complementary function by providing scientific support to the Scientific Committees, while having full direct responsibilities for the two other pillars. Process developments will ensure that the assessment is thorough, consistent, operated in the framework of an Integrated Quality Management System, performed by required competences and expertise, whilst compliance with Good Practices (e.g. GMP, GLP[7], GCP) is ensured.

The EU system should be based on a high quality initial assessment supported by several layers of peer review, and in all situations high-level expertise should be involved. For the initial assessment, sufficient time to perform the tasks adequately is necessary in order to provide the Scientific Committees with Assessment Reports of the highest quality, prepared in compliance with established guidance. The largest possible use of additional expertise should be provided all along the process. Where necessary, additional specific expertise should be provided at the level of the Committees and the Scientific Advisory Groups.

The peer review concept should ensure a quality control on the initial assessment, without duplication of the assessment already conducted. It should both relate to the content and the format, and should provide additional and complementary critical expertise views to the initial assessment.

The peer review process should be carried out in a completely transparent manner. This would be best ensured by a systematic and sufficient involvement of a peer review team from the Committees, and the additional assurance that all Committee Members have expressed their views in a timely manner. Furthermore, all aspects concerning scientific consistency and compliance with guidance and regulatory aspects should be checked by the Secretariat of the Agency. This framework will offer optimisation of timelines and opportunities for scientific discussions between the assessors and the Secretariat, and will lead to a cost efficient system.

[7] GLP: Good Laboratory Practices.

Attachment 5

Proposals for the Implementation of the European Medicines Agency Road Map

Area of Post-Authorisation Activities

Post-authorisation activities cover a wide range of areas, aiming at ensuring a continuous monitoring of the medicinal products available on the market. The area of pharmacovigilance, which is a very important aspect of post-authorisation activities, is probably one of the best examples of the EU networking model. New Community legislation will further reinforce the European Medicines Agency's coordinating role in this networking model. The Agency in close collaboration with NCAs will, therefore, have to explore how to further strengthen such concept of partnership in order to create a network of excellence at EU level.

The European Medicines Agency's vision on post-authorisation activities should be driven by a proactive conduct of pharmacovigilance, throughout the lifecycle of a medicinal product in order to further strengthen public health protection in an enlarged EU. It should lead to (1) the best knowledge of the safety profile of a medicinal product at the moment of the granting of the marketing authorisation with the scientifically most robust programme of post-authorisation studies to be performed and (2) a continuous and adequate monitoring of the safety of medicinal products, once put on the EU market.

In order to reach such objective, the European Medicines Agency will use the new legal tools such as

(1) risk management/minimisation plans, whereby the main challenge for the European Medicines Agency will be the feasibility of the implementation of such plans in all Member States, and

(2) the Agency's ability to monitor the implementation by Marketing Authorisation Holders of their pharmacovigilance obligations and to subsequently act in case of non-compliance.

In addition, the European Medicines Agency Risk Management Strategy, which underpins the Agency's proactive conduct of pharmacovigilance on the human side, will have to be further developed. A variety of activities will be undertaken, ranging from an extension of the scope of the scientific advice procedure to include post-authorisation, pharmacovigilance and risk management/minimisation aspects, to establishing a network of academic centres of excellence capable of conducting independent studies targeted on safety aspects and preferably funded from Community funds. Furthermore, particular emphasis will have to be put on ensuring that the EudraVigilance system, which is one of the key pillars of such Risk Management Strategy, is fully operational with appropriate methodologies for the effective early detection of safety signals, in order to allow successful contribution to the best evidence approach.

Finally, the European Medicines Agency Secretariat will have to further develop in order to complement its regulatory and procedural competences by scientific competences, mainly through the development of a pharmacovigilance function, in order to provide adequate support to the Rapporteurs, the CPMP and the high-level specialised expertise assisting both Rapporteurs and the CPMP. Such increased competences of the European Medicines Agency Secretariat should be developed in an enhanced Integrated Quality Management System in order to achieve an adequate level of scientific and regulatory consistency in the outcome of the scientific evaluation processes.

Attachment 6

Proposals for the Implementation of the European Medicines Agency Road Map

Area of Transparency and Communication

The European Medicines Agency began in 1995 with a small number of legal obligations to publish information about its activities, in particular the publication of EPARs. This initiative was significant in the context of the otherwise largely secretive pharmaceutical industry, particularly in Europe.

Since 1995 the Agency has continuously reviewed its Transparency Policy, leading to an increased openness, whilst having to respect some legal restraints.

The EU Review 2001 of pharmaceutical legislation will provide for even more transparency and, in addition, will strengthen the European Medicines Agency's role in the provision of information.

The new legal obligations should also be seen in the context of the new rules introduced in October 2003 on access to documents held by the European Medicines Agency. No citizen or company has yet used this new right to access documents held by the Agency, but it is a right that can be expected to be tested, taking into account the implementing rules in force from April 2004.

All this will have at least two long-term policy consequences. Firstly, the European Medicines Agency's scope and margin for self-determined manoeuvre may now be more limited. Secondly, the Agency's obligations are enforceable by citizens/companies and decisions not to release information can be more easily challenged, not just as bad administrative practice in complaints to the Ombudsman, but now also before the Courts.

The Agency will have to take strategic decisions on the level of transparency of its activities. Questions to be addressed include:

- Should the European Medicines Agency increase the level of transparency of its Management Board meetings?
  Is it possible to continue with closed-door meetings of the Management Board, when the European Food Safety Authority (EFSA) Board meetings are broadcasted life on the internet? Should the Management Board meet in public? Should its documents be publicly accessible?
- Should the European Medicines Agency increase the level of transparency of the meetings of its Scientific Committees? Should agendas and minutes be public documents? Should there be open and closed parts of the meetings?
- Should the CXMP Working Parties and the Scientific Advisory Groups meet in public? Should their meeting documents be publicly accessible?
- Should the European Medicines Agency release information on ongoing applications? For instance, by confirming that an application has been made and by providing details on the product concerned and on the status of the application?

The main challenge for the European Medicines Agency will be to determine whether the Agency wants to actively embrace its new communication mandate or take a minimalist approach.

If the strategic decision is for the European Medicines Agency to have a high level of awareness with all its stakeholders and to be on the lead in the field of provision of information on human and veterinary medicines, one has to acknowledge the resource consequences of such decision, not just in the visible areas of communication (press office, web site, publications, etc.), but also in the preparation of patient leaflets/package inserts, preparation and updating of EPARs, etc.

Finally, the European Medicines Agency should develop, in close collaboration with NCAs, a European Communication Strategy. This is particularly important in the field of communication on post-authorisation safety data which warrants a common approach at the level of all European Regulatory Authorities.

Attachment 7

Proposals for the Implementation of the European Medicines Agency Road Map

Area of Provision of Information to Patients

It needs to be emphasised that patients' approach towards the provision of information has changed significantly over the past years. The patient, having been a passive recipient of healthcare and advice, has turned into a more empowered and proactive consumer of health care. Patients are now actively looking for information on diseases and medicines since they want to be more involved in their own health care decisions. Providers of information should take due account of this trend.

An important challenge will be to provide adequate (targeted to patients), correct (preferably validated), timely and easily accessible information on medicines to patients. The European Medicines Agency vision on the provision of such information should be driven by taking the appropriate measures, resulting in better and more accessible information to patients, in order to promote the optimal use of medicines. This will require a close interaction with Member States in order to arrive at a common approach at EU level. However, optimisation and further strengthening of the current networking model through the development of the European Communication Strategy, as outlined in attachment 6, will be necessary.

In order to reach the above objective, the European Medicines Agency will develop an action plan, taking into account

(1) the outcome of the EU Review 2001 of pharmaceutical legislation,

(2) the G10 Recommendations stemming from the High Level Group on Innovation and the Provision of Medicines, and

(3) the Resolution of the Council of Health Ministers of 1 and 2 December 2003.

The Agency has already started to prepare for the implementation of these initiatives. It has created an EMEA/CPMP Working Group with Patients Organisations. Such Working Group is addressing further improvements to be achieved in the areas of transparency, dissemination of information, product information and pharmacovigilance, in order to

(1) provide information adapted to patients' needs,

(2) develop appropriate communication tools, and

(3) increase the awareness of the public in relation to the use of medicines.

The proposals for improvement from the Working Group will be the first element of the Agency's reply to the G10 Recommendations and the Resolution of the Council of Health Ministers. The recommendations from the Working Group will be subject to a consultation exercise with the Agency's partners and stakeholders. The final recommendations from the Working Group will be incorporated in an 'EMEA Strategy on Interaction with Patients'. Discussions with the European Commission and NCAs need to be started for those recommendations which require a harmonised approach at EU level. In addition, situations will arise whereby amendments to the current legal framework may need to be initiated.

Attachment 8

Proposals for the Implementation of the European Medicines Agency Road Map

Area of GXP

A European quality system, for ensuring fundamental GXP provisions are consistently achieved, is a cornerstone of any robust regulatory system. In the current changing environment which combines enlargement of the EU, the implementation of the EU Directive on clinical trials, the introduction of new technologies and new approaches to the use of technology in the manufacturing and control areas, the European Medicines Agency faces particular challenges in the years ahead.

Through the work of the GCP and GMP inspection services, the European Medicines Agency will work with all 25 EU Member States to consolidate requirements and promote European wide quality systems. On the GMP side, the work of the Joint Audit Programme for EU GMP inspectorates, supported by appropriate training, will ensure that excellence can be guaranteed across an enlarged EU. On the GCP side, special attention will be paid to bioavailability studies.

The Agency will also need to be proactive in ensuring that industry can take advantage of new pharmaceutical technologies and approaches in the manufacturing and analytical areas, as well as anticipating the implications of gene and cell therapies. Part of this work will build on existing activities organised by the European Medicines Agency to facilitate knowledge and understanding between assessors and GXP inspectors, with a view towards avoiding duplication of effort and promoting a synergistic approach that makes the best use of both community and international resources.

The new roles and responsibilities for the European Medicines Agency in the GMP coordination of both finished products and starting materials will have a significant impact on the overall transparency of Europe as regards manufacturing information. The introduction of a European wide database on manufacturing authorisations and inspection information and a register for GMP certificates creates an opportunity to provide better information to regulators and to patients, while promoting the best use of Community resources and avoiding duplication. Coordination of efforts and resources will be the cornerstone of an optimally functioning European system for supervision of manufacturers.

The European Medicines Agency will further support the above initiatives through contributions to international discussions on risk management from a quality perspective and through its cooperation with WHO in relation to regulatory information provided to non-EU countries.

The entry into force of the EU Directive on clinical trials at the same time as the enlargement creates both challenges and opportunities. The Agency will help to meet the challenge of implementation through the work of the GCP inspection services group on the harmonisation of practices, procedures, development of common approaches and joint training initiatives. The European Medicines Agency's support to the clinical trial related databases will contribute to increased communication and availability of information for regulators and appropriate access to information for patients. As in the GMP and quality assessment area, efforts to create better understanding between clinical assessors and GCP inspectors will promote synergies and robustness in the assessment and monitoring areas.

In the post-authorisation area, enhancing the supervision of the quality and safety of medicinal products on the European market will be achieved by strengthening the monitoring of product quality and safety through post-authorisation testing and pharmacovigilance inspections.

Attachment 9

Action Plan for the Finalisation of the European Medicines Agency Road Map to 2010

Action	Who	When
Preparation of European Medicines Agency Road Map	EMEA	13/01/04
Discussion at HoA/HEVRA level	-	22/01/04 HoA/HEVRA meeting
Written Comments	HoA/HEVRA	10/02/04
Preparation of European Medicines Agency Road Map – Revision 1	EMEA	25/02/04
Discussion at EMEA Management Board level	-	11/03/04
Preparation of European Medicines Agency Road Map – Revision 2 and start of 3 months consultation phase[8]	EMEA	26/03/04
Consultation with EMEA Scientific Committees	-	During April-May-June 2004
Discussion at HoA/HEVRA level	-	26-27/05/04 HoA/HEVRA meeting
EMEA Workshop with European Industry Associations (human field)	-	During April-May-June 2004
EMEA Workshop with European Health Care Professionals Associations (human field)	-	During April-May-June 2004
EMEA Workshop with European Patients Associations	-	During April-May-June 2004
Discussion at EMEA Management Board level (including preliminary feedback to the Board on the comments received)	-	10/06/04
CVMP Info Day with Interested Parties	-	17/06/04
Comments in the context of the consultation exercise	EMEA's partners and stakeholders	30/06/04
Preparation of European Medicines Agency Road-Map – Revision 3 and circulation to the EMEA Management Board	EMEA	15/09/04
Finalisation at EMEA Management Board level and subsequent publication of final document (to be accompanied by an Action Plan for the implementation of the Road Map)	-	30/09/04

[8] For the list of consulted parties, see annex. In addition, a Press Release will be issued by the European Medicines Agency and the Road Map document will be put on the Agency's website.

Annex to Attachment 9

Action Plan for the Finalisation of the European Medicines Agency Road Map to 2010

List of Consulted Parties

European Institutions

- European Commission – Enterprise Directorate-General
- European Commission – Health and Consumer Protection Directorate-General
- European Parliament – Committee on the Environment, Public Health and Consumer Policy

National Competent Authorities in the EU Member States (including Accession Countries) and EEA/EFTA Countries

- Ministries, responsible for human and veterinary medicines
- Heads of Agencies, responsible for human and veterinary medicines

European Industry Associations

- AESGP –Association of the European Self-Medication Industry
- EFPIA – European Federation of Pharmaceutical Industries and Associations
- EFPIA/EBE – European Federation of Pharmaceutical Industries and Associations / Emerging Biopharmaceutical Enterprises
- EGA – European Generic medicines Association
- EGGVP – European Group for Generic Veterinary Products
- EPFA – European Plasma Fractionation Association
- EuropaBio –European Association for Bioindustries
- Europharm SMC – European Pharmaceutical SMEs Associaton
- Eye-Care Industries EEIG
- IFAH – International Federation for Animal Health (Europe)

European Healthcare Professionals Associations

- AVC – Association of Veterinary Consultants
- CPME – Standing Committee of European Doctors
- FVE – Federation of Veterinarians of Europe
- PGEU – Pharmaceutical Group of the European Union
- UEMO – European Union of General Practitioners

European Patients Associations

- BEUC – European Consumers' Organisation
- EATG – European AIDS Treatment Group
- ECL – European Cancer Leagues
- EFNA – European Federation of Neurological Associations
- EPF – European Patients' Forum
- EPHA – European Public Health Alliance
- EURORDIS – European Organisation for Rare Disorders
- IAPO – International Alliance of Patients' Organisations

Other Organisations

- COPA COGECA – Committee of Agricultural Organisations and General Confederation of Agricultural Co-operatives in the European Union
- European Academy of Sciences and Arts
- EAVPT – European Association for Veterinary Pharmacology & Toxicology
- GIRP – European Association of Pharmaceutical Full-line Wholesalers