



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Road map to 2015

The European Medicines Agency's
contribution to science, medicines and
health

Adopted by the Agency's Management Board on 16 December 2010



The mission of the European Medicines Agency is to foster scientific excellence in the evaluation and supervision of medicines, for the benefit of public and animal health.

Legal role

The European Medicines Agency is the European Union body responsible for coordinating the existing scientific resources put at its disposal by Member States for the evaluation, supervision and pharmacovigilance of medicinal products.

The Agency provides the Member States and the institutions of the EU the best-possible scientific advice on any question relating to the evaluation of the quality, safety and efficacy of medicinal products for human or veterinary use referred to it in accordance with the provisions of EU legislation relating to medicinal products.

Principal activities

Working with the Member States and the European Commission as partners in a European medicines network, the European Medicines Agency:

- provides independent, science-based recommendations on the quality, safety and efficacy of medicines, and on more general issues relevant to public and animal health that involve medicines;
- applies efficient and transparent evaluation procedures to help bring new medicines to the market by means of a single, EU-wide marketing authorisation granted by the European Commission;
- implements measures for continuously supervising the quality, safety and efficacy of authorised medicines to ensure that their benefits outweigh their risks;
- provides scientific advice and incentives to stimulate the development and improve the availability of innovative new medicines;
- recommends safe limits for residues of veterinary medicines used in food-producing animals, for the establishment of maximum residue limits by the European Commission;

- involves representatives of patients, healthcare professionals and other stakeholders in its work, to facilitate dialogue on issues of common interest;
- publishes impartial and comprehensible information about medicines and their use;
- develops best practice for medicines evaluation and supervision in Europe, and contributes alongside the Member States and the European Commission to the harmonisation of regulatory standards at the international level.

Guiding principles

- We are strongly committed to public and animal health.
- We make independent recommendations based on scientific evidence, using state-of-the-art knowledge and expertise in our field.
- We support research and innovation to stimulate the development of better medicines.
- We value the contribution of our partners and stakeholders to our work.
- We assure continual improvement of our processes and procedures, in accordance with recognised quality standards.
- We adhere to high standards of professional and personal integrity.
- We communicate in an open, transparent manner with all of our partners, stakeholders and colleagues.
- We promote the well-being, motivation and ongoing professional development of every member of the Agency.

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1. Executive summary

This road map sets out a strategic vision for the operation of the European Medicines Agency (hereinafter 'the Agency') over the five-year period from 2011 to 2015.

It has been drafted in consultation with the Agency's European partner organisations and with the public, to ensure as broad a consensus as possible on the best approach to the Agency's fulfilment of its public mandate to protect and promote public health¹ in the European Union (EU) over the coming years.

After a brief overview of the main European and international factors that characterise the evolving operational environment of the Agency, the document sets out in some detail the key drivers for progress and change to which the Agency is subject, namely the needs to:

- ensure **efficient operation of its core business**, which is of critical importance to the continuing success of the Agency in the face of the increasing scope and complexity of its responsibilities under EU legislation;
- address **public-health needs**, through measures that include: promoting the availability of medicines for rare diseases, unmet medical needs and paediatric use; promoting the rational and better-targeted use of medicines to reduce morbidity and mortality; investigating the impact on public health of decisions taken by regulators; facilitating the availability of veterinary medicines; promoting closer coordination of activities in human and veterinary areas;
- further develop the regulatory framework for **new and emerging science**, in particular with respect to benefit/risk evaluation, potential safety issues, and ethical and environmental considerations;
- address the **impact of globalisation** in the pharmaceuticals sector, characterised by: the increasingly global nature of research, development, manufacturing and clinical-trial activities; challenges relating to the movement of clinical research to developing countries, to ethical standards and to regulatory and supervision arrangements in non-EU countries; the attendant need for closer and more intense cooperation between international partners;
- continue to review the **model for regulation of medicines** in the EU, particularly with regard to: the development of medicines; the benefit/risk balance; the point of decision-making for authorisation; post-authorisation follow-up; the growing importance of health technology assessment bodies; specific considerations relating to herbal medicines; a possible reconsideration of the extent to which legislation governing veterinary medicines is tailored to the specific requirements of this sector;
- ensure **patient/consumer and animal-health protection**, with particular emphasis on: progressing the implementation of initiatives within the framework of the European Risk Management Strategy and the European Surveillance Strategy; implementing the new pharmacovigilance legislation to address increased public demands for more refined pharmacovigilance tools and better communication on the benefits and risks of medicines; supporting the European Commission's development of a legislative framework that is more appropriate to the needs of modern veterinary medicine;
- meet **public demands for greater transparency and openness** with respect to the Agency's activities, its decision-making processes and the ready availability of up-to-date information on medicinal products, adverse drug reactions and clinical trials.

¹ Throughout this document, the term 'public health' is used to refer to both human and animal health, unless otherwise stated.

To address these drivers for progress and change, the Agency's first priority over the next five years will continue to be the successful delivery of its core business. In addition, the Agency has identified three strategic areas within which it will focus its efforts in the years ahead:

- **Addressing public-health needs,** by pursuing the following objectives:
 - stimulate medicines development in areas of unmet medical needs, neglected diseases and rare diseases, and for all types of medicines for veterinary use;
 - facilitate new approaches to medicines development;
 - apply a more proactive approach to public-health threats where medicines are implicated.
- **Facilitating access to medicines,** by pursuing the following objectives:
 - address the high attrition rate during the medicines-development process;
 - reinforce the benefit/risk-balance assessment model;
 - continue to improve the quality and the regulatory and scientific consistency of the outcome of the scientific review.
- **Optimising the safe and rational use of medicines,** by pursuing the following objectives:
 - strengthen the evidence base in the post-authorisation phase to enable better regulatory decision-making;
 - enhance patient safety by avoiding unnecessary risks to patients as a result of the use of medicines;
 - become a reference point for information on medicines evaluated by the Agency;
 - improve the decision-making process by taking due account of patient experience, thus contributing to the rational use of medicines.

Specific indicators of the expected impact/result of each of the activities in these strategic areas are identified in the body of this road map, while a separate 'From vision to reality' document (to be published in the course of 2011) will set out detailed information on the Agency's planned implementation of these activities.

The success of the Agency in implementing the vision set out in this road map will be contingent upon the availability of the necessary resources, as well as upon the continuing support and cooperation of the Agency's partners in the EU regulatory network.

2. Introduction

In 2005, the European Medicines Agency developed a longer-term strategy² to guide its proactive approach to the continuing evolution of the pharmaceutical arena in the European Union (EU). This strategy focused mainly on contributing to better promotion and protection of public health, improving the regulatory environment for medicinal products, and helping to stimulate innovation, research and development in the EU.

The Agency's 'Road map to 2015' is a continuation of this longer-term strategy, building on current achievements, but also taking due account of the changing environment in which the Agency will have to operate over the next five years. In further developing its road map project, the Agency will ensure that its vision is consistent with and complementary to strategic directions provided by the European Commission^{3,4,5,6}, the Council of the European Union⁷ and the Heads of Medicines Agencies⁸.

The 'Road map to 2015' sets out the Agency's vision, elaborates on the main drivers for progress and change that will impact on it, and explores the main initiatives to be undertaken to successfully meet the challenges it will face. This vision encompasses the Agency's strategy for both medicines for human and veterinary use, in line with the joint responsibility of the Agency⁹. It should be noted that the successful delivery of the Agency's vision

is dependent on the availability of the necessary resources. Detailed information on the implementation of the road map will be provided in the document 'From vision to reality', to be published shortly.

Striving for as broad a consensus as possible on the best way forward, the Agency discussed the 'Road map to 2015' with its partners and stakeholders. Following public consultation in 2010, which included face-to-face discussions, and subsequent consideration of the comments received, this revised version of the road map was adopted by the Agency's Management Board at its 16 December 2010 meeting, and subsequently made public.

2 The European Medicines Agency Road Map to 2010: Preparing the Ground for the Future (EMA/H/34163/03/Final).

3 European Commission's Better Regulation strategy (see [Better Regulation website](#)).

4 Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions – Safe, Innovative and Accessible Medicines: a Renewed Vision for the Pharmaceutical Sector (COM(2008) 666 final).

5 [Future Challenges Paper: 2009-2014](#), European Commission Health & Consumer Protection Directorate-General.

6 Communication from the Commission to the European Parliament and the Council: European agencies – The way forward (COM(2008) 135 final).

7 Draft Council Conclusions on Innovation and Solidarity in Pharmaceuticals (16586/1/10).

8 [A Strategy for the Heads of Medicines Agencies, 2011-2015](#).

9 An explicit reference to either sector will only be made where necessary.

3. Setting the scene: the Agency and its environment

3.1. The European Medicines Agency as a public-health agency

The mission of the Agency is to foster scientific excellence in the evaluation and supervision of medicines, for the benefit of public health. This is fully in line with the Agency's legal role and responsibilities to provide the EU institutions and Member States the best-possible scientific advice on any question relating to the evaluation of the quality, safety and efficacy of medicinal products referred to it in accordance with the EU legal provisions. The Agency's sphere of responsibilities has gradually expanded over time, in line with new EU legislation, most recently in the fields of paediatric and advanced-therapy medicinal products. Furthermore, new legislation is under way (e.g. in the fields of falsified medicines and pharmacovigilance) that will further increase the Agency's (coordinating) role in the pharmaceutical arena. As a result, the Agency's involvement in public health (within the context of the authorisation and supervision of medicinal products) has further increased and will continue to do so, thereby establishing the Agency as an important guardian of public health in the EU.

3.2. Collaboration with the Agency's partners

3.2.1. Operating within the EU regulatory network

A critical factor for the Agency's success has been the provision by the Member States of high-quality scientific resources for the evaluation and supervision of medicinal products. This provision of resources, coordinated by the Agency, is one of the features of the EU regulatory network – a concept that is unique in the world. Another feature of this network is the platform provided by the Agency for the coordination of activities at EU level (e.g. in the field of mutual recognition and decentralised medicines, and certain aspects relating to clinical trials). In its 'Road map to 2010', the Agency emphasised the need to strengthen the partnership between all EU regulatory authorities, leading to the establishment of a network of excellence at EU level. Further reinforcing this partnership will continue to be pivotal for the Agency.

When considering the Agency's environment, its partnership with other EU bodies (i.e. the European Commission and EU agencies) also needs to be taken into account, as does its collaboration with specific European bodies involved in medicines regulation, such as the European Directorate for the Quality of Medicines and HealthCare (EDQM) and the Official Medicines Control Laboratories (OMCL) network. The Agency's interaction with other EU public-health agencies in particular, such as the European Food Safety Agency (EFSA) and the European Centre for Disease Prevention and Control (ECDC), has expanded over time. Collaboration with the European Commission increasingly focuses on a deepening of the interaction in the fields of research-related work and emerging diseases.

3.2.2. Positioning the Agency on the international scene

International cooperation nowadays builds on long-established interaction in fora such as the International Conference on Harmonisation ((V)ICH), the Codex Alimentarius and the World Organisation for Animal Health (OIE), as well as collaboration with the World Health Organization (WHO) and involvement in more recent projects such as the Transatlantic Administrative Simplification initiative. Other important international activities in the pharmaceutical sphere are the mutual-recognition agreements (MRAs) and similar agreements. Further and important progress in the international field has been made through confidentiality arrangements concluded with the U.S., Japanese, Canadian and Australian health authorities. New developments relate to the interaction with standards-development organisations in the framework of the development of international standards for the definition of data structures, as well as the development of controlled and internationally agreed terminologies defining valid entries.

The coming years will see intensified efforts to further expand international cooperation, in line with the Agency's international strategy. This strategy will elaborate on the creation of synergies through collaboration, cooperation and communication with international regulatory partners, with a view towards supporting in the long term a global approach to the authorisation and supervision of medicines.

3.3. Interaction with the Agency's stakeholders

One of the key features of the Agency's interaction with stakeholders since its establishment has been dialogue with the pharmaceutical industry. While this dialogue initially focused on the innovative-medicines industry, there has over recent years been further diversification, with increasing involvement of the generics and non-prescription-medicines industries.

An element of growing importance is the involvement and participation of civil-society representatives (patients/consumers/users of medicines and healthcare professionals) in the Agency's activities, either as experts in a particular (therapeutic) field or as individuals representing their respective association. Their membership of the Management Board and some scientific committees, as well as their involvement in other parts of the Agency's work, has led to the development of specific frameworks for interaction.

Recognising the added value of patients and consumers in benefit/risk considerations – in that they enrich regulatory decisions by complementing them with the views of those directly affected by regulatory decisions – the debate currently focuses on how to achieve more structured involvement of patients in the Agency's work. Likewise, discussions are ongoing in both the human and veterinary areas on how to better engage healthcare professionals in the Agency's activities. Another trend is the increasing contribution by academia and learned societies to the Agency's work, which supports the development of regulatory science¹⁰.

Furthermore, as the scope of the Agency's role and responsibilities increases, the range of its stakeholders will extend to additional branches of the pharmaceutical sector, such as the distribution chain and the field of medical devices and diagnostics.

¹⁰ Regulatory science is defined as a range of scientific disciplines that are applied to the quality, safety and efficacy assessment of medicinal products and that inform regulatory decision-making throughout the lifecycle of a medicine. It encompasses basic and applied medicinal science and social sciences, and contributes to the development of regulatory standards and tools.

4. The Agency's drivers for progress and change

The following business drivers are shaping the future tasks of the Agency and the environment in which it operates.

4.1. Efficient operation of the Agency's core business

The main focus for the Agency over the coming years will continue to be the operation of its core business¹¹, in line with the tasks described in current and upcoming EU legislation. The Agency's roles and responsibilities have further expanded since the drafting of the 'Road map to 2010', and now cover a wide range of activities. The European Commission's impact assessments of new legislative provisions in the areas of falsified medicines and pharmacovigilance have indicated that the consequences will be very important for the EU regulatory network – and for the Agency in particular, given its coordinating role.

Efficiency will, therefore, be even more key to the successful operation of the Agency's core business. An important consequence of the growing area of responsibilities is that the Agency's tasks have become much more complex. The Agency currently comprises six scientific committees and some 35 working parties and other (scientific) fora, to which it provides scientific support. A particular challenge in this area relates to the interactions and interdependencies that exist at various levels between these fora.

4.2. Addressing public-health needs

As highlighted in the European Commission's white paper¹², there are several challenges to public health that require a new strategic approach. These cover demographic changes (including population ageing), emerging public-health threats, antimicrobial resistance, climate change (particularly in view of the emergence of new diseases) and the rapid development of new technologies (including e-health),

which will heavily impact on existing healthcare systems. An aspect that will remain high on the public-health agenda relates to the availability of medicines for rare diseases and other current unmet medical needs, such as medicines for the paediatric population. Rational and better-targeted use of medicines has been identified years ago as an important factor in reducing morbidity and mortality. Another aspect that requires careful consideration is the need to investigate the impact on public health of decisions taken by regulatory authorities, and to subsequently introduce the necessary remedial actions.

In the area of animal health, the European Commission will be implementing during the period covered by this road map the revised Community Animal Health Strategy (CAHS)¹³. The Agency is a key partner in terms of facilitating the availability of medicines for veterinary use that will be needed to deliver parts of this strategy.

The Agency's contribution to the CAHS needs to be seen within the 'One World, One Health' concept¹⁴, whereby promotion of health in animals promotes health in humans. Being an Agency with responsibility for medicines for both man and animals, it is well placed to promote closer coordination between activities in the human and veterinary areas, bringing together relevant expertise to pursue shared objectives.

4.3. New and emerging science

While new and emerging science (such as personalised medicine, nanotechnologies, novel-novel drug development, regenerative medicine and synthetic biology¹⁵, as well as advances to streamline non-clinical and clinical development) is becoming increasingly established as part of the new wave of medicines development, providing new ways to address current unmet medical needs, there are still aspects of this field that require careful consideration, primarily

11 Core business is defined as the Agency's involvement in the authorisation and supervision of medicinal products for human and veterinary use, in accordance with EU legislative provisions, including the processes supporting these tasks.

12 White Paper – Together for Health: A Strategic Approach for the EU 2008-2013 (COM(2007) 630 final).

13 Animal Health Strategy for the EU (2007-2013): 'Prevention is Better than Cure' (ISBN 978-92-79-06722-8).

14 'One World, One Health' website.

15 Synthetic biology refers to two main activities: the design and construction of new biologically based parts, novel devices and systems, and the redesign of existing, natural biological systems for useful purposes.

the appropriateness of the current legal/regulatory framework, in particular with respect to the benefit/risk evaluation and the development of tools for the anticipation of potential safety issues. There is thus a need for debate on how best to support and translate the new science into regulatory requirements. Further thought will also have to be given to aspects such as ethical and environmental considerations. Such important scientific progress will require regulators to be attuned to the new technologies in both human and veterinary fields, and to learn from research and experience in other industry sectors.

In addition, the Agency is likely to be confronted within the next few years with challenges stemming from a reappraisal of the device legislation in the EU and, in particular, activities focusing on the interaction between medical devices/diagnostics and medicinal products. Interaction between the sectors of medicinal products, medical devices and diagnostics should be facilitated to nurture a synergistic approach.

4.4. The impact of increasing globalisation

The importance of globalisation has increased over time and will continue to do so. One of the main drivers is the global nature of medicines development and research. Manufacturing and clinical-trial activities will continue to see an increased international focus over the coming years. The movement of clinical research to developing countries presents particular challenges, such as safeguarding the integrity of the data, ensuring equivalent ethical standards are met, the threat of double standards, and the need to have confidence in local regulatory and supervision arrangements. Another field of growing concern relates to the increasing manufacture of active pharmaceutical ingredients (APIs) outside the EU, and in particular the potential for substandard material to enter the supply chain.

In the area of regulation of medicines for veterinary use, the impact of globalisation will also become increasingly noticeable in terms of closer and more intense cooperation with international partners. During the next five years, particular efforts will be needed to develop, with the OIE, an appropriate approach to extending the influence and uptake of VICH guidelines beyond the existing member and observer countries. Also, in light of the recently revised EU legislation governing maximum residue limits (MRLs), closer cooperation will be required with international partners,

particularly Codex Alimentarius, in setting acceptable limits for residues of veterinary medicines in animal foodstuffs, and in risk-assessment methodologies. An increased focus on international cooperation recognises the fact that EU consumers are only really protected from risks related to products of animal origin when the same standards are applied, irrespective of whether animals are reared in the EU or elsewhere.

4.5. The model for regulation of medicines

The model for regulation of medicines is a complex concept, encompassing elements such as the requirements for medicines development, the benefit/risk balance, the point of decision-making for granting a marketing authorisation, and post-authorisation follow-up. Added complexity comes from a split of activities undertaken at national level (clinical-trial responsibility, scientific-advice handling, etc.) and at EU level (equally scientific-advice handling, assessment of paediatric investigation plans, etc.). Over the past few years, there have been several developments in each of the areas cited above that de facto mean that the current model for medicines regulation is being reviewed. A recent development in the pharmaceutical arena is the growing importance of health technology assessment (HTA) bodies on the access to market of novel medicines, due largely to increased pressure on healthcare budgets. Of particular note in this respect is the work already undertaken within the framework of the European Network for HTA Joint Action (EUneHTA JA) on the relative effectiveness of pharmaceuticals.

More specific considerations relate to the field of herbal medicinal products, where it needs to be acknowledged that the innovative concept of list entries and monographs has not really been followed up in terms of subsequent marketing-authorisation applications, and that remedial action is therefore necessary. Furthermore, aspects related to borderline issues with nutritional supplements still require resolution.

The past thirty years have seen a gradual convergence of the legislation governing medicines for human and veterinary use, leading to an improvement in the quality of veterinary medicines but also to an overall increase in regulatory requirements and in their complexity. In 2009, the European Commission recognised the need for a review, and launched an impact assessment of the veterinary medicines legislation that covered, among other

issues, whether or not there is a need to reconsider the extent to which the legislation governing veterinary medicines should, in future, be tailored to the specific requirements of this market sector.

4.6. Ensuring patient/consumer and animal-health protection

For several years, the focus within the EU has been directed towards a more proactive approach in ensuring patient safety, while continuing efforts to further improve the spontaneous reporting scheme. This resulted, in 2005, in a number of legislative changes for medicines for human use, introducing new tools such as the novel concept of risk-management plans. In addition, strategic initiatives were launched in the EU within the framework of the European Risk Management Strategy (medicines for human use) and the European Surveillance Strategy (medicines for veterinary use). In both cases, the aim is to achieve high standards of human and animal-health protection with respect to the use of medicines. Work is under way¹⁶ to further progress the implementation of the various initiatives. It needs to be recognised, however, that public opinion over time has become much more risk-averse, resulting in increased demands for more refined pharmacovigilance tools for medicines for human use, as well as better communication on the benefits and risks of medicines. The new pharmacovigilance legislation will provide an appropriate framework to address these demands. Likewise, the European Commission's review of the veterinary medicines legislation provides an opportunity to develop a framework more appropriate to the needs of modern veterinary medicine.

mation available (e.g. information on the opinion/decision-making process for the evaluation and supervision of medicinal products, on adverse drug reactions and on clinical trials).

Efforts will have to be strengthened to make up-to-date medicinal product information readily available. Providing greater transparency will entail specific challenges, such as finding the right balance between making more information and documents available more quickly and protecting commercially confidential information, while also complying with personal-data legislation. More openness of operation and increased transparency should go hand in hand with efficient and targeted communication. This becomes even more important in situations that require a coordinated approach, such as emerging public-health threats.

4.7. Demands for greater transparency and openness

For any public body in the field of medicines regulation, transparency and openness are important factors in its ability to gain, maintain and strengthen the trust of its stakeholders. Demand for information and openness on the Agency's activities will increase over the coming years, so action is needed both in terms of the tools available (for accessing documents and public database information) and the content of infor-

¹⁶ Implementation of the Action Plan to Further Progress the European Risk Management Strategy: Rolling Two-Year Work Programme (EMEA/280089/2007).

5. Addressing the drivers for progress and change

5.1. Current achievements

The 'Road map to 2010' clearly states that its ultimate objective is to ensure that the Agency adequately prepares the ground for further success in the future, building on the achievements of its first 10 years. At regular intervals^{17,18}, the Agency has reported on progress made with the implementation of its 'Road map to 2010'. Overall, the Agency largely succeeded in delivering the planned activities and initiatives and in meeting its 2010 priority objectives of top-quality scientific assessment, timely access to safe and effective medicines, continuous monitoring of medicinal products, access to information, and specific needs for veterinary medicines. Although it can be concluded that the Agency has now successfully prepared the ground for the future, further progress on the 2010 road-map objectives is still needed¹⁹. Where further work remains to be done to complete these objectives, this has been incorporated in the objectives and priorities for the next five years, as outlined in Section 5.2.

In addition, the Agency has been at the forefront in other fields, for instance the development of scientific guidelines for biosimilar and advanced-therapy medicinal products, thus paving the way for access by EU citizens to these new types of medicines. Scientific excellence (as a result of EU-wide pooling of expertise and data) has been a key strength. In this respect, it should be stressed once again that such excellent progress has been highly dependent on close collaboration between the Agency and the national competent authorities within the context of the EU regulatory network, and in particular on the valuable input of high-quality specialist expertise provided by the Member States. Another important enabler has been the Agency's continuing review of the operation of its core business, which has identified efficiency gains and allowed process improvements to be introduced.

5.2. Objectives and priorities for the next five years

5.2.1. Performing the Agency's core tasks

To address the aforementioned business drivers, the Agency's first priority over the next five years will continue to be on the successful delivery of its core business in accordance with current and new EU legislation. While the Agency's tasks have further expanded over the past years in the field of innovative medicines, access to the centralised procedure for both generic/biosimilar and non-prescription medicines has now also become a reality, and in fact constitutes an important part of the Agency's core business activities and thus its workload. It also needs to be acknowledged that the scope of the work to be undertaken in other areas did not significantly increase. This is for instance the case in the field of herbal medicinal products, although the past years have indicated the need for remedial action to address aspects such as adjusting the priority list of herbal substances, preparations and combinations thereof to the needs of the market operators, and to undertake initiatives to facilitate the uptake of the traditional-use registration scheme²⁰.

Since 2005, additional challenges have had to be addressed as a result of new legislation in the fields of paediatric and advanced-therapy medicinal products. This resulted in a marked increase in workload. From 2011 onwards, the Agency will be faced with the implementation of two new pieces of EU legislation in the fields of pharmacovigilance and falsified medicines, which will require careful planning, in collaboration with the Agency's partners and stakeholders, because of the important impact these new provisions will have on the regulatory environment.

Taking into account concerns voiced with respect to the current regulatory framework for medicines for veterinary use, the Agency will work with the European Commission and other partners in the EU regulatory network to analyse the outcome of the Commission's impact assessment and develop firm proposals designed to simplify

17 Status Report on the Implementation of the Road Map (EMA/171321/2006).

18 Second Status Report on the Implementation of the Road Map (EMA/359050/2007).

19 A third and final status report on the implementation of the 'Road map to 2010' will be prepared and published in 2011.

20 Action Plan for Herbal Medicines 2010-2011 (EMA/831327/2009).

the framework for veterinary medicines and ensure it is tailored to the specific requirements of this sector.

Efforts to strengthen the Agency's efficiency will continue in line with the European Commission's Better Regulation strategy, thereby further reducing the administrative burden. Taking into account the need to strive for the most cost-efficient way of operating, the Agency will continue to work on re-engineering and improving the processes supporting its core business. More detailed information on the measures to be taken is provided in the 'From vision to reality' document.

Successful delivery of the Agency's objectives and priorities also requires that operational and organisational aspects be carefully reviewed to verify their adequacy for the years to come. Following the publication of the European Commission's report on its evaluation of the Agency²¹, a conference was held at the Agency on 30 June 2010 to discuss the findings and recommendations made. Several recommendations relate to the complexity of interactions within the Agency's scientific fora and to the Agency's architectural capacity to deal with an ever-increasing workload. Recommendations not requiring legislative changes are addressed in the 'From vision to reality' document.

Acknowledging the Agency's achievements so far, the focus for the next period will also be directed more towards the quality of the outcome of the Agency's work, and in particular on how to increase this quality. It should also be recognised that there will be other developments and challenges in the fields of science, medicines and health that the Agency will have to face, and to which it believes it can provide an important contribution. Pivotal in achieving this aim will be to further strengthen the close collaboration and cooperation with the Agency's partners in the context of the EU regulatory network, building on the excellent progress made over the past years. In addition, in some areas the scientific and technical developments may be so important that they require coordinated consideration and debate by the wider (scientific) community, where relevant at international level, to find the best-possible answers to challenging questions on regulation and science. In these situations, the existing concept of putting in place dedicated discussion fora involving regulatory

authorities, pharmaceutical industry, academia and patients/consumers/users of medicines will be more systematically used, thereby strengthening the role of the Agency in promoting discussions with all of its stakeholders on important regulatory and scientific challenges.

5.2.2. The Agency's strategic areas 2011-2015

To address the business drivers listed in Section 4, the Agency has identified three strategic areas for the future:

- addressing public-health needs;
- facilitating access to medicines;
- optimising the safe and rational use of medicines.

Objectives in the area of addressing public-health needs will include stimulating the development of medicines for unmet medical needs (particularly novel antibiotics), medicines for rare and neglected diseases, and all types of veterinary medicines. Tackling challenges posed by the steady integration of new and emerging science into modern medicine will be a further focus of activities in this strategic area, as will the need to learn from recent public-health threats and further improve preparedness mechanisms for future threats or crises.

The Agency's focus in the area of facilitating access to medicines will be on activities designed to reduce the productivity gap that currently exists in the development of medicines. Activities in this area will include investigating the underlying reasons for the productivity gap, encouraging the use of scientific advice during the development process, and promoting early interaction between regulators and sponsors. The Agency will also explore how regulatory pathways can best align market access of new medicines with the growing knowledge over time of benefits and risks.

In the area of optimising the safe and rational use of medicines, the Agency's focus will be on minimising the risks to public health that are inherent in the 'real-world' use of medicines. Extrapolating the positive benefit/risk balance identified in a clinical-trial setting for a medicine in a given therapeutic indication for a well-defined target population to the real-life use of the medicine should be further explored. Consideration must also be given here to off-label use of medicines, which can result in adverse events that trigger (important) regulatory remedial action. It needs to be acknowledged that the Agency is limited in

²¹ European Commission – Evaluation of the European Medicines Agency – January 2010 – [Final Report](#).

its contribution to addressing this issue, but it has a role to play in raising better awareness at the level of the wider community on the rationale for its opinion/decision-making. Other activities such as improved risk-minimisation tools, post-authorisation follow-up and outcomes research will complete the Agency's initiatives in this area.

For each of the three strategic areas identified, the Agency has set specific objectives that it will target through its activities over the course of the period of this road map, together with impact/result indicators by which the Agency can measure its success in achieving those objectives, as described in detail in the following sections.

Strategic area 1: addressing public-health needs

Objectives ²²	Impact/result indicators
Stimulate medicines development in areas of unmet medical needs, neglected diseases and rare diseases, and for all types of medicines for veterinary use.	<ul style="list-style-type: none"> • Increase in the number of scientific-advice requests for medicines for unmet medical needs, neglected diseases and rare diseases, and for all types of medicines for veterinary use. • Increase in the use of specific procedures such as Article 58 procedures (under Regulation (EC) No 726/2004).
Facilitate new approaches to medicines development.	<ul style="list-style-type: none"> • Existing model for medicines regulation is adapted to enable integration of new and emerging science.
Apply a more proactive approach to public-health threats where medicines are implicated.	<ul style="list-style-type: none"> • Effective preparedness mechanisms that take due account of learnings from previous public-health threats/crisis situations are available. • The 'One World, One Health' concept is applied to link the protection and improvement of animal health with the protection and improvement of human health. • The Committee for Medicinal Products for Veterinary Use (CVMP) Strategy on Antimicrobials 2011-2015²³ is successfully completed.

Gaps in medicines development

An important public-health challenge currently faced is the lack of medicines for unmet medical needs, neglected diseases and rare diseases. One of the most critical areas concerns the limited availability of novel antibiotics for human use, often caused by unfavourable conditions for developing new effective antibiotic agents, and of strategies to limit the development of antimicrobial resistance. In addition to infectious diseases, other fields of concern with regard to gaps in medicines development are rare and neglected diseases, leading in particular to challenges for developing countries.

To address these findings, research should not only focus on the development of new medicines, but equally target known substances (looking for new therapeutic areas or improved ways of administration), thereby benefiting from a well-known safety profile as a result of wide population exposure.

The Agency plans to take the following actions:

- Investigate and analyse, in close collaboration with the pharmaceutical companies concerned, the reasons for discontinuing the development of medicines for human use, starting with selected designated orphan medicines, and propose remedial action. Any solution should favour a holistic approach, including the use of novel endpoints, different study designs and a more appropriate use of the accelerated assessment scheme for medicines intended for unmet medical needs, rare diseases and neglected diseases in the EU and beyond.

²² Only longer-term objectives, with corresponding impact or result indicators, are described in this document. Further information will be provided in the document 'From vision to reality' and the Agency's annual work programmes.

²³ CVMP Strategy on Antimicrobials 2011-2015 (EMA/CVMP/287420/2010).

- Assume a more proactive role in advising the European institutions on any gaps in medicines development, taking into account the Agency's knowledge-base on medicines under development, and on better incentives to stimulate medicines development. This should result in the establishment of a list of prioritised unmet needs, on which the public would be consulted before sending it to the responsible European Commission services. This approach could also be taken for neglected diseases in developing countries, to complement existing initiatives such as Article 58 opinions (under Regulation (EC) No 726/2004). Recent experience with the supply shortage of radiopharmaceuticals²⁴ has indicated that it would be appropriate to also carefully consider the need for the development of new imaging agents.
- Explore how best to contribute towards tackling challenges stemming from demographic changes, in particular population ageing. Taking into account current achievements in this field, the Agency will make additional efforts to ensure that the needs of elderly people are considered in the development and evaluation of new medicines and in the post-authorisation follow-up of already approved medicines.
- Launch initiatives to address the lack of development of antibiotics and the potential threat of antimicrobial resistance arising from the (mis)use of antimicrobials in human and veterinary medicine. Reference is in this respect made to the work performed within the context of the Trans Atlantic Task Force on Antimicrobial Resistance (TATFAR), to which the Agency will contribute, as well as to activities jointly undertaken by the Agency and other EU agencies such as ECDC and EFSA^{25,26}. Initiatives already launched outside the EU (e.g. in the field of tuberculosis) should also be taken into account. Specific

consideration will be given in the veterinary field to clarifying the prospects for developing novel antimicrobials for animals, taking into account the need to retain the efficacy of critically important antimicrobials in human medicine.

- Support the European Commission in implementing the revised CAHS 'Prevention is Better than Cure', by continuing its efforts within the EU regulatory network to promote the availability of medicines for veterinary use that will be needed to deliver the strategy, and those indicated for minor use and minor species in particular. In this context, the Agency will pursue approaches to facilitate authorisation of vaccines against epizootic diseases and assist where possible with bringing novel tools for disease control to market (i.e. those diseases identified as priorities within the European Technology Platform for Global Animal Health's DISCONTTOOLS project).

New and emerging science

Scientific progress over the next five years will be an important driver for change. Building on current experience with advanced therapies (cell therapy, gene therapy and tissue engineering), the Agency will have to address new challenges on the horizon relating to nanotechnologies, novel drug development, synthetic biology, and regenerative and personalised medicine. The concept of personalised medicine is steadily evolving from a theoretical concept into an integral part of modern medicine. The Agency has already been confronted with this concept, primarily in the oncology field. Some centrally authorised products already have personalised (pharmacogenomics) indications in the approved product information. Many different applications of novel nanotechnologies to medicines development are also a reality, but experience is still very limited. In addition, the field of nanotechnology is very diverse. Likewise, only a small number of applications may be seen over the next years for regenerative medicine. For these novel scientific approaches, the scientific/technical and regulatory challenges will be very significant.

The Agency plans the following actions to address these challenges:

- To advise in the field of human medicines, through pooling of specialist expertise, on the necessary adaptation of the regulatory framework to the new technologies. This will complement

24 Workshop Outcome and Recommendations – Current Use and Future Needs of Radiopharmaceuticals Labelled with Radionuclides Produced in Reactors and Possible Alternatives (EMA/150127/2010).

25 ECDC/EMA Joint Technical Report: The bacterial challenge: time to react. A call to narrow the gap between multidrug-resistant bacteria in the EU and development of new antibacterial agents.

26 ECDC/EFSA/EMA/SCENHIR Joint Report on Antimicrobial Resistance (AMR) Focused on Zoonotic Infections.

existing initiatives such as the setting-up of a dedicated biomarker-qualification procedure and the provision of regulatory and scientific support to the Innovative Medicines Initiative (IMI).

- To explore, within the forthcoming review of the legislation governing veterinary medicines, to what extent the requirements of evolving science (stem-cell technology, growth factors and other biologically active molecules, and tissue engineering) can be met within the existing legal framework and to what extent new legislation would be required. While recognising that it is impractical to develop a framework as comprehensive as in the field of advanced therapies for human use, a lack of legislation should not be allowed to be an impediment to the development of novel veterinary medicines, particularly as there is currently great interest in adapting advanced therapies for human use to veterinary applications. The methodology for assessing the safety to consumers of these new technologies and substances when administered to food-producing species will require particular attention.

Public-health threats

The H1N1 influenza pandemic in 2009 underlined the importance of prompt action in response to emerging public-health threats. Putting in place the necessary preparedness mechanisms has proven to be a very complex exercise that involves many aspects, including the availability of a dedicated legal/regulatory framework for the authorisation and supervision of medicines, rapid scientific-assessment processes, and a targeted and coordinated communication strategy. In addition, it requires the Agency to expand its interaction beyond the EU regulatory network in which it operates. Excellent collaboration between all parties in the wider EU public-health environment has been and will continue to be pivotal in addressing this challenge. While experience in this field is growing, with lessons being learned from previous pandemic-like situations and bioterrorism strategies being taken into account, there is also a need to prepare for new communicable-disease patterns caused by climate change and increased, unrestricted travel.

Recent experience with public-health threats such as the H1N1 pandemic, the contamination of rotavirus vaccines, the emergence of bluetongue, the contamination of medicinal products containing or derived from heparin and the shortage of radiopharma-

ceuticals have demonstrated the need for preparedness if regulatory authorities are to be able to cope adequately with public-health threats/crises. This requires the availability of dedicated processes and systems, as well as efficient coordination not only across the EU regulatory network, but also with non-EU regulators and with the pharmaceutical industry. Although each of these emerging situations has its own characteristics, they often have three elements in common: the complexity of the problem (including communication aspects), the global dimension and the need to find a solution quickly.

Another area of major concern is the growing threat of substandard active substances and falsified medicines. While the development of specific EU legislation is under way in these fields, the issue will remain high on the political agenda until implementation of the new legislative proposals.

Several public-health threats require the application of the 'One World, One Health' concept to be effectively addressed, whereby promoting health in man is linked with promoting health in animals. Antimicrobial resistance is one such threat that requires a coordinated approach, in terms of minimising the potential for resistance to arise from the use of antimicrobial agents in both man and animals. From the veterinary perspective, this approach is recognised within the CAHS and the CVMP Strategy on Antimicrobials.

Planned actions:

- Acknowledging that it will never be possible to have a 'one size fits all' response, the Agency will investigate – on the basis of accumulated experience, and in close collaboration with its partners and stakeholders – whether its preparedness mechanisms should be revised.
- The Agency will conduct, in collaboration with its partners and relevant stakeholders, a 'lessons learned' exercise after each major event, to further improve existing preparedness mechanisms.
- The Agency will foster the implementation of the actions proposed within both the CVMP Strategy on Antimicrobials and the CAHS, in terms of continuing and enhancing its interactions with all relevant stakeholders, as well as with the European Commission, the Codex Alimentarius and OIE, to promote prudent use of veterinary antimicrobials.

Strategic area 2: facilitating access to medicines

Objectives	Impact/result indicators
Address the high attrition rate during the medicines-development process.	<ul style="list-style-type: none"> • Increase in the percentage of successful marketing-authorisation applications for new medicinal products by encouraging that scientific advice is sought and adhered to. • Scientific information on failed medicines-development processes is made available to the scientific community.
Reinforce the benefit/risk-balance assessment model.	<ul style="list-style-type: none"> • Increased inclusion of quantitative elements, alongside an improved elaboration of the rationale for the decision/opinion in the benefit/risk considerations, for subsequent publication in the European public assessment reports (EPARs) (medicines for human use). • The concept and practice of benefit/risk assessment are embedded as part of the scientific-review process and subsequently communicated in EPARs as part of the methodology used for assessment (medicines for veterinary use).
Continue to improve the quality and the regulatory and scientific consistency of the outcome of the scientific review.	<ul style="list-style-type: none"> • Structured external surveys performed by the Agency's stakeholders on the outcome of the scientific reviews demonstrate an increase in the quality and the consistency.

Medicines-development process, early assessment and continuing dialogue

Despite the increase in research efforts in previous years, the pharmaceutical sector is confronted with the widely recognised phenomenon of the medicines-development productivity gap. Feedback has indicated that both the suboptimal management of the medicines-development process by sponsors in some instances and new requirements for medicines development have been identified as important contributing factors. In order to address the high attrition rate during the medicines-development process and the increasing productivity gap, the Agency is of the view that a number of initiatives could be undertaken to improve the situation:

- Although the concept of preparing guidelines on medicines development in the fields of both human and veterinary medicines has been in place for several years, it would seem timely to strengthen the involvement of stakeholders (and in particular pharmaceutical industry, academia/learned societies and patients' organisations) in this process, for instance by organising workshops at a very early stage of guideline development, so that stakeholders can actively contribute towards developing guidelines of the highest quality in medical, regulatory and scientific thinking. This would be beneficial both in areas that require further guideline development and in fields where existing guidance should be adapted to take account of evolving science.

- Furthermore, although the Agency is already collaborating with the European Commission, and in particular Directorate-General Research, on research-related aspects, its involvement has so far been rather fragmented. The Agency would therefore like to create a platform for dialogue with the Commission, to improve its input into the EU research agenda for medicines. This would complement current initiatives on fostering innovation in the context of IMI and the European Technology Platform for Global Animal Health, to which the Agency already provides an important contribution, and where efforts over the next years will have to continue.
- Acknowledging that the scientific advice provided by the Agency if adhered to by the sponsor increases the success rate of marketing-authorisation applications, the Agency will continue its efforts to optimise the scientific-advice process.
- Current experience with engagement of regulatory authorities in early-phase development plans of the pharmaceutical industry has indicated that it is advantageous to establish early dialogue with sponsors and to provide regulators with considerable knowledge of the data at an early stage, which in turn facilitates the scientific-review process. While it is recognised that further improvements can be introduced, there is also a need to explore whether the concept of early dialogue in the framework of medicines development could be widened, while maintaining it as a voluntary process. The concept of scientific advice could be expanded to provide continuous scientific support during the development of a medicine, combined with earlier appointment and involvement of (co-)rapporteurs, which would augment the interaction between regulators and sponsors during the development of both human and veterinary medicines. This would require clear roles and responsibilities to be defined for all parties involved.
- It needs to be recognised that even a failed medicine-development process will generate useful information and scientific knowledge that, in most instances, is currently lost, either because of aspects relating to proprietary information or because of the lack of access to these data by regulators. Taking into account the added value of such data (in terms of avoidance of repetitive and redundant animal or clinical studies, avoidance of the use of inappropriate parameters, etc.), the Agency is of the view that it would seem appropriate to explore, in collaboration with the pharmaceutical industry, what incentives could be offered to make this otherwise lost information available to the scientific community.
- The Agency will continue to strengthen its engagement with the pharmaceutical industry, the European Commission, EDQM and the European Centre for Validation of Alternative Methods (ECVAM) to promote the '3Rs' concept (replacement, refinement and reduction) in the development of medicines, replacing wherever possible the use of animals by validated alternatives.
- With respect to the veterinary sector, measures will be explored to increase both the uptake and the perceived usefulness of the scientific-advice procedure, through discussions with the pharmaceutical industry, taking into account experience gained in the field of medicines for human use, while recognising the particular requirements of the veterinary sector. Pending the development of proposals for amending the current legislative framework to cope better with the requirements of products and approaches entirely new to veterinary medicines, the Agency will promote early dialogue with applicants, to understand the regulatory and scientific challenges that they face in bringing these medicinal products to market.
- Another aspect that needs careful consideration is the area of clinical trials of medicines for human use, and two major initiatives need to be highlighted. The Conference on the Operation of the Clinical Trials Directive, held on 3 October 2007, provided a number of recommendations for further improvement. In addition, in 2009, the European Commission began an impact assessment in view of the introduction of changes to the clinical-trials legislation. An aspect that will require particular attention is the regulatory oversight of medicines development, which should be further improved. The development of new medicinal products and of the underlying basic and translational research required to bring these medicines to patients are key elements of a European Research Policy, which is of great importance in view of the development of Europe as a key location for biomedical research and pharmaceutical development. A

coherent regulatory process that can assist the development of medicines from their inception, through scientific advice, first-in-human trials, and full clinical development is an important element in enhancing the European research environment. There is a need to introduce a clear, risk-based approach so that trials of well-characterised products are simpler and quicker to initiate, and require lesser degrees of regulatory supervision, while trials of new, less well-known products can be given the resources they require and merit. Simplifying and streamlining the current processes are essential to these objectives.

- The impact of the increasing globalisation of clinical research and manufacturing and its movement to developing countries (which may be confronted with limited experience and resources, and a less developed regulatory framework) needs careful consideration. In order to address this challenge, the Agency will undertake a number of initiatives, including the following:
 - In the area of clinical research, further developing and subsequently implementing the Agency's strategy²⁷ for acceptance of clinical trials conducted in third countries, including the development of advice and guidance on ethical standards and data-quality requirements for clinical trials submitted in the EU. Furthermore, the Agency, in close collaboration with the Member State national competent authorities and its international partners, will invest in supporting capacity-building and local awareness with the regulatory authorities, research communities and pharmaceutical industry of those countries.
 - In the field of the manufacture of APIs and of finished products, the Agency will develop with the Member States the necessary framework for implementing the new anti-falsification legislation. The Agency will also build on existing collaboration with its international regulatory partners. This will not only include exchange of information (on inspection planning and outcomes) and pooling of resources to increase

inspection coverage, but will also ensure, through existing platforms where possible, a coordinated approach to improving interactions with developing regulatory authorities and capacity-building to facilitate better implementation of good manufacturing practice (GMP) and supervision for manufacturers, with respect to both medicines for human and veterinary use.

Benefit/risk assessment and communication

To address the regulators' dilemma of balancing access to market vis-à-vis the need for as complete a data package as possible prior to licensing, several factors need to be considered. Pivotal in this respect are benefit/risk assessment and communication. Work on improving the benefit/risk-balance model concentrates on three major aspects: ensuring a consistent approach, providing a better rationale for the outcome of the benefit/risk review and improving the communication with the various stakeholders. This work goes hand-in-hand with the Agency's objective to focus on further improving the quality of the outcome of the scientific review. The following activities are envisaged:

- Optimising the benefit/risk-assessment process for medicines for human use can be undertaken through a variety of initiatives. Building on current achievements, work should now focus, in terms of the methodology used, on the introduction of more quantitative elements. The robustness of the scientific review should be further strengthened through better use of expertise in the areas of statistics, decision-making and communication. Furthermore, patient empowerment and patients' participation in healthcare decisions will further stimulate the ongoing debate on the level of patients' involvement in the scientific-review process. This should lead to patients' utilities being taken into account in a more systematic way for the benefit/risk assessment. Likewise, it would seem an opportunity to debate the level of involvement of relevant practising healthcare professionals and academia/learned societies in the scientific-assessment process throughout a product's lifecycle. Work will be undertaken to align the benefit/risk-assessment methodology with activities performed by other non-EU regulatory authorities in this area.

²⁷ EMEA Strategy Paper: Acceptance of Clinical Trials conducted in Third Countries, for Evaluation in Marketing Authorisation Applications (EMEA/228067/2008).

- Further work is also needed on improving the transparency of the outcome of the scientific review, including the justification for the opinion/decision taken. This is even more important in situations where the Agency's views are not in line with the outcome of the review by non-EU regulatory authorities. Subsequently communicating the outcome of the benefit/risk assessment in the most appropriate way represents a particular challenge. The Agency will, therefore, prepare a strategy on benefit/risk-assessment communication, liaising with all stakeholders to identify their specific needs.
- In the veterinary sector, fundamental differences exist in the approach to benefit/risk assessment, where the direct risk is to the recipient animal whereas the perceptions of benefit derive from the owner, the keeper or the healthcare professional. The databases and infrastructure required for quantitative approaches to benefit/risk assessment do not exist in the veterinary sector and are unlikely to be cost-effective to develop. Current emphasis, therefore, is on the development and documentation of a systematic methodology for benefit/risk assessment, as well as on the provision of training within the EU regulatory network. Therefore, work over the coming years will focus first on more clearly embedding the benefit/risk methodology in the assessment procedure, adapting it to different types of authorisation and medicinal products (e.g. antimicrobials), and on better communication to the Agency's stakeholders about the methodology used. Other challenges will be to demonstrate within the EU regulatory network that a consistent approach to benefit/risk assessment is applied irrespective of the licensing route, and that the methodology can bring benefits in terms of availability when applied to medicines for emergency diseases and limited markets.
- Further improving the quality and the regulatory and scientific consistency of the outcome of the scientific-review processes will be a key objective for the Agency. Activities will concentrate on improving the benefit/risk-balance model as outlined above. In addition, efforts will be directed to regular external surveys with stakeholders, to monitor the outcome of scientific-review processes for medicines for human use. For veterinary medicines, better use will be made of specialised expertise during the assessment phase, and consultation will continue with stakeholders, to identify the key parameters for measuring performance of the marketing-authorisation process and to put in place systems to monitor them.
- An in-depth reflection is also needed on how to further improve the use of the legal tools for the granting of a marketing authorisation. The Agency will ensure that the criteria for a conditional marketing authorisation for medicines for human use are better adhered to, since it needs to be recognised that this concept has not really been applied as initially foreseen. Likewise, consideration should be given to whether, and in what form, the concept of conditional marketing authorisation might be introduced for veterinary medicines.
- In addition, a key issue for regulators will be whether a more 'staggered' approval (or progressive licensing) concept should be envisaged for situations not covered by conditional marketing authorisations or marketing authorisations under exceptional circumstances, for instance characterised by a better-defined or more restricted population of good responders, followed by a broadening of the population post-authorisation when more 'real-life' data are available. The Agency would like to launch a debate with all stakeholders on the appropriateness of introducing such a concept, including a consideration of appropriate incentives to support new medicines development. It should be emphasised that progressive licensing should not lead to a reduced level of evidence for first-time marketing authorisation.
- Strategies on the best way to increase the knowledge of a medicine in the post-authorisation phase need to be set up at the moment of licensing, and subsequently reviewed when new information emerges. Although risk-management plans in the human medicines field meet this aim and have been a real step forward, due account needs to be taken of provisions in the new pharmacovigilance legislation that relate to such risk-management plans, which will allow remaining uncertainties on efficacy and safety at the moment of licensing to be better addressed. Therefore, risk-management plans will be an important tool in supporting continuous benefit/risk assessment throughout a medicine's lifecycle.

Another tool for maximising the value of information generated in the post-authorisation phase – especially for orphan medicines – is the establishment and maintenance of patient registries. Furthermore, work also needs to be undertaken to improve the formulation, implementation and monitoring of post-authorisation commitments for marketing authorisations not benefiting from the conditional marketing authorisation concept, with a view to increasing the efficiency of the system. Particular attention will be paid to ensuring that compliance with these post-authorisation commitments is adhered to.

Facilitation of the relative-effectiveness assessment of medicines for human use

A number of differences have been pointed out when comparing the licensing process with relative-effectiveness and cost/benefit-assessment processes, in terms of the choice of clinical endpoints, efficacy versus effectiveness, and relative efficacy versus placebo-controlled studies. This leads to a situation whereby regulators and HTA bodies, although both aiming for the availability of medicines that make a contribution to public health, are currently applying different approaches. Calls have been made for closer interaction and collaboration between both parties of the healthcare system, while fully respecting their distinct roles and responsibilities. The High Level Pharmaceutical Forum agreed in October 2008 on a set of recommendations²⁸, including that Member States, with the involvement of the Agency, should continue their efforts to consider how EPARs can further contribute to relative-effectiveness assessments. The Agency aims to make progress in this field, albeit in a stepwise manner, while continuing to ensure that cost/benefit assessment remains distinct and separate from the licensing process. The Agency's work, therefore, will continue to be characterised by the exclusion of any economic considerations.

Two major initiatives are envisaged:

- The Agency will improve as an information provider. HTA bodies rely heavily on EPARs, and the Agency will increase its level of transparency on the outcome of the scientific-review

process as summarised in the EPARs, including the rationale for the decision/opinion, whereby more emphasis will also be put on the quantitative aspects of the benefit/risk assessment, as already elaborated upon. Furthermore, the Agency will attempt to ensure that the product-lifecycle concept is better integrated in the EPAR, so that the EPAR better meets the criteria of a 'living' document, providing up-to-date and detailed information on the benefit/risk profile of a medicinal product throughout the marketing phase.

- The Agency will engage with HTA bodies in the early stages of development of a medicine (to avoid as far as possible the appearance of two different medicine-development programmes) and throughout the medicinal product's lifecycle, in terms of alignment of regulators' and HTA bodies' evidence requirements, through initiatives such as joint approaches to scientific advice, mutual input on clinical guidelines and debating evidence requirements (including relative efficacy aspects). In view of the vast amount of data obtained through post-authorisation collection, maintaining the dialogue with HTA bodies throughout a medicinal product's lifecycle is very important, as this facilitates greater alignment of such data collection.

²⁸ High Level Pharmaceutical Forum 2005-2008, [Final conclusions and Recommendations](#).

Strategic area 3: optimising the safe and rational use of medicines

Objectives	Impact/result indicators
Strengthen the evidence base in the post-authorisation phase to enable better regulatory decision-making.	<ul style="list-style-type: none"> • A regulatory model that facilitates the post-authorisation collection of data on benefits and risks of medicinal products is put at the disposal of the regulatory system. • A pharmacovigilance framework appropriate to the needs and priorities of the veterinary sector is developed as an outcome of the European Commission's impact assessment of the legislation for veterinary medicines.
Enhance patient safety by avoiding unnecessary risks to patients as a result of the use of medicines.	<ul style="list-style-type: none"> • A revised risk-management concept that targets both novel pharmacovigilance methodologies and a risk-minimisation toolbox better adapted to reduce harm is available.
Become a reference point for information on medicines evaluated by the Agency.	<ul style="list-style-type: none"> • A high-quality, informative and targeted set of information on medicines falling within the sphere of the Agency's responsibilities is proactively put at the disposal of the EU regulatory network at the moment of licensing/updating of the marketing authorisation.
Improve the decision-making process by taking due account of patient experience, thus contributing to the rational use of medicines.	<ul style="list-style-type: none"> • Conclusions from outcomes-research projects analysing the impact of regulatory decisions on public health are used to provide input into future regulatory policy decision-making.

Patient safety

Pharmacovigilance and safety of medicines will continue to be a top priority for the Agency, with a strong focus on ensuring that both risks and benefits are monitored throughout a medicinal product's lifecycle. Avoiding unnecessary risks to patients is becoming an increasingly important factor in strategies on the protection of public health, e.g. in the context of antibiotic use. Efforts are undertaken at EU level and internationally to enhance patient safety. In the EU, the focus is on strengthening research in this field and on launching new legislative proposals aimed at rationalising and strengthening the EU framework on safety-monitoring of medicines for human use. In addition, international collaboration on medicine safety as a result of globalisation and the need for best use of resources will result in finding synergies between the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP, led by the Agency) and Sentinel

(led by the Food and Drug Administration) initiatives.

The Agency's initiatives in this field for medicines for human use will, in addition to preparing for the implementation of the new pharmacovigilance legislation, include the following:

- A revision of the risk-minimisation-measures toolbox, in the framework of the current review and learning project on risk-management plans for human use, the aim being to further reduce harm caused by the use of medicines. This should preferably be undertaken using predefined criteria for analysis drafted in collaboration with the Agency's partners and stakeholders. Taking into account the impact of certain risk-minimisation measures on the EU's health workforce (doctors, pharmacists, nurses, etc.) and the pivotal role of healthcare professionals versus patients as regards the use of medicines, particular attention will be

paid to how the risk-minimisation measures impact on the work of healthcare professionals throughout the EU. It should be recognised that this impact may vary according to the healthcare policies and systems in place.

- Progressing the European Risk Management Strategy, thereby complementing the new legislation on pharmacovigilance, targeting aspects such as capacity-building for post-authorisation monitoring; preparing for the introduction of international standards and controlled and internationally agreed terminologies in pre- and post-authorisation phases; involvement in research-related activities on pharmacovigilance methodologies, in particular within the context of the IMI framework, to investigate novel and better ways to monitor the safety and benefit/risk balance of medicines. Another good example of investment in regulatory science relates to further initiatives to be undertaken within the context of ENCePP to support decision-making on the benefits and risks of medicines.

Post-authorisation follow-up

In order to optimise the safe and rational use of medicines, more information has to be obtained in 'real-life' situations:

- As a starting point, and taking into account the provisions on post-authorisation studies in the new pharmacovigilance legislation, the focus should be on the marketing-authorisation holder's post-authorisation development plan, and should include an exploration of the kind of incentives that could be provided to pharmaceutical companies to encourage them to voluntarily include such plans in the Agency's current scientific-advice framework. Secondly, recent developments in the field of human medicines, such as a firm new legal basis to require post-authorisation studies, will augment the initial knowledge on a medicinal product's benefits and risks. This should ultimately lead to an integrated assessment of benefits and risks under real-life conditions. ENCePP is an important tool that will support the development of methods for post-authorisation data collection, the establishment of an inventory of pharmacovigilance and pharmaco-epidemiology research centres, and the creation of a register of post-

authorisation studies, thus meeting the needs of both regulators and HTA bodies.

- Taking into account increasing public concern over potential effects on the environment of the use of medicines, and building on extensive experience already gained with veterinary medicines, initiatives should be taken to look into the longer-term impact of medicines for human use on the environment. Particular attention will have to be paid to the environmental risks of nanomedicines.
- In the field of veterinary medicines, the European Commission's impact assessment of the veterinary medicines legislation will provide an opportunity to develop a post-authorisation framework that is particularly suited to the needs and resources of the animal-health sector. The Agency will consult with all involved stakeholders on how best to develop an appropriate risk-management framework, and on the extent to which it is possible to licence medicines for veterinary use at an earlier stage of development, based on the requirement to provide the necessary post-authorisation data.
- With a view to contributing to a more rational use of medicines for human use, the Agency will focus its efforts on raising better awareness among healthcare professionals of the rationale for its opinion/decision-making. The existing forum with healthcare professionals' organisations will be used to debate how this can best be achieved.

Authoritative source of information

The Agency is meeting the demand for greater transparency and openness through initiatives such as the development of policies on access to documents²⁹, on access to information in the EudraVigilance databases³⁰, and on transparency³¹. In addition, the Agency holds the following views:

²⁹ European Medicines Agency Policy on Access to Documents (related to medicinal products for human and veterinary use) ([EMA/110196/2006](#)).

³⁰ Draft EudraVigilance Access Policy for Medicines for Human Use ([EMA/187439/2008](#)) and Draft EudraVigilance Access Policy for Medicines for Veterinary Use.

³¹ EMEA Transparency Policy – Draft for Public Consultation ([EMA/232037/2009 – rev*](#)).

- Irrespective of the ongoing political debate on the best way forward for providing information on medicines to patients, the Agency should strive to become the authoritative source of information on all medicines it evaluates, both human and veterinary, for syndication to the EU regulatory network. This should also promote public recognition of the Agency as a leading authority in the field of evaluation and supervision of medicinal products. Initiatives should be directed towards the preparation by the Agency of timely, targeted and high-quality information on the medicines it evaluates. In this way, the Agency can concentrate on the quality and consistency of the information provided, and other parties can focus on ensuring maximum penetration of this information among the target audiences, and in particular patients/consumers/users of medicines and healthcare professionals, thereby fully respecting the characteristics of the EU regulatory network in this field. Strengthening the interaction with the NCAs and with organisations representing patients/consumers and healthcare professionals to build up a network of excellence at EU level will be an important target. Furthermore, joint reflection with the Member States and other interested parties on how best to address technical developments in the field of provision of information on medicines – in particular the link with e-health – is also needed.
- Work should be undertaken to put more emphasis on balanced benefit/risk communication, to contribute to the implementation of the empowered-patient concept. Aspects that will require particular consideration include how best to address the complexity of the data, as this requires careful interpretation, and determining the most appropriate time point for communication on benefits and risks when new information emerges. It will be equally important to clearly communicate to healthcare professionals and patients, using the most appropriate communication tools, the reason why the medicinal product is not indicated for use outside the approved indication.
- For veterinary medicines, the objectives in terms of transparency and communication should be the same as for medicines for human use, although it will be necessary to tailor the messages and the way in which they are delivered to the needs of the veterinary community. This will be done through surveys with the various stakeholders in the veterinary sector to understand better the types of information they would find most useful and how best they can be presented.

Outcomes research

The Agency has identified analysing the impact of regulatory decisions on public health as an important activity for the years ahead. Outcomes research in this field has begun, in line with the Agency's internal control standards, which require it to evaluate its activities. Efforts in this field will continue over the coming years, and will include the following:

- Building on current initiatives (with emphasis initially on the benefit/risk-assessment and communication model), the Agency will further engage in monitoring the use of medicines for human use, in close collaboration with its stakeholders. To gain maximum understanding of the implications of regulatory decisions, the focus for the coming years should be on outcomes research that looks at the actual versus intended use of medicines, the effectiveness of risk-minimisation measures, including aspects of feasibility in healthcare, and investigates whether the current regulatory model contributes to better therapy outcomes. The findings of this research should also be used to provide input to future regulatory policy decision-making.
- Different priorities and data sources apply to regulatory decisions in the veterinary-medicines sector. Where possible, opportunities will be taken to conduct specific outcomes-research projects in the veterinary field, focusing particularly on collecting data at EU level on the sale of antimicrobials in the Member States.

6. Implementing the Agency's road map

The Agency will implement its vision in line with the document 'From vision to reality'. This document will provide information on the prerequisites to be fulfilled and the enablers (including operational and organisational aspects) needed to allow the Agency to successfully contribute over the next five years in the fields of science, medicines and health.

In addition, to optimise the implementation of the road map, the Agency will complement its planning process by applying a multi-annual programming approach, which will equally cover a five-year timeframe. This multi-annual programming will address aspects such as workload and (human) resources forecasts, budget planning, accommodation needs, etc., and will benefit the Agency by allowing decisions to be made in a more effective and predictable way, thus helping to ensure the Agency can gradually implement its vision over the next five years. Following endorsement by the Management Board, the multi-annual planning will feed into the Agency's annual work programmes.

7. Conclusion

It is the Agency's view that the vision outlined in this 'Road map to 2015', together with the proposed solutions for addressing the challenges identified, will allow the Agency to increase its contribution to science, medicines and health, and thus to the protection of the human and animal populations of the European Union.

An important prerequisite for the successful delivery of the road map will be the further development and reinforcement of the EU regulatory network, which has already proven to be of fundamental importance to the EU's pharmaceutical sector.

The Agency is looking forward to engaging with its partners and stakeholders to successfully implement its vision for the next five years.

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