25 March 2015
EMA/201512/2015

EU Medicines Agencies Network Strategy to 2020 - Working together to improve health

Submission of comments

Comments from:

Name of organisation or individual
Health Action International
International Society of Drug Bulletins
Medicines in Europe Forum

Please note that these comments and the identity of the sender will be published unless a specific justified objection is received. In your reply please indicate whether you are replying as a citizen, organisation or public authority.

Comments should be sent to the European Medicines Agency electronically and in Word format (not pdf).

Comments should be sent to EUnetworkstrategy@ema.europa.eu and must arrive by 30 June 2015.

General comments

General comment (if any)	Outcome (if applicable) *<to be completed by the EMA/HMA>*
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: • 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	

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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 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:*	

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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 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	

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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 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.	

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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. *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.	

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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 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.	

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Public access to medicines safety and efficacy data contributes to informed decisions on treatment. Clinical trial data is not commercially confidential 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).	

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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 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.	

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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 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	

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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 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.	

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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 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	

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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 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	

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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). 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).	

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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 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	

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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 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	

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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 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	

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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?*** 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.	

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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 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:*	

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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 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	

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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”(24). 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. 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	

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''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.	

Specific comments on text

Line No. of the first line(s) affected	Comment and rationale; proposed changes	Outcome (if applicable) *<to be completed by the EMA/HMA>*
Line 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	

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