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5 EU Medicines Agencies Network Strategy to 2020

6 Working together to improve health

7 Consultation draft

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Chapter 1: Introduction to the European medicines agencies regulatory network

The European regulatory system for medicines is a unique model in the global regulatory environment. The system is based on a network of all national medicines regulatory authorities for both human and veterinary medicines from Member States in the European Union and European Economic Area, united in the Heads of Medicines Agencies (HMA), and the European Medicines Agency (EMA), working closely together in an integrated fashion. The network serves a population of over 500 million, the world's third largest population after China and India. Together, this closely integrated network ensures that patients and animals in Europe have access to medicines that are safe, effective and of good quality and that patients, healthcare professionals and citizens are provided with adequate information about medicines.

By working closely together, the network can draw on the resources and expertise of the whole EU. The network has access to thousands of experts across Europe provided by Member States and brings together this expertise and knowledge to ensure that medicines are regulated to the highest scientific standards. National Competent Authorities (NCAs) rely on each other's work to avoid duplication and share workloads and scientific competence. For example, Member States do not conduct inspections in each other's territories, avoid duplication of assessments and work together on post-marketing safety issues.

The work of the network is coordinated by the EMA and the HMA. Amongst other tasks, the EMA's responsibilities include the coordination of the scientific evaluation of those medicines that are authorised through the centralised procedure (most new active substances are now authorised through the centralised procedure) and referrals, support for innovative products (including the provision of scientific advice and qualification of biomarkers), designation of orphan status or classification as Minor Use Minor Species (MUMS)/limited market, agreement to paediatric investigational plans, as well as the coordination of the EU wide work on safety monitoring on medicines. NCA's work closely with the EMA and provide the scientific expertise for assessing centralised products, supporting innovation including centralised scientific advice, work on orphan and paediatric medicines and EU wide safety procedures through scientific resource to the various scientific committees (CAT, CHMP, COMP, CVMP, HMPC, PDCO, PRAC), working parties and experts groups of the EMA.

NCAs handle applications for all medicines that are authorised nationally or through the decentralised and mutual recognition procedure, conduct post-marketing surveillance in their territories, authorise clinical trials, provide national scientific advice, support innovation and conduct inspections. Scientific work for non-centralised products is coordinated through the coordination groups for mutual recognition and decentralised procedures, human and veterinary (CMDh and CMDv).

All NCAs are represented in the HMA. The HMA addresses key strategic issues for the network, ensures consistency across the EU, shares best practices and makes the best use of resources across the network. The HMA, including the CMDh and CMDv, works closely with the EMA and the European Commission to ensure the efficient and effective operation of the European medicines regulatory network.

In the EU, medicines are governed by a large body of EU legislation, which aims to guarantee high standards of quality, safety and efficacy of medicinal products, as well as appropriate information, and to promote the functioning of the internal market. The EU legislation today covers the whole life-cycle of a medicinal product from the research phase (clinical trials), the approval stage, manufacturing, distribution to post-marketing obligations, including sectorial legislation on orphan and paediatric medicines, advanced therapy medicinal products, as well as maximum residue limits for food safety.

There are some exemptions, notably pricing and reimbursement for human medicines, which remain a national competence. The European legislation governing medicines has been strengthened significantly in recent years in the areas of pharmacovigilance, falsified medicines and clinical trials. Drafting of new legislation on veterinary medicines is ongoing. Full and harmonised implementation of recent legislation will be a priority for the network in the coming years.

The European Commission's role in this area is multi-facetted and focuses on the following:

- Right of initiative: to propose new or amending legislation for the pharmaceutical sector;
- Implementation: to adopt implementing measures as well as to ensure and monitor the correct application of EU law;
- Risk management: to grant EU-wide marketing authorisations for centralised products or maximum residue limits on the basis of a scientific opinion of the EMA;
- Supervisory authority: to oversee the activities of the EMA in compliance with the mandate of the EMA, EU law and the EU policy objectives;
- Global outreach: to ensure appropriate collaboration with relevant international partners and to promote the EU system globally.

The European Commission is also responsible for policy initiatives in the pharmaceutical sector.

The degree of integration of the network has increased over recent years, for example since 2012 the network has strengthened its assessment of EU wide safety issues with the creation of the Pharmacovigilance Risk Assessment Committee (PRAC). Inspection activity is increasingly coordinated as well as the development of IT systems that underpin the regulatory work of the network. The network has also been jointly assessing clinical trials under the Voluntary Harmonisation Procedure in anticipation of the application of the new Clinical Trials Regulation and veterinary periodic safety reports (PSURs) in a work-share project.

With respect to the regulation of veterinary medicines, the same overall structure of the Network applies as for human medicines but on a smaller scale. In some Member States, veterinary medicines are controlled within the same agency or other government body that is responsible for human medicines, whilst in others human and veterinary medicines are regulated separately. The small size of the veterinary network reflects the much smaller size of the animal health industry compared to its human counterpart. This smaller scale and the entirely private commercial nature of the veterinary medicines market have implications for the approach that is required to ensure sustainability of both the animal health industry and the regulatory network that is required to oversee its operation.

Chapter 2: Approach to the strategy

This document outlines the high level strategy for the network for the next 5 years. It is presented, for the first time, as a single strategy for the entire network to reflect the need for a coordinated approach to address the multiple challenges and opportunities that face the network. Advances in science affect the nature of the products we regulate and the network must support new and innovative developments that contribute to public health. There is a need for efficiency and transparency, the need to address new and emerging threats, whether of a public health or criminal nature, and the need to work globally with other regulators given the increasing globalisation of the pharmaceutical industry.

This document focuses on key strategic priorities where the network can and should make a difference in the next five years. It is not a description of all the work that is and will be taken forward but a high level strategy, explaining what needs to be taken forward and why. Separate multi-annual workplans for both EMA and HMA as well as for CMD (human and veterinary) will give detailed information on the work of each component of the network (including some elements that are specific to EMA, HMA or CMD), and will also describe how the strategy will be taken forward. It builds on the previous EMA roadmap to 2015[1] and the HMA strategy document 2011-15[2].

The document presents key themes focussing on the contribution the network will make to human and animal health, optimising the operation of the network and the need to act and collaborate globally.

The elements specific to veterinary medicines of the Network strategy are elaborated in Theme 2 of Chapter 3 'Contributing to animal health and human health in relation to veterinary medicines'. In the other chapters, where reference is made to the network, this can be assumed to cover both human and veterinary parts unless it is clear from the context that it relates to human or veterinary medicines alone. The fact that about 75 percent of new diseases that have affected humans over the past decade have been caused by pathogens originating from animals or products of animal origin and the continued emergence of new pathogens reinforce the need for collaboration between those regulating human and veterinary medicines.

[1] http://www.ema.europa.eu/docs/en_GB/document_library/Report/2011/01/WC500101373.pdf
[2] http://www.hma.eu/fileadmin/dateien/HMA_joint/02-_HMA_Strategy_Annual_Reports/02-HMA_Strategy_Paper/2010_12_HMA_StrategyPaperII.pdf

Chapter 3: Strategy for the network

Theme 1: Contributing to human health

Introduction

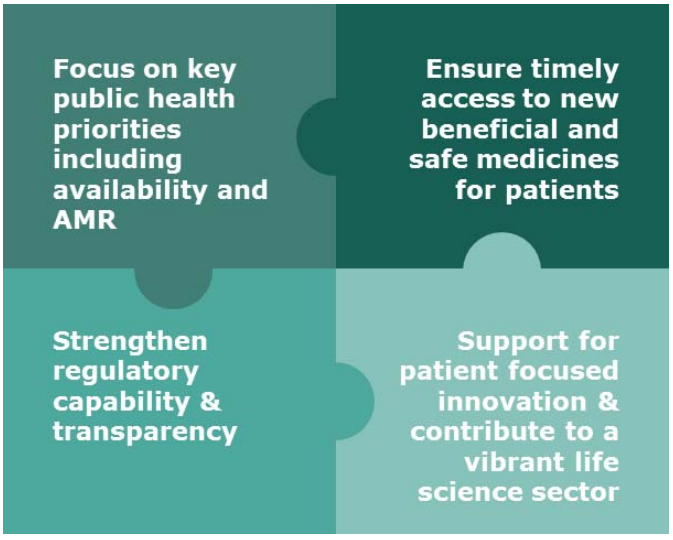
The medicines that we regulate are changing as our understanding of the scientific basis for disease evolves. We are seeing new diseases emerge and existing diseases redefined. Old problems such as antimicrobial resistance have become major public health threats and existing and new infectious diseases require new therapies. As the population ages, diseases such as dementia become more of a public health burden. New technologies are emerging and personalised medicines will represent an increasing part of the armamentarium. We are seeing new advanced therapies and more combination and borderline products.

It is important that the network keeps abreast of these advances in science to ensure that novel products can be developed optimally for the benefit of the health of the citizens of Europe. A vibrant life science sector is crucial for this and the network will need to ensure that the European regulatory environment is one that facilitates the development of novel products as well as protects and promotes public health. Costs and complexity of developing new medicines continue to increase and society is asking more in terms of timely access to novel treatments, particularly in areas of unmet need. Monitoring of products throughout their lifecycle has never been more critical.

The European regulatory framework has proven to be flexible but the range and diversity of products continues to rise. To enable promising new medicines to get to patients at the earliest opportunity requires us to explore flexible licensing pathways and a life-span approach with clinical drug development, licensing, reimbursement, use in clinical practice and monitoring viewed as a continuum.

At the same time, we must ensure that patients in the network continue to have access to existing medicines by taking action when supply issues arise, by supporting the development of generics and biosimilars and by facilitating access to medicines through appropriate classification.

This chapter outlines the major strategic initiatives the network will undertake over the next 5 years with a view to contributing to and enhancing public health.



Objective 1: Focus on key public health priorities including availability of medicines and antimicrobial resistance

The network will continue to be prepared to address public health emergencies and priorities such as antimicrobial resistance. It will also review whether there are areas that could benefit from regulatory incentives to support the development of novel products. In addition it will continue to review how to best ensure continuity of supply of good quality appropriately authorised medicines.

European citizens can expect to live longer and to live better quality lives. Nevertheless, new public health priorities are arising in Europe that the network will need to contribute to and we are faced with new public health emergencies that the network needs to respond to quickly.

Managing the threat represented by antimicrobial resistance to human and animal health will remain a high priority for the network. With respect to antimicrobial resistance in human medicine the network will facilitate access to the market of new antibiotics, particularly those against multi-drug resistant infections, and to contribute to promoting the prudent and responsible use of antibiotics. The network will continue to implement the EU Commission Action Plan, collaborate internationally and contribute to the implementation of the World Health Organization (WHO) plan to combat the rising threat of antimicrobial resistance. The Network will adopt a 'One Health' approach bringing together expertise from both human and veterinary medicine recognising that the challenge of antimicrobial resistance crosses both domains. The objectives with respect to veterinary medicine are detailed in objective 4 of theme 2 of this chapter.

The network will explore other areas that could benefit from regulatory initiatives in the next five years such as dementia. Also, the network's contribution to ensuring that the needs of special populations including children and the elderly are met should be explored to ensure that these vulnerable groups have timely access to appropriately developed medicines together with appropriate information to support their use.

The network will also explore further the needs of other special populations such as patients affected by rare diseases. To this aim a better coordination of the existing tools like the various horizon-scanning exercises for orphan medicinal products conducted by different institutions will offer a significant benefit in view of expediting the process and avoiding potential duplication of efforts.

An important aspect of ensuring the quality, safety and efficacy of particular categories of innovative biological medicines is the testing of centrally authorised products and the official control authorities´ batch release. Official Medicines Control Laboratories (OMCLs) need to ensure that the experimental assays and the reference material used to standardise the assays are updated to remain at state-of-the-art.

The Ebola epidemic has reminded us that the network must be in a position to respond quickly to public health emergencies. Although Europe, with its developed health systems, was not directly at risk of an Ebola epidemic, the network contributed to the development of vaccines and anti-viral medicines. Phase-I trials were started quickly as a consequence of the swift authorisations of these clinical trials in the network, the rapid scientific advice given and collaboration between developers and regulators. Over the next five years a priority will be to ensure that the network continues to be able to respond to public health emergencies, whether novel infectious diseases or other threats, by facilitating the early introduction of new treatments or preventative measures and learning from actions taken to address public health crises such as the Ebola outbreak.

The network is increasingly confronted with supply challenges and shortages/lack of availability of both new and old medicines. These supply issues can be caused by falsified medicines, stolen medicines, manufacturing/GMP non-compliance issues or many other factors including economic. Supply chains for medicines have become more and more complicated with an increasing trend to manufacture outside the EU. There is a continued need to ensure the quality of products wherever they are manufactured.

The Falsified Medicines Directive (FMD) introduced a range of measures to strengthen the legal supply chains and protect them from falsified medicines. The network will continue to explore how it can best address supply issues of whatever cause, including GMP issues, disruption of manufacturing processes and reliance on a single or few manufacturers for essential medicines. It will work with other bodies addressing the broader causes of supply problems. The network will also need to increase its cross border collaboration in case of supply disruptions that affect multiple Member States. In addition, greater focus will be given to the increasing threat posed by the illegal supply chain of medicines that operates mostly through websites located in third countries will also continue to need to be addressed collaboratively.

Objective 2: Ensure timely access to new beneficial and safe medicines for patients

The network will review ways to ensure timely access to novel medicines, ensuring that existing flexibilities to get appropriate medicines to patients more quickly are used to their maximum potential, by taking forward the concept of adaptive pathways and strengthening the collaboration with Health Technology Assessment (HTA)/ pricing and reimbursement bodies and healthcare professionals and patient representative bodies.

Patients increasingly demand access to new and innovative medicines at an earlier stage. Regulators need to balance the need for more information on the quality, safety and efficacy against the need for access, particularly in areas of unmet need. There is clear consensus amongst industry, regulators and HTA/pricing and reimbursement bodies that timely access to appropriate novel medicines is a priority. Participation in clinical trials is one way of giving access to patients but this is not an option for many patients and participation in trials does not guarantee access to the medicine under investigation.

The EU regulatory framework offers a number of flexibilities that allow earlier access: conditional approval, exceptional circumstances, accelerated assessment, compassionate use and treatment on a named-patient basis at Member State level. Despite these flexibilities, there is a perception that the EU is not doing enough to ensure timely access. In response, some Member States have introduced their own earlier access scheme within the existing regulatory framework. The network will need to ensure that the existing flexibilities are fully understood and prospectively planned for their use.

The concept of adaptive pathways is based on a life-span approach consisting of an early approval of a medicine for a restricted patient population, in areas of high unmet medical need, with buy-in from multiple stakeholders during development. Robust pharmacovigilance systems across the EU and the move to proactive pharmacovigilance, real-time monitoring and rapid learning systems are key enablers of this approach. The EMA pilot project on adaptive pathways to explore this approach with medicines in development will increase our understanding of how this could all work in practice. In the next five years the network will have to progress the adaptive pathways pilot, review the outcome and promote ways to ensure timely access to new medicines for patients.

Furthermore, collaboration with other key bodies such as HTA/ pricing and reimbursement bodies and patient and healthcare groups will need to be strengthened to enable appropriate decision making and sharing of information to allow optimal access. HTA/ pricing and reimbursement of medicines are essential in getting innovative medicines to patients earlier.

Further efforts should be made to incorporate patients' values and preferences into the scientific review process which could influence benefit risk decision making across the network. This is particularly important in view of the fact that patients are the ultimate beneficiaries of medicines and that, therefore, their views should be heard.

A further area for focus of the network in the coming years will be to ensure the most appropriate legal classification is applied to products and the mechanisms for allowing those that can be safely reclassified as non-prescription medicines are in place, effective and being used, thereby improving patient access.

Objective 3: Support for patient focused innovation and contribute to a vibrant life science sector in Europe

The network will work to ensure the optimal implementation of the Clinical Trial Regulation, collaborate more on supporting innovation and considering further regulatory incentives for innovation, particularly in certain areas of public health need.

To ensure access to new medicines for patients it is essential that Europe has a regulatory environment that facilitates innovation. Clinical trial activity has slowed in recent years as a consequence of increased competition globally and an unfavourable regulatory environment. Although an estimated € 30,630 million was invested in R&D in Europe in 2013 by the research-based pharmaceutical industry, Europe is consistently lagging behind the US as the place where innovators want to test and launch their products first[3].

The new EU Clinical Trials Regulation has addressed the regulatory environment for clinical trials in Europe and will take full effect by mid-2016 at the earliest, subject to the full functionality of the IT underpinning the Regulation. Under the new regulation it will be much easier to conduct trials in multiple Member States following a more streamlined process through a single European portal. The success of the regulation will largely depend on its implementation across the EU. All Member States will be modernising the ways ethics committees work to be able to comply with the legislation. The portal and database will need to be fully functional and user friendly. The network is committed to a successful and harmonised implementation of the regulation.

The network already has a strong track record in supporting innovation through national innovation offices or the EMA's Innovation Task Force, through national or EMA scientific advice, through appropriate guidance and helplines. Opportunities for greater collaboration and integration across the network and with academia will be explored to translate innovation into medicinal products. The network will also need to consider whether it gives adequate support to and an appropriate regulatory environment for those that drive innovation including SMEs and academia.

Furthermore, the network will need to reflect on what additional supportive measures may provide incentives to support beneficial innovation, including, for example, a European early stage innovative medicines designation, with subsequent optimisation of development. Many elements of such a scheme are already in place but would require repackaging and better coordination of existing services.

[3] The Pharmaceutical Industry in Figures, Key Data 2014, EFPIA, http://www.efpia.eu/uploads/Figures_2014_Final.pdf

The network will explore the opportunities for burden reduction where appropriate to ensure that regulation is never a hurdle or barrier to innovation taking into account the complexity of medicine development as well as the changing nature of pharmaceutical innovation. Over the next five years, the network will generate a discussion on the most efficient and cost effective approach to knowledge generation and evidence requirements.

Although outside of the remit of the network, HTA and pricing and reimbursement also play an important role in fostering innovation in Europe. Efforts are ongoing to bring convergence in the assessment of therapeutic added value of new medicines and patient outcomes. The network will strengthen the collaboration with HTA/ pricing and reimbursement bodies taking into account the discrete roles regulators and HTA/ pricing and reimbursement bodies have in bringing medicines to patients.

Generic and biosimilar medicines have the potential to contribute to lowering the cost of health care, can increase access to medicines and stimulate research. In the next five years, the network will continue to ensure that the regulatory framework supports the development of a broad range of generic and biosimilar medicines.

The network will continue to explore how best to include patient and societal input into pharmaceutical innovation and regulation.

Objective 4: Strengthen regulatory capability and transparency

The network will ensure that it has the capability to regulate novel products of the future, develop regulatory science, consider greater use of real world databases and increase transparency about the data that underpin regulatory decisions.

Rapid advances in science are leading to new medicines that are developed, manufactured, assessed and used in completely new ways. We are faced with personalised medicines, nanotechnology, cell and gene based technologies amongst other innovative products. The traditional methods of assessing and surveillance cannot always be applied to these products. The network will have to ensure that it understands these new and upcoming technologies.

Over the next five years the network will need ensure it has the capability to regulate the novel products of the future and to strengthen its capability to adequately assess and monitor these new medicines to assure their safety, efficacy and quality throughout the product lifecycle, as well as giving patients access to them without delay. Regulatory science, as an approach to how products are developed and regulated will become more prominent and regulators will need to work more closely with the academic community, industry and others to ensure appropriate support is given to the developments in this area.

Regulatory capability varies across the network. Some NCAs have more expertise in certain areas than others. In our networked approach to regulation NCAs rely on each other's work in the centralised, decentralised and mutual recognition procedure, EU-wide pharmacovigilance procedures, and inspections and on a voluntary basis for clinical trials. The network must ensure that all NCAs that participate in a specific type of regulatory activity continue to have the capability to do so.

The network will take forward the discussion on making individual patient level data from clinical trials available and consider if there are circumstances where this data will help the network's benefit risk based decision making.

Access to anonymised data from electronic health records has the potential to completely change the way we monitor medicines that are on the market. Such real world databases have the potential to pick up and analyse safety issues and potentially provide information about effect sizes in a real world setting and in sub populations much more quickly allowing regulators to take action at an earlier stage. Also, electronic healthcare records can be used to facilitate data collection in clinical trials, particularly those looking at outcome type data. The network will explore the use of 'big data' which has huge potential to enhance capability and reduce cost whilst respecting individual patient privacy.

The network will also continue to strengthen the pharmacovigilance capability across the network and explore new methods for monitoring products and rapidly evaluating safety issues. As part of proactively managing benefit risk throughout the life-cycle of medicines, starting early in the pre-authorisation phase, the network should do more to support early planning for post-authorisation efficacy and safety evidence gathering.

The network is already transparent about its regulatory decisions and how these decisions are made. With the EMA's policy on publication of clinical data and the Clinical Trials Regulation, the EU has set a global example for increased transparency but the network will need to consider extending this level of transparency to all of its work whilst keeping personal data and truly commercially confidential information out of the public domain.

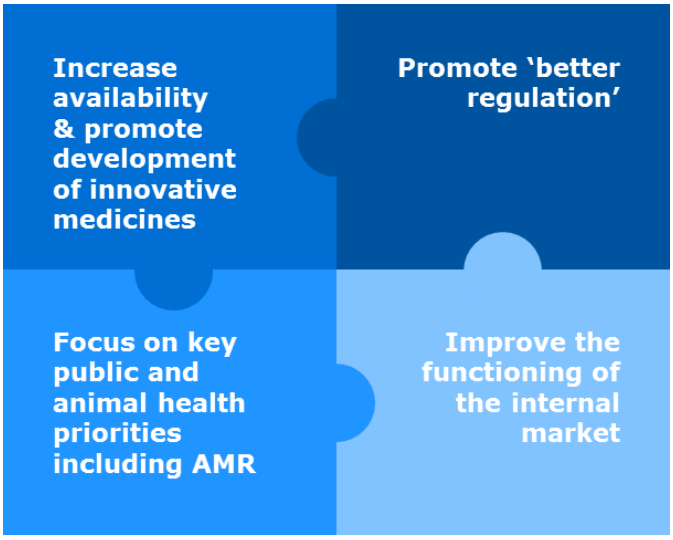
There is increasing public scrutiny on the issue of the potential risk to the environment arising from the use of medicines. The network will increase the level of transparency on the work already done during the authorisation procedure to assess and manage such risks and will explore if further measures are required.

Theme 2: Contributing to animal health and human health in relation to veterinary medicines

Introduction

The major factor influencing the strategy of the Network with respect to veterinary medicines in the next five years will be the finalisation and subsequent coming into effect of a revised legal framework. The period covered by this strategy will therefore be characterised by the network preparing for the revised legislation whilst continuing to ensure that the existing legal framework is used as effectively as possible in the period before the new legislation comes into effect.

In proposing the new legal framework, the European Commission identified four principle objectives; to increase the availability of veterinary medicines; to reduce the administrative burden on industry and regulators through applying 'better regulation'; to improve the functioning of the internal market for veterinary medicines throughout Europe; and, to minimise the risks to human and animal health that may arise from the use of antimicrobials in veterinary medicine. These same four objectives will drive the strategy of the network in the run up to the new legislation.



Objective 1: Increase availability of veterinary medicines and promote development of innovative medicines and new technologies

The network will increase the availability of all types of veterinary medicine, giving particular attention to products indicated for minor use in major species and for minor species (MUMS), as well as smaller national markets, and for technologies that are new to the veterinary domain.

The problem of a lack of availability is particularly acute with respect to products for MUMS. The network has responded through the creation of a specific MUMS scheme operated jointly by the EMA and NCAs, together with a range of measures at national level. Experience has shown that reducing the data required at the time of authorisation can act as a strong incentive to the pharmaceutical industry to market products for MUMS. A review of the MUMS guidelines will be carried out to identify the scope for further reduction in data requirements whilst still providing assurance of appropriate

levels of quality, safety and efficacy. Current efforts to extrapolate maximum residue levels to food producing animals of all species will be continued. For smaller national markets the lack of availability for veterinary products is much wider and not limited to MUMS products necessitating further considerations. Ensuring preparedness for new emerging animal diseases and diseases that spread from other continents is of high importance to the network.

A wide range of technologies that are new to veterinary medicine are now being developed that present particular challenges due to a lack of regulatory guidance and, in some cases, the fact that the existing regulatory framework does not specifically cater for them. Over the period of this strategy, the network will evaluate the success of measures recently put in place to facilitate access to market of new technologies and innovative medicines and will ensure that the new legislation is able to accommodate these new types of product. New initiatives will be explored for specific sectors to improve availability and thereby promote animal welfare.

Experience over the last years has shown that availability can also be reduced as a result of removal from the market of older medicines or removal of indications or species from the conditions of use of authorised products. The network will continue to explore ways in which attrition of existing products can be limited to situations where new threats are identified or where there are objective reasons to consider that the benefit risk balance of an existing product has changed in such a way that its authorisation should be varied or withdrawn.

The network will develop its use of the Union Database of veterinary products, as a database from which products authorised in Member States and centrally can be identified. This will both increase the usefulness of the database to veterinary surgeons who seek to identify authorised medicines under the 'Cascade' provisions of the current legislation, and help underpin the requirement of the new legislation for a suitable European database of authorised veterinary medicinal products in the future.

Objective 2: Promote 'Better Regulation'

The network will reduce the regulatory burden on the veterinary pharmaceutical industry to the greatest extent possible whilst at the same time maintaining the existing, high standards for the protection of human and animal health and of the environment and without transferring the burden to the competent authorities.

The impact assessment carried out by the European Commission in preparing their legal proposal identified that the regulatory burden on the veterinary pharmaceutical industry is proportionately substantially higher than the burden on the human industry[4] and as a consequence, the administrative burden on NCAs is also relatively high. This results from the complexity of the veterinary market which covers, for example, many different species and the need to ensure the safety of foodstuffs derived from treated animals in the case of products for food producing species. Pending finalisation of the new legislation, the network will therefore continue to pursue measures to improve the functioning of the existing legislation wherever possible. These measures will include initiatives within CMDv involving industry to address their concerns related to packaging and labelling, including the use of pictograms and working to improve the functioning of the variation procedures. The network will seek to optimise the operation and decision-making process of all authorisation procedures and cooperate to improve Industry's regulatory excellence to ensure that resources for scientific scrutiny are prioritised to the most important issues.

[4] Assessment of the Impact of the Revision of Veterinary Pharmaceutical Legislation, 11 July 2011, EPEC

The network will optimise the processes for veterinary pharmacovigilance and increase the use of IT tools, thereby improving efficiency for both industry and regulators. This is the first objective of the Veterinary IT and Data Strategy and will lay the basis for the future pharmacovigilance system envisaged in the new legislation. In addition, there is currently a disproportionately high number of reports arising from the use of veterinary medicines in companion animals whilst it is recognised that this does not reflect the balance of products used overall. The network will explore how to improve interactions with veterinary health professionals to increase reporting rates overall and particularly in the area of livestock husbandry.

The network will also undertake an extensive programme of preparation to put in place the revised processes and IT systems envisaged in the revised legislation, once the final shape of the new legislation emerges from the discussions in Council and European Parliament.

In addition, the network will follow the development of any new legislation governing the effect of chemicals on groundwater, and ensure that the process for the benefit/risk assessment of veterinary medicinal products is fully understood by stakeholders. In the event that new requirements are elaborated, the network will ensure that veterinary medicinal products comply with them.

Furthermore, the network will work with the European Commission and stakeholders to enrich the debate in the European Council on the new legislation with the aim of realising the objectives outlined in this strategy in terms of increased availability, reduced regulatory burden and adequate safeguards on the use of veterinary antimicrobials.

Objective 3: Improve the functioning of the single market for veterinary medicines within the EU

The network will seek to maximise the use of the existing legal framework to promote the effective functioning of the single market for veterinary medicines. This will include the availability of veterinary medicines in smaller national markets.

A characteristic of an effectively functioning single market for veterinary medicines is the availability across the network of a wide range of veterinary products with harmonised conditions for use. To achieve this objective, the network will continue to use the existing legislation to best effect until the new legislation comes into force. The CVMP expects to continue to process a high workload of referrals of antimicrobials and other classes of products for which the conditions of use will be both harmonised and aligned with the principles of prudent and responsible use.

The network will also develop the training systems for regulatory personnel within the framework of the Network Training Centre with the aim of achieving a shared perspective on the implementation of regulatory requirements to improve harmonisation.

In addition, the network will take into account the challenges of the internet market and will develop a strategy aimed at providing incentives and tools to increase availability in smaller national markets.

Objective 4: Focus on key public and animal health priorities including antimicrobial resistance

The network will continue to be prepared to address public and animal health emergencies and priorities including supply issues. With respect to the use of antimicrobials in veterinary medicine the aim of the network will be to minimise to the greatest extent possible the risks arising from their use in animals, whilst ensuring that sufficient antimicrobials remain available to aid in assuring a continued high level of animal health and to support food security, recognising in particular that 'healthy food comes from healthy animals'.

In addition to those actions listed under objective 1 of theme 1, the network will continue to define prudent and responsible use for classes of antimicrobials used in veterinary medicine and then take the necessary steps to ensure that the Summary of Product Characteristics (SPC) and labelling of antimicrobial products reflects responsible use in a consistent way across the EU.

In line with the European Commission Action Plan, the European Surveillance of Veterinary Antimicrobial Consumption project will continue and further refine the collection of data on the consumption of antimicrobials in veterinary medicine. This will show how successful the measures influencing prescribing patterns are.

The network will continue to work on better understanding the relationship between the use of antimicrobials in animals, the development of antimicrobial resistance and the transmission pathways between animals and man so as to target control measures effectively.

To achieve the goals regarding other public and animal health priorities the network will address emerging environmental concerns and any safety issues in a cooperative and concerted manner.

In addition, the network will continue to review how to best respond to ensure continuity of supply of good quality appropriately authorised medicines, including vaccines. This will reduce the need for Member States to have to use legal provisions that make products available other than through full marketing authorisation. The network will need to improve collaboration in case of supply disruptions or shortage that affect multiple Member States.

Theme 3: Optimising the operation of the network

Introduction

Over the past years important efforts have been made to strengthen the collaboration and cooperation between all parties in the network which is, as was stated in the introduction, a unique and successful construction in the global regulatory environment. This has resulted in various initiatives demonstrating the added value of the European regulatory authorities working together to improve health. However, a multiplicity of challenges (including health challenges, progress in regulatory science, societal trends, upcoming legislative and political changes and the impact of further globalisation) will require the network to find adequate responses and solutions to cope with these challenges in the most efficient way.

A critical success factor for the network will be to have available and at its disposal sustainable high-quality scientific and regulatory expertise able to address progress in regulatory science. The scientific and operational procedures carried out by single or various players in the network should be operationally efficient and cost-effective, minimising as much as possible the administrative burden for pharmaceutical industry commensurate with public and animal health. To continue to strengthen a network of excellence, effective communication will be paramount, whereby a proactive communication approach should be fostered at national and European level in view of the aim to strengthen public and political trust in the work of the regulatory authorities and the network. Trust not only relies on the quality of the scientific competence and the output of regulatory authorities, but also on their commitment to seek active involvement of the stakeholders (in particular patients, human and animal healthcare professionals, and the scientific community) in the work of the authorities. The network also needs to work closely with those it regulates.

The initiatives proposed in this theme to optimise the operation of the network will take into account that the network encompasses human, veterinary and joint NCAs. This approach allows the veterinary domain to benefit from the economies of scale that arise from being part of a wider network.

This theme outlines the strategic objectives of the network to optimise its operation and the main initiatives it will strive to undertake over the next five years to achieve these objectives.

Objective 1: Reinforce the scientific and regulatory capacity and capability of the network

The network will adapt the available scientific and regulatory expertise both in terms of capacity and capability to cope with changing demands.

In order to continue to achieve high-quality, fit for purpose output of the scientific review process there is a need to ensure that NCAs within the network have the necessary expertise at their disposal, both in terms of capacity and capability. Several elements need to be considered by the network for an optimal response: a clear identification of any gaps in scientific and regulatory expertise based on current and future needs, and a corresponding competence development programme, to be delivered through the EU Network Training Centre. Future needs relate to the required skills for the assessment of innovative therapies of the future, for new methodologies to support clinical trial activities (e.g. use of computer systems for capturing clinical data), for using an increasing amount of available health data, and for addressing challenges resulting from meta-data analysis. Other elements are the need to achieve common standards of scientific quality across the EU regulatory network, and to strive for state-of-the-art (scientific) guidelines.

With a view of promoting best use of the (scientific) expertise within the network, a more optimal organisation of the available expertise across the network should be considered, avoiding duplication of work, and facilitating enrichment of the expertise through more collaborative working, including enhanced outreach at national level for academic expertise. This should enable a more synergistic approach towards the organisation of the expertise within the network.

In addition, the network will continue efforts in order to strike the most optimal balance between ensuring the impartiality and independence of experts and securing the best possible scientific expertise within the network.

The network will have to ensure that it remains sustainable over the years to come taking into account an ever-increasing pressure on human and financial resources whilst the workload continues to grow. To address the sustainability challenge various initiatives have started or are ongoing, such as achieving efficiency gains through a continuous review of the business processes, supported by integrated IT systems, or the data gathering initiative, for which a pilot was launched early 2015.

Objective 2: Strive for operational excellence

The network will optimise scientific and operational procedures and continuously improve the quality of the (scientific) output within the current regulatory framework.

Over recent years various new pieces of legislation had to be implemented by the network. Some of the new legislative provisions were aiming at reducing the regulatory burden on stakeholders and the administrative burden on NCAs, but there are strong views at the level of stakeholders that there is still further room for optimising the regulatory operations. When reviewing the scientific and operational procedures at national and European level, in order to optimise both the administrative and scientific elements, particular emphasis will be put on their operational efficiency and cost-effectiveness. In addition, there is a need to make sure that the (changing) needs and expectations of the network's stakeholders are captured and well understood. This needs to be underpinned by adequate and inter-operable IT services to the network, recognising the major role that IT systems play in supporting the (regulatory) business processes and a better utilisation of available resources

within a complex regulatory environment. A coordinated approach has already been undertaken through the development of a common EU Telematics Strategy, and the network will oversee and closely monitor an efficient implementation of such strategy. It will be important to strive for the most efficient connection between the national and the EU IT systems.

Although the need for operational and scientific excellence is well understood and should be the ultimate objective, reducing administrative burden should not lead to a situation whereby the quality of the scientific work is affected which would compromise either human or animal health. Therefore, initiatives to reduce the administrative burden should go hand in hand with initiatives to further strengthen the output, and in particular the scientific quality, of regulatory processes during the life span of medicines. The availability of robust quality systems within the network is important and the well-established Benchmarking of the European Medicines Agencies (BEMA) initiative launched by HMA is a key instrument to share best practices and to look for continuous improvement. The network should ensure that the BEMA results are shared within the network to ensure transparency on best practices. Sharing best practices will allow for additional initiatives to be set up in order to mitigate discrepancies within the network. Furthermore, the BEMA methodology should be adapted to make sure that it can adequately cope with challenges related to progress in regulatory science, and can contribute to continuous improvement of the quality of the (scientific) output. The aforementioned EU Network Training Centre should result in a further enhancement of the quality of the scientific assessment.

Efforts have been made over the past years to also reduce the regulatory burden through either legislative change or other initiatives (e.g. the recent simplification in the area of variation applications). However, there are still demands by the pharmaceutical industry for further work to be undertaken in this field. Therefore, the network will consider further optimisation of the regulatory framework within the current legislative provisions. If the need for further legislative change is identified, the network will have to reflect on how this could be best taken forward.

A proportionate and effective legal framework for the regulation of medicines is important and the network has a role in influencing the development of legislation to ensure it is appropriate for future products as well as addressing current challenges.

Objective 3: Ensure effective communication of and within the network

The network will become more effective in communicating its strategic objectives, and communicating with stakeholders in crisis situations.

A key prerequisite for an efficient operation of the network is an effective communication approach. This is important in order to better communicate the remit of NCAs and defend the decisions they take to protect public and animal health. This should allow to build and maintain trust of civil society at large in the work undertaken by regulators, hereby further strengthening the reputation of regulators and their authority vis-à-vis their stakeholders. To generate understanding and trust, the network must ensure that its approach to communication supports the overall objective of safeguarding human and animal health. Only when trust can be fostered stakeholders will play their part in contributing to such an overall objective.

An important action for the network to consider will be to launch the necessary communication initiatives to help achieving its strategic objectives as laid down in this strategy document. This could be undertaken through a five year communication plan. This will ensure that communications are aligned to the overall strategy and are planned in the most effective way.

Information on medicinal products can be further improved to encourage better use of medicines by taking better into account the expectations and needs of both patients and healthcare professionals. The network will explore – together with patients and healthcare professionals – how to achieve product information more aligned with stakeholders' expectations and needs.

One of the major challenges relates to the handling of emerging events with respect to authorised medicines. Such events are mainly safety concerns or quality defects, putting into question the positive benefit/risk balance of medicines. Important progress in this field has been made since 2010 by putting in place a coordinated approach within the network towards communication on such emerging events. This has allowed adopting whenever possible a proactive approach towards communication within the network, fostering as much as possible a consistent message towards the stakeholders. Nevertheless, the network will have to continue ensuring its outputs are usable, authoritative and reliable. To make further improvement in this field, it will be imperative to even better understand the expectations and needs of its stakeholders, in particular patients and healthcare professionals, so that the necessary measures can be taken.

A special point of focus relates to regulators' responses to health emergencies. Although each health crisis always has its own specificities, experience has taught the importance in such situations of timely, consistent and effective communication to the public at large. The network, therefore, will have to consider how to further improve its communication in case of health emergencies, in particular as regards a better coordination of communication on emerging health threats across the network.

Objective 4: Strengthen the links with other authorities and with stakeholders

The network will reinforce its collaboration with other authorities engaged in making medicines and medical devices accessible to patients, and to further improve interactions with its stakeholders.

HTA/ pricing and reimbursement bodies have an important role in providing access to medicines to patients. The network will strengthen the interaction and collaboration between regulators and HTA/ pricing and reimbursement bodies, taking into account their discrete roles, to further enrich the robustness of the scientific review whilst facilitating timely access to medicines (see also theme 1, objective 2).

A number of events in the past years in the field of medical devices have underlined the need to provide for a more robust regulatory framework and new legislation is now underway to address such need. There will, however, remain areas, irrespective of the national situation, where collaboration between medicines regulators and medical devices regulators will have to be strengthened, such as in the field of combination products, companion diagnostics, borderline products, and ancillary medicinal substances. The network will explore how such collaboration could be reinforced. In addition, depending on the outcome of the discussions on the new legislation on medical devices, further areas for collaboration with medical devices authorities may be identified, learning from areas of best practice including NCAs who already have joint medicines and devices responsibilities.

Ensuring that the needs and expectations of its stakeholders are being addressed should be an important target for the network. It is, therefore, paramount that the views of stakeholders are captured and listened to, especially with respect to those who develop, prescribe and use medicines. The network will put in place more streamlined mechanisms to obtain regular feedback from key stakeholders on the operation of its activities and the quality of its output, which may result, as also

explained in objective 2 in the current theme, in a revision of the scientific and operational procedures to optimise their functioning.

Increased cooperation will be sought with the other decentralised Agencies of the EU such as the European Chemicals Agency (ECHA), the European Centre for Disease Prevention and Control (ECDC) and the European Food Safety Authority (EFSA) in areas of common interest.

Theme 4: Contributing to the global regulatory environment

Introduction

The network has a long history of developing effective cooperation within the EEA and is therefore well placed to contribute to greater collaboration outside its borders. The trend towards globalisation of pharmaceutical activities, in particular the growth of clinical trial activity in countries outside the EU, increasing reliance on manufacture in developing countries and associated concerns about ethical considerations and counterfeit operations present challenges for the network within a global context.

Greater complexity of global supply chains and reliance on clinical data generated outside the EU create a strong public health need to ensure that these activities are properly monitored and controlled, as well as opportunities to develop greater links with international regulators who face the same challenges. All regulators worldwide are facing increasing economic constraints, in the context of which international collaboration can provide opportunities to create synergies, avoid duplication and facilitate work and information sharing.

All components of the network have been contributing to international activities by participation in harmonisation activities such as the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), the International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products (VICH), as well as supporting non–EU regulators through work with WHO, the Organisation for Economic Co-operation and Development (OECD), the World Organisation for Animal Health (OIE) etc. for over 20 years. As the world of medicines regulation has expanded globally, the need to strengthen regulatory systems worldwide as described in the 2014 World Health Assembly (WHA) resolution has become a priority. Smaller and emerging non-EU regulators are looking to the network for support and capacity building and the EU model is increasingly explored as a model for other regional harmonisation initiatives. Opportunities to support these initiatives in a coordinated manner across the EU network need to be explored.

A growing trend to include pharmaceutical activities in trade negotiations between the EU and third countries has implications for the network, as does the emergence of new international networks and coalitions where a coordinated and consistent approach should be taken, avoiding all unnecessary duplication, and ensuring both adequate network representation and appropriate feedback.

Objective 1: Assure product supply chain and data integrity

The network will intensify measures to continue to assure product, supply chain and data integrity within increasingly complex global supply chains.

Industry figures show that about 80 percent of active pharmaceutical ingredients used in medicines authorised in Europe are manufactured outside the EU. While there continues to be substantial finished product manufacture within the EU, the EU also imports a significant percentage of pharmaceuticals and/or products which have been partially or fully manufactured outside the EU. The complexity of international supply chains present risks of errors and occasionally counterfeits or product diversion. Key to ensuring supply chain integrity is to make sure that all steps in the supply chain are adequately controlled and monitored, both at an individual company level and through appropriate regulatory oversight including inspections and audits. Sharing of information between regulators responsible for oversight of different manufacturing stages and ensuring that the same standards are applied irrespective of manufacturing location will help minimise possible problems.

Closely linked to these challenges is the need to ensure the integrity of the data on which regulatory decisions about medicines are based. Concerns about data integrity may arise for many reasons e.g. poor training, inadequate implementation or occasionally due to suspicions of falsification. The integrity of the data in the studies used to support market authorisation is fundamental to trust and confidence in the products themselves.

The network will work with global partners to address the challenges posed by increasingly complex supply chains, global industries and falsified and counterfeit medicines.

Mechanisms to facilitate greater information sharing to enhance oversight including common approaches to identification of suppliers and supplier sites and linkages between inspection databases will be explored by the network.

The network will ensure that all suspicions of problems with data integrity are thoroughly investigated working closely with other international partners where these data may have been generated or used.

Efforts to understand the drivers behind inadequate practices will be made with a view towards promoting a culture of compliance and trust.

Objective 2: Convergence of global standards and contribution to international fora

The network will take a lead role in convergence of global standards assuring appropriate representation in international fora and will put in place mechanisms to strengthen cooperation with non-EU regulators in a consistent and integrated manner.

The globalisation of pharmaceutical operations is a driver for convergence of international standards and approaches. If equivalent standards of good manufacturing practices and good clinical practices are applied in countries which supply pharmaceuticals internationally and in which clinical trials are performed, the opportunities for cooperation and mutual reliance can be strengthened thus facilitating better use of collective resources, avoiding duplication and sharing of best practices. Similarly, international electronic standards are key to effective information sharing and need to be implemented across the network.

The network is built on the equivalence of standards and approaches and is therefore well placed to facilitate the extension of these standards and approaches in other regions. Aspects of the EU falsified medicines directive implemented in 2013 helped to establish principles of international trust and cooperation and stressed the value of supervision of manufacturers by local regulators and mutual communication.

The network has traditionally supported established fora such as the International Conferences of Harmonisation (ICH and VICH), the International Regulatory Cooperation on Herbal Medicines (IRCH) and Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S) with a view towards contributing to convergence of global standards. One of the aims of the reform of ICH spearheaded by the European Commission since 2011 is to become more inclusive by opening up to new members and countries. Similarly VICH has embarked on a global outreach initiative. Members of the EU network also actively support the work of WHO and OIE in developing standards and in training and capacity building.

The emergence of new cooperative mechanisms between international regulators such as the International Coalition of Medicines Regulatory Authorities (ICMRA), the International Pharmaceutical Regulators Forum (IPRF) and the International Generic Drug Regulators Pilot (IGDRP) provide opportunities for the EU network to contribute to the future shape of international collaboration.

Countries such as China and India have become important suppliers to the network, both in terms of manufacturing and as countries where increasing number of clinical trials, including bioequivalence trials, are performed and the regulators in these countries are key partners for the network and in the context of other international convergence mechanisms and networks.

The network, in close cooperation with WHO, will take a lead role in convergence of global standards through existing fora aimed at harmonisation and convergence of approaches.

An integrated and consistent approach to cooperation with countries such as India and China will be promoted by the network.

Mechanisms will be put in place to ensure that participation in international fora is representative and consistent and that feedback is provided to the network.

Objective 3: Ensure best use of resources through promoting mutual reliance and work-sharing

The network will promote best use of collective global resources by improving information and work sharing with non EU regulatory partners and encouraging adoption of European regulatory approaches.

Changes in the economic environment which place ever increasing pressure on limited resources combined with greater understanding of the similarity of challenges faced by regulators worldwide have increased the opportunities for work-sharing and mutual reliance in the area of medicines regulation. The network with a history of Mutual Recognition Agreements (MRA) on GMP as well as its own established cooperation mechanisms is well placed to further widen these collaborations. Political initiatives in the form of trade agreements between the EU and non-EU countries increasingly include pharmaceuticals as an area of cooperation. Recent examples include the TTIP, CETA and FTAs with Japan and Singapore. Such agreements can provide opportunities to extend reliance on GMP and GCP inspections with those authorities who already apply equivalent standards and it is important that the network contributes actively to these discussions. Similarly increasing focus on the need for cooperation on the evaluation of generic medicines have recognised the European regulatory system

as a model to be followed and a pilot collaboration mechanism has been launched involving both decentralised and centralised procedures. Extending these approaches to innovative medicines should also be explored.

The network will explore the opportunities presented by draft trade agreements and other mechanisms to promote greater mutual reliance on inspection outcomes in both, human and veterinary medicines.

The network will also work to strengthen mutual reliance, trust and synergies in order to achieve better use of collective resources/work products, avoiding duplication and sharing of best practices.

In the area of generic medicines evaluation, the network will review and build upon the information sharing pilots to promote the leveraging of regulatory authorities' collective resources.

In addition, the network will improve the mechanisms in place to share information with other regulators across the globe on products throughout their life cycle.

Furthermore, opportunities to leverage resources in other areas and to increase reliance of other regulators on European Assessments and outputs will be explored.

Objective 4: Support training and capacity building and promote the EU regulatory model

The network will build on existing approaches to training and capacity building for non-EU regulators in order to promote international best practices.

As mentioned in the introduction to this theme, non-EU regulators are increasingly looking to the network for support and capacity building and as a model for their regional harmonisation initiatives. Taking into account the limited resources available, increasing demands for capacity building and collaborative approaches amongst regulators worldwide should be met by first identifying mutual priorities and then establishing mechanisms to deliver a coordinated response across the network. The network will build on existing training and capacity building approaches such as the GCP and Pharmacovigilance inspector training courses, the Paediatric medicines regulatory network and ICH and VICH training and IPRF activities to greater promote international practices in developing countries to the benefit of the network.

The network will review training and capacity requests received through different organisations to ensure these can be addressed in a synergistic manner using the collective resources of the network.

Glossary

BEMA	Benchmarking of European Medicines Agencies Steering Group
CAT	Committee for Advanced Therapies
CETA	Comprehensive Economic and Trade Agreement
CHMP	Committee for Medicinal Products for Human Use
CMDh	Co-ordination group for Mutual recognition and Decentralised procedures – human
CMDv	Co-ordination group for Mutual recognition and Decentralised procedures – veterinary
COMP	Committee for Orphan Medicinal Products
CVMP	Committee for Medicinal Products for Veterinary Use
EEA	European Economic Area
EMA	European Medicines Agency
EU	European Union
FMD	Falsified Medicines Directive
FTA	Free Trade Agreement
GCP	Good Clinical Practices
GMP	Good Manufacturing Practice
HMA	Heads of Medicines Agencies
HMPC	Committee on Herbal Medicinal Products
HTA	Health Technology Assessment
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
ICMRA	International Coalition of Medicines Regulatory Authorities
IGDRP	International Generic Drug Regulators Pilot
IPRF	International Pharmaceutical Regulators Forum
IRCH	International Regulatory Cooperation on Herbal Medicines
MRA	Mutual Recognition Agreement
MRL	Maximum Residue Limit
MUMS	Minor Use Minor Species
NCA	National Competent Authority
OECD	Organisation for Economic Co-operation and Development
OIE	World Organisation for Animal Health
OMCLs	Official Medicines Control Laboratories

810	PDCO	Paediatric Committee
811	PIC/S	Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme
812	PRAC	Pharmacovigilance Risk Assessment Committee
813	SME	Small and medium-sized enterprises
814	SmPC	Summary of Product Characteristics
815	TTIP	Transatlantic Trade and Investment Partnership
816 817	VICH	International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products
818	WHA	World Health Assembly
819	WHO	World Health Organization