

# **The Heads of Medicines Agencies Strategy Paper**

Developing the Heads of Medicines Agencies Strategy for the European Medicines  
Regulatory Network – A Discussion Document

## **Executive Summary**

### **Introduction**

This document is a contribution from the Heads of Medicines Agencies (HMA) to enhance protection of public and animal health within the European Economic Area (EEA) as a response to the evolving regulatory environment: enlargement, legislative changes brought about by the implementation of new legislation, changing public health needs and a reaction to changes and developments in the pharmaceutical industry.

HMA represents human and veterinary national competent authorities (NCAs) for medicinal products in the EU Member States and the EEA-EFTA States, Iceland, Liechtenstein and Norway (region referred in this document as EEA). Together, these authorities work in partnership in the European Medicines Regulatory Network (EMRN or the Network), with the European Medicines Agency (EMA) and the European Commission.

It should be acknowledged that NCAs operate in different legal frameworks, with some having responsibilities for health products other than medicines, and all having a range of different funding arrangements and governance processes. However, the role in regulating the quality, safety and efficacy of human and/or veterinary medicines is the issue that unites them all within the HMA.

The EMA has its status, role and responsibilities clearly defined in the Community legislation and the EMA Roadmap for 2010 clearly focuses on the implementation of its obligations. Although EMA has a primary role in coordinating the resources of NCAs to operate the centralised procedure, NCAs have the additional responsibility to effectively operate the Mutual Recognition (MRP) and Decentralised (DCP) procedures, as well as overseeing the large number of nationally-licensed medicines across Europe.

Equally, the EMA has a central role in monitoring the safety information on medicinal products in the European market, but it is the NCAs who are responsible for gathering this information and conducting effective pharmacovigilance within their territories.

In the area of clinical trials, NCAs have the responsibility of authorising and monitoring the safety of trials within their territories.

Officials from NCAs come together at the EMA in different working groups, working parties and advisory groups and make decisions that have general impact on, centrally, MRP, DCP and nationally authorised products, and the role of EMA in producing harmonised scientific guidance is fully recognised.

This document is the result of a collective exercise involving the strategic view taken by practitioners in the many different fields of regulation and the input from partners and stakeholders of the Network. HMA proposes a number of strategic orientations based on the analysis of the regulatory environment that is constantly evolving. Therefore, this document should be considered as a working document reflecting the thinking and strategic views of HMA at one point in time that will be updated periodically as a result of

the analysis of experience and the regular dialogue with partners and stakeholders of the Network.

### **Purpose of the document**

This strategy document represents the perspective of the HMA of the functioning and future development of the European Medicines Regulatory Network, where the individual and collective contribution of the national competent authorities to the operation of the Network is acknowledged and enhanced.

In order to fulfil the goal of the Network which is to enhance the protection of public and animal health in the EEA by ensuring that patients, animals and animal owners have access to medicinal products which are of a high standard of quality, safety and efficacy through effective action in all aspects of the regulatory process, this HMA Strategy Paper complements the EMEA Roadmap. The aim of the Strategy Paper and the proposals within it is to enhance the operation of the Network through effective coordination of national resources, a shared mandate with EMEA for some pan European matters, the provision of focus for leadership within the Network and a mechanism for communicating the views of the HMA to the European Commission and the EMEA. These objectives should be underpinned by a clear mission and vision that would consolidate HMA's specific role.

### **Strategic orientations**

#### Patient Safety

- To implement proactive and effective pharmacovigilance at European level based on pharmacovigilance at national level taking a risk-based approach.
- To enhance communication on all aspects of potential safety concerns within the Network.
- To ensure delivery of safety information in a coordinated, timely and accessible manner across the Network, enhancing cooperation between the scientific staff involved in decision making and communications staff.
- To foster means to measure the impact of safety communications.
- To promote the concept of benefit-risk balance in medicine regulation among patients, patient groups, health care professionals and the public in general.
- To ensure that knowledge on medicinal products is available to enable doctors and veterinarians to make rational choices about medicines and enable patients and animal owners to make decisions about their healthcare on an informed basis.

#### Operation of the Network

##### *MRP and DCP*

- To ensure that there are common standards of a high quality and predictable outcomes in the MRP and DCP.
- Support concerted efforts to ensure uniformity and timely availability of product information across the EEA.
- To exercise an appropriate level of management and supervision of their representatives on CMD(v) and CMD(h).
- To provide a level playing field for industry on public and animal health issues and in the implementation of the Community legislation across the Network.

### *Expertise*

- To maintain the expertise necessary to regulate Member States' domestic industry, coordinate and manage pharmacovigilance and inspect manufacturing sites within its own territory.
- To ensure that NCAs staff are of a sufficiently high quality to meet national needs and the needs of the Network.
- To provide an effective training scheme for the Network with the aim of matching the training needs in the scientific/regulatory field.
- To consider the role HMA could play in the development of specialised centres of expertise.

### *Resources*

- To foster more effective ways of reducing duplicate work done in NCAs, through work and information sharing.
- To cooperate in order to meet the legal requirements (timelines, templates, scientific guidelines) applicable in the MRP and in the DCP.
- To provide the human resources for formal working parties and groups, advisory groups and sub-groups at the EMEA as well as to working groups reporting to HMA that together make the system work.

### *Cooperation*

- To develop greater synergies with European and International bodies (DG Enterprise, DG SANCO, DG Research, the EDQM, OMCLs, the WHO, the OIE and the FAO) in order to maximise the benefits of the interaction with these bodies.
- To strengthen the coordination of inspection and laboratory control services envisaging a new collaborative approach with pharmaceutical industry to deal with pharmaceutical crime, liaising more closely with national and international law enforcement bodies.
- To implement a global risk management by means of strengthening the cooperation between the services responsible for assessment, inspection and quality control within NCA and at the level of the Network.
- To encourage contacts at all different levels, at the policy level, at the administrative level and the scientific level for the sound functioning of the Network amid of the legal processes underpinning the Network.
- To encourage informal and formal exchanges of knowledge as well as benchmarking with the attempt to identify and disseminate best practice and develop mutual recognition as an effective means of enhancing the overall capacity of the Network.
- To encourage collaboration between NCAs responsible for human medicines and NCAs responsible for veterinary medicines.
- To consider variables that are largely outside the remit of medicines regulation such as systems of access to healthcare provision or social insurance systems and reimbursement aspects when making decisions at European level and take them into account when discussing the future of European cooperation in medicines issues.

### *Communication*

- To make the multi-dimensional role of the Network clearer to stakeholders and to make the contribution required of the Member States to fulfil EMEA's legal obligations more transparent.

- To develop effective media relations aligned with HMA communications strategy in order to communicate with stakeholders on the activities of the Network and to deal with issues in the high-profile area of public and animal health.
- To bring greater transparency into the regulatory process.
- To participate in the debate at EEA level and foster its own dialogue with stakeholders in order to aid the development of trust, social responsibility, market transparency and professional ethics within the Network.
- To ensure a consistent message across the Network minimising mixed, or mistimed, messages from different partners.

### *Stakeholders*

- To foster the most effective way of regulating human and veterinary medicines in the EEA while meeting the needs of stakeholders in a balanced way.
- To recognise the global nature of development, manufacture, distribution and use of medicinal products.
- To recognise the legitimate role of stakeholders in contributing to the HMA Strategy within the Network.
- To develop robust and effective relationships with stakeholders in order to bring:
  - appropriate input into the planning and policy making of the NCAs, ensuring that they are proactive and anticipate stakeholder issues.
  - added legitimacy for the agencies' policies, decisions and actions.
  - awareness of issues of importance to the stakeholders.
  - the opportunity for the development of policy in a consultative way, enabling stakeholders to ask questions and give their opinion on the NCAs' decisions and policies.
  - networks and alliances based on trust and the effective flow of information to and from the target groups.

### *Information Technology*

- To support an EU Telematics Strategy that provides systems required by Community legislation and set up by EMEA with high quality and reliable data provided by all members of the Network.
- To develop additional systems necessary to optimise the exchange of information and communication at all levels of the regulatory process within the Network.

### *National contexts*

- To manage the impact of the national contexts (expectations of citizens, health care professionals and politicians) on the functioning of the Network.
- To take into account national social attitudes towards openness and transparency, perceived conflict of interests on the part of the regulator and attitudes towards the pharmaceutical industry.
- To identify the issues where a « one size fits all » approach is not possible.

### *Supporting Innovation*

- To support the innovation of new products by the pharmaceutical industry.
- To ensure that internal and external scientific and regulatory assessors at NCA have sufficient skills and knowledge to advise effectively all applicants, including small and medium sized enterprises.
- To increase the scope of inspection and laboratory control activities in line with innovation and legislative change.

- To ensure that innovative products come to market as safely as possible without unduly delaying or hindering clinical research that can lead to beneficial healthcare innovation.
- To harmonise national implementation of the Clinical Trials Directive ensuring consistency of approach, particularly for multi-centre trials taking place across the EEA.
- To take a risk-based approach in order to strengthen in a coordinated way the assessment of high-risk clinical trials aiming to protect the health of trial participants.
- To recognise and involve academic research and work by Non-commercial research organisations.
- To support the development of the strategic research agenda of initiatives such as the Joint Technology Initiative on Innovative Medicines and the European Technology Platform on Global Animal Health, enabling the optimisation of resources and contributing to the increased competitiveness of European pharmaceutical/biotech industry.

#### Distribution and access to medicines

- To improve availability of information on available medicinal products within the Network, especially with products of low volume, low price and specialised products intended to treat severe and/or rare diseases.
- To look at solutions even at legislative level to improve availability of both human and veterinary essential medicines for minor species and/or smaller markets.
- To support regulatory initiatives that would speed up access to the market of medicinal products aimed to any form of public and animal health emergency.
- To coordinate actions with wholesalers and pharmacists and competent public-health authorities involved in the distribution networks and implementation of GDP requirements in order to secure a safe distribution process.
- To ensure a harmonised approach to the pre- and post-authorisation controls placed on veterinary products.

#### Work Plan

This document concludes with a work plan based on the strategic orientations put forward above (published at

[http://www.hma.eu/uploads/media/HMA\\_Strategy\\_Work\\_Plan.pdf](http://www.hma.eu/uploads/media/HMA_Strategy_Work_Plan.pdf)).

Each of the actions has a timeline and relevant HMA working groups were identified to implement them. Many actions of this plan will be implemented together with EMEA.

This document and the work plan have been updated to reflect the views of stakeholders and the ever changing environment in which the Network operates. Regular follow up of the strategy and actions is envisaged in the coming years and partners and stakeholders will have the opportunity to contribute to build a stronger Network.

## **The Heads of Medicines Agencies Strategy Paper**

Developing the Heads of Medicines Agencies Strategy for the European Medicines Regulatory Network – A Discussion Document

### **Chapter 1: Introduction**

1. This paper is a contribution from the Heads of Medicines Agencies (HMA) to enhance protection of public and animal health and part of the ongoing debate about the most effective way of regulating human and veterinary medicines in Europe, meeting the needs of our stakeholders in a balanced way. The strategy is a work in progress, i.e. the HMA acknowledges that the European Medicines Regulatory Network (EMRN or the Network) will be faced with new challenges which are not considered in this paper, that these challenges will be met as they arise and that the strategy and this paper will be revised regularly to reflect the new challenges.
2. The HMA which is the network of the Heads of human and veterinary regulatory agencies for medicinal products in the EU Member States and the EEA EFTA States, Iceland, Liechtenstein and Norway (referred to hereafter as the EEA) recognises its role as an important partner in the regulatory network. Being a partner in the regulatory network entails responsibility for the functioning of the network and the HMA acknowledges this responsibility by giving its vision of the future development of the Network in this paper. In this development it is obvious to recognize the global nature of development, manufacture, distribution and use of medicinal products.
3. The HMA is established to provide a forum for the co-ordination and exchange of views and proposals on issues concerning the European System of Medicines Regulation and the HMA's role within that System. Some of its key tasks are to
  - provide a focus for leadership,
  - devise and deliver practical solutions to problems arising,
  - provide a mechanism for communicating the views of HMA to the European Commission and the EMEA, and
  - work for the interest of the European citizens in promoting the positive benefit-risk balance of medicinal products.
4. The aim of this paper is to foster enhancement of the whole Network for the proper protection of public and animal health and in this respect it is complimentary to the EMEA Road Map to 2010. HMA has adopted the paper in the full recognition that the strategy will develop over time and that other stakeholders have a legitimate role in influencing its development.
5. Following the adoption by the HMA in November 2005 of the first version of the paper, the HMA agreed in April 2007 to revise the paper to take into account comments made by stakeholders in the consultation process and to reflect the evolving nature of the environment in which we operate.

An analysis of the responses from stakeholders was conducted – both a document outlining the responses and the analysis are published at the HMA website (<http://www.hma.eu/63.html>).

This revised Strategy Paper was adopted by the HMA at its meeting in November 2007.

The paper still builds on the work conducted by the six Drafting Groups, which looked at individual aspects of the operation of the regulatory system. The Drafting Groups, which were chaired by a Head of Agency and consisted of high-level staff of the NCAs, dealt with

- Communication and Information,
- Scientific Assessment Process
- Inspection, Laboratory Control and Enforcement,
- Scientific Resources,
- Pharmacovigilance and
- IT Information Systems.

The Drafting Group reports were particularly important as they represented a strategic view taken by practitioners in the many different fields of regulation under the chairmanship of a Head of Agency. Furthermore, they represent the commitment of time, resource and effort from officials from a majority of the EEA and the foundation on which the strategy document is largely built.

## **Chapter 2: Aim of the Paper**

6. The paper aims to expand on the role that the National Competent Authorities (NCA) of the EEA should play, collectively and individually, in the operation of the Network.
7. It falls into four distinct parts. Firstly, chapter 3 explores the current regulatory environment by examining:
  - the legal framework
  - the building blocks of the network (NCAs, the HMA and the EMEA);
  - the Networked model as a multi-dimensional force;
  - the NCAs in their national context;
  - the interdependencies and blurred boundaries between national and European responsibilities.
8. Chapter 4 reflects the fact that each NCA has a variety of stakeholders. Taking account of their needs in a balanced and appropriate fashion, whilst ensuring that public and animal health protection remains a focal point, is at the heart of the strategy. Further consultation with stakeholders is essential for the development of this strategy and for the establishment of the force of the HMA identity.
9. Chapter 5 makes proposals to enhance the current system and promote its further development. There are five over arching issues to consider:
  - Public and animal health,
  - Patient Safety,
  - The operation of the current system,
  - Supporting innovation,
  - Distribution and access to medicines.
10. A revised Work Plan based on the conclusions drawn from the earlier parts of the paper was adopted by the HMA at its meeting in February 2007. The revision of the work plan was carried out to ensure its implementation in due time by bringing the actions and their priorities in line with the strategy and assign responsible actors within the Network to carry out the actions – the revised work plan is published on the HMA website ([http://www.hma.eu/uploads/media/HMA\\_Strategy\\_Work\\_Plan.pdf](http://www.hma.eu/uploads/media/HMA_Strategy_Work_Plan.pdf)).

11. The reports from the six Drafting Groups can be found on the HMA website (<http://www.hma.eu/74.html>).

### Chapter 3: Context

12. This chapter defines the current context in which the Network operates. It is important to note that the context is a dynamic one: For example, the Network needs to grow and build on its previous successes, particularly to ensure that the dual challenge of the further centralisation of the medicines regulatory system and of new demands in the non-centralised procedures is met. The 2001 Review of Medicines Legislation, while it has established a wider group of products which must use the Centralised Procedure, has also strengthened the Mutual Recognition Procedure and established the Decentralised Procedure. This has increased the need for collaboration between NCAs and rendered fruitful cooperation even more important.

#### The Legal Framework

13. This is not an exhaustive description of the current legal basis for the regulatory system which operates but it should be stated that the basis for the Network is set out in Community pharmaceutical law. In fact, the Regulation establishing the Centralised Procedure and the EMEA and the Council Directives, implemented in national law, which underpin the operation of the MRP and DCP are the legal mechanisms underpinning the Network. This gives the Community Institutions (the Council, the European Commission and the Parliament) a clearly defined remit which is matched by that of national governments and institutions. The European Commission, in particular, plays an important role in ensuring that there is a level playing field in the implementation of the Community law in this field and is, of course, the Licensing Authority for the Centralised Procedure. The specific legal framework which is currently in place presents a balance of Community and national law which predates how the different parts of the Network operate. Of course, national law in this field may add responsibilities to specific NCAs.

#### The building blocks of the Network: the National Competent Authorities, and the EMEA

14. There are currently more than 40 NCAs in the EEA. There is agreement that all agencies have a role to play in the Network despite differences in their available resources. Nationally, the agencies play a variety of roles: Some are jointly responsible for human and veterinary medicines, whilst some are only responsible for one or the other: Some deal with medical devices and reimbursement arrangements, as well as medicines regulation. All have different national interests to balance and different legal bases, funding arrangements and governance processes under which they operate.
15. The NCAs' role in regulating the quality, safety and efficacy of human and/or veterinary medicines is the issue which unites them all. It is through the HMA that they come together to discuss them. Not a statutory body, Article 1 of the Guideline for Heads of Medicines Agencies (adopted May 2003 and amended February 2005 to reflect the organisational changes of the HMA) explains its mission: Two of its key tasks are to provide a focus for leadership within the Network and to provide a mechanism for communicating the views of the HMA to the European Commission and the EMEA. The creation of a Management Group and a Permanent Secretariat are key developments designed to give the HMA an identity in its own right in the Network. They are key to the success of completing these aspects of its mission.

16. Conversely, the status, role and responsibilities of the EMEA are clearly defined in the new legislation and in a variety of official documents, most succinctly in the EMEA Road Map to 2010. Its overall responsibility for the operation of the Centralised Procedure is clear and undisputed and it enjoys the full support of the NCAs in this. The concept of the shared mandate for other pan European matters, including safety and quality issues, referrals and product harmonisation, and communication of information on Centralised Products and for certain international contacts, has also become a legal reality. Again, by agreement, it has at its disposal the resources of the NCAs in achieving many of these tasks.

#### The Network as a multi-dimensional force

17. There is agreement on the concept of a networking model and the need to enhance cooperation to make the Network work more efficiently, which is a shared responsibility between the EMEA, the European Commission and the HMA. The EMEA Road Map holds the same concept and ideas. The networked model operates on a number of different dimensions and is supported by differing forms of formal and informal communication between all of the different players in the Network:
- In the Centralised Procedure, for example, the EMEA has a primary role in coordinating the resources of the NCAs in the assessment of applications, the monitoring of the safety of products on the market, in the inspection of manufacture of such products, and also in the quality control of these products through the links with the EDQM. Community law, guidelines and Standard Operating Procedures strictly define roles and interactions between the different players. Rightly, in this dimension, the EMEA is at the hub of the network, in which NCAs operate.
  - On other levels, for example in the Mutual Recognition Procedure (MRP) and in the new Decentralised Procedure (DCP), the contact is primarily between NCAs. This is a formal system too, with timelines, templates and the requirement to adhere to scientific guidelines set down in Community law but operated by the NCAs. They meet in a setting which has been given a legal form with the implementation of the 2001 Review, but need to cooperate in order to make this system work. Issues previously encountered include the fact that the Community law in this field is not directly applicable and as such implemented in national legislation and that there is a direct impact on national healthcare delivery processes and patients. In the current global market both formal and informal contact to make this system work is more important than ever.
  - Other formal systems exist: the Pharmacovigilance Working Parties for human and veterinary medicinal products (PhVWP), the Inspectors Groups (IG) and many of the sub groups of CXMP including working parties and scientific advisory groups, all provide a forum for officials from the NCAs to come together to make decisions directly about, or having general impact on, centralised, MR, DCP and national products. In the area of sampling, for example, Official Medicines Control Laboratories network (OMCLs network) monitors centralised products on behalf of the EMEA and there is a collaborative approach for sampling and testing both Centrally Authorised and Mutual Recognition products. The “dual mandate” of such bodies, composed essentially of officials from the NCAs, is a development this paper will come back to.
  - There are other participants in the Network: DG Enterprise and other parts of the European Commission (DG SANCO and DG Research), the Council of Europe

and its various bodies including the European Directorate for the Quality of Medicines & Healthcare (EDQM) and the World Health Organisation (WHO) and the World Organisation for Animal Health (OIE) or Food and Agriculture Organisation (FAO) for veterinary medicines. While the coordination of some of these activities is attributed by law to the EMEA, greater synergies need to be developed by HMA in order to maximise the benefits of working with these bodies.

18. Of course, the legal processes mentioned above underpin the whole of the Network, but it must be understood that a variety of contacts at all different levels, at the policy level, at the administrative level and the scientific level, are necessary to the functioning of the Network. The impact of decisions taken in one NCA can have an impact on operations in another: Industry stakeholders are interested in a level playing field and public and animal health issues know no national boundaries. This last dimension is the most difficult to define but is key to the future operation of the system. Many, though not all, of the suggestions for strengthening or enhancing the Network will fall within this dimension.

#### National Competent Authorities in their national context

19. It is recognised that the NCAs operate in a national context as well as a European one while EMEA's context is primarily European. The NCAs also operate in daily contact with citizens, healthcare professionals and politicians. This fact adds an important dimension to the operation of the Network, making cooperation and communication even more important. National stakeholders can put very different expectations on NCAs, and influence how they act at EU level.
20. Although the Community pharmaceutical legislation is based essentially on the Single Market provisions of the EU Treaty, the primary stakeholders obviously include patients and healthcare professionals who operate in quite different healthcare delivery systems. These range from centralised systems with controls on access to healthcare provision and certain therapies to systems based on social insurance with reimbursement arrangements which are also quite varied. The growth of generic prescribing is a healthcare delivery issue which has an obvious link to the work of the regulator. While these variables are largely outside the remit of medicines regulation, they have an impact on issues such as access to medicines "over the counter" and the application of safety decisions in prescribing practice. These issues have an undeniable impact on medicines regulation at national and European level. These issues need to be considered more fully when making decisions at European level and taken into account when discussing the future of European cooperation in medicines issues. In the veterinary medicines field, in addition to the variation in the distribution arrangements in place nationally, variety in the practice of animal husbandry and the differing importance of species to be found in certain territories can also have an impact.
21. The pharmaceutical industry is a global one and, literally, a global response is needed in many cases. However, the nature of the industry differs from country to country and this also has an impact on national and EU policy. While some countries have a broadly based innovative industry, others have significant generics industries. All regulatory bodies have a greater or lesser impact on the competitiveness of the industry that they regulate. In a number of practical ways, particularly in the "skills mix" of the NCAs, local industry has an influence on the regulator too. In a discussion of the potential for specialisation the need for each NCA to, at the very least, maintain the expertise to regulate its domestic industry, coordinate and manage

pharmacovigilance and inspect manufacturing sites within its own territory should be underlined.

22. Social and cultural conditions and attitudes vary too. These can be defined in law: Restrictions still apply to the marketing of certain products, such as abortifacients, in some parts of the EEA and attitudes to veterinary diseases can affect the local approach to the authorisation of veterinary medicines. Less obviously, social attitudes towards openness and transparency, perceived conflict of interests on the part of the regulator and attitudes towards the pharmaceutical industry also vary from country to country. Some NCAs are subject to rigorous scrutiny by national Parliaments, the press and various Non Governmental Organisations, while others operate in relative isolation from such matters. In addition, patients, patient groups, healthcare professionals and the public in general all have a relatively low level of knowledge of benefit-risk balance in medicine regulation. In some cases, this amounts to a positive mistrust of industry and the regulator, an additional complication to the business of regulation.

#### Interdependency and blurring the boundaries

23. It is true that many issues differentiate the NCAs from one another and from the EMEA. However, from an analysis of the many issues which bind them together, one message is clear: there is a mutual interdependency which exists in spite of the differences. The Centralised Procedure is strengthened by the contribution of internal and external expertise from the NCAs. However, the MRP, DCP and national procedures still command the largest resource commitment from NCAs, due to the volume of applications, and so it is crucial to the successful operation of the Network that NCAs continue to retain and develop their core skills.
24. The interdependency of the various EU authorisation procedures can be demonstrated by the analysis of the products on the market place. Each Agency, while it commits resources to the Centralised Procedure, also needs to retain or build the competence to participate in the authorisation of a variety of products through the MRP and DCP and monitor their safety in use and in manufacture. In addition, those NCAs with a responsibility for pricing and reimbursement make these arrangements for centralised and nationally authorised products. All NCAs are responsible for the distribution of Centralised Products on their markets. For veterinary medicines, a large proportion of National Markets remains un-harmonised and can be expected to remain so for some time. That creates concerns as far as availability of veterinary medicines is concerned for minor use and minor species.
25. Another is the fact that the boundaries are often blurred: GXP IWG and PhVWP both now have shared mandates and address issues of concern in the MRP, DCP and the Centralised Procedure. They meet at the EMEA and the Secretariat is provided by it, but they are composed of national officials. Referrals are also dealt with at this Community level. In the same way, the OMCLs network is currently developing the sharing of competencies for products authorized through the Mutual Recognition system. This dual mandate means that a one size fits all approach is often not possible, especially where the national implementation of decisions is concerned.

#### **Chapter 4: Stakeholders**

26. The Network has a number of stakeholders. If a stakeholder is defined as an individual or group that can influence, or be influenced by the NCAs' actions, then the list is a long one. The principal stakeholder groupings for any medicines regulatory agency are:

- Patients and carers,
- the general public,
- healthcare professionals,
- pharmacies and wholesalers,
- animal owners and food producers,
- the pharmaceutical industry,
- healthcare policy makers,
- national governments,
- the European Institutions
- other NCAs in the Network,
- other non-EU regulators,
- other international bodies such as the WHO, the European Food Safety, Authority, OIE, OECD, EDQM, etc.

27. The list grows if some of the new challenges facing the Network are also considered: For example, in order to counteract pharmaceutical crime, the NCAs and the EMEA will need to liaise more closely with national and international law enforcement bodies. The media, while not a stakeholder in its own right, represents interest of the general public and also provides an excellent means of communication with stakeholders. Effective media relations are an essential aspect of the communications activities of the Network dealing with issues in the high-profile area of public health. It is acknowledged that relationships with the media and identifying the most appropriate methods of harnessing the power of the media to support the message being conveyed by the Network are important. Therefore the Network needs an active approach to the media which outline relations aligned with its communications strategy to derive some benefits rather than underestimating the influence of the media.

28. Robust and effective relationships with stakeholders will bring:

- appropriate input into the planning and policy making of the NCAs, ensuring that they are proactive and anticipate stakeholder issues.
- added legitimacy for the agencies' policies, decisions and actions.
- an awareness of issues of importance to the stakeholders.
- the opportunity for the development of policy in a consultative way, enabling stakeholders to ask questions and give their opinion on the NCAs decisions and policies.
- networks and alliances based on trust and the effective flow of information to and from the target groups.

29. Individual NCAs conduct a dialogue at national level with many of their stakeholders. This dialogue has, so far, been largely managed by the EMEA at European and global level. We have already seen how multi-dimensional the network is, and the extent to which the NCAs operate across these dimensions. It is appropriate, therefore, for the HMA, representing the NCAs, to participate in the debate at EU level too and foster its own dialogue with stakeholders. This will aid the development of trust, social responsibility, market transparency and professional ethics within the Network

30. The networked approach means that managing and communicating in the regulatory relationship is complex. Decisions are more regularly reached at European level. This process can in itself make effective and timely dialogue difficult but ensuring a consistent message across the regulatory network has also proved difficult – with stakeholders receiving mixed, or mistimed, messages from different partners. Other

issues such as commercial sensitivities surrounding drug information and its dissemination also intervene and impact on our ability to share information with the wider community.

31. To summarise, stakeholders need to be engaged fully in the process of developing the HMA Strategy as we need to be aware that they have particular demands and requirements from the Network. Balancing the different interests of the different stakeholders is key. This can sometimes be a difficult process but is helped by basing the various relationships on the need to protect public and animal health through effective regulation.

## **Chapter 5: Moving Forward: Enhancing the Current System and Promoting Further Development**

32. Although chapter 3 of this paper has set out some of the constraints on further development of the European Medicines Regulatory System, further analysis also highlights areas where there is considerable scope for progress to be made. These strategic conclusions can be grouped together under five headings:

- Impact on public and animal health protection
- Patient Safety
- Operation of the European Medicines Regulatory Network
- Access issues
- Supporting Innovation

33. There are also more detailed, practical issues identified in these documents which will need to be considered further by the various committees, sub committees and working groups of the EMEA and HMA. This is covered more fully in the Action Plan.

### Impact on public and animal health protection

34. The contribution played by medicines regulation to the protection of public and animal health, by ensuring that patients, animals and animal owners have access to medicinal products which are of an appropriate standard of quality, safety and efficacy is often underestimated by health policy makers. Another contribution to the protection of public and animal health is to ensure that medicinal products and knowledge are available to enable doctors and veterinarians to make rational choices about medicines. It is, however, the primary task of the regulator and any enhancement to the current system must improve or maintain our capacity in this field.
35. The corner stone of public and animal health protection is effective action in all aspects of the regulatory process. A part of this is the assessment of the benefit-risk balance which may vary in the Member States of the Network due to differences in clinical practice in the Member States. Such differences may influence the approach taken by a NCA.
36. Suggestions to ensure general enhancement of the assessment process are made but the following issues apply to the licensing process in particular:
- Robust, high quality assessment will be best achieved by preserving the Rapporteur/Co-rapporteur approach in the Centralised Procedure, with Peer Review concentrating on the quality of the assessment process. While such a system would be optimum in the MRP and DCP, it was recognised that the

involvement of a number of Concerned Member States (CMS) each considering parts of the dossier, provided the opportunity for quality assurance and achieving consensus.

- The need to resolve some of the underlying problems faced in the operation of the MRP is recognised. While there are the obvious successes of the MRP the failure to properly define the concept of significant risk to public health, a tendency to allow national interests to hold sway over the Community one and a disconnect between activity at a national level and the Community approach also needs to be acknowledged.
- Central to the licensing process is the fact that the internal and external scientific resources of the entire NCA are brought to bear on a dossier. Even in CXMP, members are briefed by their officials and advised by internal and external experts. HMA bears a particular responsibility in ensuring that its own staff is of a sufficiently high quality to meet national needs and the needs of the Network.
- Mechanisms need to be found to ensure that issues raised are based on scientific grounds or in some occasion linked to the differences in clinical practice in Europe. This is particularly the issue when dealing with the harmonisation of “nationally” licensed products of long standing.
- IT support, in the form of video and tele conferencing, the variety of databases set up under EU legislation and coordinated by the EMEA, are also essential.
- Communications at all stages of the process needs to be optimised. Pre submission scientific advice should be obtained from CXMP or from a NCA by the applicant. At this stage, discussion between the applicant and the Reference Member State (RMS), and between the RMS and CMS should also become the norm in more complex cases. This is part of the quality assurance process and should lessen the need for National Competent Authorities to raise issues during the procedure. New or revised IT solutions will need to be considered to facilitate this stage of the process.

37. Effective pharmacovigilance is also key to the protection of public and animal health and the maintenance of confidence in the medicines regulatory process. The work already carried out by the Working Group on European Risk Management Strategy is recognised and strongly supported. The opportunity to create the best pharmacovigilance system in the world, with a linked Network, scientific centres of expertise and significant animal and human populations is identified. However, some challenges – of linking diverse healthcare delivery systems and efficient use of resources – have also been identified.

38. Exploiting the wide population base for pharmacovigilance purposes is one of the key objectives of the Network. There are a number of aspects to this:

- Boosting data capture: The creation and management of national reporting systems is one of the cornerstones of pharmacovigilance and is built on the close proximity between patients and healthcare professionals and each NCA. The different methods of healthcare professional and patient reporting across the Network have given different results in terms of numbers of adverse drug reactions (ADR) reported. The Network can help all NCAs reach a consistent standard of quality and reporting rates through fostering learning from one another and sharing best practice. However, the EMEA also has a role to play: all NCAs are now contributing their ADR data to Eudravigilance.
- Signal Detection and confirmation: Development of more sophisticated techniques, such as data mining, are needed to fully utilise the data captured.

Other methods of signal detection and confirmation also need to be brought into play at national and European level. In particular, more extensive use of epidemiological databases should be encouraged. This is an area where central coordination, and perhaps funding, could play a bigger part.

- Regulatory decision making: Nationally and centrally, communicating and implementing the regulatory decision is a key step in the process. Co-ordination of messages across national boundaries is one issue: Time zones may be different but more fundamentally because of local conditions, varying from the local healthcare delivery system to the level of local press interest, there may be difficulties in the harmonised implementation of decisions. This needs to be recognised in the decision making process. European procedures on safety issues often take long as it takes time to achieve a robust assessment involving all relevant NCAs and fulfil the procedural obligations but the lengthy timescale may mean that NCAs act independently due to national reasons during the procedure which may increase the difficulty in harmonising the implementation of decision. Therefore every effort should be made at every level to shorten the timescale.
- Proactive pharmacovigilance: The European Risk Management Strategy present the opportunity to on going reassessment of benefit-risk of products in use and, possibly, an opportunity for managing the entry of innovative products onto the market in a way which allows safety concerns after launch to be managed, but ensures that patients and animals have access to the products that they need.

The 2001 Review of Community pharmaceutical legislation introduced an additional regulatory obligation on NCAs: to carry out inspections at the premises of Marketing Authorisation Holders to ensure that they comply with the pharmacovigilance requirements of the legislation. As this is a new requirement, there are opportunities to share best practices in undertaking inspections, with a view to promoting a consistent approach across the Network. As this becomes more established the possibility of worksharing may be explored. By developing such coordinated actions, NCAs will be in a position to monitor not only the due implementation of classical pharmacovigilance requirements, but also of the risk-management plans that have begun to be build on the basis of the 2004 directive with a view to strengthening post-marketing surveillance with a wide range of tools. The progress achieved in developing EudraVigilance paves the way for further progress in the effectiveness and reactivity of pharmacovigilance in Europe.

39. Animal health protection plays an equally important role but veterinary pharmacovigilance is not as far advanced in terms of infrastructure and policy development as human pharmacovigilance. Some NCAs have to work hard to improve pharmacovigilance and a variety of mechanisms for learning from one another may be considered. Antimicrobial resistance is important to both the regulation of human and veterinary medicines and, of course, issues such as drug residue monitoring in animals is particular to veterinary medicines. Steps must be taken to ensure that these issues are adequately addressed. As with pharmacovigilance in human medicines, decisions need to be implemented in a timely and coordinated manner across the Network. In this respect, the findings on communication of pharmacovigilance information or of safety issues apply equally to veterinary medicines.

40. Finally, the measures to be taken to improve the overall contribution to public and animal health have been identified. They include:
- Moving with the times: Increasing the scope of inspection and laboratory control activities in line with legislative change, reacting to the re-structuring and globalisation of manufacturing and the advent of a range of new therapies (gene therapy, cell therapy and biotechnology).
  - Dealing with pharmaceutical crime: The opportunities for clinical trials misconduct and fraud increase as the industry becomes increasingly global, and can have a considerable impact on trial subjects and public health generally. Counterfeiting and diversion are also increasing and seem likely now to threaten the legitimate supply chains of the EEA. In this regard, the coordination of inspection services and laboratory control must be strengthened and a new collaborative approach with pharmaceutical industry must be envisaged.
  - Global risk management: Risk management plans must not forget to pay attention to all aspects of potential safety concerns, including quality aspects that can be monitored using the national laboratory of controls. The approach to dealing with quality issues, once identified, could be strengthened by better cooperation between the services responsible for assessment, inspection and quality control within each NCA. There is also the need for greater coordination between NCAs and between EMEA and EDQM. The need for enhanced communications in this field, covering all aspects of inspection, enforcement and laboratory control has both a harmonising effect and is also an effective use of resources.

#### Patient Safety: Facilitating Patient Choice

41. The needs of individual patients need to feature highly in the HMA strategy if it is to be relevant to their expectations:
- The key to the relationship is to ensure that the information provided is relevant to the needs of patients and enables them to make decisions about their healthcare on an informed basis.
  - Healthcare professionals also need information to be provided in a timely and accessible manner so that their prescribing choices can be influenced by information coming from the regulator.
  - Animal owners, food producers and veterinary surgeons need the same level and quality of information, albeit tailored to their particular needs.
42. At national level some competent authorities have made more progress than others have in terms of developing their approach to communications and to building the relationship with patients and healthcare professionals. In the multi-dimensional network there is a gap which needs to be filled at HMA level and an effort must be made to improve communication on national and MR products.
43. The introduction of the equivalent of the European Public Assessment Rapport (EPAR) for MRP, DCP and nationally licensed products is also fundamental to the introduction of greater transparency into the assessment process. However, the product information prepared by NCAs, or prepared by others but regulated by them, is one of the main interfaces between the regulator and the citizen – the patient or the healthcare professional. The need to ensure that the information prepared at the time of product launch, the Summary of Product Characteristics and the Patient Information Leaflet, need to be of a uniform standard and up to date is recognised.

While some of this is governed by legislation, a concerted effort on the part of those involved in the assessment process also needs to be made. Investment also needs to be made in making these documents accessible electronically, if needed, perhaps through a HMA web portal.

44. The issue of communication of safety information has also received a great deal of attention. There are four key points to make:
- Legislative amendment and, in many countries, a changing social and cultural environment means that communication needs to be firmly embedded in the working lives of regulators.
  - NCAs are often in the best position to maintain close contact with local patient organisations and healthcare professionals, often ensuring faster and more effective communications on key issues.
  - In terms of incident management taking the regulatory decision is only the beginning of the story and sufficient time and attention needs to be given to ensuring that the messages are being heard and acted upon by those who need to do so.
  - There also needs to be appropriate measurement of the impact of safety communications.
45. Above all the need for all information, and particularly crisis management information, to be given in a coordinated, timely and accessible manner across the Network is underlined. It is recognised that this is a difficult task: Poor coordination may put other NCAs in a difficult situation and it also gives the impression that the European Medicines Regulatory Network is fragmented. The need to observe rules of commercial confidentiality, dealing with cultural and political differences and resource issues also present difficulties. This requires particular cooperation between the scientific staff involved in decision making and communications staff.
46. Recognising the need to improve the Network's activity in this field, a four step approach is suggested to improve the Network's communication, whilst at the same time offering learning opportunities at national level:
- The establishment of a communications network consisting of communication leads in each NCA to simplify and facilitate the flow of information at national level and between the NCAs and the EMEA.
  - A communications survey: what mechanisms are currently available and where best practice can be learnt.
  - The establishment of "standing groups" to examine specific issues arising out of the communications survey.
  - The communications tool kit: best practice templates to be adapted for local use and mechanisms for cooperation (e.g. Extranet), with the aim of introducing consistency without rigidity.
47. In the current Information Technology age, greater use should be made of information and communication technology services. Tools such as voice over IP and video conferencing can be used to facilitate communication between regulators and need to be developed. Moreover, tools to ensure that patient information and safety information can be managed effectively (websites, national product information databases) could also be developed.

#### Operation of the Network

48. The multi-dimensional nature of the Network has already been demonstrated. The differences between the NCAs, pressure on resources, tensions between their national and European roles and the lack of an external visibility of the HMA and the informal, but underpinned by delegated national competence, way that much of the system operates, all have an impact on the operation of the system. These issues need to be addressed if the function of the Network is to be enhanced.

### ***Role of the HMA***

49. Despite the fact that HMA's role and function have no statutory basis, HMA has managed, through informal cooperation, to launch major initiatives (e.g., the European Risk Management Strategy) and monitor the implementation of new legislation (e.g. the Clinical Trials Facilitation Group). It is acknowledged that the lack of external visibility has had an impact on the role that HMA has been able to take in coordinating the activities of the Network. Some difficulties have been experienced in achieving consistency of approach and maintaining dialogue with industry and patient groups.
50. The necessity to develop HMA's distinct identity is recognised and there has been real progress in this field: The creation of the HMA-MG and its supporting Permanent Secretariat (HMA-PS), brings continuity to the business of HMA and, with the Presidency of the day, provides a focus for much of the business of HMA. This work needs to be consolidated, with a clear mission and vision for the HMA. It needs to be given a visible presence and made more relevant to the citizens of Europe - through a functioning and useful website, and making it part of the "one stop shop" for medicines information at European level.

### ***Supervision of the MRP and DCP***

51. In a more tangible way, HMA needs also to exert more influence over the operations of the MRP and the DCP and over safety issues at EU level, especially where these concern national or MR products. In principle, this should not be problematic as national officials meet in a number of groups with a shared mandate (the IG, the PhVWP, as well as the CMD(h) and CMD(v), the OMCLs network advisory group), to conduct the business of the MRP and DCP. HMA also receive regular reports on the operation of some of these bodies and the Rules of Procedure of some of them have been revised to enable the HMA to advise on particularly difficult political issues.
52. HMA's overall aim must be to ensure that there are common standards of a high quality and predictable outcomes in the MRP and DCP. Adherence to properly defined guidelines, guaranteeing a supply of high quality and properly qualified staff, the development of enhanced, Community-wide, training, IT support and increased communications are all key in this process. It should meet this aim by exercising an appropriate level of management and supervision of their representatives on CMD(v) and CMD(h).

### ***Relationship with EMEA***

53. The mutually supportive nature of the relationship with the EMEA is positive and needs to be maintained for the benefit of the European Medicines Regulatory Network. The EMEA has shared its vision for the implementation of the new medicines legislation in the Road Map and the resource requirement it is laying on the NCAs is becoming clearer. The recent discussion of new approach to scientific advice is an example of how transparent and open the EMEA must be in its approach to the resources it needs and the contribution required of the Member States. In their

public portrayal of the Network, the HMA and the EMEA need to make the multi-dimensional role of the Network clearer to stakeholders and to make the contribution made by the NCAs to all parts of the Network more transparent.

### ***National Competent Authorities specialisation***

54. The extent to which NCAs participate in the European Medicines Regulatory Network must be a decision taken by each Agency. There are a number of factors to consider: The EMEA requires access to resource to ensure the smooth operation of the Centralised Procedure, and has already sought to assess the resource that individual Authorities may wish to devote to it. It is important that most NCAs contribute to some extent to ensure that decisions continue to reflect the wish of the whole Community. The large number of nationally authorised and MR products also mean that due regards needs to be taken of the skills mix which exists in each NCA. Specialisation might lead to a monopoly situation with a negative impact on both the Centralised Procedure and the MRP and DCP. It might also make it more difficult for NCAs to meet their national requirements. NCAs need to have access to expertise to assess new therapies and diseases. Specialisation may not be permanent as it is often dependent upon a few key staff and may lead to increased variability of work load volumes. On the other hand, when faced with new technologies and increasingly innovative medicines, centres of expertise become increasingly attractive. The HMA might consider if it should play a role in the development of such centres.

### ***Common Training***

55. There is a need to ensure that the outcomes of regulatory decision making were robust and effective and had validity at European level. Enhanced training of assessors is identified as one way of reinforcing confidence in the Network. Under this perspective it has been highlighted that there is a need for a strategic approach for the provision of training in the Network. There is also need for a better coordination of existing training activities already performed by NCAs and other institutions and organisations together with an improved matching between the training necessities in the scientific/regulatory field and the training opportunities actually provided. In order to find realistic solutions, HMA has put in place a forum with the aim of identifying the best way of proceeding along these lines and the most adequate operational tools.

### ***Learning from one another***

56. The differences between the NCAs in terms of skills mix and over all capacity to implement the Community acquis in the field of medicines legislation is clear. However, there is a strong desire to exchange knowledge through a variety of means. Twinning, twinning light, and informal and formal exchanges of knowledge and benchmarking all enhance the operation of the system. These exercises have been quite successful. The idea of formal or informal twinning arrangements as a desirable within their fields is introduced. While the Benchmarking of European Medicines Agencies (BEMA) Project constitutes a Network wide attempt to identify and disseminate best practice, "sectoral" benchmarking between smaller groups of NCAs has been identified as an effective means of enhancing the overall capacity of the Network.

### ***Resource***

57. The availability of resource has already been identified as an issue. The review of the legislation introduces a number of new obligations for the EMEA and new and increased tasks for NCAs. The implementation of the paediatrics regulation will also imply a number of additional tasks both at European and at national level. These changes have a strong impact on the Network, in particular with regard to the workload, complexity of tasks, need for more specialised expertise and effective co-operation at the Community level. For example, the extended mandatory scope of the centralised procedure for human medicines will result in a significant increase in the number of “initial applications”. The range of complexity: from highly complex applications for new innovative product classes emerging from new technologies all the way through to generic products that raise few new scientific issues will also increase. The obvious increase in the threat posed by counterfeit medicines means that strategies will need to be developed and resources allocated to it. The increasing importance of effective communications at national and Network levels also implies an investment in resources to meet this new requirement. If the Network is to be successful, a flexible approach to the allocation of resource to European projects needs to be taken. More effective ways of reducing work which is duplicated in different NCAs, including such measures as sharing inspection reports, sharing information on laboratory testing, processing Periodic Safety Updates Reports (PSURs), the assessment of paediatric data and even conducting signal detection and generation in pharmacovigilance, need to be identified and put in place. NCAs should endeavour to find the most effective way to make its limited resources available optimising its deployment for the operation of the Network.

#### Supporting Innovation

58. It would be a failure of the Network's public and animal health role if it did not support the innovation of new products by the pharmaceutical industry, as this would deny patients and healthcare professional's access to cutting edge medicines and new technologies. On the other hand the regulator must ensure that such products come to market as safely as possible. Striking that balance is a key aspect of regulating clinical trials. Authorising clinical trials is a national responsibility for NCAs, but governed by the Clinical Trials Directive. The aim of the regulatory framework is to protect the health of trial participants and, in this respect, the Network is currently putting emphasis on strengthening in a coordinated way the assessment of potentially high-risk, first-in-man clinical trials. As there is a clear public health interest in enabling timely and effective clinical research that can lead to beneficial healthcare innovation, NCAs and stakeholders regard consistency in the national implementation of the Clinical Trials Directive as a priority. Greater harmonisation will ensure consistency of approach, particularly for multi-centre trials taking place across a number of Member States. The Clinical Trials Facilitation Group and its subgroups are working towards reducing the extent of additional national requirements, with a view to bringing the overall regulatory burden imposed by the Network more into line with the requirements of the EU Directive. The ongoing development of EudraCT as a central repository of information on the content, commencement and termination of clinical trials in the EU, enables better overall supervision of trials and strengthened protection of participants. Non-commercial clinical research plays an important role in understanding the nature of products and the credibility of the system. The role of academic research and work by other research organisations must also be recognised as they are key stakeholders in the work of the Network and operation of the EU system.

59. Many innovative products now come to market via the Centralised Procedure, and the contribution made by the NCAs has already been recognised here. However, not

all such products come via this route and suggestions, including pre-submission scientific advice and co-ordination between the RMS and CMS, which will enhance the assessment process are made. As stated above, multiple involvement of NCAs in the assessment process (or at least in parts of the dossier) better training, greater reliance on guidelines and IT support in the form of a scientific memory database is called for. If adopted, these proposals would lead both to a robust assessment, which all NCAs can endorse, and a quicker, safer entry of the product onto the market, in the interests of both public and animal health and the Marketing Authorisation Holders.

60. Supporting innovation is identified as an important issue. For example, NCAs need to constantly ensure that their internal and external scientific and regulatory advisors have sufficient skills and knowledge to advise effectively all applicants, including Small and Medium-sized Enterprises (SMEs). Identifying and maintaining such sources of advice becomes increasingly difficult as science advances, particularly when matched with the need to ensure that advisors are free of conflict of interest. As the benefit-risk profile of many innovative medicines becomes increasingly a matter of constant review and supervision, the new approach to more proactive pharmacovigilance and, as yet undeveloped, new ways of monitoring the safety of such products in use becomes even more important. Inspection of the manufacturing and distribution of new technologies is also an issue: NCAs need to decide now whether to develop an expertise in this field and put in place recruitment strategies or strategies to diversify the current skills set of their staff. The work being done to develop learning circles in PIC/S in these areas is particularly relevant. Supporting innovation also requires that the NCAs should make their best efforts to take due account of the specific situation of innovative SMEs, often focused on biotech.
61. A variety of procedural changes also need to be considered to ensure that the service provided to industry is optimal. Many of these are based around IT issues. The range of IT systems which can be harnessed to support the work of the NCAs is large. E-submission is the gold standard but it is clear that some NCAs are likely to be using this as the norm much more quickly than others. It could also be enhanced by linking it to tracking systems and associated information's systems supporting the life cycle management approach being adopted by industry and some regulators. The enhancement of Eudranet to provide work spaces for collaboration in assessment and other communication systems such as tele- and video-conferencing is key to the success of the MRP and DCP.
62. The legal position of the EMEA as the co-ordinator of European databases is clear but the partnership arrangement which underpins it needs to be re-evaluated. Much of the data, which supports the EU system, is collected and fed into the system by the NCAs. As such there are legal issues (data protection and intellectual property issues) which need to be resolved. The resourcing of such systems, too, presents some difficulties. The NCAs may need to consider adding some of their own resource to that provided by the EU if the enhancements which are needed to the system are to be made in time for them to be effective. The long term interoperability of the whole EU telematics system also needs to be considered further. The Telematics Strategy may need to be updated in the light of legislative changes to be introduced and the additional demands being placed on the IT infrastructure of the Network
63. Due account should be taken by HMA of initiatives such as the Joint Technology Initiative on Innovative Medicines and the European Technology Platform on Global Animal Health, both established by the European Commission. The overall objective of the projects are to remove bottlenecks hampering the efficiency of the

development of new medicines, and where research is the key to resolve current obstacles for the European pharma/biotechnology industry to become world leaders. Industry together with relevant stakeholders (such as EMEA, national regulatory agencies, patient organisations, healthcare providers, healthcare policy makers, payers/insurers, SMEs, academia and member states), is developing a strategic research agenda identifying critical scientific gaps in which more pre-competitive research is urgently required. Such a platform at EU level should ensure the maximum utilization of resources and is expected to provide socio-economic benefits for the European citizens and animal owners (e.g. improved access to better medicines), as well as contributing to the increased competitiveness of European pharma/biotech industry at large.

#### Access to and distribution of Medicines

64. Many of the issues identified above have a direct bearing on the availability of medicines for human and animal use. Although supply chain issues are not fundamentally regulatory issues, actions taken by the regulator can have an impact on the availability of medicines. In particular, availability of both human and veterinary essential medicines in smaller markets has become more of a problem as regulatory requirements are increasing. Different solutions at legislative level might need to be looked at. It might be investigated if accelerated approval at national level is a way of dealing with this issue. Public research, development and incentives should be investigated as well.
65. Any regulatory action, from delay in the license issue, safety action or variation of a product already being marketed or a suspension of the manufacture or distribution of the product at the regulator's request, can have an impact on access to a particular medicine. Many of the measures suggested above – from better communication at the application stage through to improving patient information, will mitigate against a delay being introduced unnecessarily by the NCAs. There is an additional dimension as concern grows about the availability of products designed to limit the spread of, or treat pandemic flu, deal with bioterrorist attack, incursion of an exotic animal disease into the EU or some other form of emergency. The beginnings of action are being seen here at European level – the EMEA has been active in this field and HMA is also considering its own role.
66. The changes within the pharmaceutical industry, most notably, the move of manufacture outside the European Union are also a key factor. There is also an obvious extension of the supply chain. This has a public health impact as there may be more chances for the guidelines on Good Distribution Practice to be breached. Particular emphasis should be given to areas that can be seen as posing specific risks to the overall network: ensuring the availability of adequate resources for GXP and pharmacovigilance inspections, dealing with negative inspection outcomes in a timely and coordinated way when multiple products and multiple competent authorities are involved and improving the distribution networks and implementation of GDP requirements to improve control and help combat counterfeits. Third country inspections are resource intensive and more sharing of information on these inspections with other NCAs, WHO, MRA partners, PIC/S, EDQM and others might rationalise the use of scarce resource. Within the borders of EEA, securing a safe distribution process relies both on NCAs and other competent public-health authorities and on wholesalers and pharmacists, whose professionalism and vigilance can greatly contribute to safeguard the reliability and credibility of the distribution chains.

67. It is perhaps in the field of animal health that there is the most obvious supply issue. Although it is impossible to ensure that there are medicines for all species and all indications, there is a need to ensure that there is a database of products available and up to date information on them. Changes mentioned elsewhere in this paper, such as improvements in time frames, training and better approaches to communication and risk-assessment/management between regulatory authorities should ensure that the regulator does not impose an unnecessary obstruction on the entry of products onto the market. However, veterinary NCAs could go further in their collaboration to ensure that there are synergies and duplication of work between NCAs is avoided. NCAs should ensure a harmonised approach to the pre- and post authorisation controls placed on veterinary products. More collaboration between NCAs responsible for human medicines and NCAs responsible for veterinary medicines should also be encouraged. The HMA has addressed availability of veterinary medicines by adopting a report on the matter in February 2007 – the report can be found at the HMA website <http://www.hma.eu/204.html#c1197>.

The problem of supply of veterinary medicines persistent within the whole EEA is even more evident in small markets where also a question of availability of medicinal products for human use is present. Member states with small markets face problems of availability of human medicinal products, especially with products of low volume, low price and specialised products intended to treat severe and/or rare diseases. Finding solutions for patients' needs should be the ultimate priority. Namely the existing legal framework is not adequate to face such problems. It is mostly intended to face specific drug shortage, specific threats or patient specific needs. Lack of a significant assortment of medicinal products shall also be dealt with effectively.

## **Chapter 6: Introduction to the Work Plan**

68. The Work Plan which follows is based on the position put forward in this paper. It is constructed along the same lines as chapter 5 of the paper and the recommendations are divided into 5 themes: Public and Animal Health Protection; Patient Safety; The Operation of the Current System; Supporting Innovation; Distribution and Supply of Medicines. The recommendations are strategic in nature and concerned with enhancing the function of the Network as a whole.
69. Being concerned with strategy rather than the operation of a specific part of the network, regime or procedure within it, the Work Plan does not contain all of the detailed arguments which are put forward. Relevant HMA working groups have been identified and timelines set for each proposed area of action. Regular follow up of implementation should be ensured at HMA meetings.

## **Chapter 7: Conclusion and next steps.**

70. While the commitment has been given that this will be a largely resource neutral exercise, implementing the Work Plan should be seen as a re-allocation or a short term investment of additional resource in many cases. The Work Plan and this paper have been updated to reflect the views of stakeholders, the HMA and the ever changing environment in which we operate.

## The Heads of Medicines Agencies Strategy Paper

### HMA Strategy Paper Work Plan

Revision February 2007

The HMA Strategy Implementation Group (SIG) undertook the task of analysing the recommendations for action by the Network in the HMA Strategy Paper Work Plan, in line with the mandate given by HMA. The revised HMA Strategy Paper Work Plan that resulted from this work was adopted by HMA on 8 February 2007 during the meeting they held in Dresden.

Cooperation of the members of the Network in terms of visibility, information and work sharing, learning of best practice from one another and harmonisation of the interpretation of European legislation are at the heart of the work plan, with a view to improving the operation of the Network and the quality of its regulatory activity making the best possible use of available resources.

HMA-relevant working groups were identified for each action involving working groups with HMA mandate and European Working Groups that include guidance for medicinal products under the remit of MRP/DCP.

The creation of two new groups is proposed (the HMA National Communication Professionals and the HMA Training Project Team). Implementation timelines for actions range between Q1-2007 and Q2-2008.

HMA acknowledges that actions on some important areas such as the implementation of the clinical trials directive, distribution activity, and some specific aspects of innovation are not sufficiently addressed by the work plan and should be included in future updates.

No	Recommendation	Groups involved	Timeline
1	HMA should be more involved in the operation of the scientific/regulatory European groups with responsibilities for both national and European issues (e.g. CMDs, Ad hoc Inspectors Groups, PhVWP) as well as groups directly reporting to HMA. It should receive regular updates from relevant bodies that include national medicinal products/activities within their remit, so it can keep abreast of developments and reinforce decision making. The mandates of relevant working groups should explicitly include the reporting procedure to HMA.	HMA-MG/PS, HMA-relevant WG	Q2-2007
2	HMA should ask CMD(h) and CMD(v) to consider the optimum ways of ensuring that high quality	HMA-MG/PS, CMDs	Q2-2007

	robust assessment and European consensus are maintained in MRP and DCP with the view to promoting adequate functioning of the system, including overall satisfactory involvement of NCAs.		
3	In addition to mechanisms already set out in the legislation, HMA and EMEA should consider ways of strengthening cooperation between NCAs in the pre-submission phase and once a procedure has started. A report should be prepared for consideration by the HMA.	NCAs, EMEA, CMDs	Q2-2008
4	HMA should get regular feedback and closely monitor progress in the implementation of the recommendations set by the HMA Strategy Paper in the field of pharmacovigilance in both human and veterinary sectors, based on the close cooperation between NCAs and EMEA.	ERMS FG, PhVWP, ESS Group, HMA-PS	Q2-2007
5	A veterinary group should be established which will survey the resource available to veterinary pharmacovigilance and address potential weaknesses in the system. It should learn from the experience of the ERMS FG.	HMA(v)	Completed
6	Enforcement issues (e.g. in the areas of clinical trials fraud, counterfeiting and internet sales of prescription only medicines) should be given a higher profile at HMA level, operating through and with the Enforcement Officers network and in consultation with the EMEA-AHIG and with the OMCLs. There should be regular reporting to HMA by relevant groups.	NCAs, EMEA-AHIG, EDQM, HMA-MG/PS, HMA-WGEO	Q1-2007
7	CMD(h) and CMD(v) should be asked to consider how, within the current legal framework, steps can be taken at European level to ensure that the quality of the SPC, leaflet and label all meet a high quality standard and are useful and relevant to patients, carers, animal owners and food producers and Health Care Professionals/veterinary surgeons, taking into account the work done by the QRD group in cooperation with CMDs. There should be a report back to HMA.	CMDs, EMEA-QRD, HMA-PS	Q1-2007
8	A procedure must be established to ensure that there are common outcomes in the application of the legal requirement to produce National Public Assessment Reports, even if the approach is different from one NCA to another.	NCAs, CMDs, HMA-PS	Q1-2008
9	HMA must formally recognise the Communications Group which has met informally under the Dutch presidency and ask it to consider and implement the solutions paper prepared by the Communications and Information Drafting Group.	NCAs, HMA-MG, EMEA	Q1-2007
10	The vision and mission of the HMA is to be re-assessed and given greater publicity to ensure it is seen as a viable and effective body within the Network	HMA-SIG, HMA-WGV, HMA-MG	Q2-2007
11	Arrangements in place for, and the functions of, the HMA website should be reviewed. This should be a gateway to information about the HMA role, the network itself and medicinal products available.	HMA-WGV, (BfArM, ANMV)	Q1-2007
12	A project team should be established to consider in greater detail the proposals made by the Drafting	HMA-MG, NCAs, EMEA	Q2-2007

	Groups for enhancing cooperation on the training of NCA staff, taking account of the EU Competence Development Strategy outlined in EMEA's Roadmap. This includes the possibility of establishing a European assessors' academy.		
13	The BEMA SG should be asked to ensure that its Report into the 1st Benchmarking Cycle provides an analysis of best practice in key areas across the Network, so that the aim of the benchmarking exercise, i.e. raising performance levels and learning from one another, can be met.	BEMA SG, HMA-MG/PS	Completed
14	Sharing experience through specific benchmarking activities on particular topics, complementary to BEMA, should be considered as a way to promote best practice within the Network and its working groups, e.g. sharing of information on outcomes of laboratories of control activity through OMCLs, on experience gained through twinning projects, on Joint Audit Programme (JAP) of GMP inspectors activity, etc.	NCA's, EMEA, EDQM, HMA-PS	Q1-2008
15	Subject to legal requirements and operational concerns, efforts to implement work sharing across the operational areas of medicines regulation in the veterinary and human sectors should be encouraged.	HMA-relevant WG, EMEA, HMA-MG/PS	Q1-2007
16	The link between evaluation, inspection and laboratory controls must be reinforced. Scoping exercises and recommendations should be carried out.	NCA's, HMA-relevant WG, EMEA, EDQM	Q4-2007
17	HMA should ensure that there are sufficient skills in place across the Network to deal with new technologies. A survey of resource, horizon scanning, establishment of learning sets and a timetable for the production of guidelines and standards could be considered, taking into account the work already undertaken by EMEA and in association with the Commission.	HMA-Training-PT, HMA-Resource Planning WG, NCA's, EMEA, EDQM, EC	Q2-2008
18	The EU telematics strategy should be reviewed, to ensure that the strategy continues to meet the wider needs of the Network, supporting more collaborative working and fostering innovation.	HMA Tandem Support WG, EMEA, EC	Q2-2007

## Glossary

ACRONYM	DESCRIPTION
<b>AHIG</b>	Ad Hoc Inspectors Groups (equivalent to Inspectors Services Groups)
<b>ANMV</b>	Agence Nationale du Médicament Vétérinaire
<b>BEMA</b>	Benchmarking of Medicines Agencies
<b>BfArM</b>	Bundesinstitut für Arzneimittel und Medizinprodukte
<b>CMD(h)</b>	Coordination Group for Mutual-Recognition and Decentralised Procedure (human products)

<b>CMD(v)</b>	Coordination Group for Mutual-Recognition and Decentralised Procedure (veterinary products)
<b>CMDs</b>	Coordination Groups for Mutual-Recognition and Decentralised Procedure
<b>DCP</b>	Decentralised Procedure
<b>EC</b>	European Commission
<b>EDQM</b>	European Directorate for the Quality of Medicines
<b>EMEA</b>	European Medicines Agency
<b>EMEO</b>	European Medicines Enforcement Officers
<b>EO</b>	Enforcement Officers
<b>ERMS</b>	European Risk Management System
<b>ESS</b>	European Surveillance Strategy
<b>EU</b>	European Union
<b>FG</b>	Facilitation Group
<b>GMP</b>	Good Manufacturing Practice
<b>HMA</b>	Heads of Medicines Agencies
<b>HMA(h)</b>	Heads of Medicines Agencies (human sector)
<b>HMA(v)</b>	Heads of Medicines Agencies (veterinary sector)
<b>MG</b>	Management Group
<b>MRP</b>	Mutual Recognition Procedure
<b>NCAs</b>	National Competent Authorities
<b>OMCLs</b>	Official Medicines Control Laboratories
<b>PhVWP</b>	Pharmacovigilance Working Party
<b>PS</b>	Permanent Secretariat
<b>PT</b>	Project Team
<b>QRD</b>	Quality Review of Documents
<b>SG</b>	Steering Group
<b>SIG</b>	Strategy Implementation Group
<b>WG</b>	Working Group
<b>WGV</b>	Working Group on Visibility