17 December 2015
EMA/848469/2015
Chief Policy Adviser

Overview of comments received on "EU Medicines Agencies Network Strategy to 2020"

Comments

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
01	General	I am a veterinarian, consulting in regulatory affairs and pharmacovigilance and often get questions within pharmacovigilance human but due to veterinary medicines. As there are many databases in different languages available to report the adverse event, few reporting is done by (animal) doctors, MAH or Distributors when there is no pharmacovigilance department due to the time effort it cost. Therefore there lays a chance to make the results from databases more efficient by using one obliged database (Eudravigilance (VET)) in the EU and a direct help desk on the web. Also more advertisement on tv (within the EU one same advertisement) how to report an adverse	

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		event to the Authorities or the MAH for example due to lack of efficacy by farmers could give indirectly new light to signal detection. More inspections/ audits on reporting by MAH of veterinary medicines on AE and PSUR writing and sales, could give new light on signal detection as not only the originator companies but also the generic vmp companies have influence on the resistance of antibiotics due to their sales. Set up one webpage with Availability of (V)MP in case of urgency with 1th, 2nd and 3rd choice of (V)MP authorized per species and indication regulated by the Authorities, harmonize them within the EU could be efficient. The CASCADE could be made electronically by linking active substances authorized per country, per species and indication. Have (V)MP send per post with an obliged stamp or sticker for more control of products sold electronically in and outside the EU. Than one new page on HMA for different links to epidemiology and resistance on antibiotics (results for PSUR implementation) by third parties with scientific based results per country. Many people do not know how to find this information and it costs time to explore databases or good websites with already existing links to this information. I could be of help in structuring this mixup of links and contents on the web and therefore I hope I may be of use for the implementation of the EU network strategy.	
02	General	The ECNP suggest making psychiatric drugs a priority, given the enormous (and increasing) burden of psychiatric disorders to the European population.	
02	Page 8	The ECNP expresses its support to the adaptive pathways scheme	
02	Page 9, objective	An important innovation that would accelerate brain research would be to exempt phase 1 and 2 trials for the need for GMP production. This would save small companies and	

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	3	academic groups vast sums of money in terms of drug supply	
	Page 9, objective 3	Remove the Schedule 1 status (i.e. move to Schedule 2) from many drugs that have medicinal properties but which are also used recreationally – e.g. MDMA and cannabis – this would make them available to doctors and patients without increasing risk of diversion. For supporting evidence see these papers: • Nutt DJ (2015) Illegal Drugs Laws: Clearing a 50-Year-Old Obstacle to Research PLOS Biology – • Nutt DJ (2014) Medical cannabis: time for a comeback? The Pharmaceutical Journal http://www.pharmaceutical-journal.com/opinion/comment/medicinal-cannabis-time-for-a-comeback/20067185.article Sessa B and Nutt D (2015) Making a medicine out of MDMA. Brit J Psychiatry 206, 4–6. doi: 10.1192/bjp.bp.114.152751	
03	General	Thank you for the opportunity to comment on this important strategy document. It is clearly an important step forward and will certainly prove to be a valuable framework in which to improve efficiency, facilitate and co-ordinate the work in the area of EU human and veterinary medicines. From our perspective a particularly striking element is that the strategy covers a network with the Member states (Heads of Medicines Agencies). We understand that although the network is not formally foreseen in the legislation, it plays an important role in implementing the legislation in your field of expertise. ECHA too has co-operation and facilitation arrangements with the Member States. These take the form of expert groups such as the meeting of the Competent Authorities for REACH (1) and CLP (2) (CARACAL) and the Biocides Competent Authority Meeting, which advises the European Commission and ECHA on questions related to the implementation of the legislation. These groups are composed of representatives of Member State and EEA-EFTA Competent Authorities, as well as a number of observers from non-EU	

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		countries and stakeholders such as industry and trade associations. However, in the striving to increase our own efficiency and the efficiency of the implementation of legislative areas in which we work, we would welcome the opportunity to learn more about moving towards a similar arrangement as you have developed with the network of Member States. We are pleased to see ECHA is named in relation to increased cooperation in theme 3, objective 4 of the strategy. We also see opportunities to strengthen our work together to optimise the synergy in our areas of common interest. In addition to learning more about the Network of Heads of Agencies, in the annex to this letter we highlight some areas where we believe we can focus our joint energies, but recognise that this level of detail may better fit into a multi-annual work programme (MAWP), rather than this strategy. Our MAWPs are medium-term strategy documents which set out our envisaged work for five years and are available on our website. These are supplemented by five year review reports and annual work programmes. Importantly in the context of EMA's strategy document, we are working with the Commission and our stakeholders on a strategy for ECHA's contribution to meeting the 2020 goals established at the World Summit on Sustainable Development. We take this opportunity to wish EMA well with this important step forward in developing the Heads of Medicines Agencies Network and look forward to our continued collaboration. (1) Regulation EC No 1907/2006 on the registration, evaluation, authorisation and restriction of chemicals. (2) Regulation EC No 1272/2008 on the classification, labelling and packaging of substances and mixtures.	
04	General	The consultation draft outlines a comprehensive strategy for the EU Medicines Agencies	

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		Network. Issues and challenges and high level strategies for addressing them are very clearly presented. The strategy overall is fully supported by NICE.	
04	General	In building more joined up processes to ensure timely patient access to treatments that are clinically effective and affordable, closer collaboration between regulators and HTA agencies is needed. It is pleasing that this need is reflected in the consultation draft. We consider, however, that this is such an important issue that this message can be strengthened in a number of areas of the consultation draft both to emphasise the opportunity for closer collaboration and to reflect the strong progress that has already been made. Specific comments related to the theme of closer regulator / HTA agency collaboration, are shown below.	
04	98-99	There is an opportunity to improve the overall working of healthcare systems through closer cooperation and collaboration between regulators and HTA agencies. Strong progress in this area has already been made, for example the EMA Adaptive Pathways pilots involving multiple stakeholders including HTA agencies and the EMA / multiple European HTA agencies parallel scientific advice service. Expanding on lines 98-99 to highlight opportunities for closer interaction with HTA agencies and reflecting the significant progress made would be very helpful at this early, introductory section of the strategy document.	
04	240-274	Ensuring timely access to new beneficial and safe medicines for patients as outlined in Chapter 3, Theme 1, Objective 2 is fully supported by NICE. Initiatives to support timely access, such as the adaptive pathways work, are likely to make the post marketing authorisation data collection and vigilance even more important than they are now. It may be helpful to reflect this through expanding the explanatory text under Objective 2.	
04	241 263-266	NICE fully supports the proposal to take forward the concept of adaptive pathways and strengthening the collaboration with HTA / pricing and reimbursement bodies, healthcare professionals and patient representative bodies (box below line 241 and expanded in	

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		lines 263-266).	
04	292-297 307-312	Lines 292-297 provide a useful summary of the network's support to innovation. To support research and development and subsequent adoption of innovative products, it is essential that development plans take account of evidence requirements for HTA as well as regulatory approval. The network is already active in this area through the EMA / European HTA agency parallel advice and through supporting the EUnetHTA Shaping European Early Dialogue (SEED) initiative. Lines 307-312 partially address the role of HTA and pricing / reimbursement in fostering innovation in Europe but do not capture the importance of integrating regulatory and HTA perspectives and evidence requirements in clinical research and development. A new paragraph combining lines 292-297 and 307-312 and emphasising the importance of considering both regulation and HTA from the earliest stages of innovative product research and development would be very useful.	
04	319-361	NICE welcomes the consideration of transparency, data availability and data sharing as outlined in Chapter 3, Theme 1, Objective 4. Progress here will be relevant to and supportive to NICE's work.	
04	616-620	NICE fully supports the proposal to strengthen the interaction and collaboration between regulators and HTA and pricing / reimbursement bodies (lines 616-620).	
05	General	The European Haemophilia Consortium (EHC) welcomes the opportunity to comment on the HMA/ EMA Strategy to 2020. The EHC welcomes the inclusion of patients as equal stakeholders in many of the strategy items proposed by the Network's strategy. The EHC notes that the EMA is quite advanced in including patients' representatives in its work and it hopes that this will only be continued and reinforced in the next five years. Furthermore, the EHC hopes that other Members of the Network will follow the EMA in its lead for patients' inclusion in their work carried at national level. The EHC believes that patients can provide a unique insight in the use of medicinal products. Furthermore, the	

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		final objective of the activities of the Members of the Network is to ensure a high level of health protection for patients and to facilitate the work of healthcare professionals, so it only seems natural that patients should be actively included in the work of the Network.	
05	255-270	The EHC supports the Network's strategy in strengthening its capacity to assess safety of novel therapies. In this regard, the EHC strongly encourages the Network to promote the reporting of adverse events, not only in the post-authorisation phase but throughout the whole development process of the product, including in clinical trials. The EHC believes that patients, physicians and regulators have the right to be made aware of potential side effects of medicinal products under development. In fact, withholding this information would not only be unethical but potentially lead to patients being exposed to similar and unnecessary adverse events when undergoing clinical trials with other sponsors developing similar products. The EHC believes that physicians and patients should not be withheld by confidentiality clauses to report adverse events resulting from the use of products in clinical trials to regulatory authorities. This point is in line with the adaptive pathways approach and the more proactive approach to pharmacovigilance outlined in lines 255 to 259. It is also in line with the Network's strategy to incorporate patients' values and preferences into the scientific review process to influence benefit risk decision making (lines 267-270).	
05	346-347	The EHC supports the Network's strategy in regulating novel products and strengthening its capability to assess their safety, efficacy and quality. In this regards, the EHC strongly encourages the Network to accept submissions of adverse events collected by larger databases rather than just small post-marketing surveillance studies. This is in line with the network's strategy to explore the use and potential of 'big data.' (lines 346-347) This is also in line with the Network's strategy to improve use of available health data (lines 523-534).	
06	General	In general, we note and appreciate the effort, depicted by the 2020 Strategy, to rely on	

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		the network of authorities and on new technologies to shape policy which is responsive to the needs of patients and the complexity of the current economic scenario. In this sense, we see a number of points of contact with our 2015-2019 Strategy, which aims at promoting technologies to enhance privacy and data protection; to identifying cross-disciplinary policy solutions and to work with other authorities in order to speak with a single European voice. In particular, we appreciate that the 2020 Strategy emphasises the opportunities and potential that Big Data may bring about for medical research and sets to explore such possibilities with an eye on data protection. We also focus on the social benefits of Big Data, particularly in the context of mHealth (see specific comments below), and are in the process of assessing the most adequate safeguards to allow a full exploitation of such potential to the benefit of patients and users.	
06	338	We share the opinion of the EMA that access to patients' electronic health records and the use of Big Data will enhance the potential and opportunities of drug research and afford a more timely response to the needs of the population. At the same time, we consider that the use of Big Data brings with it substantial responsibilities in ensuring that individual rights to privacy and data protection are not harmed. In this respect, we point to our analysis of Big Data in the recently published EDPS Opinion of mobile health (mHealth), available at https://secure.edps.europa.eu/EDPSWEB/webdav/site/mySite/shared/Documents/Consultation/Opinions/2015/15-05-21_Mhealth_EN.pdf	
06	348	We share EMA's opinion that pharmacovigilance is a crucial activity in order to ensure good manufacturing, quality and safety of drugs, both in human and in animal health. To the extent that pharmacovigilance entails the reporting of personal information concerning the patients or the animal's keepers and owners, however, data protection safeguards should apply, in order to preserve the individual rights of these persons.	

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06	353	We welcome EMA's commitment to keep personal data out of the public domain. In fact, as technology develops, opening new possibilities to apply it to healthcare, personal data will come under increasing pressure. It is important to preserve individual rights to privacy and data protection and ensure that individuals enjoy the right to choose how and for which purposes their data should be used.	
06	678	In the course of our activity, we have examined the data protection implications of possible solutions against drug counterfeiting. To the extent that such solutions entail the use of databases and record the personal information of natural persons involved in the supply chain (e.g. employees of the marketing authorisation holder, agents, pharmacists, etc.) data protection safeguards should apply to preserve the rights of these persons.	
07	General	In general Fellows of the Royal College of Pathologists welcomed this consultation and the initiative it represents. Concerns were expressed about whether fungal pathogens and antifungal resistance had been considered and included. This clearly links with agricultural use of azoles as a risk factor. Another but more global concern is that after ketoconazole lost its licence there are no mould active oral antifungals on the WHO[1]s essential medicines list. Co-infection with TB is very common in many countries and lungs with TB cavities are at very high risk of developing chronic aspergillosis with high annual mortality in the absence of treatment. Resistance to antifungal agents is a growing global problem that requires urgent attention. The impact of agricultural and horticultural use of antifungals is not considered. Tri-azole antifungal agents are the mainstay of treatment for invasive fungal infections and in the absence of effective treatment these infections are lethal. Tri-azoles also offer the most cost effective approach, and antifungal stewardship programmes aim at	

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		restricting their unnecessary use in order to spare their activity. At the same time, azole fungicides are widely used for crop protection and material preservation. Millions of kilograms of tri-azole agents are used in the regular spraying of crops and food commodities in the Europe each year. Despite this, fungi continue to decimate major food crops such as wheat, and barley.(1) The recent flooding and global disasters are likely to result in an increased need for fungicides as environmental disruption triggers dispersion and moist conditions promote fungal growth.(2) Ongoing climactic change and global warming exacerbate the problem.(3) This is relevant to human disease as the main source for human fungal pathogens is the environment. Azole resistance in one of the most important fungal pathogens, Aspergilllus fumigatus, has emerged rapidly over the last decade and this has been clearly linked to azole fungicide use in agriculture.(4) The prevalence of aspergillosis is not clearly defined and although invasive disease is rare and confined to immunocompromised populations, the burden of chronic respiratory disease in terms of asthma, allergic bronchopulmonary aspergillosis and chronic pulmonary aspergillosis affects millions of individuals worldwide.(5) Improvements in medical care have resulted in a growing population of immunocompromised patients at risk for severe fungal infections. There is strong evidence that antifungal resistance results in clinical failure and higher mortality rates (6, 7). Azole resistance of Aspergillus was first noted in the 1990's and has risen steadily since.(7, 8) Early cases were shown to arise from a variety of de novo mutations in patients on long-term therapy for chronic respiratory conditions. However, more recently a clonal resistance mechanism has been identified in both patient and environmental isolates. Whilst most prevalent in the Netherlands, it has now spread globally(9-13)and represents a significant public health problem.(14) This specific TR34/L98H mutation consists of a tandem repeat of 34 bases (TR34) within the promotor region of the CYP51A gene, combined with a leucine to histidine amino acid substitution (L98H).	

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		Azole resistance is found in up to 26% of environmental surveillance isolates in Europe and in TR34/L98H mutation is present in 50% of these.(4) Interestingly, the TR34/L98H mutation has not been the most frequently reported resistance mechanism in the UK but this should be interpreted with caution as data are extremely limited. (15) Importantly, this TR34/L98H mutation linked resistance is not only found in environmental isolates of Aspergillus but also in clinical isolates from patients with no previous azole antifungal exposure. It appears that the patients have become infected with an azole resistant environmental strain. The mutation confers pan-azole resistance to itraconazole, voriconazole, posaconazole (16) as well as many azoles widely used in agriculture. Global spread of this resistance mechanism has been linked to the selective pressures exerted by massive agricultural fungicide usage. (17) Whilst direct evidence linking resistance to pesticide use is lacking, the circumstantial evidence is overwhelming.(16, 18) Recently, another environmental mechanism of resistance has been identified and associated with clinical treatment failures in patients. (17) This too has been linked to agricultural use of fungicides and highlights the need for the medical and mycological establishment to invest in robust surveillance and identify azole resistance as a research priority. Recent analysis has highlighted that mycology in the UK receives only 2% of funding allocated for research in human infectious diseases.(19) Little of this is directed at global health and translational research is relatively poor. However a lack of investment and succession planning remain and this coincides with the burgeoning problems of antifungal drug resistance, emerging infections and increasing antifungal drug expenditure as well as increased morbidity and mortality. 1. Control ECfDPa. Risk assessment on the impact of environmental usage of triazoles on the development and spread of resistance to medical triazoles in Aspergillus species. In: Stockholm E, editor. Stockholm: ECDC Stockholm; 2013. 2. Benedict K, Park BJ. Invasive Fungal Infections after Natural Disasters. Emerg Infect	

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		Dis 2014(Mar). 3. Garcia-Solache MA, Casadevall A. Global Warming Will Bring New Fungal Diseases for Mammals. Mbio. 2010;1(1). 4. Chowdhary A, Kathuria S, Xu J, Meis JF. Emergence of azole-resistant Aspergillus fumigatus strains due to agricultural azole use creates an increasing threat to human health. PLOS Pathogens. 2013;9(10):e1003633. 5. Brown GD, Denning DW, Gow NAR, Levitz SM, Netea MG, White TC. Hidden Killers: Human Fungal Infections. Sci Transl Med. 2012;4(165):165rv13. 6. Arendrup MC, Mavridou E, Mortensen KL, Snelders E, Frimodt-Moller N, Khan H, et al. Development of Azole Resistance in Aspergillus fumigatus during Azole Therapy Associated with Change in Virulence. Plos One. 2010;5(4). 7. Howard SJ, Cerar D, Anderson MJ, Albarrag A, Fisher MC, Pasqualotto AC, et al. Frequency and Evolution of Azole Resistance in Aspergillus fumigatus Associated with Treatment Failure. Emerg Infect Dis. 2009;15(7):1068-76. 8. Mortensen KL, Jensen RH, Johansen HK, Skov M, Pressler T, Howard SJ, et al. Aspergillus Species and Other Molds in Respiratory Samples from Patients with Cystic Fibrosis: a Laboratory-Based Study with Focus on Aspergillus fumigatus Azole Resistance. J Clin Microbiol. 2011;49(6):2243-51. 9. Astvad KMT, Jensen RH, Hassan TM, Mathiasen EG, Thomsen GM, Pedersen UG, et al. First Detection of TR46/Y121F/T289A and TR34/L98H Alterations in Aspergillus fumigatus Isolates from Azole-Naive Patients in Denmark despite Negative Findings in the Environment. Antimicrob Agents Chemother. 2014;58(9):5096-101. 10. Bader O, Weig M, Reichard U, Lugert R, Kuhns M, Christner M, et al. cyp51A-Based Mechanisms of Aspergillus fumigatus Azole Drug Resistance Present in Clinical	

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		Samples from Germany. Antimicrob Agents Chemother. 2013;57(8):3513-7. 11. Lockhart SR, Frade JP, Etienne KA, Pfaller MA, Diekema DJ, Balajee SA. Azole Resistance in Aspergillus fumigatus Isolates from the ARTEMIS Global Surveillance Study Is Primarily Due to the TR/L98H Mutation in the cyp51A Gene. Antimicrob Agents Chemother. 2011;55(9):4465-8. 12. Seyedmousavi S, Hashemi SJ, Zibafar E, Zoll J, Hedayati MT, Mouton JW, et al. Azole-Resistant Aspergillus fumigatus, Iran. Emerg Infect Dis. 2013;19(5):832-4. 13. Steinmann J, Hamprecht A, Vehreschild MJGT, Cornely OA, Buchheidt D, Spiess B, et al. Emergence of azole-resistant invasive aspergillosis in HSCT recipients in Germany. The Journal of antimicrobial chemotherapy. 2015;70(5):1522-6. 14. Vermeulen E, Lagrou K, Verweij PE. Azole resistance in Aspergillus fumigatus: a growing public health concern. Current Opinion in Infectious Diseases. 2013;26(6):493-500. 15. Fraczek MG, Bromley M, Buied A, Moore CB, Rajendran R, Rautemaa R, et al. The cdr1B efflux transporter is associated with non-cyp51a-mediated itraconazole resistance in Aspergillus fumigatus. J Antimicrob Chemother. 2013;68(7):1486-96. 16. Snelders E, Camps SMT, Karawajczyk A, Schaftenaar G, Kema GHJ, van der Lee HA, et al. Triazole Fungicides Can Induce Cross-Resistance to Medical Triazoles in Aspergillus fumigatus. Plos One. 2012;7(3). 17. Verweij PE, Snelders E, Kema GHJ, Mellado E, Melchers WJG. Azole resistance in Aspergillus fumigatus: a side-effect of environmental fungicide use? Lancet Infectious Diseases. 2009;9(12):789-95. 18. Stensvold CR, Jorgenson LN, Arendrup MC. Azole-resistant invasive aspergillosis: relationship to agriculture. Curr Fungal Infect Rep. 2012;6:178-91.	

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		19. Head MG, Fitchett JR, Atun R, May RC. Systematic analysis of funding awarded for mycology research to institutions in the UK, 1997-2010. BMJ Open. 2014;4(1):6.	
08	General	The European Directorate for the Quality of Medicines & HealthCare (EDQM), a Directorate of the Council of Europe, welcomes the opportunity to comment on the EU Medicines Agencies Network Strategy to 2020 - Working together to improve health. The EDQM is pleased to see the Heads of Medicines Agencies (HMA) and the European Medicines Agency (EMA) working closely together to make sure that patients and animals in Europe have access to medicines that are safe, effective and of good quality. The EDQM is supportive of the high level strategy for the regulatory network for the next 5 years and welcomes the collaborative work that has gone into the development of the objectives that this strategy contains. We would, however, and on behalf of the expert members of the European Pharmacopoeia Commission (Ph. Eur.), users of the Ph. Eur., the OMCL network and holders of EDQM certificates of suitability ask for consideration of the following comments before finalisation of the strategy document.	
08	53-128	The EDQM/European Pharmacopoeia is a significant part of the European regulatory network and therefore should also be represented in this chapter (see also lines 524-526). By inclusion of the Ph. Eur. in chapter 1, the Ph. Eur. would be covered as part of the European network mentioned on several occasions in the document, especially in Themes 3 & 4. The integration of the Ph. Eur. as an actor and key player of the European Regulatory Network would especially make sense in view of lines 571-579.	
08	59		Add: …fashion, <u>supported by other European organisations such as the European Directorate for the Quality of Medicines & HealthCare (EDQM) of the</u>

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			Council of Europe.
08	69		Add: …work together on official batch control for biologicals and post-marketing surveillance and safety issues.
08	91		Add: In the quality sector, the work of HMA is supported by the EDQM (for example by the European Pharmacopoeia, the certification of suitability procedure and the coordination of official batch release and market surveillance).
08	213		Add: …batch release, both run in collaboration with the EDQM.
08	211-215	Collaboration with the Ph. Eur. Commission and its group of experts on setting quality standards for biological products could be mentioned in this paragraph (or at least the need for further strengthening of the existing cooperation).	
08	213		Delete: "at"
08	226		Replace: "old" with "well-established"
08	228		Replace: "complicated" with "complex"
08	335		Add: …recognition procedure, official batch release, EU-wide…
08	526		Add: Other elements ~~are~~ include the need to achieve common standards of

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			scientific quality across the EU regulatory network, and to strive for state-of-the-art (scientific) guidelines., and in order to reinforce the regulatory capacity of the network, support for the maintenance and development of practical testing expertise in the Official Medicines Control Laboratories.
08	528		Add: …considered in collaboration with partner organisations (such as the EDQM as coordinator of the OMCL network and in charge of the certification of suitability procedure), avoiding…
08	580	1. For this objective, the collaboration with partners such as the EDQM should be strengthened. 2. Part of this objective should be to optimise communication within the network and not just in 'crisis situations' or to outside stakeholders. This concept is mentioned in the title but not reflected in the highlight box.	
08	613-640	The EDQM is an organisation which collaborates on a regular basis with EMA and NCAs on a number of activities. We believe that the EDQM should be mentioned in this section	
08	614	Collaboration with other organisations active in this field should be strengthened	Add: …accessible to patients, and in ensuring their quality, and…
08	640		Add: Considering the role of the EDQM, both in establishing common

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			quality requirements for medicines in the European Pharmacopoeia and ensuring their application via the certification of suitability procedure as well as the EDQM's coordination of the Official Medicines Control Laboratories Network activities which are critical to many of the objectives outlined in this document, the network should strengthen the interaction and collaboration with the EDQM taking into account their discrete roles, to further enhance the robustness of the regulatory system.
08	645	It is commonly agreed that about 80% of APIs used in Europe are sourced from outside the EU (as mentioned in line 674). Moreover, for a number of APIs, a European source is no longer available. Therefore it is relevant to add the manufacture of APIs alongside pharmaceutical activities and clinical trials;	Add: …pharmaceutical activities, in particular the manufacture of active substances and the growth of clinical trial activity in countries outside the EU…
08	672	Please clarify the text: "supply chain" singular is used in the title of this objective but throughout the text there is a mixture of "supply chain" and "supply chains" used.	
08	681-683	The current International API inspection programme could be mentioned as an example of international initiatives for information sharing on manufacturing sites and GMP compliance.	
08	723	IGDRP is no longer a pilot and is now a programme	Replace "the International Generic Drug Regulators Pilot (IGDRP)" by "the

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			International Generic Drug Regulators Programme (IGDRP)"
08	729		Add: …with WHO and EDQM, will…
08	800	IGDRP is no longer a pilot and is now a programme	Replace "the International Generic Drug Regulators Pilot (IGDRP)" by "the International Generic Drug Regulators Programme (IGDRP)"
09	General	The Association of Clinical Research Organizations (ACRO) represents the world's leading, global clinical research organizations (CROs). Our member companies provide a wide range of specialized services across the entire spectrum of development for new drugs, biologics and medical devices – from discovery, pre-clinical, proof of concept and first-in-man studies through post-approval and pharmacovigilance research. With more than 110,000 employees engaged in research activities around the world (including 30,000 in Europe), ACRO advances clinical outsourcing to improve the quality, efficiency and safety of biomedical research. Each year, ACRO member companies conduct more than 9,000 clinical trials involving nearly two million research participants in 142 countries. On average, each of our member companies works with more than 500 research sponsors annually. ACRO thanks the European Medicines Agency (EMA) and Heads of Medicines Agencies (HMA) for the opportunity to submit comments on the "EU Medicines Agencies Network Strategy to 2020". ACRO fully supports this EMA and HMA initiative to establish a single coordinated strategy for the network, reflecting the need for a coordinated approach by the EMA and the national competent authorities to support biomedical innovation and ensure timely access to safe and effective medicines for EU patients. ACRO welcomes this and future opportunities to provide to the network the expertise available within its member companies for consultation and comment on relevant issues in the field of	

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		human medicines.	
09	53-128	The Introduction to the document defines the role of the EU Medicines Agencies Network as ensuring 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." Understandably, the Introduction focuses on regulatory activities to support the availability and use of safe and effective medicines in the EU. However, we consider that this section of the document would be strengthened significantly by also highlighting the activities undertaken by the network to discharge its regulatory responsibilities while at the same time promoting and supporting biomedical innovation and the improvement of public health in the EU. We also note that the document makes no statement about accountability for delivery of the strategy, and consider that the document would be much more forceful if specific accountabilities were defined.	
09	186-239	ACRO supports the focus on preparedness to address key public health emergencies and priorities. The document identifies some key priorities as antimicrobial resistance, and the availability of medicines for treating dementia and for use in special populations such as children and the elderly. ACRO recommends that a formal list of public health priorities is developed in consultation with a broad range of stakeholders in order to ensure that agreement is reached on the most urgent priorities, and to ensure that effort is directed to these by the development of an action plan, also developed in conjunction with a broad range of stakeholders, for each priority identified.	
09	240-274	ACRO supports the objective of ensuring timely access to new beneficial and safe medicines for patients. However, ACRO notes that the network plans to achieve this by 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	

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		(HTA)/ pricing and reimbursement bodies and healthcare professionals and patient representative bodies. While we agree that all of this should form part of the approach, we recommend that EMA and HMA does not rely solely on the flexibilities within existing regulatory pathways but also looks more widely to consider new approaches and pathways that would further facilitate timely access to beneficial and safe medicines. ACRO was disappointed to see that a proportionate risk-based approach to medicines regulation was not highlighted as an element of this objective, as we consider that this is a fundamental principle of effective and efficient regulation. We also note that the collaborative bodies identified in this section are (implicitly) within the EU. We acknowledge that a separate section of the document (Theme 4) addresses international collaboration, but consider that international cooperation between regulators is such an essential element in ensuring the timely access of EU patients to safe and effective medicines that we recommend this is also highlighted in the current section of the document.	
09	275-318	ACRO is pleased that the document identifies support for patient focused innovation and contribution to a vibrant life science sector in Europe as a key objective for the network. As noted above, we are concerned that some other parts of the document do not adequately highlight the role of the network in facilitating biomedical innovation and improving public health. We are especially pleased that the document commits the network to ensure optimal implementation of the new Clinical Trial Regulation (536/2014) and acknowledges that the decline in EU clinical trial activity over recent years has resulted from an unfavourable regulatory environment. Line 288 recognises that the success of the Clinical Trial Regulation will depend on its implementation across the EU, and ACRO fully endorses this statement. To this end, and to help reverse the global perception of the EU as an unfavourable regulatory environment for clinical trials, ACRO recommends that the network consults widely with stakeholder groups to consider how the Clinical Trial	

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		Regulation can be implemented successfully across the EU, and develops and publishes a detailed plan of the steps that it will take to ensure this is achieved. In order to regain global competitiveness in clinical research, particular stakeholder concerns that would need to be addressed include a clear statement from the network that review timelines stated in the Regulation will be considered as maxima and that everything possible will be done to work to shorter timelines, sponsor concerns about the publication of detailed information about specific clinical trials prior to marketing authorisation, the Annex VI labelling requirements that may adversely impact EU competitiveness by limiting innovation and increasing administrative burden and cost, and the planned "gentleman's agreement" for a clock-stop over the Christmas/Epiphany period, which will create the impression to the rest of the world that Europe's regulators are closed for business as far as clinical trials are concerned during this period.	
09	319-361	ACRO fully supports the network's stated objective to 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. These are all important developments that will significantly improve the timely access of safe and effective medicines to patients. As noted in the text, however, many of these developments have implications for data privacy and the protection of personal data. Currently, there is no harmonised EU position on requirements for the protection of personal information collected during health research, leading to significant administrative burden and expense for those conducting such research across the EU. It is unlikely that the forthcoming EU Data Protection Regulation will include the required level of granularity to address this, and so ACRO recommends that an important, additional element of the network strategy should be to work with Data Privacy Commissioners across the EU to develop a harmonised EU position on requirements for the protection of personal data collected in biomedical research. Additionally, as noted earlier, we acknowledge that a separate section of the document	

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		(Theme 4) addresses international collaboration, but consider that international cooperation between regulators is essential in the development of regulatory science, and recommend that this is also highlighted in the current section of the document.	
09	513-539	ACRO supports both the objective to reinforce the scientific and regulatory capacity and capability of the network, and the actions identified.	
09	540-579	ACRO agrees with the objective to optimise scientific and operational procedures and continuously improve the quality of the (scientific) output within the current regulatory framework. We note that this will be underpinned by adequate and inter-operable IT systems and therefore strongly recommend early and continuing consultation with stakeholder groups representing organisations that will be required to submit data to the IT systems as new systems and standards are developed. The text rightly emphasises the need for robust quality systems within the network. However, the document does not address the need for accountability and stewardship to ensure appropriate cost controls and streamlining of operations. While recognising the complexity of this in a network comprising national competent authorities funded by EU Member State governments and the centrally (EU)-funded European Medicines Agency and European Commission, ACRO considers that an important element in optimising the operation of the network is to ensure that EU tax payers and user fee payers can be assured that they receive value for money from the operation of the network, and this aspect appears to be missing from the document.	
09	580-612	ACRO supports both the objective to ensure effective communication of and within the network, and the actions identified	
09	613-639	ACRO supports both the objective to strengthen the links with other authorities and with stakeholders, and the actions identified. ACRO welcomes the opportunity to provide to the network the expertise available within its member companies for consultation and comment on relevant issues. We note that the network plans to put in place more	

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		streamlined mechanisms to obtain regular feedback from key stakeholders on the operation of its activities and the quality of its output, and recommend that these mechanisms allow for stakeholders to raise and discuss concerns prospectively with the network and are not confined to providing feedback on specific topics requested by the network.	
09	672-697	ACRO supports both the objective to assure product supply chain and data integrity, and the actions identified	
09	698-734	ACRO is greatly encouraged that 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. In ACRO's view, such activities are key to facilitating timely access to safe and effective medicines for patients worldwide. We were surprised to note that the examples of new cooperative mechanisms between international regulators did not include the Global Coalition of Regulatory Science Research, as the European Medicines Agency has participated in this coalition, which has the potential to make a significant contribution to the development of regulatory science and facilitate innovation in biomedical research.	
09	735-761	ACRO supports both the objective to ensure best use of resources through promoting mutual reliance and work-sharing with regulators in other territories, and the actions identified.	
09	762-775	ACRO supports both the objective to support training and capacity building and promote the EU regulatory model, and the actions identified. ACRO thanks the European Medicines Agency (EMA) for the opportunity to submit comments on the "EU Medicines Agencies Network Strategy to 2020."	

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10	General	EFSA believes the 'EU Medicines Agencies Network Strategy to 2020 - Working together to improve health' is a comprehensive framework for the network in the coming years. In particular EFSA welcomes the detail and clarity provided on • the process of putting together a joint-strategy EMA with MSs medicines agencies for the next 5 years • the rationale for putting the emphasis on the network and the added-value of the network instead of focusing on EMA. • how EMA is working with national bodies when it comes to transparency and access to data and sees a common interest in the areas of : • 'Contributing to animal health and human health in relation to veterinary medicines' (Theme 2) which provides several objectives/goals which EFSA supports. • Antimicrobial resistance (AMR), in particular in two of the themes: Theme 1 on 'Contributing to human health' and Objective 4 of Theme 2 on 'Focus on key public and animal health priorities including antimicrobial resistance'. • The promotion of a one health approach that the EMA's network is adopting.	
10	General	In the area of EFSA's regulatory activities, potential synergies are noted in the areas of • Theme 1 on 'Contributing to human health'- Objective 4 'Strengthen regulatory capacity and transparency' • Theme 2: Contributing to animal health and human health in relation to veterinary medicines – Objective 2 Promote 'Better Regulation' and EFSA looks forward to closely following and supporting activities in these areas. Although it has been made clear in Chapter 2 on 'Approach to the Strategy' that the	

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		Strategy is meant to be a high level strategy and not a description of all the work that will be taken forward, the document would have greater impact and clarity if there were some indications of actions/methods/tools/milestones/measurement that could be applied to reach the objectives formulated. Therefore it is difficult to assess the probability of achieving the objectives of the Strategy. Certain activities could be listed within a timeline without details. Regarding Objective 4: 'Strengthen the links with other authorities and with stakeholders' of Theme 3, it is noted that the section is rather short especially on the links with other authorities. It is suggested that EMA provides more detail on the interagency collaboration activities that are on-going in that area. In the coming years, cross support between EFSA and EMA experts will continue to be important and EFSA believes it would be beneficial to provide more detail on how such collaboration could be strengthened. Interagency cooperation will continue to be essential to achieve the objectives in areas of mutual interest such as animal health, AMR, one health approach. In the same Theme, Objective 2 'Strive for operational excellence' highlights the requirement for inter-operable IT services. In addition to internal services within the network, EFSA believes this is increasingly important between agencies.	
10	General	Overall the division into strategic themes with objectives - To make this structure easier to follow for the reader would recommend differentiating the typeface (font/colour) of a 'Theme' and the Objectives as currently the difference is minimal and not so easy to follow.	
10	General	There is an overabundance of imprecise, inactive verbs to describe activities that need to take place within the 5 year period, such as 'explore', 'will explore', 'will continue to explore' or 'will have to progress', 'will need to be strengthened', will need to consider', 'will need to reflect' . Using more active verbs and phrases which are specific would make the overall document more credible and compelling to read (e.g. lines 202, 207, 232, 261, 264, 295, 296, 298, 302, 305, 317, 471, 592, 596, 626, 752, etc.)	

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11	General	In relation to propose new or amending legislation for the pharmaceutical sector: EFPC proposes to look at unnecessary flaws in legislation now. Proposing Anti-Biotics (AB) to be on Doctor's prescription only, we propose to the EMA for an advice to nations. This is in the interest of reducing resistance to AB. Also adjustment in the legislation concerning unwanted and harmful variation in prescription, over prescription of drugs and waste should be addressed.	
11	204	In addition we would suggest to mention in particularly handicapped people and deprived groups in the society like Roma in order to assure an accurate communication.	
11	217	Public health emergencies: it should be emphasized that due to moving populations not only the risk for spread of infectious diseases has increased but also the continuity of care which is hampering the provision of adequate pharmaceutical care.	
11	241-242	Strengthening the collaboration with health care professionals: This would include the concern of Primary Care professionals for: • The risk for over-medication • Ensure the full scope for non-pharmaceutical treatments as well	
11	317	Bottom up initiative via Community Primary Care services will be crucial to achieve this.	
11	596	For this a specific working group to connect with Primary Care professionals would be highly relevant. We are in the process of developing such working group with a range of partners/stakeholders active in Primary Care and we would be very keen to get support from the EMA to continue this process and being financially supported by the European Union in performing this crucial task.	

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11	606	Once more, also in these emergency situations a lot has to be done on community level by primary care professionals in prescribing the correct medication, informing other stakeholders and the public; this would require a pro-active communication with primary care professionals, so a need for a special working group for this.	
12	General	No comments on the Strategy document.	
13	General	BEUC welcomes the opportunity to comment on the EU Medicines Agencies Network Strategy to 2020. To better address public health needs and optimise the safe use of medicines for human use in Europe, we encourage the EU Medicines Agencies to address the following: • The network's strategy should be more representative of the needs of all patients, rather than highly focusing on a narrow group of patients with unmet medical needs. • The trend to make new medicines available earlier must not be at the expense of the safety of medicines. All patients, including patients seeking early access to a medicine for unmet medical needs, deserve the same protection. • We welcome a discussion on knowledge generation and evidence requirements for medicines access. We strongly believe that 'early access' programmes should be limited to subset of medicines to treat genuine unmet medical needs or rare diseases. In this way, early access programmes should remain the exception and should not become the rule. • The term 'novel' suggests newer although it doesn't necessarily communicate that the products should be better than existing alternatives, which is what all patients deserve. Therefore, we suggest the term 'novel' be replaced with the term 'added therapeutic value' throughout the document. • European regulators can play a leadership role by stimulating sponsors to study and	

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		submit data on the comparative effectiveness of new medicines in the application for market authorisation. The earlier a medicine's comparative efficacy is known in the medicines lifecycle, the greater the benefits for pricing and reimbursement decisions, the faster access to medicines of added value, and the more informed decisions by healthcare providers and patients can be achieved. • The network strategy can acknowledge overconsumption and inappropriate prescribing as key challenges and integrate their reduction into the long term goals of the network. • In response to public health emergencies, we would like to see the rapid introduction of preventative and treatment measures that have been proven to be safe and effective. • Greater attention to drug shortages, particularly the economic factors that cause them, and the coordination and dissemination of information about them, would be beneficial to consumers. Optimise the balanced involvement of stakeholders in the network's activity while appropriately handling potential conflicts of interest.	
13	General	As concerns medicines for veterinary use, BEUC would like to make the following recommendations: • If we welcome the work undertaken by EMA to update the SPCs of antimicrobials and integrate references to the prudent and responsible use of antimicrobials, we also believe that the strategy should mention the possibility to restrict, or even forbid, the veterinary use of certain antimicrobials deemed of critical importance for human health. This is particularly relevant as the EMA will help the European Commission identify which antimicrobials should be on the two lists mentioned in the new Veterinary Medicines Regulation – i.e. the list of antimicrobials restricted in	

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		veterinary medicine and the list of antimicrobials forbidden off-label. BEUC encourages EMA to prioritise the evaluation of modern cephalosporins and fluoroquinolones, which are used in livestock while being used as a last resort solution in patients with difficult-to-treat infections. For more information please access the BEUC position paper on antibiotic use in livestock and the BEUC position paper on the European Commission's proposals to tackle antibiotic resistance in the Veterinary Medicines and Medicated Feed legislations. • A record system for consumption data will greatly improve transparency and help determine where most efforts must be devoted. To do so it is important to collect relevant information and combine different kinds of data to get a full picture of antibiotic use in livestock. Consumption data should provide information on the duration of treatment, the dose administered, the number of animals treated, the therapeutic indication and the administration route. It is particularly important to monitor and record any metaphylactic use as this practice is not substantiated by any scientific studies but rather validated because of organisational matters. Ideally consumption data should be collected at farm level and at veterinarians' level to get a full picture of the true situation on the ground. In addition any off-label use should also be collected. For more information please access the BEUC position paper on antibiotic use in livestock and the BEUC position paper on the European Commission's proposals to tackle antibiotic resistance in the Veterinary Medicines and Medicated Feed legislations. • The new Veterinary Medicines Regulation might abolish the ranking system which helped determine what antimicrobials are most suitable when there is no drug available for the species and/or the indication. This means that antimicrobials only	

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		authorised in humans could be administered to food-producing animals. As such the EMA should update antimicrobials SPCs to reflect on the need to use antimicrobials only allowed in human medicine as a last resort solution after all veterinary medicines have been deemed unsuitable. For more information please access the BEUC position paper on antibiotic use in livestock and the BEUC position paper on the European Commission's proposals to tackle antibiotic resistance in the Veterinary Medicines and Medicated Feed legislations.	
13	163	Rationale: Polypharmacy, or the use of multiple medicines, is on the rise and it often goes hand-in-hand with inappropriate prescribing, or medicines for which the risks outweigh the benefits and for which there are effective, safer alternatives. Medicines are prescribed to treat symptoms or diseases that can also be addressed by lifestyle changes or non-drug therapies, which are often highly effective, lower cost and potentially safer options for patients and healthcare systems. We suggest that the challenge of polypharmacy and inappropriate prescribing also be acknowledged in the strategy for the network.	Text: As the population ages, diseases such as dementia become more of a public health burden. **Polypharmacy and inappropriate prescribing can lead to serious and preventable adverse events, particularly in older people**.
13	167 Also at 241, 246, 319…	Rationale: The term 'novel' suggests *newer* although it doesn't necessarily communicate that the products should be better that existing alternatives. Only products that are better than existing alternatives will give patients the added value they need. Therefore we suggest the term 'novel' be replaced with the term 'added therapeutic value' throughout the document.	Text: It is important that the network keeps abreast of these advances in science to ensure that ~~novel~~ products **of added therapeutic value** can be developed optimally for the benefit of the health of the citizens of Europe.
13	173	Rationale: Experiences in the US show that expedited regulatory evaluation programmes have resulted in safety implications for patients, including a higher risk of serious adverse drug reactions (ADRs) and higher rate of patient information leaflet (PIL) revisions for dose, safety and efficacy issues (1). We suggest this challenge be more	Text: Monitoring of products throughout their lifecycle has never been more critical, **as more information is needed on the benefit-risk balance of medicines, particularly those to**

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		clearly acknowledged, substantiating the need for continuous monitoring. (1) Kesselheim et al. JAMA 2011;305:2320-6 Berlin. Am J Pub Hlth 2009;99:1693-8	**which early access has been granted**.
13	175	Rationale: In BEUC's view, the trend to make new medicines available earlier must not be at the expense of the safety of medicines. Consumers expect that all licensed medicines have been proven to be safe before reaching the market. All patients, including patients seeking early access to a medicine for unmet medical needs, deserve the same protection.	Text: To enable promising new medicines to get to patients ~~**at the earliest opportunity**~~ **in a timely manner** requires us to **establish their safety profile before exploring** flexible licensing pathways and a life-span approach with clinical drug development, licensing, reimbursement, use in clinical practice and monitoring viewed as a continuum.
13	187	Rationale: Forward looking regulatory initiatives are often best started by taking stock of what has already been accomplished in the field of regulatory incentives, particularly for orphan medicines and paediatric medicines. BEUC encourages the EU network of Medicines Agencies to host a public consultation and independent analysis of past regulatory incentives to bring products of added therapeutic value to the market, prior to embarking on future regulatory initiatives. Lessons learned from the past can inform best practice in the future.	Text: It will also ~~review whether there are areas that could benefit from~~ **conduct an independent analysis of past** regulatory incentives to support the development of novel products **and, based on the results, determine whether there are areas that could benefit from future incentives.**
13	203	Rationale: Vulnerable groups such as older people and children are susceptible to overprescribing and inappropriate use of medicines. BEUC recommends that the network strategy acknowledges overconsumption as a key challenge and integrate its reduction into the long term goals of the network.	Text: 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

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			have timely access to appropriately developed medicines together with appropriate information to support their use **and reduce overconsumption**.
13	221	Rationale: Patient safety is the centerpiece of any response to public health emergencies. BEUC would like to see the rapid introduction of preventative and treatment measures that have been proven to be safe and effective. The case of Tamiflu has illustrated that all balanced public health responses need to be based on established safety and efficacy of medicines, verifiable through access to clinical trials data, prior to medicines purchase and use.	Text: 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**~~ **timely** introduction of new treatment or preventative measures **proven to be safe and effective**, and learning from actions taken to address public health crises such as the Ebola outbreak
13	226	Rationale: Economic factors have featured prominently in some cases of drug shortages in the EU, therefore, BEUC proposes to state this more clearly.	Text: These supply issues can be caused by falsified medicines, stolen medicines, manufacturing/GMP non-compliance issues, ~~**or many other factors including**~~ economic **factors and many others**.
13	235	Rationale: Greater attention should be paid to informing healthcare professionals and patients of impending or actual drug shortages, especially considering the cross border aspects of drug supply.	Text: The network will also need to increase its cross-border collaboration in case of supply disruptions that affect multiple Member States, **in particular to rapidly coordinate and disseminate information about**

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			shortages or impeding shortages to healthcare professionals and patients.
13	167 Also at 241, 246, 319…	Rationale: The term 'novel' suggests *newer* although it doesn't necessarily communicate that the products should be better that existing alternatives. Only products that are better than existing alternatives will give patients the added value they need. Therefore we suggest the term 'novel' be replaced with the term 'added therapeutic value' throughout the document.	Text: It is important that the network keeps abreast of these advances in science to ensure that ~~novel~~ products **of added therapeutic value** can be developed optimally for the benefit of the health of the citizens of Europe.
13	243	Rationale: Access to medicines earlier in their lifecycle is sought by patients with unmet medical needs who want to expand their treatment options. Whereas patients whose medical needs are met do not have the same motivation to pursue so-called 'early access'. This nuance should be addressed in the text.	Text: Patients **with unmet medical needs** 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
13	245	Rationale: In general, regulators are the 'guardians' of medicines safety and efficacy and it is their responsibility to balance the highest safety & efficacy standards with access. As this is a statement of their general responsibility, we suggest to remove the reference to unmet need.	Text: 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~~.**
13	246	Rationale: The original statement should clearly be linked to medicines of added therapeutic value. Although new medicines with only marginal benefits compared to competitors can create some price competition between patented medicines, it doesn't	Text: There is clear consensus amongst industry, regulators and HTA/pricing and reimbursement bodies that timely

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		tend to lead to price reductions in practice (2) and can detract from investments from other, much needed areas of research. (2) Hollis, A. (2004). Me-too drugs: is there a problem. WHO report.	access to ~~appropriate novel~~ medicines **of added therapeutic value** is a priority.
13	260	Rationale: Consumers expect that all marketed medicines are proven safe and this same approach must be taken to all 'timely access' measures for medicines.	Text: 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**, while still ensuring that expedited access is not at the expense of medicines safety**.
13	265	Rationale: When considering HTA/pricing and reimbursement mechanisms, BEUC finds it important to consider the policy context of each country and respect the autonomy of each health system to choose which technologies and medicines it wishes to use. Studying the comparative efficacy of medicines can help enable access to the most optimal and safest treatments for patients. The earlier an assessment of comparative efficacy can take place in the medicines lifecycle, the quicker decisions about pricing and reimbursement can be made down the line, the faster medicines of added value can reach patients, and the more informed decisions can be made by healthcare providers and patients about the best available therapy. Moreover, European regulators can play a leadership role by stimulating sponsors to study and submit data on comparative effectiveness at the application for market authorisation. The EMA has already embraced the comparative efficacy criterion in situations where there are concerns about the safety or inferiority of a new drug (3).	Text: 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 **that respects national competencies** and sharing of information to allow optimal access. **To this end, the network will consider how to stimulate the collection and submission of data on the comparative efficacy as part of the application for market authorisation of a new product for all conditions for which alternative treatments**

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		(3) European Medicines Agency. Reflection paper on the need for active control in therapeutic areas where use of placebo is deemed ethical and one or more are available. EMA/759784/2010. November 2010.	**exist. This will facilitate future** HTA/ pricing and reimbursement **decisions ~~of medicines~~ that** are essential in getting innovative medicines to patients earlier.
13	267	Rationale: By including stakeholders in the various working groups, the network proves to be inclusive and responsive to societal needs and expectations. In this respect, it is vital to achieve a balance of stakeholders represented and to take into account possible conflicts of interest.	Text: 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. **Due attention should be given to achieving a balance of stakeholders participating in consultations, and a transparent declaration of any conflicts of interest they may have.**
13	271	Rationale: Medicines that change classification from prescription to over-the-counter (OTC) products can obtain one year of data exclusivity, which can prevent competing products from gaining market authorisation on the basis of the same data. Blocked competition keeps prices high for consumers. BEUC suggests to remove the reference to 'improving patient access' because affordability following a switch to OTC can be an issue for some consumers.	Text: 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~~.**

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13	280	Rationale: A reliable and efficient regulatory environment is needed to protect and uphold consumers' right to access safe and effective medicines. In most EU member states, the financial crisis bears some responsibility for the cuts in public R&D expenditure, not an unfavourable regulatory environment.	Text: Clinical trial activity has slowed in recent years as a consequence of increased competition globally **and strain on public budgets following the financial crisis**. ~~**and an unfavourable regulatory environment.**~~
13	307	Rationale: An unaffordable medicine is just at inaccessible for patients as a medicine that doesn't exist. BEUC would like to see references to HTA, pricing and reimbursement take a balanced approach to innovation to ensure that the results of medicines R&D are affordable for consumers and healthcare systems.	Text: Although outside of the remit of the network, HTA and pricing and reimbursement also play an important role in fostering ~~**innovation**~~ **innovative and affordable products** in Europe.
13	309	Rationale: The results of added therapeutic value assessments should serve to minimise the use of drugs with marginal benefits and ensure the most optimal treatments are affordable for patients and healthcare systems. The latter objective should be communicated more clearly when describing the network's objectives.	Text: 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 **in order to increase access to the best available therapies**.
13	167 Also at 241, 246, 319…	Rationale: The term 'novel' suggests *newer* although it doesn't necessarily communicate that the products should be better that existing alternatives. Only products that are better than existing alternatives will give patients the added value they need. Therefore we suggest the term 'novel' be replaced with the term 'added therapeutic value' throughout the document.	Text: It is important that the network keeps abreast of these advances in science to ensure that ~~novel~~ products **of added therapeutic value** can be developed optimally for the benefit of the health of the citizens of Europe.

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13	330	Rationale: BEUC supports the EMA to optimise its interaction with stakeholders while taking into account possible conflicts of interest. For example, the systematic involvement of the EMA at an early stage of the drug development process could influence the final assessment of the product and open the door to possible conflicts of interest.	Text: 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, **while also addressing potential conflicts of interest to maintain public trust in regulators' (perceived and actual) independence**.
13	331	Rationale: Considering the EMA has regular and systematic exchanges with patients, consumers and healthcare professionals, we suggest these groups also be named in the text.	Text: 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, **patients, consumers, healthcare professionals**, and others to ensure appropriate support is given to the developments in this area.
13	346	Rationale: While BEUC welcomes the potential for large healthcare datasets to contribute to medical advance, it reminds the network that patient data belongs to individual patients. Therefore, patients' individual informed consent should be sought before their	Text: The network will explore the use of 'big data' which has huge potential to enhance capability and reduce cost

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		information is collected, transmitted and shared.	whilst **ensuring individual informed consent for data use** and respecting individual patient privacy.
13	355	Rationale: The new European Medicines Agency policy on publication of clinical data represents a major step towards transparency. However, we are concerned that the regulation and the EMA policy only applies to new medicines - which effectively leaves out most of the medicines prescribed to or purchased over the counter by consumers. We consider it essential that the results of all past clinical trials are reported. The EMA should ensure that all data related to the efficacy and safety of medicines, submitted to regulatory authorities (at national and supranational levels) is publicly available, including all pre-market clinical data and post-authorisation studies.	Text: 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 **only** truly commercially confidential information out of the public domain. **In particular, the network will consider how greater transparency can be given to clinical trials data held by regulators supporting medicines licensed before 2015.**
13	461-462	Rationale: See general remarks on veterinary medicines.	Text: **The network will also liaise with other food safety bodies to develop an international strategy to combat antimicrobial resistance**.
13	461-462	Rationale: See general remarks on veterinary medicines.	Text: **The network will collect data on the use of antimicrobials in veterinary medicine to determine which policy options should be**

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			recommended.
13	461-462	Rationale: See general remarks on veterinary medicines.	Text: **The network will also provide recommendations to the European Commission on the antimicrobials that should be restricted or prohibited in veterinary medicine, and in particular when they are used outside the terms of the license, because they are deemed of critical importance in human medicine.**
13	470	Rationale: See general remarks on veterinary medicines.	Text: **The framework will be regularly evaluated to make sure any important information that would help better monitor and map antimicrobials use in veterinary medicine is collected.**
13	473	Rationale: See general remarks on veterinary medicines.	Text**: In particular, EMA should continue to cooperate with EFSA and ECDC to identify high resistance to antimicrobials in animals and humans and how they can be interlinked.**
13	481	Rationale: See general remarks on veterinary medicines.	Text: **The network will also provide guidance as to the use of any new antimicrobials to ensure they are**

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
			used responsibly and any resistance phenomenon is minimised.
13	532	Rationale: In recent years, the EMA has introduced progressively more rigorous policies to handle conflicts of interest between its agency and its stakeholders. Although there is still room for improvement, the EMA's policy on handling conflicts of interest can encourage national competent authorities with weaker or without such policies to adopt similar measures. Ultimately, the network should work towards an upwards harmonisation of handling conflicts of interest throughout Europe.	Text: 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. **To this end, the network will pursue a high standard of handling conflicts of interest, particularly by introducing new or reinforcing existing policies at all national competent authorities.**
13	571	Rationale: Regulatory efficiencies can result in benefits for the pharmaceutical industry and consumers, such as faster access to medicines proven safe. BEUC reminds the network that any legislative changes to reduce regulatory burdens must uphold the highest standards of safety, efficacy and quality to ensure consumer protection.	Text: Therefore, the network will consider further optimisation of the regulatory framework within the current legislative provisions **and in a manner that upholds the highest standards of safety, efficacy and quality to ensure patient safety**.
13	596	Rationale: BEUC encourages the network to seize the opportunity to learn from the EMA's structures for stakeholder consultation (i.e. Patients & Consumers Working Party, Healthcare Professionals Working Party, public written consultations, public meetings, etc.) and integrate these mechanisms in the work of national authorities, particularly	Text: The network will explore – together with patients and healthcare professionals – how to achieve product information more aligned with

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		concerning product information.	stakeholders' expectations and needs. **This can be achieved through the EMA's own consultation fora and also through greater consultation of patients, consumers and healthcare professionals, by the national competent authorities.**
13	634	Rationale: BEUC suggests that the key stakeholders should be made explicit and the network should actively strive for a balance of stakeholders.	Text: The network will put in place more streamlined mechanisms to obtain regular feedback from **a balanced group of** key stakeholders**, such as patients, consumers, healthcare professionals, and pharmaceutical companies** 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.
13	699	Rationale: Regulators are the 'guardians' of medicines safety and efficacy and it is their responsibility to balance the highest safety & efficacy standards with access. This core objective should be emphasised when referring to the network's leadership role in a global context.	Text: 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 **uphold patient safety and** strengthen cooperation with non-EU regulators in a consistent and

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			integrated manner.
14	General	GIRP is very much supportive of the excellent work of the EMA and is committed to working with the Agency where needed and demanded within the scope of responsibilities of pharmaceutical full-line wholesalers on improving the legislative and regulatory environment for the safe, efficient and effective distribution of medicines for European patients.	
14	92-102	GIRP is supportive of all new and ongoing revisions of European legislation mentioned in this consultation document. New and improved legislation and regulation can enhance the environment in which wholesale distributors operate in order for them to provide timely, safe and continuous supply of medicines to pharmacies, hospital and other healthcare professional for patients. However, it is important that legislation and regulation takes proportionate account of the individual activities and levels of responsibility of the different operators in the pharmaceutical supply chain. For instance, when obligations are being placed on wholesale distributors, it is important that facilitating obligations are placed on upstream and downstream operators, to ensure that wholesale distributors are effectively able to comply with their obligations. Post marketing surveillance is of utmost importance for national competent authorities when it comes to the oversight of the pharmaceutical supply chain. It is often the case that post marketing surveillance systems involve the requirement for operators in the pharmaceutical supply chain to record certain information about the products. Often we see the requirement for wholesale distributors to record the batch number and expiry date of the different types of products (medicinal products, veterinarian medicinal products, medical devices). It is essential that any requirement to record such information at the level of the wholesale distributor is based on the availability of information in a suitable machine readable format for wholesale distributors and for their	

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		data capture and storage. Not requiring the manufacturer or importer to ensure that such information be available in machine readable format, results in wholesale distributors being faced with an insurmountable challenge of having to record such information manually. The manual recording of such information results in a high number of errors. Manual recording also substantially slows down the speed of product commissioning and delivery. Finally it is important to mention that new requirements such as the one just mentioned are introduced in a proportionate and pragmatic way to the extent that they do not hinder the continuous supply of products to European patients. In summary, new legislation should not shift post marketing surveillance responsibilities and duties onto the shoulders of wholesale distributors. Legislation and regulation needs to take proper account of the actual activities and responsibilities of wholesale distributors in the supply chain. Wholesale distributors should not be burdened with post marketing surveillance activities which typically lie in the hands of national competent authorities or which are part of the marketing/manufacturing authorization holder or importer obligations. Wholesale distributors are authorised, in accordance with the principles and guidelines of Good Distribution Practices, to carry out wholesale distribution activities. Any legislative or regulatory obligation which would lead wholesale distributors to interfere with the packaging or the product itself would require additional licensing such as Manufacturing authorisations. Therefore, new legislative or regulatory obligations need to reflect the nature of activities and responsibilities of the wholesale distributors.	
14	178-180 + picture	It is important to mention that access to medicines is not only about authorising the placing of new products on the market. Pharmaceutical full-line wholesalers provide a framework for the safe, effective and efficient distribution of all medicines authorized to be marketed in the various national markets. Pharmaceutical full-line wholesalers provide the full range of medicines, in range and depth, to pharmacies, hospitals and other	

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		healthcare providers, within a very short timeframe. The timely access to safe medicines for European patients can only be fully guaranteed by ensuring that a sustainable framework is in place for the actual distribution of medicines by operators such as pharmaceutical full-line wholesalers. Therefore, as part of the strategy for the network, due account of the actual activities and responsibilities of pharmaceutical full-line wholesalers in the overall health care system should be taken into account. When speaking about ensuring "timely access to new beneficial and safe medicines for patients" the entire distribution chain and its compulsory cooperation needs to be duly considered.	
14	203-206	GIRP members (pharmaceutical full-line wholesalers) ensure that all medicines are available whenever and wherever needed so that even the most isolated patient can receive the most specialised medicine in a safe and timely manner. GIRP members guarantee the highest levels of supply chain quality, integrity and excellence. They are the trusted supply chain partners for manufacturers, pharmacists, healthcare professionals and, above all, patients. We would fully support public health priorities which focus on the issue of availability of medicines. We would encourage full and optimised recognition and use of the existing distribution network which is in place and operated by pharmaceutical full-line wholesalers. The contribution that the distribution network of pharmaceutical full-line wholesalers provide is often overseen in the discussion when it comes to ensuring medicines availability.	
14	221-224	GIRP would like to inform that the pharmaceutical full-line wholesalers can play a key role in crisis preparedness and in times of public health threats and pandemics. In some countries where wholesale distributors are legally obliged to carry out a public service obligation they are typically required to have buffer stocks over a defined period of time.	

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		Involving wholesale distributors in crisis and emergency planning can be important for national competent authorities in terms of inventory management of medicines and for making such medicines available whenever and wherever needed. For this purpose GIRP has an emergency contact list in place.	
14	225-236	Concerning the issue of shortages and lack of availability of medicines, GIRP would like to highlight that it stands ready to support initiatives which will help address these issues. While understanding the remit of the activities of the EMA, it is important to look at the issues from a holistic point of view. Shortages and the lack of availability of medicines are not only issues concerning manufacturing and GMP non-compliance. GIRP has published on its website (www.girp.eu) a reflection paper which sets out wholesaler distributors' perspectives on the root causes and possible solutions for mitigating the impact of shortages. It is therefore important to bring all stakeholders including pharmaceutical full-line wholesalers together to look at the root causes and to find common solutions which can help mitigate the problems arising from shortages and a lack of availability of medicines. The EMA can take a lead in facilitating the bringing together of all stakeholders in the pharmaceutical supply chain and public bodies to discuss these concerns and to find together measures which will address the issues mentioned here. GIRP therefore supports targeted initiatives that might look at these issues in a wider context.	
14	380-381	GIRP certainly lends its support to a strategy which will contribute to animal health and human health in relation to the availability of veterinary medicinal products. The European institutions are currently working on revising the legislative framework for veterinary medicinal products. GIRP widely supports the new legislative developments in this field. However, as mentioned in our initial remarks on supporting for operators in the distribution chain a better regulatory environment, it is important that new obligations reflect the actual activities of the various operators. When wholesale distributors will be required to record certain information (e.g. batch number and expiry date) on the outer	

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		packaging of veterinary medicinal products, it will be important that such information be available in machine readable format. It is therefore crucial that the legislation ensures that upstream operators (marketing/manufacturing authorization holders and or importers) are obligated to place such information on the outer packaging in machine readable format.	
14	412-426	As already mentioned previously as part of the strategy to promote better regulation, it is important that regulation only sets obligations which are reflective of the actual activities and responsibilities of the various operators in the supply chain. Time and time again we see obligations being placed on wholesale distributors to record certain information from the outer packaging of products. Typically, the requirement involves wholesale distributors to record the batch number and expiry date of the products. However, in order for wholesale distributors to effectively comply with this requirement, it is important that the regulation obligates marketing/manufacturing authorization holders and importers to make this information available on the outer packaging in a suitable machine readable format. Furthermore, the machine readable codes should be standardized.	
14	482-503	GIRP members stand willing and ready to take active involvement in the discussions with national regulatory agencies. It is often the case that representatives from the wholesale distribution community are not informed and not involved when important issues concerning Good Distribution Practices and Good Manufacturing Practices, which have a distribution perspective, are being discussed by national regulatory agencies in the presence of other stakeholders.	
14	580-589	As a stakeholder, GIRP supports this objective and believes that there is a need for effective communication between the network and stakeholder organisations such as ours.	

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		In order to achieve a better and smarter regulatory framework it is important to have a high level of understanding of the role of the different stakeholders and their organisations in contributing to achieve the current thoughts as outlined in the strategy.	
14	598-607	GIRP believes it has a role to play in helping address the major challenges related to the handling of emergency events with respect to authorised medicines. GIRP maintains an emergency contact list which can be used by central and national regulatory agencies in times of public emergencies. The emergency list is available on our website and the login details have been provided to the European Commission. GIRP members stand ready and are willing to take an active part in discussions which will lead to a better coordinated approach to the handling of public emergencies. GIRP members have been involved in dealing with public emergencies in the past such as during the H1N1 crisis and other pandemics.	
14	613-629	With respect to objective 4 we would like to highlight, in the area of medical devices, it is important that the new legislation and other initiatives, such as the development of the unique device identifier system, will include obligations and requirements which are proportionate to the activities and responsibilities of distributors.	
15	General	In order to be most efficient and effective during implementation activities, EFPIA and EBE suggest that the Strategy to 2020 include prioritisation of objectives and when possible timelines for the actionable items. While appreciating that this document is intended primarily to outline its overarching strategy, the Strategy to 2020 has voluminous aspects which will require thoughtful implementation efforts. Therefore, we presume that the EMA/HMA intends to develop task prioritisation, resource allocations, and project plans necessary for realising this strategy. We very much welcome the joint effort form the EU Network to collaborate on a common Strategy to 2020; however, as the strategy is being implemented it would be necessary	

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		to understand how the EMA, HMA, and other stakeholders will divide the activities to achieve the presented strategic objectives. Prioritization, resourcing, and new initiatives should be fully communicated and established through consultation with stakeholders. It is important that implementation does not delay patient access to new medicines nor increase burden on Regulators or on Industry. As helpful, industry would be very interested to be involved and provide input during these next stages. EFPIA and EBE propose that EMA/HMA develop a communication plan to ensure that all of the concerned stakeholders remain informed on the progress. The EMA/HMA may consider a stakeholder meeting to allow discussion of project prioritisation. Also, the EMA/HMA could, perhaps, release an update report at least annually or at an annual meeting gathering all stakeholders. The Strategy to 2020 mentions that "(t)he network will take forward the discussion on making individual patient level data from clinical trials available." As written, this statement is of most concern to EFPIA and EBE across the Strategy to 2020 document. EFPIA and EBE recognize the benefits of providing appropriate access to patient level clinical trial information to enable further research. First, as framed in its data sharing principles (http://transparency.efpia.eu/uploads/Modules/Documents/data-sharing-prin-final.pdf) EFPIA continues to believe that companies are best placed to provide access to patient level data under a controlled access model, especially given the recent efforts by companies conjointly (e.g. clinicalstudydatarequest.com) or separately (e.g. Yoda Project). These initiatives include a review of the scientific rigour of research proposals before providing access to anonymised patient level data to reduce the risk of erroneous concerns about safety or false hopes of a potential benefit for patients. Second, EFPIA has significant concerns about and reservations on uncontrolled access to patient level information from clinical trials. Patient level data from clinical trials should	

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		not be broadly or proactively provided if there is a reasonable likelihood of re-identification. Making such data available for downloading by researchers does not provide adequate protection of privacy, as the downloaded data may be combined with other information, increasing the risk of re-identification. To reduce this risk, access to patient-level data from clinical trials should be in a secure environment that does not allow downloading of the data. In summary, EFPIA believes that organised provision of patient level data from clinical trials properly falls within the remit of the clinical trial sponsor, and the industry can share such data in a way that effectively safeguards patient privacy and scientific rigour. Given the successful initiatives under EFPIA' s data sharing principles EFPIA is not convinced and therefore does not support that EMA provides access to patient level data from clinical trials, even for cases where EMA should request such data in the future. Digital health is not specifically mentioned in the draft Strategy to 2020 of the Network. This is a field that is currently not utilised to its full potential for meeting patient needs. At the same time technology is evolving and more and more solutions are being developed. Therefore, we suggest that the Network considers inclusion of the necessity/possibility for digital solutions for patient and healthcare focused innovation as part of its Strategy to 2020.	
15	183-184	The Strategy to 2020 prominently mentions "(s)upport for patient focused innovation & contribut(ion) to a vibrant life science sector." One way to assist in the vibrancy of the EU life science sector is through a balanced regulatory system which is interpreted with flexibility to advance scientific innovations. The EMA/HMA has another opportunity to demonstrate this balanced approach to regulation through ongoing implementation efforts of the new EU Clinical Trials Regulation. The impact of additional requirements must be assessed to ensure that the EU remains a welcoming place to conduct clinical research. As an example, the trend toward greater transparency of patient-level data	

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		may have an effect on the ability to recruit patients into EU clinical trials. This will help ensure that EMA/HMA and involved stakeholders do indeed contribute to facilitate a "vibrant life science sector".	
15	186, 276 and 299-300	There are several statements about the importance of "considering further regulatory incentives for innovation" and a note about "a European early stage innovative medicines designation". EFPIA and EBE believe that an EU environment that has adequate incentives for innovation is critical to realising a vibrant life science sector. Industry would appreciate the opportunity to discuss potential regulatory incentives further with EMA/HMA to assist in determining which incentives would indeed achieve a positive result, if implemented. There are likely multiple policy options that should be fully explored and would not compel an update to the pharmaceutical legislation.	Propose adding to the Strategy to 2020 a statement such as "EMA/HMA will discuss potential regulatory incentives with stakeholders to gain insight into which incentives would achieve a positive result, if implemented."
15	225-239	The drug shortage issue is a priority for the EU and we consider that this topic could benefit from a more detailed description. The Network should ensure that expectations and responsibilities are well defined and publicised so that stakeholders are able to readily comply. Editorial Comment: The following sentence seems incomplete: "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."	
15	240-241	EMA/HMA have usefully underscored the desire to "ensure timely access to novel medicines" and mention some areas of flexibility that may facilitate this (e.g., conditional approvals). Another approach to assist with this goal would be to reduce the timeline from positive opinion to Commission decision for centrally authorised products. By condensing the timeline of this decision making process, patients would have faster access to new treatment choices and innovation would be further encouraged. While it is	

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		understood that this process is under the "risk management" responsibility of the European Commission, a shortening of the processes is mainly in the hands of Member States. In particular, a strong cooperation with the national Agencies and their governments with the goal to speed up the review by the Standing Committee in the Decision Making process should be envisaged, in particular where a CHMP opinion was preceded by an accelerated assessment. Likewise, the network should consider ways to improve the process timelines for national products and the national phase for MRP/DCP products.	
15	240-274	The EMA has also recently implemented an adaptive pathways pilot. Industry intends to take advantage of every opportunity to engage EMA/HMA and other involved stakeholders during the pilot and upon its completion during the likely transition to a permanent pathway. EFPIA and EBE views adaptive regulatory pathways as an essential approach to ensuring that patients have timely access to innovative new medicines. However, as these adaptive pathways are still experimental during the pilot phase, the Strategy to 2020 should indicate that the network will also consider alternative approaches with similar aims, such as those being discussed within various initiatives (e.g., Innovative Medicines Initiative (IMI). This section and the reference to adaptive pathways should take account of the fact that the expectation of more targeted medicines in the future with clearer evidence on efficacy in a smaller number of patients requires new considerations for benefit-risk assessments. This will be even more applicable as extensive safety data will be generated over time, including post approval. Intensive scientific and regulatory discussions between the EMA and the Network will be needed to achieve consistency in approaches and to ultimately realise implementation of such approaches.	
15	257	As the Strategy to 2020 references the importance of engaging 'stakeholders' at multiple places, it would be helpful to clarify that stakeholders oftentimes include Industry.	

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15	265-266	The EMA/HMA identifies that "HTA/ pricing and reimbursement of medicines is essential in getting innovative medicines to patients earlier" and comment that one method is to ensure closer collaboration between the regulators, HTA/ pricing and reimbursement bodies and patient and healthcare groups. Earlier discussions with HTA/ pricing bodies at the stage of scientific advice and introducing parallel assessment would complement this approach with the aim to reduce the time between regulatory and reimbursement approval. Further considerations would be welcomed on how the needs and input of HTA/pricing and patient bodies can be incorporated into the Strategy to 2020.	
15	267-270	The Strategy to 2020 explains that "(f)urther efforts should be made to incorporate patients' values and preferences". These efforts in partnering with patients should also be coordinated, as much as reasonable, through international partnership, including other stakeholders such as the FDA, and other regulators; HTA bodies and payers globally; medical and other relevant professional organizations; and a critical mass of biopharmaceutical companies. This cooperation will assist companies in having a global medicine development strategy. The voice of the patient will then continue to be enhanced in the decision making process. In addition, IMI projects may offer a viable platform to develop methodologies for such approaches.	
15	271-274	The Network mentions a willingness to focus on possibilities for re-classifying certain products to non-prescription when they can safely be used in order to improve patient access. Given the challenges and experiences to date, the Strategy to 2020 (or subsequent implementation communications) should provide additional strategic details for how this might be optimally achieved.	
15	305-306	The Strategy to 2020 notes that "(o)ver the next five years, the network will generate a discussion on the most efficient and cost effective approach to knowledge generation and evidence requirements." We offer that the Network should also consider building on other related initiatives at a European level (e.g. IMI GetReal), at a national level (e.g.	

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		CASMI in the UK) and globally (e.g. with U.S.).	
15	307-312	"Efforts are ongoing to bring convergence in the assessment of therapeutic added value of new medicines and patient outcomes." EFPIA and EBE emphasize the need to improve the knowledge on appropriate patient outcomes and related metrics.	
15	322-323	"We are faced with personalised medicines, nanotechnology, cell and gene based technologies amongst other innovative products." There is a need for multi-stakeholder initiatives by the Network on topics where cooperation and convergence are necessary to foster the concept of personalised medicines and adaptive approaches, for instance cooperation of Biobanks and patient registries.	
15	326-327	"Over the next five years the network will need to ensure it has the capability to regulate the novel products of the future and to strengthen…." EFPIA and EBE wish to recognise the ongoing active role of members of the Network in the EU's IMI and believes that this is an important way to facilitate achievement of this objective. There is also the training/talent development aspect: are there sufficient links to schools/universities to identify talent early and ensure there are sufficient incentives (not just financial) for these individuals to pursue a research/technical-oriented career with regulatory authorities? Other important approaches that EMA/HMA will undoubtedly take are to engage stakeholders during technical workshops and in novel guideline development. Regular initiatives are needed to ensure leverage of knowledge of evolving science between industry, academia and regulators. Industry is willing to contribute to this and IMI could certainly be an important partner for this.	
15	338-339	Please refer to EFPIA and EBE input on data privacy under General Comments on data privacy. EFPIA and EBE fully support a multi-stakeholder debate on this critically important issue	

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15	341-347	The Strategy to 2020 notes that the "network will explore the use of 'big data' which has huge potential to enhance capability and reduce cost whilst respecting individual patient privacy". EFPIA and EBE agree with the emphasis on the importance of 'big data'. Access to anonymised data from electronic health records has the potential to make many changes to the ways in which we develop drugs and ensure their appropriate use once on the market. It will be important for the Network not only to "explore the use of big data" but also to encourage life sciences companies to submit evidence based on e-health records data. This is in line with EFPIA and EBE's recent open letter inviting the Competitiveness Council in the European Union (EU) to establish a working group on big data in healthcare (1). Though, as noted above, the risk of data breach of the EMA owned databases should be fully considered with all stakeholders including privacy experts. (1) http://www.efpia.eu/uploads/Competitiveness_Council_2-3_March_2015.pdf	
15	353	The Strategy to 2020 states "The network is already transparent about its regulatory decisions and how these decisions are made". While the EMA provides decision transparency through the European Public Assessment Reports (EPARs), a commensurate level of transparency on a local level may not be available in some cases. Therefore, initiation of publishing of assessment reports and regulatory decisions made by all NCAs should be included in the strategy.	
15	354	"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…" Biopharmaceutical companies are committed to advancing public health goals through responsible sharing of their clinical trial data in a manner which is consistent with the following imperatives: • Safeguarding the privacy of patients;	The Strategy to 2020 could provide additional detail on how the EMA and HMA intend to work with stakeholders to ensure that clinical trial information is shared responsibly, while ensuring patient anonymity and protecting

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		• Preserving scientific rigor and the trust in the regulatory systems; and • Maintaining incentives for investments in biomedical research.	commercially confidential information and continuing to support the development of innovative new treatments.
15	363-3481	Given its principal mission, EFPIA and EBE will not comment here on the animal health aspects of Theme 2.	
15	494-496	The Strategy to 2020 states that "…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". EFPIA and EBE fully agree with this essential element of the Strategy to 2020. In fact, the Nature Reviews article noted that "(e)ffort should also be made to address unnecessary bureaucracy in regulatory procedures in general…" It is likewise important that network fees are judiciously managed thus minimising as much as possible the administrative and cost burden for the pharmaceutical industry.	
15	502-503	"The network also needs to work closely with those it regulates." EFPIA and EBE continue to fully support this goal and believe that there are already good model examples as to where this has been effective including the EMA-industry stakeholder platforms that have been established for key topics and procedures. EMA hosted a productive meeting with industry on 24 April 2015.	
15	527-531	In terms of promoting the best use of expertise, it may be beneficial to note that the necessary expertise to enable global development may reside beyond the EU. For example, the Strategy to 2020 could add the underlined text below.	"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

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			more collaborative working, including enhanced outreach at national level for academic expertise and international expertise. This should enable a more synergistic approach towards the organisation of the expertise within the network and enhance international cooperation.""
15	535-536, 544-548	The Strategy to 2020 recognises that there is "…an ever-increasing pressure on human and financial resources whilst the workload continues to grow" for the network and "to optimise both the administrative and scientific elements, particular emphasis will be put on their operational efficiency and cost effectiveness". Just as the model for R&D is continually evolving, the corresponding regulatory model will besides continue to concurrently adapt. With every EMA/HMA initiative, regulatory policymakers should query if a more efficient and effective way is possible.	
15	539	According to the Strategy to 2020, an integrated IT system or data gathering initiative was piloted in early 2015. We would appreciate additional clarity about the referenced and/or related initiative(s).	
15	535-536, 544-548	The Strategy to 2020 recognises that there is "…an ever-increasing pressure on human and financial resources whilst the workload continues to grow" for the network and "to optimise both the administrative and scientific elements, particular emphasis will be put on their operational efficiency and cost effectiveness". Just as the model for R&D is continually evolving, the corresponding regulatory model will besides continue to concurrently adapt. With every EMA/HMA initiative, regulatory policymakers should query if a more efficient and effective way is possible.	
15	552-555	"A coordinated approach has already been undertaken through the development of a	We are proposing the following change

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		common EU Telematics Strategy". As there is a good level of ongoing development work on EudraVigilance, PSUR repository, and EU Clinical Trials Database and Portal, EFPIA and EBE will continue to engage in dialogue with EMA/HMA as it awaits efficient functionality of these pending systems.	in the text: "It will be important to strive for the most efficient connection between the national and the EU IT systems as well as for a gradual convergence of national systems."
15	591-592	The network envisions a "five year communication plan". As suggested in the General Comments, EFPIA and EBE support an annual update on progress towards achieving this strategy. Also, we hope that the overall communication approach allows for bi-directional communication with EMA/HMA on its Strategy to 2020.	
15	594-597	We welcome further improvement of the information to patients and healthcare professionals. The Strategy to 2020 states that "The network will explore – together with patients and healthcare professionals – how to achieve product information more aligned with stakeholders' expectations and needs." As industry is a key source of information on medicinal products, EFPIA and EBE have been developing proposals in this area, in anticipation of the Commission's review of shortcomings in current requirements for product information. Further, it would be useful to state an intention to consider not just the content of product information but the method of dissemination. In particular, the use of electronic media to ensure timely access to updated information to both healthcare professionals and patients. This may contribute to enhancing patient health literacy levels and ultimately benefit compliance and adherence.	
15	616-620	"The network will strengthen the interaction and collaboration between regulators and HTA/pricing and reimbursement bodies…" Efforts across the Network to facilitate regulatory and HTA/pricing and reimbursement body interactions are critically important for global development of new medicines. It would be useful to gain greater clarity on how the Network intends to strengthen collaboration with other key bodies such as HTA/pricing and reimbursement bodies.	

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15	648-653	"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" and identify how international collaboration can provide "opportunities to create synergies, avoid duplication and facilitate work and information sharing." Although the Strategy to 2020 refers more to the work sharing on GMP and global supply chain activities, we would welcome the further consideration of local in-country testing in this collaborative initiative. Local in-country testing can pose significant resource demands on Industry and Regulators alike. Therefore, benefit would be expected from a more collaborative, work sharing approach wherein the local testing results of one NCA might be taken by other NCAs in the region, avoiding duplication of effort.	
15	654-663, 729-732	"Smaller and emerging non-EU regulators are looking to the network for support and capability building". The Strategy to 2020 also emphasizes "cooperation with countries such as India and China". The network continues to serve as a champion of regulatory science and its commitment to the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceutical for Human Use (ICH) is commendable. As medicine development truly is a global venture, EFPIA and EBE support EMA/HMA in engaging with other regulatory agencies as they develop capabilities and to identify aspects for greater compatibility. Additionally, the strategy should also mention the continuation of cooperation with countries where partnerships have already been well established, such as the U.S.	
15	691-693	"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."	It would be helpful if more clarity was provided for how this will be accomplished and how information will

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
			be shared on this initiative.
15	694-695	"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." It will be appreciated if information on the process is fully described, and in those instances, specific details are shared with the relevant company.	
15	735-736	EMA/HMA seek to "(e)nsure best use of resources through promoting mutual reliance and work-sharing". Significant partnership already exists between the U.S. FDA and EU Network, both bilaterally and internationally particularly through the ICH. EFPIA and EBE consider that there are additional opportunities to develop even greater streamlined processes and procedures including, for example, for Good Manufacturing Practices (GMP) and Good Clinical Practices (GCP) Inspections, clinical trial applications and for paediatric development planning. While there are ongoing formal government discussions on some of these topics, it is still possible to achieve improvements on 'mutual reliance' and 'work-sharing' even today. In addition, the concept of establishing "centers of excellence" in Europe for various topics, such as the assessment of applications for clinical trials and marketing authorisations, should be considered. The section summary box states that the primary objective of the Network will be to encourage the adoption of European regulatory approaches. Although harmonisation across the EU region could be a good model for other regions, it is hoped that the Network will similarly be open to exploring and adopting best practices from other regions as applicable.	
15	760-761	In the same spirit of mutual reliance and when approached for collaboration, EFPIA and EBE believe that the EMA/HMA should foster partnerships with other non-EU regulatory authorities to allow them to rely on European assessments and inspections. Indeed, the lack of adequate resources faced by regulators in certain regions of the world can	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		contribute to delays in approval of medicines in these regions.	
15	762-763	"Support training and capacity building and promote the EU regulatory model." EFPIA and EBE, along with other regulatory stakeholders, may be supportive collaborators in securing expertise for certain capacity building topics.	
16	General	All the partners of the REGenableMED project are aware of the existence of this draft strategy. We welcome the opportunity to review this document on "EU Medicines Agencies Network Strategy to 2020- Working together to improve health." Generally, we believe this document is much needed and timely. If the Network is successful in achieving its strategic objectives, it will lead to major advances in the development and clinical uptake of advanced therapies in the European Union. Moreover, while the strategy rightly underlines the need to take into account the points of views of patients, healthcare professionals, industry and academia, we would also like to highlight the specific contributions of social scientists working in these areas. For example, social science research projects such as REGenableMED systematically elicit and track the positions of relevant stakeholders, and the changing business models of medicines producers (particularly relevant to line 631 of this draft). It should also be valuable to the Network in the context of Theme 1 Objective 2 on "Ensure timely access to new beneficial and safe medicines for patients" and Theme 3 Objective 1 on "Reinforce the scientific and regulatory capacity and capability of the network".	
16	Page 6, 165-177 and 621-629	The emergence of complex advanced therapies and combination and borderline products (including medical devices and diagnostics), which don't have a clear regulatory and commercial route to clinic, highlights the need for progressively adaptive and flexible regulation that is capable of evolving with emerging scientific knowledge and new technologies. The REGenableMED project is generating a sound evidence base for decision-making by looking at these issues within business model, value chains and	

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		broader innovation ecosystems perspectives. The one-size fits all pharmaceutical model is clearly not fit for purpose when it comes to complex and highly differentiated regenerative medicine therapies.	
16	265-266	The role of horizon scanning organisations should also be recognised as an important conduit in getting innovative medicines to patients earlier.	
16	302-306, 313-316	Modern therapeutic development spans pharmaceuticals, biologics and new pathbreaking approaches such as regenerative medicine. Therefore, policy approaches must move more explicitly away from the notion of conventional pharmaceutical innovation, which has an established regulatory framework, and business model to move products from the laboratory to the clinic. In contrast, emerging health technologies such as regenerative medicine are faced with continuing uncertainty about their pathways to market, and the regulatory burdens are greatest for the SMEs and smaller organisations that are at the cutting edge of technology development. A whole innovation ecosystem approach is needed that attends to the scientific, clinical, regulatory and pricing/reimbursement pathways to clinic, and recognises the complex mix of organisations and institutions now needed to develop advanced therapies.	
16	319	In order for the network to develop capabilities to regulate novel products of the future by developing regulatory science, there is also a need to re-imagine the design of clinical trials and type of data required for novel health technologies such as regenerative medicine, which again might be quite different from conventional pharmaceutical products or other advanced biologicals.	
16	616	We especially welcome the recognition of the need for closer coordination between HTA and regulation.	
16	659	The involvement of the Network with the Council of Europe, and especially with the European Directorate for the Quality of Medicines & Healthcare should be highlighted and	

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		collaboration could be strengthened.	
17	Theme 1	The following summary of issues relevant to this theme is based partly on reports prepared by Tait as contributions to the work of the UK Emerging Science and Bioethics Advisory Committee (ESBAC) (UK Department of Health, 2012-14). It also draws on more recently completed research projects on regenerative medicine, stratified medicine and antimicrobial resistance (AMR). Within the broad range of constituencies represented on ESBAC (https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/328623/Membership.pdf) there was a sense of frustration related to the governance approaches being applied to many health related technologies, seen as leading to a crisis in funding for new health technologies, abandonment of many promising initiatives, and requiring re-thinking of the relationships between innovation, governance approaches and ethical or societal safeguards. For the development of drugs and diagnostics, stratified medicine to cell therapies and regenerative medicine problems were identified arising from governance processes that unnecessarily constrain innovation, requiring better health-related policies that could deliver positive health outcomes more rapidly and efficiently than is currently being achieved. The work of ESBAC in this area included the development of an integrative governance framework to guide policy makers facing the wide range of potential boundary-crossing interactions that can have fundamental impacts (positive and negative) on the nature and timing of emergence of novel biomedical science and technology, and also on the broader scale and scope of national and international innovation systems.	
17	Obj. 1	Policy – Innovation interactions In considering the interactions among regulatory and policy drivers and innovative health care developments, different issues arise depending on the extent to which the technology is disruptive or incremental for the company developing it (Objective 1).	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		Most novel health care technologies involve incremental innovation that fits well within companies' existing business models and within pre-existing regulatory systems, improving competitiveness or delivering marginal improvements to existing health care products or processes. In such cases regulatory systems have evolved over decades bringing in piecemeal accretion of changes to regulatory systems as new, unexpected hazards have emerged. The outcome is a system that has become inflexible and difficult to modify in ways that are appropriate to the latest scientific and technological advances and opportunities. A disruptive technology potentially leads to revolutionary improvements in healthcare or addresses currently unmet clinical needs. It also challenges companies' established business models and innovation strategies. Regulation to ensure safety, quality and efficacy will be necessary but there may be no clear regulatory precedent. Alternatively, the presumed regulatory precedent may prove difficult to implement in the new context, for example as for stem cell therapies (Mittra et al., 2014). For both disruptive and incremental innovation, many regulatory systems have become too onerous even for large companies and this, combined with the increased difficulties in finding new candidate products for currently unmet needs, has led to drug development pipelines that are no longer sufficiently populated to ensure continued survival even of large multinational companies in their present form (Tait et al., 2007). The pressures for change from large companies are now being added to those of smaller companies and patient groups, linked to government desires to support innovation in order to stimulate economic growth.	
17	Obj. 1&4	Relevant to Objectives 1 and 4, an example of the power of regulatory change to improve the innovative capacity of an industry sector, arises from the incentivisation of the development of antimicrobial drugs to meet the AMR challenge. Tait et al. (2014) demonstrated that recent adaptations in US Food and Drugs Agency guidelines for clinical trials have reduced the R&D costs of antimicrobial (AM) drug development by	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		~50%. However, in an example of the reverse trend, the same study showed that the development of the accurate, rapid, and inexpensive in vitro diagnostic (IVD) tools that will be required to detect the nature of the infectious agent and its susceptibility to specific AM drugs, is likely to be negatively affected by future changes to tighten IVD regulations in the EU, and to bring them closer to those of the US (already seen as severely inhibiting the development of novel diagnostics).	
17	Obj. 2&3	Small start-up companies, with a greater potential than multinationals to deliver truly novel disruptive innovation, lack the resources to meet regulatory challenges and so focus their attention on the incremental innovation strategies of multinational companies, this being their only viable exit strategy. The end result is an overall sectoral innovation system that is rigid and inflexible, focusing on incremental rather than disruptive innovation (Tait, 2007). The costs and inflexibility of regulatory systems are thus limiting the number of potentially safe novel products that can be developed and are an important factor contributing to the difficulties companies experience in maintaining well-populated drug development pipelines (Objectives 2 and 3).	
17	Obj. 3	Governance Guideline 2 Where a product such as a new drug carries a strong potential social benefit, regulators should consider using policy incentives, such as market mechanisms, infrastructure investment or regulatory 'fast tracks', to minimise delays in development (Milne and Tait, 2009; Omidvar et al., 2013) (Objective 3). Using policy or regulatory initiatives to incentivise the development of novel health-related products has been very effective, for example in the case of orphan drugs, vaccines and treatments for AIDS, and the approach could be more widely adopted, particularly in the case of more disruptive innovations.	
17	Obj. 3	Governance Guideline 3.	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		When considering which regulatory precedent to invoke, particularly for potentially disruptive technologies, a useful ground rule would be to choose the regulatory system in operation for the industry sector for which the innovation is path-dependent, rather than one for which it is path-breaking (Tait et al., 2006). Policy makers and regulators are becoming more aware of the impact of their decisions on innovation futures. Regulatory decisions made early in the development of new products can profoundly affect the innovation potential of entire industry sectors and indeed the capacity of countries and regions to compete in global markets (Objective 3). There is a history of decisions taken in early stages of product development, that are then difficult to change, and have unforeseen and counter-productive outcomes. For example, stem cell therapies are likely to be path-breaking for a pharmaceutical company, but to be path-dependent for the small companies already working in areas related to tissue transplantation. The outcome of the decision to regulate stem cell therapies as if they were drugs rather than surgical procedures is that the probability of successful development of such therapies has been considerably diminished, with longer delays than would otherwise have been the case (Tait, 2007).	
17	Obj. 2	In addition to being the object of regulation, biomedical science and technology (particularly the development of in vitro and in vivo diagnostics) can have an important role in supporting regulatory change, to maintain safety and efficacy of products and processes while improving the efficiency of the regulatory systems themselves (Objective 2). Examples include: eliminating some aspects of a potential risk; providing faster, cheaper or more ethical routes to generation of evidence for regulatory decisions; or adaptive licensing based on new scientific developments	
17	Obj. 2,3&4	Integrative governance framework for innovative health care technologies The Integrative Governance Framework, based on Innogen Institute research, includes the following guidelines.	

<table>
<tr><th>Stake-holder no.</th><th>General/ Line no.</th><th>Stakeholder comments</th><th>Proposed changes by stakeholder, if any</th></tr>
<tr><td></td><td></td><td>Governance Guideline 1

Enabling, discriminating regulation works better and faster than regulation that is constraining and indiscriminate (Chataway et al., 2006), as summarised in the table below.

<table><tr><td>Enabling regulation</td><td>Provides encouragement or inducements to undertake a desired course of action
Affects the speed with which a particular regulatory policy is able to exert its influence</td></tr><tr><td>Discriminating regulation</td><td>Discriminates among products to favour those that deliver the desired policy aim
The extent and appropriateness of its discrimination among products or processes will determine a policy’s effectiveness in guiding product development in particular directions</td></tr><tr><td>Constraining regulation</td><td>Creates disincentives to undertaking undesirable actions</td></tr><tr><td>Indiscriminate regulation</td><td>Regulates all products in a class similarly regardless of their properties</td></tr></table>
For example, for the regulation of diagnostic devices for stratified medicine applications, the role of small companies is likely to be constrained by the requirement to adapt their product development cycles indiscriminately to those of multinational companies developing the companion drug. The outcome is likely to be a reduction of innovative activity in this area as only multinational companies will be willing/able to develop such devices (Mittra and Tait, 2012) (Objectives 2, 3 and 4).</td><td></td></tr>
<tr><td>17</td><td>Obj. 2&4</td><td>The Innogen Institute Independent Review on Antimicrobial Resistance considered</td><td></td></tr>
</table>

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		Regulation-Innovation Interactions in the development of Veterinary Antimicrobial Drugs and Diagnostics (Scannell and Bruce, 2014). The findings of this supplementary Report are particularly relevant to Objectives 2 and 4 within Theme 2. This research found that the current policy environment is discouraging investment to develop innovative antibiotics for use in animals – drug companies do not see a convincing case to invest in novel AM drugs for animals when the nature of the market into which the drugs will emerge is so uncertain. The problem is the expectation that future regulatory or policy instruments will limit, or even ban, the use of novel animal AM drugs in animals. Future stewardship programmes to limit the use of novel AM drugs in human health systems are likely to make it politically difficult to allow the use of these novel drugs or their close analogues in animals, and there will be little reason to develop niche candidates for the small and less profitable animal market compared to a human market supported by government incentives. The expected reduction in the use of AM drugs in veterinary medicine has implications for animal welfare, for the economics of food production, and potentially for the transmission of zoonotic infections to the human population. These factors will increase the importance of having rapid and cheap animal diagnostics, of the discovery and development of new vaccines, of improvements in animal genetics, and of good animal husbandry practices and agricultural biosecurity.	
17	Obj. 4	The costly and time consuming nature of current regulatory systems are among the primary reasons for the current shape of health-related innovation systems, dominated by the strategies of large multinational companies (Objective 4).	
17	Obj. 4	Governance Guideline 4 For governance or regulatory decisions taken at an early stage in the development of innovative technologies, there should be scope for adaptation of policies and regulations as more is learned about the relevant benefits and risks of a technology, product or	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		process, including the development of regulatory science as an important component of the process of regulatory adaptation (Objective 4). Given the uncertainties inherent in the early development of innovative health care technologies, particularly where the innovation has the potential to be disruptive of current innovation trajectories and therefore to have an important impact on the capacity to meet future health care needs, it will be important for the implementation of the EU Medicines Agencies Network Strategy that regulatory systems have greater adaptive capacity than those currently in operation. The challenge is for regulations to be capable of evolving as scientific and technical knowledge expand and as uncertainty about the eventual nature of products, processes, benefits and risks is resolved and at the same time to facilitate developments that are safe and effective and also meet ethical and other stakeholder concerns while maintaining choice for the majority of citizens.	
17	Obj. 1-3	In the context of Objectives 1 – 3, particularly related to personalised and stratified medicine, relevant issues include the need to draw on a broader base of data inputs on genomics, patient behaviour and healthcare system differentiation. Public private partnerships (PPPs) have been a focus of strong interest in this context (Mittra, 2013) and although the number of such partnerships is growing, their rationale and basis for collaboration remain unclear (Chataway et al., 2012). Such collaborations are at the core of a set of new life science policies in the UK but there is little indication in the policy documents of clear boundaries for these partnerships (Omidvar et al., 2014), in part due to the lack of empirical evidence at the system level for conceptualising what is still a relatively new approach. The PPP mechanism has also been tested in the developing country context (Hanlin et al., 2007; Smith, 2009), for example through the International Aids Vaccine Initiative and the Global Alliance for Vaccines and Immunisation. However, the challenge of getting public and private sectors to work together is also relevant here.	

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17	Obj. 4	Objective 4 refers to support for training and capacity building to promote the EU regulatory model. The Innogen Institute Masters Programme on Management of the Bio-economy, Innovation and Governance (BIG) (http://www.sps.ed.ac.uk/gradschool/prospective/taught_masters/h_n/msc_management_bioeconomy_innovation_governance) covers many of the issues raised in the EU Medicines Agencies Network Strategy. It is already contributing to this objective and is planning short courses and CPD initiatives that will extend its influence more widely.	
18	225-229	Medicine shortages - would like to see more of a commitment here to actively dealing with the problem of medicines shortages.	
18	272-273	This paragraph talks about reclassification from POM to OTC status. From a PGEU perspective, it would be better to see the EMA take a more positive, proactive position in relation to reclassification.	
18	632		Suggest addition of word "supply". "…..captured and listened to, especially with respect to those who develop, prescribe**, supply** and use medicines
18	674-675	80% of active ingredients used in medicines authorised in Europe come from outside the EU. This is contributing to medicine shortages where the often single source of an ingredient runs dry. Could the Network commit to encouraging more diverse sources of raw materials to reduce the risk of shortages?	
19	General	We welcome the approach of a joint strategy for the EU medicines agencies network, in particular: 1. A single strategy is presented for the entire network to reflect the need for a coordinated approach;	

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		2. The strategy has a clear structure of 4 themes identified as major, each of them with 4 objectives – this will make it easier to monitor and measure advances; 3. The strategy provides for "flexibilities that allow earlier access" to new and innovative medicines, to ensure timely access for patients; 4. Appropriate importance is given to robust pharmacovigilance systems across EU (proactive pharmacovigilance, real-time monitoring and rapid learning systems); 5. A strong emphasis is put on patient-focused innovation and efforts will be made to better "incorporates patients' values and preferences".	
19	General	We strongly support the need for: 1. **Adaptive regulatory pathways**. This point is particularly relevant in regards to DG RTD Health initiatives on personalised medicines and on rare diseases. We have several projects and topics addressing the needs for stratified therapeutic interventions. 2. **Collaboration with HTA agencies**. We request to be associated more concretely with stronger efforts on parallel scientific advice between the network and HTA agencies. Since innovative patient-focused health research is also at the core of the policy and funding objectives of DG RTD, we also request to be fully associated to the related activities (such as the mentioned 'EMA innovation task force' and the 'innovative medicine designation', p. 9 of the document) of the EMA and the network in order to reap the full benefits of a synergistic policy in this area.	
19	General	We also welcome the strong emphasis on antimicrobial resistance and the need to respond to public health emergencies. On the latter issue, we request an even stronger and more concrete commitment to explore regulatory pathways in the absence of human efficacy data.	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
19	General	Although the Innovation Task Force and Adaptive licensing are mentioned, there is no specific reference to the CAT or to ATMPs. The network examines how to create a more favourable environment for ATMP developers, especially those from academic, clinical and SME sectors.	
19	General	The document could be better supported with more statistical data.	
19	53-129	This Chapter should include some data, such as number of medicines approved every year by EMA and/or NCAs, average approval time.	
19	71-81	This paragraph is somewhat confusing. The description of the work of EMA and the NCAs, respectively, are formulated in such a similar manner that they sound redundant and the differences are not easy to grasp.	
19	77		Typo: NCAs (not NCA's)
19	92-102	Including a short summary table with the most relevant EU legislations, including those described as 'drafting of new legislation on veterinary medicines is ongoing' would be appropriate.	
19	113	This sentence is somewhat confusing in this context: don't policy initiatives exactly consist in proposing new or amending existing legislation for the pharmaceutical sector described in the first bullet point on line 104 (in combination e.g. with the last bullet point on line 111)?	
19	146-147	We assume the key themes correspond to the key strategic priorities mentioned on line 139? If yes, both sentences could be merged. If not, please clarify.	
19	154		To more explicitly endorse and give visibility to this approach insert '…reinforce the need for **a 'One Health' approach with** collaboration between

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
			those…'
19	166	Clarify "borderline products". Do you mean products for which it is unclear in which category they fall?	
19	173		To give even stronger visibility to this important issue (treated also in lines 263-266 and 616-620) add at the end of this paragraph: 'This requires collaboration between stakeholders determining access (patients, industry, regulatory, HTA and pricing and reimbursement authorities)'.
19	186-239	Objective 1 seems mostly focused on infectious diseases and antimicrobial resistance. While this is undoubtedly a crucial area of focus, it is nevertheless surprising that chronic diseases (which constitute the largest burden in terms of number of patients and healthcare costs incurred) are not put more forwarded. Dementia is just mentioned in one line.	
19	196	It is written that the network will continue to implement the EU Commission action plan on AMR. This sounds as if the EMA and national regulatory agencies are the only ones implementing this strategy. It should be stated instead that the network contributes to implementing this strategy.	
19	197		To make a clearer reference to the name of the document add '…implementation of the World Health Organization (WHO) **global action** plan to combat the rising threat…

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
19	202	Neurodegenerative diseases (including dementia) are one of the major threats for the health and well-being of EU citizens. It is surprising that the EMA strategy is not more developed in this regard. How does EMA plans to be involved in the WHO/G7 strategy?	
19	207-210	The statement that "existing tools like the various horizon- scanning exercises for orphan medicinal products conducted by different institutions will be better coordinated" should be better explained. The Strategy could mention a possible platform to share information and updates between network members. There is no mention of what new knowledge will be exclusively generated by this better coordination of the existing tools and is not already available from other sources.	
19	224	To strengthen the efforts for regulatory pathways for medical countermeasures add at the end of this paragraph: 'This will include efforts to consider regulatory pathways for products against pandemic pathogens, for which efficacy data in humans cannot be obtained prior to an outbreak.'	
19	263-266	This is indeed a very important item and it would be useful to see more details on how EMA further plans its collaboration with HTA authorities. This can also be linked to lines 307-312.	
19	284-291	Those lines describe in some doubtful, unconvincing terms the future implementation of the EU Clinical Trials Regulation (foreseen by mid-2016 at the earliest). All efforts should be put in place to ensure the success of this regulation, which will have major impact on conducting clinical trials and delivering new medicines in Europe. It will help make Europe a better place to test new medicines, thus increasing its appeal to international innovators in the biomedical sector.	For example, to avoid the misunderstanding that the Regulation needs to be implemented into national legislation and to avoid to unnecessarily offend existing Ethics structures delete and rephrase as follows: '…following a more streamlined process through a single European portal. Members States are likely to modernise the ways ethics committees work to be able to comply

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
			with the legislation.
19	292-297	This section is most welcome, but also described in rather vague terms. Could something be added regarding EMA's strategy regarding its participation/collaboration to H2020 projects? This can also be linked to lines 302-306	
19	319 and following	Not addressed in this section is the question of how long it takes the network to take decisions on marketing authorisation requests. The network has very stable review times over the years. In the past that made Europe competitive but other regulators (US, Swissmedic and others) are getting much faster, so that Europe loses competitiveness. This is an important question that should be addressed in the strategy, namely how the European network will ensure that it comes rapidly to decisions, in light of high pressures from all sides (outside world, resources, expectation of industry, etc.).	The first paragraph of this section as drafted implies that regulatory science is about understanding new technologies. The last sentence of the second paragraph of this section actually captures what is needed very well. It is proposed to move lines 329 to 332 up and then continue by saying something along the lines of: "…this includes dealing with the rapid advances…."
19	329-332	See previous comment. How does EMA plans this in practice and in particular, what is EMA's strategy regarding its participation/collaboration to H2020 projects?	
19	527-531	The positive words about the aim of mobilising the available scientific expertise within the network, a more optimal organization of the available expertise across the network and avoiding duplication of work should more strongly be coupled with the message how this information will be disseminated to national academic experts (who are the potential targets).	
19	549-555	Regarding IT systems, it needs to be emphasised that these systems need to be operationally secure in order to guarantee the protection of personal data and	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		commercially confidential information.	
19	571-580	This is indeed an important point. Under Theme 2 (animal health), this is addressed within a specific objective on "Promote better regulation". Can such an objective not be further developed for human health as well, explaining better what are the potential regulatory bottlenecks?	
19	620	Here and/or in the paragraph lines 243-246 add a more concrete commitment to increase efforts to further develop parallel scientific advice add a phrase such as: 'In particular, possibilities to obtain parallel scientific advice from regulatory agencies and HTA agencies will be strengthened in order to facilitate rapid access for patients.'	
19	689-690	Mention which global partners.	
20	General	AESGP welcomes the new approach of defining one comprehensive strategy for the entire network of medicines agencies. AESGP appreciates the commitment of the network as outlined in the draft strategy to ensure: • the most appropriate legal classification is applied to medicinal products, • the mechanisms for allowing medicinal products that can be safely reclassified as non-prescription medicines are in place, effective and being used. However, AESGP would welcome it if – in order to honour the commitment to appropriate legal classification – the network undertook to: • enhance the scientific expertise and understanding of the particularities of non-prescription medicines, • use the recently developed methodology ("Brass model") for quantification of risks and benefits in assessing switches to non-prescription status.	

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		AESGP understands the principles of "Better Regulation" and administrative burden reduction as applying to all areas regulated by the EU and asks in particular that they are applied by the network to well-established substances. In order to implement a policy of avoiding and reducing the administrative burden for the industry, it will be imperative that senior management of the network is actively involved in the exercise: following an invitation by the HMA and EMA, a limited number of areas, where the administrative burden could be reduced, should be identified by stakeholders. These topics should be subject of technical scrutiny by the relevant expert group of the network followed by a dialogue with stakeholders about concrete opportunities for administrative burden reduction. Senior management should monitor the process ensuring that all arguments are carefully considered while not reducing the level of public health protection.	
20	225	Objective 1 focuses among others on the availability of medicines. One problem is the availability of herbal, homeopathic and anthroposophic medicinal products: A study commissioned by the EU Commission (see http://ec.europa.eu/health/files/committee/73meeting/73plus/study_report.pdf) states that there is an availability problem of herbal medicinal products and homeopathic and anthroposophic products (HAMPs). The study mentions as possible problem drivers divergence in national procedures and approaches to herbal medicinal products and HAMPs (p. 7). One problem is e.g. the incomplete and ineffective implementation of simplified registration procedures of herbal medicinal products and HAMPs in the Member States (p. 8). More than 100 million EU citizens use homeopathic and/or anthroposophic medicinal products. These are long-standing European traditions. Complementary medicine plays an important role in the health systems of EU Member States. Given the fact that these medicinal products are widely used among the EU citizen, we suggest that the EU Medicines Agencies Network should examine possibilities to improve and assure the	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		availability of these medicinal products.	
20	639 Theme 3; Objective 4	AESGP underlines the necessity of further developing the rules for herbal medicines so that this significant market in Europe remains competitive; cooperation with EFSA is indeed encouraged to find a good balance between the different categories of products (food and medicinal products).	
21	225	EHN recommends to take into consideration the latest WHO Model List of essential medicines (April 15), providing good examples of CVD-related medicines that are crucial for any healthcare system. http://www.who.int/medicines/publications/essentialmedicines/EML2015_8-May-15.pdf A lot of experts discuss the availability of medicines. EHN believes it is important to follow the guidelines elaborated by evidence-based analysis, such as the one published by the WHO.	
21	244	Correct and balanced information is crucial. Make sure patients' associations are also consulted.	
21	245	Assessment of new medicines not only on benefit/risk ratio, but also comparing to existing medicines	
21	255	Smaller trial populations could bring medicines earlier to market, but need a solid and continuous assessment of pharmacovigilance.	
21	278	EMA's leading role in the new clinical trials regulation is welcome. EC, EMA and HMA should now make sure its implementation is correctly undertaken.	
21	317	It is essential that patients' associations are consulted in terms of access to medicines. Such an important topic needs all stakeholders at the table.	

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21	318	There is a trend of involving patients in research's projects, from small trials to big international projects. The EMA should be at the forefront of this movement by promoting participation of patients in research. Guidelines on how researchers or the science people can collaborate with patients' would also be welcomed.	
21	322	All stakeholders should be consulted. The efforts in cell and gene therapies of small research centers (academic, foundations) should be supported.	
22	General	In places the document suffers from a lack of differentiation between human/veterinary medicines. Equally in other places elements which might also be of value in veterinary medicines are restricted to human medicines.	
22	General	No reference is made to EDQM, another key player in EU standards for medicines. It would be helpful it was clarified how EDQM in future will fit into the overall strategy of control of medicines.	
22	General	It is disappointing that there is no reference to efforts to support 3Rs, be it in the EU or through regulatory convergence and influencing third countries.	
22	General	IFAH-Europe appreciates the chapter on "Promote 'Better Regulation'". As pointed out in the document, the impact assessment for the review of the veterinary medicinal products legislation has identified that the veterinary sector suffers from a disproportionately high administrative burden, at 13% of the sector's turnover. This is double that calculated for the human medicines sector. The veterinary sector fulfils equivalent regulatory requirements (plus consumer safety requirements) to the human medicines sector, and yet operates in a market 1/40th of the size (2.6% of the human medicines market). This necessitates implementing the most efficient regulatory procedures possible. The impact and significance of these facts will no doubt be a driving force behind the EU Medicines Agencies Network Strategy to 2020, bearing in mind that new VMP legislation will not come into force until the end of this strategic period.	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
22	82-86	NCAs are responsible for all medicines enforcement activities, so suggest this important element is added to the list of their activities.	
22	94-95	Current EU legislation does not control clinical trials for animals, although it is anticipated that future legislation will although it will differ significantly from that which applies to human medicines.	Please amend the sentence to read: "The EU legislation today covers the whole life-cycle of a medicinal product from the research phase (clinical trials of human medicines), …"
22	99-100	Strengthened legislation only currently relates to human medicines.	Proposed change: Please amend the sentence to read: "The European legislation governing human medicines has been strengthened significantly in recent years in the areas of pharmacovigilance, falsified medicines and clinical trials."
22	107-108	Opinions are issued by the Scientific Committees, e.g. CVMP, and not EMA.	Please modify the sentence to read: "Risk management: to grant EU-wide marketing authorisations for centralised products or maximum residue limits on the basis of a scientific opinion of the expert scientific committees of the EMA;"
22	135		Please amend the sentence to include animal health as well: "…innovative developments that contribute to public

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			and animal health."
22	136		Please amend the sentence to include animal health as well: "…transparency, the need to address new and emerging threats, whether of a public or animal health"
22	271-272	It is not clear if this section applies to veterinary medicines. Anyhow it is considered that ensuring the correct legal classification is a matter to be handled at a national level in view of the different distribution systems that exist.	
22	452-454	The wording implies that harmonization will proceed under the current legislation, without specifically highlighting that this can only happen in the case of a serious risk, or on a voluntary basis.	Please modify the sentence to read: "In the case that serious risks are identified, the CVMP will ~~expects~~ will process ~~a high workload of~~ referrals of antimicrobials and other classes of products to align the relevant information in the Summary of Product Characteristics ~~for which the conditions of use will be both~~ harmonized and aligned with the principles of prudent and responsible use".
22	460-461	It is disappointing that in this section there is no reference to the need for new antibiotics for use in animals. Lines 193-4 specifically dealing with antibiotics for people states … "will facilitate access to the market of new antibiotics".	Please modify the sentence accordingly
22	698-699	In this section on convergence of global standards and contribution to international fora,	

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		the absence of any reference to Codex is notable.	
22	729-730	Regulatory convergence is equally important in veterinary medicines, where OIE has a key role. Convergence in the area of pharmacovigilance is considered to be a key area.	Please amend the sentence to read: "The network, in close cooperation with WHO and OIE, will take a lead role in convergence of global standards, particularly in the area of pharmacovigilance ..."
23	General	1. The terminology should be clarified. The draft network strategy variously refers to "innovative", "novel" and "new" products, without defining what this means. Not everything that is new can be considered innovative or novel. In EPF's view "new" is a neutral word whereas "innovative" implies new products that have value - that bring benefit to patients' quality of life, and by extension benefit to society. 2. In the context of medicines, it is important to define what constitutes "innovation" in this positive sense and to adopt a consistent approach. Recently, the updated report "Priority Medicines for Europe and the World" (2013), the reports of the Belgian EU presidency on "Innovation and Solidarity", and the 2014 Council conclusions "Innovation for the benefit of patients" have raised similar questions of what should be considered 'valuable' innovation, and how this should be adequately incentivised and rewarded. This conversation should take place with the involvement of all relevant stakeholders at European level. 3. To ensure that innovation brings real value to patients, patient involvement needs to be taken as a strategic approach and integrated across the entire innovation chain at EU and national level. Developing a framework for patient involvement is one of the main recommendations of the WHO Priority Medicines report.[1] Patient involvement in the regulatory process is indispensable, particularly with the	

[1] Chapter 8, "New approaches to promoting innovation"

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		emergence of novel, more flexible approaches to regulatory approval, such as conditional marketing authorisations, which promise faster patient access but also involve potentially greater uncertainty and potentially greater risks, at the time of authorisation. EPF suggests that the EU Medicines Agencies Network provides an optimal platform for developing such a strategic approach to integrate patient involvement into the regulatory process, including in Member States where this is currently lacking. The EMA model for involving patients and consumers is widely seen as an example of good practice with potential for replication, but could be promoted more proactively towards national authorities. The network could play a valuable role in sharing and mutual learning, inter-alia through closer links with the Patient and Consumer Working Party. Although we appreciate that specific activities will be defined in annual work plans, those work plans will be based on the high-level priorities outlined in the Network Strategy. Therefore, this topic needs to be explicitly included as one of the priorities of the Strategy.	
23	88	*The term "good practices" should be used, since what is "best" depends on the definition and who is doing the defining. This comment applies throughout.*	… ~~best~~ **good** practices …
23	204	*Rationale: The term "vulnerable groups" is unnecessary labelling – not all children or older persons are by definition vulnerable. In this context we prefer the term "specific populations".*	"… ensuring that the needs of ~~special~~ **specific** 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

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			support their use."
23	253	*Rationale: the meaning of the last sentence is unclear. From the patient perspective, more coordination between Member States is needed to ensure that the same opportunities of accelerated access are available to patients across the EU.*	"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, **better coordinated** and prospectively planned for their use."
23	267	*Rationale: stakeholder engagement at national regulatory agencies – particularly the involvement of patient organisations – is key to integrating a meaningful patient perspective into policy. The EMA experience of the added-value provided by patient organisations can and should be used to enhance awareness and improve patient involvement with national competent authorities.* *The document eventually produced by the "impact assessment" working group of the PCWP can be used as an effective advocacy tool in this respect.* *The network could also function as a forum for mutual learning, including connecting with patient and consumer organisations – for example through joint meetings, and having an observer from the network at the PCWP.*	"Further effort 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. **The network should give more visibility and develop recommendations or guidance as**

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			appropriate for national competent authorities, based on the EMA experience of patient and consumer involvement."
23	276	*Rationale: objective 3 is "support for patient-focused innovation" so the description should be in line.* *The description should be explicit about the meaning of innovation as new products that bring value/ benefit for patients. This is the kind of innovation that needs to be incentivised.*	"The network will work to ensure the optimal implementation of the Clinical Trial Regulation, collaborate more in supporting **patient-focused** innovation and considering further regulatory incentives for **valuable** innovation, particularly in certain areas of public health need."
23	317	*Rationale: see our comment above (line 267).*	"The network will continue to explore how best to include patient and societal input into pharmaceutical innovation and regulation **at EU and national levels**."
24	General	The European Society for Medical Oncology (ESMO) welcomes this consultation published jointly by the EMA and HMA on the EU Medicines Agencies Network Strategy to 2020- Working together to improve health. ESMO is appreciative of the importance given to discussions with stakeholders throughout the process of approving medicines. We are supportive of the EMA/HMA strategy, and we would like to see the role of	

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		stakeholders, such as scientific societies, strengthened in the EU Medicines Agency Network Strategy 2020. ESMO agrees with the themes and objectives outlined in the Consultation draft. Given the complexities of the regulatory processes, there is a need to improve the understanding of these processes for the stakeholders who are directly affected.	
24	98 and 103-112	The mandate of European Commission on pricing and reimbursement for human medicines should be clarified. In the draft it is stated clearly that pricing and reimbursement for human medicines are not regulated by the EU legislation and that they are left to national competent authorities. Whereas this is acceptable for reimbursement in that is strictly related to national policies and local economy of each Member State, it may be less clear to the EU citizen why pricing should not be harmonized in the EU. The sustainability of innovative anticancer drugs is at risk. The cost of novel drugs is creating a huge gap in access to medicines across Europe with consequent intolerable disparities among EU citizens. Even countries with less economic restraints will soon struggle to sustain health expenditure for cancer drugs. The initiatives of the European Commission to harmonize the HTA assessment of new drugs through the establishment of EUnetHTA (2005) and the HTA network (2013) are acknowledged. However, a transparent discussion on pricing at centralized level should be promoted, too.	
24	240-272	ESMO endorses the priority for timely access to innovative drugs and welcomes the multiple initiatives that are being adopted to ensure it. However, if in the scope of the paper, any practical initiatives related to the collaboration with HTA bodies and even more with pricing and reimbursement bodies would be welcome. We stress that even if the cost/efficacy evaluations are under the domain of each EU country, there is no reason in principle why the efficacy assessment should be different from one country to another. More harmonization on this would be a big step forward, even if pricing remains different and the willingness to pay may obviously differ across the EU. Involvement of	

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		national HTA bodies in the scientific advice process provided to companies developing new drugs may be of help as well.	
24	275-318	Clinical Trials Regulation: ESMO appreciates EMA/HMA's acknowledgement of the impact that the Clinical Trials Regulation (CTR) will have on the way innovation will occur across Europe. ESMO believes that the correct and harmonized implementation of the Clinical Trials Regulation is indeed very important to improving the way trials are done across Europe, and to foster pan-European clinical trials. ESMO hopes that the EMA/HMA will work together with stakeholders to ensure that the Regulation is implemented appropriately across the EU, especially on aspects that are to be independently implemented by the Member States (such as Article 28 (2) on the use of data beyond the end of the scope of a clinical trial).	
24	275-362	ESMO Magnitude of Clinical Benefit Scale: ESMO is aware of the initiatives that are being pursued by EMA with regard to the development of new tools to assess the benefit/risk of new anticancer drugs. ESMO would also like to take this opportunity to mention the Magnitude of Clinical Benefit Scale (MCBS) that was launched in May 2015. It is a "validated tool to assist oncology clinicians in evaluating the most effective anti-cancer medicines for their patients", but can be replicated across disease areas. Its aim is to provide a "rational, structured, and consistent approach to 'stratify' a drug's clinically meaningful benefit."	
24	482-640	Meetings with scientific community and relevant stakeholders: The recent (April 2015) EMA- ESMO-Rare Cancers Europe workshop on a very rare cancer (chordoma) indicates that the EMA is open to receiving input from patients, healthcare professionals, academia, statisticians and industry representatives, and to provide advice during the drug development process, as necessary. As this workshop was the first of its kind, ESMO would encourage the EMA to use this platform for additional disease areas where there is a high-unmet need. Such constructive dialogue between key stakeholders will provide regulators and stakeholders the information needed to make decisions on new	

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		medicines (timely access; involving patients in the process; and increase its transparency) and improve the methodology of clinical trials too. ESMO would like to see experts from all relevant parties present at these discussions, who will be able to provide advice on decisions, without having any conflicts of interest.	
25	General	EGA, representing the European generic and biosimilar medicines industries, very much welcome the first common EMA/HMA Strategy Paper for the regulatory network. Regulators play an extremely important role in protecting public health and assuring access to medicines. However, the strategy paper is mainly focused on facilitating access to new, innovative medicines (words: "innovative, novel, innovation, new medicines" are mentioned more than 50 times; for comparison "generic/ biosimilar" are cited only 5 times). We believe that the strategic thinking on how to contribute best in achieving those objectives shall be broader than focusing almost exclusively on supporting innovation. Innovation and scientific progress are indeed a key pillar of the pharmaceutical industry and shall be supported as much as possible. However, access of the majority of the population to essential, first-line, quality treatment should not be neglected but, rather, be given equal consideration as one of the regulators' strategic objectives for 2020. It shall be noted that currently more than half of the European population is treated with generic and biosimilar medicines. This is expected to be around 70% in 2020 to assure sustainability of the European healthcare systems. The regulators' network shall also have a comprehensive strategy on how to support the objective of essential and fundamental patient access to treatment, in line with the EU 10 Patients' Rights (http://ec.europa.eu/health/patient_safety/docs/2015_eu_patients_factsheet_en.pdf) in the longer term, and on how to support generic and biosimilar medicines industries in order to fulfil this expectation. A strong regulatory framework providing citizens with	

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		quick access to safe and high-quality products is also at the core of the proposals of the Luxembourg Presidency of the Council of the European Union.	
25	82	The role of the NCA in handling the vast majority of all MAs in the EU should be highlighted as it is a huge task for the authority. Proposal: "NCAs handle the vast majority of all MAs in the entire EU (medicines that are authorised nationally or through the decentralised and mutual recognition procedure*, containing well known active substances and being mainly generic medicines).*	
25	132	The EGA welcomes a common EMA/ HMA Strategy Paper as an important step forward to better integration of all partners in the regulatory network. Closer cooperation and agreement on common strategy will help to achieve common objectives much more easily.	
25	142	Although the common Strategy Paper itself is already a major achievement, the translation of the high level strategic objectives into a work plan is critical. From our point of view, the ideal situation would be to have one common work plan with clear indications of leading role/ responsibility and timelines. As our understanding is that EMA and HMA will elaborate separate work plans, a reassurance needs to be given that efficient coordination and alignment between HMA and EMA will be in place to avoid incompatibility, contradictory solutions and duplication of tools to achieve strategic objectives.	
25	158	Regulators play an extremely important role in protecting public health and assuring access to medicines. We believe that their strategic thinking on how to contribute best in achieving those objectives shall be broader than focusing almost exclusively on supporting innovation. As mentioned in the general introduction, innovation and scientific progress being a key	

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		pillar of the pharmaceutical industry, shall be supported as much as possible. However, access of the majority of the population to essential, first-line quality treatment should not be neglected but, rather, given equal consideration as one of the regulators' strategic objective for 2020. It shall be noted that currently more than half of the European population is treated with generic and biosimilar medicines. This figures is expected to rise to around 70% in 2020 in order to assure sustainability of the healthcare systems. Proposal: The regulators' network shall also have a comprehensive strategy on how to support the objective of essential and fundamental access to treatment in the long term and how to support generic and biosimilar industries to fulfil this expectation.	
25	178	The support of the network for patients' access to generic and biosimilar is mentioned *"when supply issue arise"*. In our opinion, it is already too late to resolve this issue smoothly. Proposal: One of the strategic priorities of the network shall be a deep analysis of why supply disruptions happen and how the regulators, together with industry, can prevent them. This issue needs to be approached holistically, looking at all actors within the supply chain and by taking account of the multitude of contributing factors, including regulatory and economic issues. As the regulators' network is already engaging in the dialog with Pricing and Reimbursement Authorities for the purpose of the HTA, we see an opportunity for a common policy aimed at preventing supply disruptions as an additional topic for discussion with PR authorities.	
25	186	It is not EGA's intention to question the need for the development of medicines for rare diseases and special populations. However, from a public health perspective, we want to highlight the importance of cost–efficient treatments for chronic diseases affecting the	

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		largest population and identified by the WHO as 'essential medicines' and as such being of key priority in view of demographic trends and lifestyle. Proposal: The public health priorities shall not be only focused on dealing with "emergencies/small populations" but also with tackling key challenges of the largest "general" population consuming the majority of healthcare budgets.	
25	231	The continuity of safe medicines supply in the legal framework and the fight against the illegal supply of falsified medicines are essential activities in which efforts from the network need to be pursued. Regarding the continuity of medicines supply, the EGA would like to highlight that a harmonised approach on communication of information on quality and manufacturing potential supply disruption by MAHs to CAs, as has been proposed as part as a collaborative industry effort in 2015. Regulators are now in a position to assess whether an EU agreement on a template reporting form and common trigger could be a strategic objective for the network, allowing (1) a facilitated coordinated action between CAs and (2) the gathering of standardised data by CAs for the trending of underlying causes, while considering mitigation strategies. In many instances, supply chain issues as summarised above arise due to the wide geographic spread of the supply operations, the multiplications of operators and the complexity of regulatory and economic systems. Proposal: Key recommendations for the strategic EMA and HMA workplans are: • To consider regulatory dialogue platforms with key source countries as key forums to raise awareness and address technical or regulatory issues upfront	

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		• To favour transparency of regulatory enforcement action outcomes (e.g. all GxP information) • To consider creating dialogue opportunities with 'new' operators in main non-EU countries actively supplying the EU (e.g. brokers, API intermediate manufacturers, CROs) as a means of raising awareness on EU regulators' expectations with industry support. • To increase regulatory convergence with historic partners (e.g. the US FDA or PICS members) as a means to promote standards globally.	
25	240	The timely access to medicines for patients is presented from the perspective of timely access to novel medicines by exploring the new regulatory pathway (adaptive licencing) and HTA/ Pricing and Reimbursement bodies. Without undermining the importance of fast access to novel medicines (especially those which bring breakthrough innovation and provide solution for unmet medical need), the timely access as a strategic objective shall apply to all medicines. Proposal: The network shall put in place mechanisms which will guarantee a timely access to all medicines.	
25	275	All effort to create favourable conditions for R&D activities in Europe are very welcome and are needed to strengthen the European Pharmaceutical industry. Again, the support of the network is expressed in terms of the development of novel medicines, although our sectors would also welcome the regulators' support in developing generic, value added and biosimilar medicines (including the support for single development programs).	

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25	313	Generic and biosimilar medicines are presented only as a source of savings and stimulation for research by originator companies. It needs to be mentioned that generic and biosimilar industries spend 9-17% of their turnover on R&D (based on internal EGA survey). The meaning of "innovation" shall not be only associated with NCE but also with the added value offered by products with known active substances. This type of innovation shall also be supported by the network as a key means to improve patients' health outcomes.	
25	348	EGA fully supports early detection of potential safety signals, and the rapid evaluation of safety issues, which should be pragmatic with actual end benefit to patients and not simply the collection of additional product information. For multisource generic medicines, it is of great importance that assurances are made regarding efficient ways of dealing with pharmacovigilance activities without duplicating assessment, avoiding multiplication of signals and assuring consistency in the assessment of medicinal products with the same active substance. The intended simplification and removal of duplication in community pharmacovigilance procedures with consequent efficiency gains for both the pharmaceutical industry and medicines regulators is not visible but is both welcome and anticipated.	
25	358	The role of the EU regulatory network will be extremely important in the upcoming EU strategy on pharmaceuticals in the environment. We take the issue of pharmaceuticals in the environment seriously. We wish to address current concerns through an open and constructive dialogue with stakeholders and policy-makers, taking into account environmental and public health aspects as well as their policy ramifications. We are also actively engaged in minimizing the impact of our activities on the environment and the unintended consequences of the use of medicines.	

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		Proposal: In terms of possible input, it is important that EMA and NCAs • Raise awareness about the value of the existing environmental risk assessment • Consider possible refinement to the current approach to ERA; the European pharmaceutical industry represented by the Association of the European Self-Medication Industry (AESGP), the European Federation of Pharmaceutical Industries (EFPIA), and the European Generic and biosimilar medicines Association (EGA), has already made proposals on this topic and would welcome further discussion with EMA and national experts • Supports careful consideration of the existing balance in the current regulatory framework between access to medicines and environmental considerations.	
25	482	EGA recognises the effort that has been made by the Network to strengthen the collaboration between all players in the system in recent years. Building trust in the network, several successful work-sharing initiatives, plus the availability of technical solutions and IT tools offer significant opportunities for further optimisation of effective functioning of the network. All future initiatives optimising the functionality of the network shall create a win-win situation for the authorities and industry in terms of removing administrative barriers and making the entire system much more cost-effective. Proposal: The element of cost/ efficiency and impact on regulators/ industry resources shall be routinely assessed in all future initiatives and detailed proposals in the work plans.	
25	540	EGA fully endorse this objective and considers it as one of the top priorities of the	

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		network. EGA also agree with points for improvements/ opportunities identified in this chapter. The huge potential of IT solutions to support regulatory processes and operational costs-effectiveness; prevent duplication of assessment; streamline MA procedures and optimise variations process have been also identified by the EGA members as top priorities to be discussed by the regulatory network. EGA has developed several recommendations on how to improve regulatory efficiency and to strive for operational excellence which will be shared with the EMA/HMA (highlights in the Annex).	
25	580	EGA fully supports the view that information on medicinal products is to be further improved to encourage better use of medicines by taking into account the expectations and needs of both patients and healthcare professionals. This approach is particularly relevant for biosimilar medicines. Although the EMA and a number of national regulatory agencies have provided information on biosimilars to both patients and healthcare professionals or have provided clear positions on their respective websites, EMA/HMA are encouraged to make coordinated information efforts regarding biosimilar medicines to ensure increased patient access to innovative biotherapeutic treatments and to support the sustainability of the national healthcare systems. Despite the fact that Europe is leading worldwide regarding the legal and regulatory framework for biosimilars, and that these medicines have behaved in the market place since 2006 as expected by the regulators, the approval process continues to be misunderstood and challenged. The most recent example of such misunderstandings are the conclusions of the OPECST (Office Parlementaire d'Evaluation des Choix Scientifiques et Technolgiques) in France. We call upon EMA/HMA, that, each time such a misunderstanding occurs, the approval system is explained and the regulatory decisions to protect public health are defended. This should enable civil society to build and	

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		maintain trust in the work undertaken by regulators, hereby further strengthening the reputation of regulators and their authority vis-à-vis their stakeholders. We fully support that "*to generate understanding and trust, the network must ensure that its approach to communication supports the overall objective of safeguarding human and animal health and that only when trust can be fostered, stakeholders will play their part in contributing to such an overall objective".*	
25	608	The ability of the Network to communicate clearly in crisis situations has improved and recent events illustrated a coordination of initial messages which proved beneficial and largely effective in containing media outburst. Where communication issues have arisen is when EU processes (e.g. referral) are side tracked by national parallel procedures. While completely lawful and useful in certain circumstances (e.g. taking account of a specific national context), these can lead to confusion in the public health message, and misunderstandings, particularly as with the cross-border healthcare directive provisions, patients are aware and expect that medicines will be considered in a similar fashion in the different EU Member States. Proposal: The launch of national parallel procedures should be carefully thought through, particularly in terms of communication and public health messages.	
25	613	As was already expressed above (comments on 178 line), with a view to preventing supply disruptions and assuring long term sustainability of the healthcare system, the scope of the dialogue with Pricing and Reimbursement Authorities shall be extended.	
25	641	EGA fully support the stance taken by the EMA/HMA in the context of the global regulatory environment. The support of the network to achieve the single development program for biosimilar/ generic/ complex generic/ value added medicines will be highly appreciated as a part of the Strategy 2020.	

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		In addition, since the EU pioneered the regulatory framework for biosimilar medicines and continues to inspire the world, the EMA/HMA network has therefore a key role in continuing to support the implementation of the highest standards around the world regarding biological products, including biosimilar medicines. Such a commitment is expected by the 67th World Health Assembly's Resolution on *Access to biotherapeutic products including similar biotherapeutic products and ensuring their quality, safety and efficacy (1)* as well as the Resolution on *Regulatory system strengthening for medical products (2)*. To increase regulatory capacity in developing countries, Twinning projects involving experienced and less experienced national drug regulatory authorities (NRAs) should be promoted and supported. Such Twinning projects, based on the secondment of experts from experienced to less experienced NRAs, can deliver specific and guaranteed results as demonstrated by the very successful Twinning projects launched in the EU in May 1998 to support EU accession countries in meeting the Acquis Communautaire. As expressed above (line 231), the EU Network has an instrumental role to play in international trade agreements and regulatory dialogues, convergence efforts and information sharing (with regulators, industry and 'new' operators), awareness raising. Regarding the EU Network's participation in international regulatory forums, we support greater involvement but also reflection on ways to prevent the multiplication of parallel 'convergence' discussions which can only lead to redundancy and ineffectiveness. Where concrete and practical approaches are being developed and considered (e.g. to simplify multi-country registration), one key element for the success of these initiatives will be to involve the primary users of the scheme, i.e. industry. In the era of telematics discussions, it is important to anticipate as early as possible issues of submission tools and platforms, resource accessibility and systems	

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		interoperability which can otherwise pose significant practical hurdles. Regarding capacity building, and referring back to the global geography of pharmaceutical operations, while the EU regulatory network should pursue all work-sharing possibilities, it is also beneficial that where mutual trust with partners in some areas is still at an early stage, the EU network should have a capacity and capability building programme so that all regulated aspects of the medicines production or testing receive a similar level of attention. (1) WHA67.21 http://apps.who.int/gb/ebwha/pdf_files/WHA67/A67_R21-en.pdf (2) WHA67.20 http://apps.who.int/gb/ebwha/pdf_files/WHA67/A67_R20-en.pdf	
26	General	The BioIndustry Association (BIA) welcomes the opportunity to submit these comments and observations on the draft EU Medicines Agencies Network Strategy to 2020 - Working together to improve health. We very much welcome that the European Medicines Agency (EMA) and the Heads of Medicines Agencies (HMA, which brings together all national medicines regulatory authorities in the EU and EEA) jointly developed a "single strategy for the entire network to reflect the need for a coordinated approach to address the challenges and opportunities that face the network". The strategy document acknowledges the need for a strengthened collaboration within the network over the next 5 years, drawing on the resources and expertise of the whole EU, as well as the need to work globally with other regulators. This will help to improve Europe's attractiveness as a location for clinical research and development of novel medicines. The BIA fully supports the commitment in the strategy document "to seek active involvement of the stakeholders" and the "need for the network to work closely with	

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		those it regulates". The strategy document focuses on key strategic priorities of importance to BIA member companies operating across the life science sector in the UK and Europe, in particular: • Support for patient focused innovation • Provide incentives to support innovation, e.g. a "European early stage innovative medicine designation" • Progress the adaptive pathways pilot and promote ways of ensuring timely access to new medicines for patients • Ensure optimal implementation of the EU Clinical Trials Regulation • Strengthen collaboration with health technology assessment (HTA)/pricing and reimbursement bodies to facilitate in getting innovative medicines to patients earlier • Ensure the network has the capability to regulate the novel products of the future • Explore the opportunities for regulatory burden reduction While separate multi-annual work programmes will describe how the strategy will be taken forward by the EMA and HMA, it is important that the work plans are complementary and the activities aligned with the strategic priorities set out in the strategy document. The BIA and its member companies look forward to continue the dialogue with the EMA and the national medicines regulatory authorities to the ultimate benefit of patients. For the development of novel technology products, we believe in the benefits of engaging the life science industry in regular dialogue so that assessors get a better understanding of emerging technologies as these evolve.	

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27	General	On behalf of the European Centre for Disease Prevention and Control I would like to thank you for an opportunity to comment the EU Medicines Agencies network Strategy to 2020. The document provides a good overview of areas where the network will focus its activities with an objective to contribute to public health. However throughout the document the links to public health authorities at national/EU level and possible collaborative actions are not mentioned. However in the areas of e.g. antimicrobial resistance, availability of medicines (including vaccines), response to public health emergencies, and post-authorisation studies of vaccines early contacts between regulatory and public health authorities (and industry) would be beneficial in having a full picture of the matter at stake and in planning possible actions.	
28	General	EUCOPE welcomes the opportunity of being involved in 'EU Medicines Agencies Network Strategy to 2020 – Working together to improve health' and supports HMA/EMA's initiative to build a common long-term strategy for the entire network of Competent Authorities which will reflect the need for a coordinated approach to address multiple future challenges and opportunities. We agree that as advances in science and technology affect the nature of regulated medicinal products, the network must support new and innovative developments that contribute to public health. EUCOPE understands that HMA/EMA's document intends to build a high-level strategy for the next five years and that this strategy will be developed in detail through separate multi-annual work programmes which will define specific priorities and milestones. We appreciate the opportunity to contribute to this exercise and welcome HMA/EMA's further interaction with external stakeholders in the implementation of the strategy. Furthermore, all parties will benefit greatly during the execution and implementation if there is a regular integrated status report (with appropriately defined metrics to measure the implementation). When reflecting on the allocation of resources to prioritized tasks and project plans, EUCOPE would encourage HMA/EMA to refer to on-going pilots (Adaptive pathway,	

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		EUnetHTA's Joint Actions 2&3, STAMP, Early access scheme, parallel advice....) so that its strategy to 2020 ensures continuity with ongoing efforts. There is a concern that the steadily increasing demand will outweigh the allocated resources. The long-term sustainability of the Network should be reviewed to ensure Europe's regulatory system performance whilst facilitating and supporting innovation. EUCOPE supports the spirit of the strategy and is generally aligned with the focus areas identified and the proposals on how to enhance integrated and collaborative work amongst regulatory bodies and other stakeholders in Member States across Europe and how to tackle the key challenges in the granting of patient access to innovative therapies. The current document has highlighted the need to ensure that at the European level the different owners of various agendas and priorities start a comprehensive debate on how to respond to the multiple challenges faced by Europe regarding its future competitiveness, the health of its ageing population and its leadership in a high-growth sector. We would like to encourage the Network to take active part into the following issues: 1. Improve attractiveness of Europe for research and development in life sciences through reducing red tape and good implementation of recently introduced legislation (e.g. implementation of the Clinical Trials Regulation to attract clinical trials in Europe); 2. Become a global leader in regulatory standards, e.g. for biological products (originator and biosimilars), and personalised medicines at global level; 3. Suggest a balanced policy agenda that responds to the different needs of our societies, our health systems and our competitiveness, e.g. data disclosure, environmental legislation. This requires good coordination among different	

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		Directorates-General, establishing guiding principles for balanced policy making and clear priority setting; 4. Ensure appropriate incentives, such as the data exclusivity regime, are well designed to incentivise investment in research and development of new medicines. The comments below go in the same direction as the general spirit of the strategy, while providing an additional perspective to the key issues identified and to go one-step further in the explanation of the strategic direction the network could take in tackling these challenges.	
28	202-210	EUCOPE strongly supports the focus on special populations such as patients affected by rare diseases. EUCOPE also welcomes the intention to avoid duplication of efforts for a faster and better patient access to orphan drugs (i.e. avoiding a duplication of regulatory assessment, e.g. significant benefit by the COMP vs. benefit/risk assessment by the CHMP as well as a "recognition" process of the first regulatory assessment by the HTA: significant benefit demonstrating the product value). A flexible and integrated approach to the existing framework for orphan drugs also through an "adaptive path" would allow the provision of pragmatic access solutions to patients facing an unmet medical need. "*The network will explore other areas that could benefit from regulatory initiatives in the next five years such as dementia*". As recognized by the EU Commission[1], the rise of other major and chronic diseases is an issue and does require a more integrated approach and proper initiatives (for example oncology). However, we would welcome a clarification of how 'other areas' are to be explored/identified. *1 http://ec.europa.eu/health/major_chronic_diseases/diseases/index_en.htm*	
28	245-246	EUCOPE welcomes the reinforced collaboration between the network and Health	

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		Technology Assessment (HTA)/pricing and reimbursement bodies as well as patient and healthcare groups, to ensure timely access to medicines. The continuity of the Network system should be secured: national authorities should not reassess elements previously considered at the European level, but rather complement them. A reassessment would undermine the European regulatory framework for medicines and result in unnecessary and unjustified delays in access to innovative medicines. The collaboration with HTA/pricing and reimbursement bodies should preserve existing regulatory pathways and avoid the multiplication of requirements for approval. This is especially true as regards the criteria of the orphan designation. Any duplication or contradiction by national authorities of the assessment conducted by the EMA should be avoided in order to assure patient access for these often life-threatening diseases.	
28	253-254	EUCOPE welcomes this intention to ensure that the existing regulatory flexibilities (i.e. CMA, EC, AA) are fully understood and properly used by the Network. This intention should be expanded to other external Stakeholders (HTA, payers, patients).	
28	255-262	EUCOPE welcomes the focus of the EMA on adaptive pathways in the next five years, in its study of the practicalities of the system, and how it would ensure timely patient access to innovative medicines. We would encourage EMA to look at how the successive steps of the market access process, from marketing authorisation to reimbursement, could be better aligned to ensure all accelerated market access schemes for patients with high unmet medical needs are efficient.	
28	263-266	See comment under lines 245-246 above. We agree that timely access to new innovative medicines is a priority and we support pathways facilitating this priority. The current adaptive pathway scheme is set-up to engage multiple stakeholders (regulatory, HTA, pricing and reimbursement) during drug development. However, there is a need to further discuss appropriate patient involvement in contextualising and embedding the appropriate Benefit/Risk methodology.	*"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 **and timely** decision making and sharing of information to allow optimal access. **An***

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		We encourage involvement of the entire Network in related IMI initiatives.	***essential part of this cooperation will be to ensure that HTA/pricing and reimbursement bodies can maximise the use of the scientific assessment done at EMA level and therefore avoiding duplication.*** *HTA/ pricing and reimbursement of medicines are essential in getting innovative medicines to patients earlier."*
28	267-270	EUCOPE fully supports the intent to further integrate patients' values and views into the work of the network. It is important to put patients at the centre of pharmaceutical regulatory decisions, as they are the end-users of the innovative products we develop. Where possible, patient representatives should be involved in the decisions to bring an innovative medicine to the European market.	
28	278-291	EUCOPE is fully aligned with the HMA/EMA planned focus on ensuring the optimal implementation of the Clinical Trials Regulation, to secure a regulatory environment that triggers innovation in Europe. The network should take it as an absolute priority in the years to come. Clinical trials are essential to development but are also a way of providing access to innovative therapies to European patients. The implementation phase is critical to allow National Competent Authorities to cooperate in a consistent way. In order to ensure a smooth implementation of the regulation, it is also important to avoid the duplication of assessments in the regulatory procedure between the National Competent Authorities and the ethics committees.	*"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*

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			*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****, and the duplication of assessments conducted by ethics committees in the framework of the central procedure by regulatory authorities, and vice versa, should be avoided****. The network is committed to a successful and harmonised implementation of the regulation****, allowing National Competent Authorities to cooperate in a consistent way****. Concerning transparency and public availability of data and information on clinical trials, a balanced approach is needed to protect public health and foster the innovation capacity of European medical research, thus supporting the EU as a location for innovative research that results in the development of new products and research into new and better uses of existing products.***

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28	298-301	EUCOPE welcomes the HMA/EMA initiative towards a European early stage innovative medicines designation. The industry had a very good experience with the 'breakthrough designation' scheme that was developed in the US and would support any initiative that would bring a similar system in Europe. This is particularly welcome by smaller biotechnology companies that are highly innovative. Adaptive pathway to patients or any early path should include early incentive scheme.	
28	307-312	See comment under lines 245-246 above. In addition, the methodology used to assess the therapeutic added value of new medicines needs to be scientifically sound, flexible enough to take into account the specifics of different therapy areas, such as rare diseases and not delay patient access.	*"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.* ***This assessment needs to be scientifically sound, flexible enough to take into account the specificities of different therapy areas, such as rare diseases and prevent delays in patient access.*** *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."*
28	317-318	See comment under lines 267-270 above.	

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28	341-347	*"Access to anonymised data from electronic health records has the potential to completely change the way we monitor medicines that are on the market…. The network will explore the use of 'big data', which has huge potential to enhance capability and reduce cost whilst respecting individual patient privacy."* 1. We recognize that high quality data will be an important asset in decision-making. However, regulators should ensure that the data collected during drug development could flow into regulatory data systems and further to other healthcare environment stakeholders. 2. Data demanded for input into regulatory systems should be critically assessed for their added value versus the additional cost and data quality risk. 3. The use of international data standards and the development of interoperable systems are paramount to support global medicine development and patient access. The Network could work towards these developments and ensure a good synchronization of regional implementation timelines. 4. In the light of recent hacking of IT systems, EUCOPE would like to stress the need for IT security and encourage the network to develop an advanced, overarching and harmonized policy on IT system security.	
28	353-357	EUCOPE welcomes the network being transparent about its regulatory decisions and how these decisions are made as well as the EMA's policy on publication of clinical data and the Clinical Trials Regulation. Another important output regarding regulatory decision-making and transparency is the product information. Product information has the greatest impact on ensuring safe and effective use of a medicine in practice. However, as recognized by various stakeholders there are opportunities for significant improvements. From this perspective, it would be considered	

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		appropriate to include a vision on the development of product information in the next 5-years with regard to the content and structure and effective dissemination.	
28	516-526	EUCOPE supports the network's initiative for constant improvement in the scientific and regulatory expertise of its members. We believe a particular emphasis should be given to the training of other external stakeholders such as ethics committees as their assessment capability may vary across Member States, particularly in terms of the procedural rules for the authorisation of clinical trials and risk-management plans. We would encourage the network to develop specific training programmes to ensure all ethics committees across the European Union have the same level of expertise and understanding.	*"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 programmes, 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.* ***In particular, training should be provided to ethics committees to ensure a consistent***

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			level of knowledge for the assessment of clinical trials across EU Member States. *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."*
28	540-579	EUCOPE would like to support the network's efforts to strive operational excellence. We are particularly thankful for the opportunity the EMA gave to external stakeholders to contribute to its work on the reduction of administrative burden. We would encourage the continuation of such stakeholder meetings for the sound implementation of the strategy. We believe that stakeholders should keep working together towards a more flexible approach which will optimize regulatory processes, especially in the field of pharmacovigilance. Today, the different layers imposed by the pharmacovigilance legislation and the many stakeholders involved complicate the process, create duplication or the development of contradictory views. We believe that a more integrated approach would be favoured by all stakeholders. Ideally, the process would favour continuity of responsibility and alignment between decisions taken at European level and what is applied by national authorities. This would ease the burden for businesses which struggle to maintain their registered products, and would allow them to keep investing in innovative therapies.	*"Over the 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.* ***For the system to be more efficient, stakeholders should work together to ensure regulatory processes are optimised in future with a reduction***

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			of the layers and a more integrated approach, thus avoiding the various stakeholders potentially working in silos and duplicating work, especially in the field of pharmacovigilance. This will enable pharmaceutical companies to remain competitive and highly innovative in Europe.*"*
28	594-597	*"Information on medicinal products can be further improved…more aligned with stakeholders' expectations and needs"*. The regulated product information must become a useful and trusted reference for informing prescribers and patients about medicines. 1. Modern IT and social media development should be explored to offer additional communication channels in a changing society. This can contribute to enhancing patient health literacy levels and ultimately benefit patient compliance and adherence. 2. In addition there is a need to further streamline the dissemination of the product information. The EU agency network would see benefits in an up-to-date integrated database containing the product information of all approved medicines in Europe. 3. Finally, we would like to encourage the network to consider an open stakeholder consultation on biosimilars labelling. Currently, the EMA follows the "generic approach", pointing to the EPAR as the more comprehensive document containing necessary information about biosimilars. Results from a survey of the Alliance for Safe Biologic Medicines (ASBM) among European physicians, however, showed that the EPAR was the least preferred document while the SmPC was the next most	*"The network will explore – together with* ***industry,*** *patients and healthcare professionals – how to achieve product information* ***and any lay summary (RMP, CSR)*** *more aligned with stakeholders' expectations and needs."*

Stake-holder no.	General/ Line no.	Stakeholder comments	Proposed changes by stakeholder, if any
		important resource. *Source: EBE (2014), Tell me the whole story: the role of product labelling in building user confidence in biosimilars in Europe; GaBi Journal 3;4; www.gabi-journal.net* Available information for patients is including not only in the Patient Information but also several lay summary (RMP, CSR), which may be complex and should be more aligned with patients' expectations.	
28	616-620	Comment and rationale: See comment under lines 245-246.	
28	630-636	We support the overarching aim of Objective 4 of Theme 3, stating that "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." However, we would like to see an explicit reference to the importance of patients' involvement in regulatory processes in this section.	*"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* ***patient representatives and*** *those who develop* ***and*** *prescribe ~~and use~~ medicines. The network will put in place more streamlined mechanisms to obtain regular feedback from key stakeholders on the operation on 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."*

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28	698-734	We fully support increased dialogue among global regulators. However, considering standardisation in most cases is still a challenge within EU, let alone in the rest of the world, new standards and requirements impacting global development and submission operations should simultaneously be implemented on a global level. Specifically, the implementation of IDMP should be synchronized between regions as products are developed and licensed globally. 1. The implementation of agreed standards and guidelines should be better co-ordinated and managed on a global level (e.g. ICH). 2. A mapping of global discussions of related ongoing initiatives would be beneficial to clarify and streamline the interactions.	
28	713-720	The International Conference of Harmonisation (ICH) would be a valuable tool towards international harmonization in the field of pharmacovigilance, to export Europe's best practices in risk-management plans, as these are so crucial to patients worldwide independently of the region of the world where they receive treatment.	*"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.* ***ICH could also look at new potential processes for harmonisation, such as***

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			pharmacovigilance where it is important to ensure an equal level of safety for patients across the globe."
28	774-775	"The network will review training…the collective resources of the network." Globalisation has an impact on all facets of drug development. As the EU system is widely recognized as one of the mature regulatory frameworks in the world, sharing of these experiences and best practices are supported. Especially, regarding products/regulations, which are demanding new approaches, for example biosimilars scientific assessment / regulation. We welcome initiatives such as the FDA program for their staff (regulatory project managers) to visit pharmaceutical companies. We would encourage a similar program for the Network.	
29	General	Vaccines Europe thanks EMA for the opportunity to provide comments on the EU Medicines Agencies Network Strategy to 2020: Working together to improve health (EMA/MB/151414/2015), which is broadly supported. Vaccines Europe is the specialized vaccines industry group operating within the European Federation of Pharmaceutical Industries and Associations (EFPIA). It represents innovative research-based global vaccine companies as well as small and medium-sized enterprises operating in Europe. Vaccines Europe supports the EFPIA/EBE comments, however wants to draw the Heads of Medicines Agencies (HMA) and the European Medicines Agency (EMA) attention to some vaccine's specificities for their consideration: Development of new vaccines will require innovative technologies that are inherently complex. Early dialogue with regulatory agencies and policy makers is needed to	

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		• Evaluate the project feasibility and sustainability; • Agree on success criteria of pivotal studies (definition of endpoints, etc) ; • Maximise chances of success of implementation of new vaccines in national recommendations; • Design and enable post-approval program In line with objective 2, progressive development and access would be essential for any new innovative vaccine, which implies continuous dialogue with regulators, Health Technology Assessment (HTA), payers, health care professionals, patients, as well as national vaccine recommendations committees on what evidence will be required to bring a medicine to the patient and what could be needed post-launch. To help overcoming these challenges the Agency needs to maintain the vaccine expertise that already exist in the Vaccines Working Party and to enhance further their interaction with other EMA Committees to allow a comprehensive understanding of the vaccine specificities when applying to new development concepts. In addition, it would be important to maintain an on-going dialogue during the drafting of vaccines-specific guidelines/policies, i.e. at the stage of the concept paper and before their finalization. Vaccines Europe supports the Agency efforts to facilitate the early introduction of new treatments or preventive measures in cases of public health emergency. To be ready in time with the needed measures, there is a need to incentivise Public Private Partnerships, as well as to facilitate mutual recognition of US & EU marketing authorization. A coordination mechanism for US and EU regulators should be set up to share information and seek to identify common standards, manufacturing requirements, and testing procedures to expedite marketing approval of vaccines that are needed to address public health emergencies. Vaccines Europe also supports further interaction between the EMA and Agencies outside	

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		of the EU and International Organisations/Forum (WHO, ICH etc.) in particular with regard to the public health threats. Finally, Vaccines Europe is ready to collaborate with the agency at the time more granular proposals are made as part of multiannual work plan.	
29	161-163	A holistic approach to fight antimicrobial resistance that includes the development of new vaccines should be part of the strategy.	"Old problems such as antimicrobial resistance have become major public health threats and existing and new infectious diseases require new ~~therapies~~ **therapeutic and preventive medicines**
29	225-227	In the case of vaccines, the purchasing system (such as tenders) and market structure may cause inflexibilities and negatively impact the number of suppliers available to react to shortages.	… These supply issues can be caused by falsified medicines, stolen medicines, manufacturing/GMP non-compliance issues or many other factors including economic and **market structure (e.g. purchasing models not adapted to address scarcity of products such as tender process).**
29	241	For vaccines there are other recommending bodies then HTA involved.	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

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			Technology Assessment (HTA) **and other recommending committees as relevant**/ pricing and reimbursement bodies and healthcare professionals and patient representative bodies.
29	263	The concept of adaptive pathways should also consider including collaboration with vaccine recommendations committees at national level.	'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. ***For vaccines, collaboration will also need to be established with national vaccine recommendations committees to enable earlier public access to innovative vaccines.***'
29	309	Please add text to consider collaboration with vaccine recommendations committees at national level for vaccines.	'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. ***For vaccines, collaboration***

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			will also need to be established with national vaccine recommendations committees.'
30	General	EuropaBio welcomes the opportunity to comment on the Consultation draft of the EU Medicines Agencies Network Strategy to 2020: Working together to improve health (EMA/MB/151414/2015, hereafter "Network Strategy"). We consider that the Network Strategy is well presented and addresses the majority of the areas that will be important in the upcoming years. The strategy contains a good focus on supporting innovation, as well as on increased collaboration both within the network and between the network and various external stakeholders. We believe this strategy could improve Europe's attractiveness as location for development of novel medicines. We also thank you for recognising the need to decrease the regulatory and administrative burden and associated costs of compliance in the EU. EuropaBio suggests that: • A prioritisation of the objectives is introduced. This prioritization should be determined through consultation with stakeholders. • Annual updates should be published to inform stakeholders of progress. • A statement is added to mention implementation of societal medicines should never delay patient access to new medicines nor unnecessarily increase burden on regulators or industry. • A paragraph is introduced to mention that a critical assessment of which (outdated) company requirements can be safely abolished without compromising public health or be more efficiently integrated should be conducted before 2020. This exercise should be done in order to (i) ensure long-term sustainability of the Network, (ii) to	

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		further reduce the burden on SMEs and (iii) to improve attractiveness of Europe for research and development in life sciences. Finally, as biotech industry representative, EuropaBio wishes to express the support of its members for the implementation of the strategy in coming years. We call on the Network authorities to always look at industry as a committed partner and key stakeholder who is willing to engage in dialogue and provide necessary expertise in order to deliver on public health objectives.	
30	202-204	When giving examples of areas that could benefit from regulatory incentives to support the development of novel products, the draft only mentions "dementia".	We suggest indicating that there are other areas that could benefit from such incentives, as follows: *The network will explore other areas that could benefit from regulatory initiatives in the next five years such as dementia and* ***areas of unmet need****.*
30	224	Many potentially interesting approaches to expedite the approval process and avoid duplication of efforts have been developed as part of the Ebola epidemic (for the approval of pandemic vaccines) such as allowing the rolling submission of data and expediting the MA process. These approaches could be relevant in other areas/for other forms of public health emergencies.	Hence, we suggest the following addition to line 224: *"[…] public health crises such as the Ebola outbreak.* ***Similarly, the Network will explore opportunities for expanding the scope of the available means for dealing with public health emergencies beyond the Ebola epidemic, namely to novel complex therapies".***
30	253-254	We believe that a discussion is needed on whether and how the existing flexibilities could be improved or amended to better reflects the needs of society.	Hence, we propose the following addition:"*[…] The network will need to*

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			ensure that the existing flexibilities are fully understood and prospectively planned for their use. ***It will examine whether these flexibilities should be amended or adapted to better respond to societal asks in terms of timely access to novel treatments, particularly in areas of unmet need".***
30	255	We support the inclusion of the Adaptive Pathways pilot as a potential way to ensure timely access to medicines. However, the strategy does not discuss any alternative approaches to ensuring timely access. As the Adaptive Pathways approach is experimental and because barriers still exist, the strategy should recognise the need to consider alternative approaches. STAMP is one such example of an alternative method, which displays similar aims.	
30	263-266	We encourage the Network to reinforce support for the local level implementation of all activities related to facilitating timely access to novel medicines, especially between national medicine regulators and HTA bodies. In particular we call on all national competent authorities to seek alignment with each other in the way they interpret and apply flexibilities vis-à-vis companies, in order to avoid duplication and minimise the administrative burden for industry.	*HTA/ pricing and reimbursement of medicines are essential in getting innovative medicines to patients earlier.* ***All activities implementing these functions at local level should be appropriately resourced and regularly reviewed in order to ensure alignment is kept and unnecessary administrative burdens are avoided".***
30	267-268	We believe efforts in partnering with patients should be coordinated, as appropriate, through international partnership with other stakeholders, such as other regulators, HTA	*"[…] Further efforts should be made to incorporate patients' values and*

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		bodies and payers, medical professional organizations and industry. This cooperation will assist companies in having a global medicine development strategy.	*preferences into the scientific review process which could influence benefit risk decision making across the network* ***and globally"*****.**
30	268-270	The voice of the patient should be increased in decision making at the EMA, promoting patients from observer at CHMP to at least input into discussion.	*"[…] 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.* ***The Network will explore the scope for including patient's representation at the level of the CHMP for centrally authorised products"****.*
30	298-301	The strategy discusses an interesting proposal to introduce a European early stage innovative medicines designation. We think a 'European early stage innovative medicines designation' could be a good incentive. Further details on this would be useful. It would also be helpful to recognise that a similar designation exists in the US. The network should aim to collaborate with the FDA on how development of important new medicines could be optimised globally.	
30	302-306	We agree with the EMA that there is a need to decrease the regulatory and administrative burdens and associated costs of compliance in the European Union. We believe that it may be possible achieving significant process in this area, without compromising the need to ensure a high level of public health protection.	Hence, we propose the following addition: *"[…] 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*

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			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. ***The network will also examine how to reduce administrative burdens and associated costs and outline best practice in the Member States on implementing EU legislation in the least burdensome way".***
30	346-347	The use of international data standards and the development of interoperable systems are paramount to support global medicine development and patient access. The Network should be fully engaging in these developments and better synchronize regional implementation timelines.	*"[…] 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 seek as much as possible alignment with similar approaches in this filed from others regions of the world".***
30	353-357	Responsible data sharing (whilst ensuring that the privacy of patients is protected, the integrity of the regulatory decision-making is respected, and incentives for investment in biomedical research are maintained) is supported. Therefore the strategy paper's commitment to ensuring that 'truly commercially confidential information' is kept out of the public domain is welcomed. Another important output regarding regulatory decision making and transparency is the	

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		product information. The product information has the greatest impact on ensuring safe and effective use of a medicine in practice. We suggest including a vision on the development of product information in the next 5-years with regard to the content and structure and effective dissemination.	
30	527-531		*"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* ***international*** *expertise through more collaborative working, including enhanced outreach at* ***international and*** *national level for academic expertise. This should enable a more synergistic approach towards the organisation of the expertise within the network".*
30	540-555	We suggest mentioning the platform meetings, which have proven very useful and of importance to enhance communication with stakeholders, as this would allow for faster improvements and optimization of day-to-day operations, which benefits patients and competitiveness.	
30	562-564	We are very interested to learn more about BEMA's achievements and upcoming activities. We strongly encourage having periodic publications/press releases of BEMA's methodology and main results.	
30	594 - 597	We believe there is scope to further streamline the dissemination of product information.	

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		The Network is still lacking an up-to-date integrated database containing the product information of all the approved medicines in Europe.	
30	596-597	We suggest clarifying that industry will be consulted on this initiative and offered a chance to take active part with regard to its implementation. In addition we raise the point on need for alignment on the use of guidelines regarding product information for centrally authorised and nationally authorised medicines. Sharing information between member states and between them and the EMA is important for sponsors as well as agencies but if this sharing does not happen using the same language it may create confusion and result in suboptimal outcomes for biotech companies and patients. For instance, using the correct controlled vocabularies and the function of the xEVMPD (Extended EudraVigilange Medicinal Dictionary) is critical for safety reporting. If the "*network will explore […] how to achieve product information more aligned with stakeholders' expectations and needs"* we would appreciate the possibility to survey existing practices and to verify that the templates, required vocabularies and guideline regarding development of product information texts (i.e. SmPC, labels and package leaflets) required by national regulators and the Agency are consistent with each other.	*"[…] The network will explore – together with **all relevant stakeholders, including** patients~~, and~~ healthcare professionals **and industry**– how to achieve product information more aligned with stakeholders' expectations and needs".*
30	616-620	Efforts across the network to facilitate earlier and continuous regulatory and HTA/pricing and reimbursement body interactions are critically important for the global development of new medicines. Going forward, such bodies need to be adequately resourced.	*"[…] The network will strengthen the **funding,** 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 […]"*

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30	731-732	This section discusses cooperation with countries such as India and China; it would also be useful to mention the maintenance of links with countries where partnerships are already well-established. For example, between the EU and the US.	
30	735-737	The section summary states that the primary objective of the network will be to encourage the adoption of European regulatory approaches. We welcome commitment to taking a lead role in convergence of global standards and strengthening cooperation with non-EU regulatory authorities to support global medicine development. We agree that the harmonisation across the EU could be a good model for other regions, but it is also hoped that the network will be open to exploring and adopting best practices from other regions where these offer greater efficiencies.	
30	774-775	We encourage the EMA and the national agencies in the Network to take part in training activities for their staff offered by industry without compromising their impartiality and objectivity as assessors. In this sense, we would be happy to provide updates to the HMA-EMA staff "on the science side" of recent developments in the biotech market. A successful example of this is the FDA program for their regulatory project managers to visit pharmaceutical companies. We would encourage a similar program for the Network. We are ready to discuss specific opportunities for collaboration in a separate forum, e.g. suggesting training topics and providing training experts or organising information sessions during the HMA or EMA meetings in the future.	
31	General	Health Action International (HAI), International Society of Drug Bulletins (ISDB) and Medicines in Europe Forum (MiEF) are pleased to contribute to the public consultation on the EU Medicines Agencies Network Strategy to 2020 (1). In our view, in order to be able to carry out its public health tasks, the EMA needs to:	

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		• Be weaned off a fee-for-service relationship with pharmaceutical companies through public funding from the European Union; • Reconsider its proposal to give systematic scientific advice in exchange of fees which places the Agency in a position of conflict of interest; • Focus on evaluating evidence (scientific data) from clinical studies that have been designed to meet health needs, and assess the benefit-harm balance of medicinal products on a comparative basis (therapeutic advance); • Improve and enforce its transparency requirements to effectively prevent conflicts of interest and ensure access to regulatory data: pre and post marketing information, clinical data, pharmacovigilance data, as well as a central registry of all data; • Encourage the interaction with independent civil society representatives; • Prevent expedited marketing authorisations such as adaptive pathways from becoming the rule rather than the exception, if no genuine unmet medical need is at stake, so as to prevent unnecessary exposure to avoidable harm. **The independence of the European Medicines Agency is paramount** In order to understand how EMA's priorities and functioning have evolved, one should be aware that the Agency is very heavily funded by pharmaceutical companies. Industry funding has progressively increased since 1995 when the EMA was established. In 2015, the collection of pharmaceutical companies' fees will amount to more than 83% of the Agency's overall budget (2). In contrast, the fees collected by the US Food and Drug Administration (FDA) from drug companies submitting applications for marketing authorisations for human medicines and/or biological products represent about 60 percent of the FDA's overall budget (3). To guarantee the EMA's independence, and prevent difficulties in sustainability due to	

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		fewer applications and subsequent fluctuations in fee revenues, any direct financial relationship between the Agency and industry should be avoided. This could be achieved by restructuring EMA's funding so that fees would make up but a small proportion of its overall budget. **Robust policies on conflicts of interest must be in place to safeguard public health** The independence of the regulatory process is crucial to ensure that public health is not supplanted by private interests. To guarantee independence, medicines agencies and national competent authorities must have in place robust policies of conflicts of interest, for its management board, staff and experts. In this regard, we regret EMA's recent decision to weaken its policy on conflicts of interest for experts. There is no rationale behind the Agency's decision to decrease cool-off periods and to maintain an arbitrary classification system that allows unjustified situations whereby experts with conflicts are permitted to engage in the EMA's policies and their decision-making. Since the EMA is considered a benchmark to many national drug regulatory agencies, we urge them to reconsider and to reverse its policy (4). *Concrete measures by competent authorities and medicines agencies to increase expertise include*: 1. Reinforcing the number and skills of experts who are independent from pharmaceutical companies 2. Significantly reinforcing agencies' in-house expertise. 3. Diversifying and cross-compare the viewpoints of the various experts in committees and working groups (epidemiologists, primary healthcare providers, patients, etc.). 4. Bringing in new heads of working groups and committees, new institutional representatives, etc., on a regular basis, so as to increase the number of experienced	

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		people and to enhance skills. 5. Extending the requirement of transparency to all the work done by regulatory agencies and other competent authorities (including making available the documents used to develop positions or make decisions). 6. Implementing a system of independent verification of declarations of interests. 7. Implementing a system of sanctions in case of non-disclosure of interests. 8. During meetings of committees or other working groups, hearing from the participants who have an interest in the company involved (either directly or as a competitor), e.g. the clinical trial investigators; then requiring all participants (experts or others) who have an interest (be it major or minor) in any company involved to leave the room, during the discussion leading up to a position being taken or a decision being made. 9. Implementing and applying sanctions in case of participation of somebody in a position being taken or a decision made, in case of an interest in the company affected by the position or the decision. 10. Maintaining a public register of all documents detained, as requested by the European ombudsman **The mandate of EMA and national drug regulatory authorities** The role of 'support to innovation', as understood by the EMA and national medicines agencies as *optimising industry's return on investment* frequently conflicts with the agencies' main mission of evaluating and regulating drugs and medical devices. This *innovator* role, which also encompasses the provision of early scientific advice, should be closely monitored and subject to full transparency, so as to minimize regulatory capture. Those officials/experts participating in the provision of scientific advice should not be	

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		involved in the assessment of the pharmaceutical product at a later stage. **The benefit-risk assessment of health products needs to be evidence-based** Since 1965, the criteria for marketing authorisation in Europe are the demonstration of a medicine's efficacy, safety and quality. Efficacy is usually demonstrated in clinical trials, in which the effects of the new drug are often compared to placebo rather than to "the best therapeutic option available" for the same indication. And frequently surrogate outcomes are deemed sufficient which do not necessarily translate into tangible benefit for patients. Consequently, some drugs constitute a step backwards, unnecessarily exposing patients to adverse effects when other safer treatments exist. The paucity of new medicines that offer even a modest therapeutic advantage stands in stark contrast to the large number of new products that expose patients to unjustified risks. The majority of new medicines are "me-too" drugs and not "innovative" since they do not have an added therapeutic value (5,6). Rather than lowering the requirements for market authorisation of new drugs, as proposed in the adaptive pathways concept, the EMA should establish a compulsory demonstration of a new drug's **therapeutic advance** when compared to the best available therapeutic option. This would act as an incentive to reorient research and development towards unmet health needs -for which there's no adequate treatment -and true therapeutic progress. Therapeutic advance should be the 4th criterion to be demonstrated when applying for a marketing authorisation. The therapeutic advance of a new medicine would be appraised in comparison with existing treatments, and demonstrated by relevant clinical data collected from comparative clinical trials. Clinical trial results would then need to indicate the extent to which the new medicine would be more effective or safer than the existing standard treatment, specifying the relevant patient population.	

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		In order to implement more stringent criteria for market authorisation, concrete measures include: 1. The requirement for pharmaceutical companies filing marketing authorization applications to include complete results of clinical trials comparing the new drug against the drug(s) of reference, in their optimal conditions for use. 2. A change in legislation at the European level requiring that marketing authorisation applications demonstrate the added therapeutic value and packaging safety of new drugs with a high level of evidence, demonstrated in the normal conditions of use. 3. The provision of public financing for comparative clinical trials that allow drugs to be objectively rated among therapeutic strategies (including non-drug options), in terms of their risks and their benefits. **Transparency in decision-making: access to documents is a right of EU Citizens and an institutional duty of the EMA** The EMA's transparency requirements are enshrined in the EU directive 200/83/EC which regulates pharmaceutical products, as well as in the EU freedom of information Regulation (Regulation 1049/2001) which governs public access to documents at European Union's institutions and agencies. Health is a field where the decisions of EU institutions affect citizens' daily lives. The accountability and public scrutiny of Health Authorities' decisions are only possible when the public has access to both the body of evidence and the rationale on which decisions are based. Unfortunately, in 2015, despite their clear mandate to uphold transparency, the European Medicines Agency (EMA), the Heads of Medicines Agencies (HMA) and the National Drug Regulatory Agencies still fail to provide full public access to scientific evidence about the effects of medicines on human health. In practice, an overly broad	

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		definition of "commercially confidential information" is used to defend this secrecy. This leads to undue delays in access to documents, even if they contain no commercially confidential information as the EU Ombudsman's investigations of complaints have shown (7,8). Concrete measures to achieve widespread transparency include: 1. Increasing the transparency of debates, position-taking and decision-making: detailed agendas of meetings announced ahead of time; documents upon which experts have made statements (documents supplied by companies and those obtained elsewhere). All clinical data or other data that are important in making recommendations (presentations, etc.) must be made public. 2. Ensuring that experts' minority opinions are expressed, by requiring that the voting results be included in minutes, with the details and the justification of the minority opinions, position by position or decision by decision (video recording or verbatim reporting of the sessions would allow this objective to be met). 3. Making minutes of meetings available online and readily accessible, within two weeks after the meeting. 4. Ensuring the follow-up (traceability) of recommendations made at each level of regulatory agencies, administrative and ministerial authorities in charge of medicines, with publication, when applicable, of the reasons why recommendations were not taken into account. 5. Giving access to PRAC's opinion at every stage: before drug approval, on Periodic benefit-risk evaluation reports, etc. **Public access to medicines safety and efficacy data contributes to informed decisions on treatment. Clinical trial data is not commercially confidential**	

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		information Public access to full clinical data, including raw data, is particularly important to protect public health as it allows for comprehensive independent analysis, enhancing knowledge about the real effects of medicines and allowing comparative effectiveness reviews (9). Patients, consumers and healthcare professionals have long been deprived from having access to this important information. The EMA has prevented full disclosure under the guise that giving public access to commercially confidential information would jeopardize commercial interests. ***Implementation of the Clinical Trials Regulation*** The recently adopted EU Clinical Trials Regulation has the potential to significantly increase public access to clinical trial data. Regulators – and in particular the EMA in its key role of managing the EU clinical trials database- must uphold the principle that clinical trial data held by regulatory authorities is information of public interest. Any definition of commercially confidential information is to be interpreted narrowly and should never override disclosure of clinical trial data. The EMA must in fact fully comply with the Regulation on access to documents and the Treaty on the Functioning of the European Union, which identifies the ”protection of health and life of humans’’ as an overriding public interest. (7) Moreover, under Regulation No 1049/2001 on access to documents, confidentiality is an exception: ”In principle, all documents of the institutions should be accessible to the public. However, certain public and private interests should be protected by way of exceptions’” (Regulation 1049/2001, recital 11). In our view, the EMA’s ‘Draft proposal for an addendum, on transparency, to ”the Functional Specifications for the EU portal and EU database to be audited’’ is unacceptable and at odds with the principles enshrined in Regulation (EU) No 536/2014	

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		and the transparency advances it promised to bring, especially that of increasing the reliability and robustness of clinical data. The EMA's has the responsibility to protect and strengthen public health. However, its interpretation of Regulation (EU) No 536/2014 does little to meet the needs of patients and the public across the European Union yet goes a long way to soothe the requests of "clinical trial sponsors" such as the pharmaceutical industry, by introducing limited disclosure as the norm and by providing all the flexibilities sponsors need to circumvent their legal obligations to disclose clinical trial data. By allowing for redactions of clinical trial data, on the grounds of commercial confidentiality, the EMA is compromising public health and diminishing public trust in regulatory-decision making (10). A redefinition and narrowing of the notion of commercially confidential information is essential to prevent the EMA from relying solely on the self-classification by the sponsor of the information that may undermine the sponsor's economic interest or competitive position. Any exception to disclosure rules should only involve the removal of specific elements of information within a document and never be applied to an entire section or certain types of documents. ***Access to de-identified clinical trial participants' data: an essential step for secondary analysis*** EMA's views have dramatically changed since November 2012, when it announced that it would "proactively publish clinical- trial data and enable access to full data sets by interested parties" –to allow for reanalysis of trials' results. It is important to distinguish patient personal data from de-identified participants' data. Participants accept to put themselves at risk, taking part in clinical trials, hoping that their participation will benefit society through the advancement of science. Furthermore, according to EU regulations, data submitted to regulatory authorities during a marketing authorisation procedure is submitted in non-identifiable form. Currently applied	

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		anonymisation methods safeguard patient confidentiality. Only in very specific cases (e.g., rare diseases) additional measures might be required to prevent re- identification. There is no public health rationale in preventing access to de-identified data by researchers and the European Medicines Agency should strive to ensure public access to these data in the future implementation of its access to clinical trials policies. Granting public access to raw data is crucial to minimise dangerous practices of reporting bias, which overrate the benefits of a drug while underestimating its harm. Moreover, industry-funded research often benefits from public funded research bodies (access to investigators and research teams at publicly research sites; public funding for basic research through EU grants and Member State funding, etc.). This is an additional argument that all data from biomedical research is made publicly available. ***Trade agreements should not hamper affordable access to needed medicines nor hinder clinical data transparency.*** As noted in the HMA/EMA draft strategy paper, political initiatives in the form of free trade agreements between the EU and non-EU countries increasingly include pharmaceuticals as an area of cooperation. This is the case in the Transatlantic Trade and Investment Partnership, the Comprehensive Economic and Trade Agreement and other free trade agreements with Japan, Singapore and South Korea. The inclusion of a 'Pharmaceutical annex" with provisions on the regulation of pharmaceutical products in these trade agreements often undermines public health, for example, by including principles that should govern pricing and reimbursement decisions that limit the freedom of Member States to tailor their pricing and reimbursement strategies to provide sustainable access to medicines in favour of an increased voice for the pharmaceutical industry in these decision making processes (11). It is of utmost	

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		importance to ensure that agreements being currently negotiated: a) do not hamper by any means affordability of needed medicines, b) do not limit or restrain Member States' competence to negotiate price and reimbursement decisions c) do not impede public access to medicines' safety and efficacy data under the guise of trade secrets protection enshrined in trade agreements. **Timely access to medicines shall not be in detriment of patient safety** Whilst timely access to needed medicines is important, faster access should not take place to the detriment of patient safety. The concept of ''innovative medicines" should be attributed to medicines addressing true unmet medical needs and with added therapeutic value when compared to the best available treatment. Existing flexibilities for market access - e.g. conditional approval, exceptional circumstances, compassionate use, accelerated assessment- should only be applied in duly justified circumstances. Communication to patients and their carers about the potential benefits of conditionally-approved medicines should not be overestimated, nor should their potential harms be underestimated. Treatment under conditional marketing authorisation must be closely monitored and any adverse drug reactions should be reported and published. **Adaptive pathways: deregulation under the guise of increased access, with patients and society picking up the tab** According to data from the European Commission, the timelines for drug licensing have drastically shortened over the last 10-20 years, sometimes posing threats to patient safety (12). Premature licensing is achieved at the expense of proper evaluation, leading	

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		to more harm to patients (13,14). Years of experience show that in Europe, the US and Canada, pharmaceutical companies frequently do not honour their commitments on post-authorisation evaluation of medicinal products (15,16,17). It should also be noted that the move to extend conditional marketing authorisation to all new medicines was rejected by the European Parliament and the Council in 2010. The current pharmacovigilance legislation further underscores that: "*It is essential that a strengthened system of pharmacovigilance does not lead to the premature granting of marketing authorisations*" (18). The EMA's 'adaptive pathways' approach – which builds on the proposal for an adaptive licensing approach to all new drugs (19) - raises numerous concerns from a public health point of view. First, adaptive pathways aims to grant marketing authorisations based on lower requirement for evidence, for instance by taking on board surrogate endpoints in detriment of clinically relevant outcomes to save costs and time. Since the marketing authorisation is granted based on limited data, patients will be potentially exposed to the harms of a medicine which has not been subject of a thorough evaluation. Evidence from the US from the last 16 years has shown that drugs approved once the legislation on expedited drug approvals had been passed were more likely to be withdrawn or receive a new black-box warning than drugs authorised prior to the bill's passage (20). Second, there are potential consequences to patients' safety when the burden of evidence is shifted from pre-marketing to post-marketing. That also means that the risk is shifted to the patients and the cost to the public. The drug's evaluation is to be rolled out once the medicine is already on the market, but in reality post-authorisation commitments are often not honoured. It could prove extremely difficult to gather	

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		additional clinical data on a drug once it has been authorised. Third, the European Medicines Agency's pilot project, launched in March 2014, seems to be an ideal tool to circumvent democratic process. It paves the way for the deregulation of marketing approval procedures and increases industry's control over other healthcare stakeholders: health technology assessment (HTA) bodies (influence on pricing and reimbursement decisions), prescribers and patients (increased control over prescriptions, access to personal data, direct-to-consumer communication). Fourth, adaptive pathways come with an additional measure to the concept: "a prohibition on product liability suits during the initial marketing period" by injured patients or payers. This insidious measure clearly defends the interests of the manufacturers. Patients and healthcare professionals will not only have to agree to use a medicine which has not been adequately tested, but also end up not being able to prosecute the company if something goes wrong. This places desperate patients in a particularly vulnerable and unprotected position, which is clearly unethical. Fifth, the legal basis for a number of aspects of the adaptive pathways approach is missing, e.g. the power to force manufacturers to conduct post-licensing studies. Last but not least, the spill-over effect: Implementing adaptive pathways could lead to a situation whereby premature marketing authorisations become the rule rather than the exception, even when no genuine public health need is identified, therefore putting EU citizens' health at risk. **Scientific advice to pharmaceutical companies = risks of regulatory capture** The provision of confidential "advice" to pharmaceutical companies on their development plans for new medicines in exchange for fees – is a potentially harmful practice that the EMA is now trying to extend to national health technology assessment (HTA) bodies in the European Union (EU) (21).	

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		The provision of scientific advice by regulators to the regulated, in exchange for fees, holds an inherent risk of regulatory capture. This is further accentuated when the committee responsible for providing advice on marketing authorisation procedures is concomitantly involved in scientific advice procedures. To minimise the risk of regulatory capture, committee members deciding on marketing authorisation should not be involved in the provision of scientific advice. Scientific advice should be transparent to allow independent scrutiny and enhance public trust. Detailed reports of the scientific advice provided by regulators to pharmaceutical companies during drug development and pre-registration process should be published at the time of decision on trial, or not later than 12 months after the end of the trial. This information cannot be considered commercially confidential information as there is a clear overriding public interest in disclosure. Instead of providing customised advice to pharmaceutical companies, we urge the EMA to write up ad hoc guidelines that help drug manufacturers make development decisions that address genuine public health needs. Potential guideline deviation should be addressed through written exchange only and subject to transparency requirements (see above mentioned recommendations). European public assessment reports (EPARs) and similar national regulatory documents should include an additional section summarising scientific advice given by the EMA at each stage of the development process. This information would not only facilitate better understanding of the data provided, but also allow for an assessment of the role of scientific advice in the approval of new medicines. **Medicines agencies and price and reimbursement bodies shall collaborate while maintaining their different roles** ***Cost-effectiveness assessment needs to remain independent from the Drug Regulatory Agencies***. The EMA wants to be recognised as the "leading authority" in the	

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		evaluation and supervision of medicines. It intends to work more closely with health technology assessment (HTA) bodies to make sure that their assessments are not too divergent. It is necessary to recognise that the aims of EMA and HTA are not identical. Whereas for EMA efficacy, safety and quality are legally sufficient criteria, HTA needs to assess the comparative effectiveness measured in patient relevant outcomes (morbidity, mortality, quality of life). Pharmaceutical companies are increasingly challenging health technology bodies' recommendations when these do not serve their commercial interests. They would like HTA bodies to be bound by drug regulatory agency decisions. HTA bodies have expertise in comparing relative effectiveness of medicines as well as in cost-effectiveness assessment. They play a major role at the national level role in the sustainability of Member States' social insurance systems and should therefore remain fully independent of Drug Regulatory Agencies as well as from any influence of pharmaceutical companies. Rather than trying to "harmonise" the methods of HTA institutions and limit their scope, or to support approaches that would not take into account the varied aims of the assessments and the context, systems and priorities of different Members States. A sensible form of cooperation would be that EMA demands that new drugs are tested against the best available treatment and for meaningful endpoints. EMA's role furthermore is to act as a provider of information. It should provide HTA bodies and the scientific community with complete assessment reports, as well as any relevant data corroborating its decisions. Once again, openness and transparency are crucial to enabling others to build on EMA's work. **Pharmacovigilance should be a major priority for the EMA and regulatory**	

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		network ***Access to pharmacovigilance data*** Adverse drug reactions (ADRs) are reported by health professionals and patients to facilitate the accumulation of scientific knowledge, and to prevent otherwise avoidable ADRs and drug-induced harm. In August 2014, the European Medicines Agency (EMA) organised a public consultation on the revision of its 2011 policy on the access to the European pharmacovigilance database EudraVigilance, which created the public interface adrreports.eu. Reports of suspected adverse drug reactions are coded using standardised terminology and then registered in EudraVigilance as "Individual Case Safety Reports, ICSR". In practice, however, this process can strip spontaneous reports of individual cases of clinical significance. That is why access to narrative summaries of individual cases needs to be provided along with quantitative data. Unfortunately since 2012, the public interface Adrreports (www.adrreports.eu) has provided access to only a limited number of quantitative information, e.g. the number of individual cases associated with a given substance, but it does not give access to a listing of case summaries ("Narrative Case Summary"). As major contributors of spontaneous reports of adverse drug reactions, it is unjustifiable for healthcare professionals, consumers and patients to have such limited access to EudraVigilance. In its draft revision document, the EMA proposed to share more data with marketing authorisation holders (MAH), which made sense since they are required to develop periodic benefit-risk evaluation reports about their drugs. Nevertheless, drug regulatory agencies have to closely monitor the MAH pharmacovigilance activities in order to avoid	

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		data being misinterpreted or withheld as recently happened on several occasions. The EMA also proposed to give research organisations, on request, "access to ICSR data sets similar to those provided for MAHs in response to justified research requests". However, the EMA set up restrictive conditions for granting access to researchers, e.g. the signature of confidentiality agreements. The EMA also demanded to "view any publication resulting from EudraVigilance data before submission (…). [and that] any issues raised by the Agency (…) must be addressed to the satisfaction of the Agency before submission for publication". However, EMA's central role does not give it the right to monitor how the data are used or to censor scientific discussion. Anonymised narrative summaries of cases should be made available. Considerations about the re-identification of patient level data cannot be exaggerated. As rightly emphasised by EMA regulators ''(…) standards for de-identifying personal data are available and continue to evolve to ensure adequate protection''(22). Additional safeguards can be applied in exceptional circumstances. We encourage the EMA in its Eudravigilance policy to support public health by: • proactively providing public access to useful qualitative data such as anonymised summaries of cases; • granting public access to consumption data of drugs in the EU; • providing access to all drug regulatory authorities' assessment reports of MAH's periodic benefit-risk evaluation reports (former Periodic safety update reports); • not forcing researchers to sign "confidentiality agreements". ***PRAC Public Hearings: missing in action?***	

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		Five years have passed since the adoption of the directive and regulation on Pharmacovigilance, another three years since the first PRAC meeting, but the PRAC Public Hearings have not yet been implemented. They are a long awaited and welcomed initiative but several major improvements are still needed to make the most of these hearings. We encourage the EMA to ensure that EU pharmacovigilance public hearings are as transparent and independent as the public sections of advisory committees in the USA (23). EMA's draft rules (published in 2014) allowed pharmaceutical companies to use public hearings as a platform to minimise/deny genuine safety concerns, as companies would be systematically granted "the opportunity to present its/their view(s) to the participants during the public hearing" by the EMA (1). In contrast, the US Food and drug administration (FDA) guidance on advisory committee prevents "the sponsor whose product is under review" from participating in the open panel of public hearings (2). The EMA proposed non-public hearings "where a marketing authorisation holder or another person intending to submit information that has confidential data relevant to the subject matter of the procedure" (1). We underline that non-public hearings hinder public scrutiny and should be reserved to protect whistleblowers, and should not offer MAHs an opportunity to influence the decision-making process. Moreover, instead of being reluctant to organise live-broadcast and web-streaming of public hearings by adding everywhere the condition "when technically feasible", we expect the EMA to make the most of modern communication tools to ensure wider participation by the general public. ***PRAC 's role and independence should be reinforced*** The Pharmacovigilance Risk Assessment Committee (PRAC) is the committee at the European Medicines Agency that is responsible for assessing and monitoring safety	

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		issues for human medicines. On two recent occasions, the recommendations of the PRAC have not been duly followed: 1. On 10 January 2014, the PRAC recommended that Protelos/Osseor should no longer be used to treat osteoporosis, due to its risk of cardiovascular harm. Nonetheless, the CHMP opted not to recommend a suspension, but just introduced some restrictions to its use. 2. On 8 November 2013, the PRAC recommended the suspension of diacerein-containing medicines, due to their gastro-intestinal side effects and liver toxicity. Rather than accepting the PRAC position and withdraw the market authorisation(s), the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human just endorsed on 19 March 2014 a set of recommendations to restrict the use of diacerein-containing medicines. Both pharmaceutical products are still being marketed in the EU, despite their disproportionate risk of harm. *Concrete measures to achieve a robust and proactive pharmacovigilance include:* 1. Ensuring that decisions in pharmacovigilance matters are made independently from marketing authorisation committees. 2. Encouraging the undertaking and the public financing of post-marketing authorisation studies, as decided by the marketing authorisation or pharmacovigilance committees. 3. Applying sanctions, in particular financial penalties, for non-completion within the designated time period of post-marketing authorisation studies that marketing authorisation or pharmacovigilance committees have requested from marketing authorisation holders. 4. Publishing in a timely manner all pharmacovigilance data likely to encourage	

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		healthcare professionals and patients: to report the adverse effects experienced with this or that drug; to take special precautions; or to reconsider current treatments. 5. Making decisions to suspend or to withdraw marketing authorisation without delay, on the basis of an unfavourable risk-benefit balance, particularly when there is an alternative treatment with a better risk-benefit balance; with the benefit of the doubt given to the patient and not to the drug. 6. Requiring that the withdrawal of a drug from the market be preceded by online publication of the minutes of the pharmacovigilance committee that proposed the withdrawal, as well as the documents underlying that decision. **Preventing otherwise avoidable medication errors** The document does not identify any priority in the prevention of medication errors nor does it put forward measures to encourage the rational use of medicines. We urge the EMA to improve the quality of packaging to minimise the medication errors in practice. Guidelines on naming, labelling and packaging of medicinal products should be reviewed to proactively address patient safety concerns. In addition, packaging, labelling and package leaflets should be subject to user testing both in the hospital and in ambulatory settings. The comprehensive results of such tests should be thoroughly assessed by Drug Regulatory Agencies before granting a marketing authorisation. **Encourage generic and biosimilar competition to enable affordable treatment** Increasingly, and this is only exacerbated by the current economic crisis, Member States are under greater strain to provide universal access to care and to needed medicines. Most notably, more than 100 influential oncologists have described current prices of cancer medicines as: "astronomical, unsustainable and even immoral"( ). Recently, the exorbitantly high price of Sovaldi° (sofosbuvir) a new Hepatitis C drug was heavily criticised by NGOs, consumers, patients, carers, and healthcare professionals worldwide.	

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		Generic competition is an effective tool to bring medicine prices down. Prices tend to drop 25% a year after generic entry and 40% two years after entry (25,26). These savings translate across the health system: average savings are estimated to be almost 20 percent after the first year, and 25 percent after the second year (22). Unnecessary delays in generic and biosimilar market entry have a negative impact on drug affordability and increase the overall expenditure on medicines. **Any decision to switch a prescription medicine to non-prescription must be evidence-based and have patient safety and rational use in mind** The HMA/EMA proposed strategy paper refers to the need to ensure that mechanisms to re-classify medicines from prescription-only to non-prescription ‘’are in place, effective and being used, thereby improving patient access’’(1). We warrant extreme caution in any attempt to change the legal classification of medicines. These decisions should be evidence-based and have the best interests of patients in mind (i.e. high standards of patient safety). In addition, the potential for misuse and/or irrational use should be adequately weighed. **Medical Devices: a priority not to be ignored** The EMA should also include another important aspect in its work plan to 2015: medical devices’ evaluation. The medical devices market is rapidly expanding. The EMA should be structurally adjusted to be able to scientifically assess medical devices being marketed in the European Union. The US Food and Drug Administration can rely on the expertise of its Center for Devices and Radiological Health (CDRH) which is responsible for regulating companies that manufacture, repackage, re-label, and/or import medical devices sold in the United States. The EMA and the network of regulatory agencies, some of which are already responsible for regulating devices at national level, should further consider how to best address this important priority and uphold their responsibility to protect patients’ health.	

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31	171	"Costly and complex" development of medicines **Debunking pharma myths on the costs of the current pharmaceutical model and its Research and Development** The pharmaceutical industry generated higher profit margins than any other industrial sector in 2013, and is likely to have remained the most profitable sector in 2014. However, the majority of this revenue is not reinvested in R&D. The DG Competition enquiry revealed that between 2000 and 2007 pharmaceutical companies spent around 23% of their turnover on marketing and only 17% on R&D (23). The cost of a new drug discovery was claimed to be $1.3bn (£834m; €1bn) in 2011, but this figure, which comes from the industry-supported Tufts Center, is likely to be at least a fourfold overestimation. Researchers have recalculated the Tufts Center figures using a more comprehensive methodology to include cheaper drugs in their calculation and drugs produced in part with public funds or tax credits. They found a mean cost closer to US$90 million per new drug and a median cost of US$60 million (27). Recent estimates from the same Tufts Centre have suggested that a new drug costs $2.6 bn to develop (28). Consumer advocates and NGOs have criticized the new figures saying that critical information was missing from the analysis and that it was mere propaganda. The real costs of R&D remain unknown – even the director of pharmaceutical company GlaxoSmithKline called the "1 billion estimate [of R&D costs] one of the greatest myths of the industry" - and estimates of the industry and independent analysts vary greatly. (29)(30) 1. HMA, EMA. EU Medicines Agencies Network Strategy to 2020. Consultation draft, EMA/MB/151414/2015, March 27, 2015. Page 9. 2. http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_co	

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		http://english.prescrire.org/en/79/549/49237/4104/4091/SubReportDetails.aspx 11. https://www.oxfam.org/en/research/trading-away-access-medicines-revisited 12. European Commission Directorate General Competition. "Final Report of the Pharmaceuticals Sector Enquiry"; 8 July 2009. ec.europa.eu :426 pages. 13. Carpentier D et al. "Drug review deadlines and safety problems" N Engl J Med 2008; 358: 7 pages. 14. Frank C et al. "Era of faster FDA drug approval has also seen increased black-box warnings and market withdrawals" Health Aff 2014; 33(8): 6 pages. 15. US Government Accountability Office "Drug safety – Improvement needed in FDA´s postmarket decision-making and oversight process" Report GAO-06-402, 2006. www.gao.gov: 63 pages. 16. Carpentier D "Can expedited FDA drug approval without expedited follow-up be trusted" JAMA Internal Medicine 2014; 174 (1): 95-97. 17. Lexchin J "Notice of compliance with conditions: a policy in limbo" Healthcare policy 2007; 2 (4): 114-122 (+ annexes: 5 pages). 18. "Directive 2010/84/EU of the European Parliament and of the Council of 15 December 2010 amending, as regards pharmacovigilance, Directive 2001/83/EC on the Community code relating to medicinal products for human use" Official Journal of the European Union 31 December 2010: L 348/74-L 348/99. 19. Eichler H-G et coll. "Adaptive Licensing: Taking the Next Step in the Evolution of Drug Approval"Clinical Pharmacology & Therapeutics (2012); 91 (3): 426–437. 20. Frank C et al "Era of faster FDA Approval has also seen increased black-box warning	

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		and market withdrawals" Health Affairs 2014 ; 33(8) : 1453-1459 21. AIM, HAI Europe, ISDB and MiEF "Providing "scientific advice" to pharma industry undermines the independence of regulatory authorities" Joint consultation response to the EMA's public consultation on its `Best practice guidance for pilot EMA HTA parallel scientific advice procedures'; 15 July 2014: 6 pages. http://english.prescrire.org/en/79/549/49233/3696/3469/SubReportDetails.aspx 22. Eichler HG, Pétavy F,Pignatti F et al. Access to patient-level trial data- A boon to drug developers. NEJM doi:10.1056/NEJMp1310771 (2013) 23. US Food and Drug Administration (FDA) "Guidance for the public, FDA advisory committee members, and FDA staff: the open public hearing at FDA advisory committee meetings" Final guidance; 15 May 2013: 13 pages. 24. Laurance, J. (2013). Makers of anticancer drugs are "profiteering," say 100 specialists from around the world. British Medical Journal (BMJ) 346:f2810. 25. Kanavos, P., Vandoros, S., Irwin, R., Nicod, E. and Casson, M. (2011). Differences in costs of and access to pharmaceutical products in the EU. Policy department economic and scientific policy. Brussels. 3.6. Access to generic medicines in EU member states and the benefits of generic competition: p70. 26. Executive Summary. Final Report DG Competition Sector Inquiry Summary. http://ec.europa.eu/competition/sectors/pharmaceuticals/inquiry/communication_en.pdf 27. Light D and Lexchin J "Pharmaceutical Research and Development: What Do We Get for All that Money?" BMJ 2012; 344: 5 pages 28. Mullard A "New drugs cost US$2.6 billion to develop" Nature Reviews Drug Discovery 2014; 13, 877.	

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		29. Light, D. and Lexchin, J. (2012). Pharmaceutical research and development: what do we get for all that money? British Medical Journal (BMJ). 345. 30. Adams, B. (2013). GSK chief: drug prices should be lower. PharmaTimes Online. http://www.pharmatimes.com/article/13-03-18/GSK_chief_Drug_prices_should_be_lower.aspx [accessed August 6th, 2014].	
32	General	The European Coalition to End Animal Experiments (ECEAE) currently represents 24 animal welfare member organisations across 22 European countries including 18 EU Member States. The ECEAE is the only pan-European organisation exclusively representing animals used in experiments. The ECEAE is an independent, campaigning organisation funded exclusively by donations from individuals and from its member organisations. We are disappointed to not see recognition of the issue of animal testing within the strategy. There are well known animal welfare (ethical) and scientific issues with the use of animals in the pharmaceutical sector. 95% of drugs fail in clinical trials because reliance on non-clinical tests, including animal based models and toxicity tests, are unable to adequately predict neither efficacy nor safety. The new Directive on the protection of animals used for scientific purposes (Directive 2010/63/EC) strives to achieve "the final goal of full replacement of procedures on live animals for scientific and educational purposes as soon as it is scientifically possible to do so". The need to "phase out" animal testing was recently reiterated by the European Commission in a statement this June in response to a petition by 1 million EU citizens calling for an end to animal testing. We feel the EMA strategy should be aligned to this purpose. We feel it is important even in such a top level strategy document to recognise the issue of animal testing for pharmaceuticals and to include additional efforts that the Agency and the HMA working together can make to reduce the sector's reliance on animals. In response to requests from the animal protection community, including ourselves, the	

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		EMA set up the JEG3Rs in 2010 to look at ways to replace, reduce and refine the use of animals (the 3Rs). The work of this committee should be mentioned in the strategy and broadened to include the HMAs who have a greater responsibility in the authorisation of existing medicines as well as the enforcement of the Directive 2010/63/EC. We include general suggestions for suitable Objectives where the EMA could improve its activity on the issue of animal testing.	
32	Theme 1 Obj. 2	Work in this area could also contribute to the reduction in animal use by identifying and eliminating unnecessary or unreliable animal tests that can also slow down the access to market. One example is eliminating the rodent carcinogenicity study that takes 2 years to complete, costs 1 million Euros and has an accuracy of less than 50%. This is currently an ICH project which has been supported by -and needs additional support - from the EMA and HMAs. The critical path initiative in the USA explicitly recognised the failure of animal testing in helping speed up the access to market. An EMA and HMA project to look at the issue of the poor translation of animal research (including safety testing) to clinical trials would be incredibly helpful in this area.	
32	Theme 1 Obj. 4	A commitment to sharing best practice in alternative methods between regulatory authorities with cooperation from industry and stakeholders would fit here and would be most welcome. For example a project to work together to root out redundant animal testing in existing and new market authorisations including batch safety tests would be very important. For example, we are concerned about requirements in market authorisations for batch safety tests that have been replaced or removed from the European Pharmacopeia. Unless authorities review existing authorisations these will not be removed and animals will continue to be used unnecessarily. This is a task that the JEG3Rs has taken up but appears to have limited capacity for. This is precisely something that the HMA and EMA	

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		can do together since it relies on looking at existing market authorisations, many of which may be national and not central.	
32	Theme 3 Obj. 1	There appears to be some duplication in objectives to Theme 1 (objective 4). Our comments on that objective could equally fit here.	
32	Theme 3 Obj. 4	There is a need for greater engagement with stakeholders in general, particularly the need for more open meetings. There is also a need for greater engagement with sector specific, accredited stakeholders, which could take the form of annual stakeholder meetings as well as permitting greater transparency and feedback from stakeholders through participation as observers in relevant committee meetings and expert working groups on scientific and procedural topics. Greater engagement with the EDQM to facilitate the uptake of alternative methods that are in the European Pharmacopeia in the requirements for new and existing authorisation is also greatly needed. Greater engagement with pharmaceutical companies to facilitate the use of alternative methods is also needed. An exploration of why alternatives are not used more frequently to support market authorisations needs to be made as the reasons are unlikely to be purely scientific. Industry may need to be encouraged to submit supporting evidence from alternative methods which the EMA reviews to determine if in fact (in retrospect) they could have been relied on. Unless industry and regulators cooperate in this way we will not replace animal testing.	
32	Theme 4 Obj. 2	It should be mentioned that the EMA will continue to develop, support and promote 3Rs efforts at the ICH and VICH to reduce the use of animals, promote modern technologies as well as the efficient use of resources.	
33	76	Comment: after paediatric investigational plans, insert (PIPS)	

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33	81	Comment: should include recognised patient organisations.	
33	178	Comment: this is the first time that patients "in the network" are referred to and appears to describe the role of patient as a "consumer". The valuable work patient representatives have contributed to the work of the Agency over the past decade is being ignored.	
33	207-210	Comment: patients with rare diseases do not only require orphan medicinal products. There are products, such as immunoglobulins, that do not fall under the category of "orphan medicinal products" but are vital for patients with primary immunodeficiencies.	Proposed change (addition in bold and italics): "To this aim a better coordination of the existing tools like the various horizon-scanning exercises for orphan medicinal products ***and other medicines to treat rare diseases*** conducted by different institutions will offer a significant benefit in view of expediting the process and avoiding potential duplication of efforts".
33	229	Comment: Manufacturing outside the EU. Therefore there should be increased collaboration amongst other agencies, such as FDA in order to avoid duplication and harmonize these efforts.	
33	270	Comment: their views should be heard.	Proposed change: their views should be taken into consideration.
33	313-316	Comment: we need to ensure that the new medicines marketed as generics and biosimilars have the same quality, safety and efficacy profiles as the innovative medicines.	Proposed change (addition in bold and italics): "In the next five years, the network will continue to ensure that the regulatory framework supports the

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			development of a broad range of generic and biosimilar medicines, ***with the same quality, safety and efficacy profile as the original medicines***."
33	331	Comment: with the academic community	Proposed change (if any): with the academic community and expert patient community
33	582	Comment: is an effective communication approach.	Proposed change: should be an effective and collaborative communication approach
34	General	Thank you for offering the opportunity to comment on the EMA Strategy 2020. After consulting the IPFA members organisations I am pleased to inform you that we have no comments to add.	
35	241-242	Although we fully appreciate the need to get lifesaving medicines to patients as quickly as possible we find that this chapter insufficiently reflects the fact that a substantial amount of medicines entering our markets has little to no added therapeutic value (1). It is in the interest of the European citizen that added therapeutic value is assessed before granting a marketing authorisation. This issue should be prioritised at EU level and added therapeutic value should be mainstreamed in policies of the European Medicines Agencies. It would benefit the European citizen more than recent approaches such as "adaptive pathways", which will weaken evaluation requirements. Contrary to conditional marketing authorisations (MA) or compassionate uses, it will not be restricted to situations where there is an unmet medical need, but rather used to speed up the marketing authorisation procedure for all new medicines even if they do not meet a public health need. Moreover, evidence on added therapeutic value would help national	

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		reimbursement agencies in their decision-making. Linking the reimbursement of a drug to its added therapeutic value makes it less profitable to develop "me-toos", and the pharmaceutical industry will thereby be stimulated to invest more in medicines that address public health needs. The European Parliament, the European Commission and the Council of Ministers acknowledges the importance of added therapeutic value in new medicines both for the benefit of public health and to stimulate the development of truly innovative medicines and a competitive European pharmaceutical market. (2)(3) (1) http://data.consilium.europa.eu/doc/document/ST-15838-2014-INIT/en/pdf (2) http://data.consilium.europa.eu/doc/document/ST-15838-2014-INIT/en/pdf (3) http://www.europarl.europa.eu/thinktank/en/ document.html?reference=IPOL_STU(2015)542219	
35	645-647	Although the consultation draft highlights the growth of clinical trial activity in countries outside the EU and mentions ethical concerns, no specific reference is made to the ambitions that have been set out by the EU medicines agencies Reflection Paper. (4) (4) http://www.ema.europa.eu/docs/en_GB/document _library/Regulatory_and_procedural_guideline/2012/ 04/WC500125437.pdf	
35	672-673	We suggest to add a reference to the protection of clinical trial subjects outside the EU.	
36	General	In the Network Strategy document I note a number of areas where you may wish to consider how the EMCCDA and its network of National Focal Points could help strengthen the data available to your network. In particular, I am thinking your work to strengthen the pharmacovigilance capability across the network (line 348). The European Union Early Warning System on New Psychoactive Substances setup by the Council Decision, and of which the EMA is a partner, is uniquely placed to identify signals of misuse and	

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		abuse of psychoactive medicinal products. Recently this has included potential signals on pregabalin, quetiapine, and bupropion. In turn, at the request of the EMA, the EMCCDA and its partners collected information on the abuse, misuse, and dependency linked to the use of these medicines for use by the EMA's Pharmacovigilance Risk Assessment Committee. Similarly, in respect to your objective to focus on key public health priorities such as the availability of medicines (line 186,211,187) and how supply issues can be caused by falsified medicines (lines 225-226), which is compounded by a globalised supply chain (lines 689-690), you may wish to explore the utility of the data we collect through the Early Warning System in order to achieve better this objective.	
36	637-639	Given this close, excellent, cooperation may I suggest that you consider including the EMCDDA in the list of decentralised Agencies that you wish to strengthen links with.	