BEUC POSITION ON THE EUROPEAN MEDICINES AGENCY ROAD MAP TO 2015

Contact: Ilaria Passarani – health@beuc.eu
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BEUC, the European Consumers' Organisation
80 rue d'Arlon, 1040 Bruxelles - +32 2 743 15 90 - www.beuc.eu
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Summary

BEUC welcomes the European Medicines Agency roadmap to 2015 and the fact that the Agency is now under the supervision of the European Commission's Directorate General for Health and Consumers.

To better address public health needs and optimize the safe use of medicines we encourage the EMA to:

- Proactively publish more information and documents, especially in relation to pharmacovigilance and clinical trials;
- Ensure that conditional marketing authorisation remain the exception and not the rule;
- Take immediate action in case of non compliance with the terms of the marketing authorisation;
- Continue the efforts of providing high quality information to the public;
- Optimize the interaction with stakeholders taking into account possible conflicts of interest;
- Explore with the Institutions alternative funding mechanisms;
- Consider the possible conflict of interests in providing systematic scientific advice;
- Develop specific methodologies for the assessment of nanomedicines;
- Provide HTA bodies all relevant information while remaining fully neutral;
- Foster the collaboration with the European Food Safety Authority for borderline products;
- Include in the Road Map a reference to homeopathic medicines.

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1. Preliminary remarks

BEUC, the European Consumers' Organization, welcomes the European Medicines Agency (EMA) roadmap to 2015 and its strategic objectives especially in the context of the new structure of the Commission and the fact that the Agency is now within the portfolio of the Commissioner for Health, and no longer a competence of the Commissioner for Enterprise and Industry. We are confident that this change will contribute to better ensure coherence and consistency in the formulation and in the implementation of EU policies affecting pharmaceuticals.

2. Transparency

BEUC strongly welcomes the EMA initiative to develop a comprehensive transparency policy. Transparency is an essential element in building consumers' trust and confidence in the Agency and ultimately in medicines. The EMA scientific opinions have a big impact on public health and on patients' safety. The opinion making process should be fully transparent and ensure accountability. In this respect, we welcome all the EMA initiatives aimed at better explaining the regulatory procedures, as well as the formulation of the scientific opinions.

In particular, we consider very positively the EMA intention to proactively publish more documents and information, including the agendas and minutes of EMA scientific committees[1]. On this last aspect we believe it is possible and desirable to go even further by publishing the decisions taken, details of votes and explanations of votes, including minority opinions, as already foreseen by article 126b of Directive 2004/27/EC on the transparency obligations of authorities. The minutes should be written in a way that it is understandable also by those who didn't attend the meeting.

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.

We also believe that the Periodic Safety Update Reports (PSURs), and at least the EMA assessment of PSURs, should be published. It is not the case at the moment and we hope this will change once the new EU legislation on pharmacovigilance will enter into force. Finally, we encourage the EMA to ensure the register of ongoing and completed clinical trials is made available, as it is done by the US Food and Drug Administration (FDA).

3. Benefit/risk assessment

BEUC strongly believes the conditional marketing authorisation should remain the exception and should not become the rule. In the provisions currently in force (Regulation 507/2006), a centralised conditional marketing authorisation may be granted only if the risk/benefit balance is positive: the benefit to public health outweighs the risks inherent to the fact that additional data are required and that unmet medical needs will be fulfilled. We ask for these criteria not to be changed or interpreted in a "flexible manner".

1 The EMEA Transparency policy, September 2009.

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With regard to post authorisation commitments, the experience[2] shows that in many cases where companies were required to conduct post-authorisation safety studies, they failed to do so. A report[3] of the United States Government Accountability Office (GAO) published in September 2009 revealed that "from 1992 through November, 2008, the Food and Drug Administration (FDA) asked pharmaceutical companies to complete 144 studies associated with 90 drug applications, and that companies had completed just two-thirds of the requested studies. 15 of the 52 uncompleted studies have been pending for more than five years, and several have been pending for more than eight years". The FDA has authority to speed a medicine's removal from the market if the sponsor fails to complete a required confirmatory study with due diligence or if such a study fails to confirm the medicine's benefit. But, the GAO report outlines that the agency has never exercised this authority, "even when such study requirements have gone unfulfilled for nearly 13 years," nor has it ever specified the conditions which would prompt it to take such action.
The report also adds that "weaknesses in FDA's monitoring and enforcement process hamper its ability to effectively oversee post marketing studies".
The result is that doctors and patients remain unsure whether some critical medicines used to treat illnesses like cancer and heart disease are actually beneficial. The experience of the US highlights that it is of upmost importance, not only to introduce stricter requirements for the conditional marketing authorisation, but also to provide the EMA and the national medicine agencies with the powers and the appropriate tools to enforce the legislation.
The risk is to expose a large group of the population to unnecessary and avoidable risks especially if the medicine in question doesn't address unmet clinical needs and a safer alternative is already available. Evidence[4] shows that the already increasingly premature licensing of medicines, at the expense of proper evaluation, leads to more pharmacovigilance issues further down the line.

4. Authoritative source of information

We fully support the statement of the Road Map paper indicating that the EMA "should strive to become the authoritative source of information on medicines". BEUC doesn't support the current Commission proposal to relax the existing rules with regard to information that pharmaceutical companies can provide directly to consumers as we believe it falls short in making a clear distinction between information and advertising and it will give companies the possibility to choose on which disease and on which medicines to provide the information and to what extent. In addition we believe it opens the door to disease mongering giving rise to detrimental consequences, including a push towards high margin and life style medicines, an increase on health care costs, a bias against non-drug therapies and a pressure on the doctor/patient relationship.
Therefore, we asked the Commission and the Member States to develop a more comprehensive information strategy that truly responds to consumers' information needs and that fosters and promotes the existing sources of information starting with the valuable high quality information provided by the European Medicines Agency.

2 Lexchin J "Notice of compliance with conditions: a policy limbo" Healthcare policy 2007; 2 (4) :114-122.

3 FDA Needs to Enhance Its Oversight of Drugs Approved on the Basis of Surrogate Endpoints, United States government Accountability Office, September 2009. The full report is available at http://www.gao.gov/new.items/d09866.pdf

4 Carpentier D et al. "Drug review deadlines and safety problems" N Engl J Med 2008; 358:1354-1361.

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The Agency invested a lot in the provision of information to the public and made many efforts to make this information more understandable (e.g. Quality review of document (QRD), involvement of the patients and consumers working party (PCWP) in the readability test of package leaflets and European Public assessment report (EPAR) summaries) and more accessible (e.g. new web site). This information already exists and should be fully exploited.

5. Interaction with the stakeholders

BEUC values highly the cooperation with the European Medicine Agency and looks forward to continue working closely with the Agency, thus bringing the perspective of the medicines' end users. BEUC has been member of the EMA patients and consumers working group since its establishment in 2003 and we consider it as a good example of stakeholders' involvement in the activities of a public authority.

By including stakeholders in the various working groups, the EMA proves to be inclusive and responsive to societal needs and expectations. In this respect, it is vital to maintain a clear distinction between stakeholders and the scientific experts from the national authorities not only in terms of the interest they represent (the first ones partial interests, the second one general interest), but also in terms of the expertise they can provide.

When involving stakeholders, it is also essential to take into account that the people attending the meetings are not there in their individual capacity and that they represent an organisation. In other words they should be considered not only as "a consumer" "a patient" or as "a health care professional" but also as "lobbyists". They are there to bring the perspective of their members (provided that those involved in the EMA activities are EU umbrella organizations) and to advocate in the interest of the organization they represent.

And for consistency with the EU transparency policy we think that all those interests groups involved in the EMA work should be encouraged to register in the EU lobby register.

All those involved in the EMA activities fill in a declaration of conflict of interest which is available on the web site or upon request. To increase transparency but also consistency with the forms for declaration of conflict of interests used by other EU agencies (e.g. ECHA, EFSA etc) we suggest a revision of the existing form[5] by clarifying that not only those who are "employed" by an organisation but also those who work as volunteer or cover any other role in an organisation should disclose if the organisation receive funding from pharmaceutical companies (page3 of the form). In addition, to ensure consistency with the form for declaration of conflict of interests used by other EU agencies (e.g. ECHA, EFSA etc), we suggest adding two additional activities, namely "research funding" and "interest of close family members".

This is particularly relevant also with regard to the increasing contribution by academia and learned societies to the EMA work, given that university often receive funding by private companies.

5 http://www.emea.europa.eu/pdfs/general/direct/conflicts/Annex2-DeclarationofInterest.pdf

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6. Independency

The EMA is an independent and authoritative agency of the European Union. The contribution of pharmaceutical companies to its budget – which amounts today to more than 80% of the overall budget, and progressively increased since the Agency was established in 1995 - is disproportionate considering the EMA mission to address public health needs. Therefore we encourage the EU institutions to explore alternative funding mechanisms for the Agency also taking into account that its counterpart in the US, the Food and Drug Administration – relies on industry fees for less than 25% of its budget.

The Road map suggests an early dialogue between the agency and the companies – including an earlier appointment of the rapporteur for the approval dossier – in order to facilitate the review process. This would certainly help companies in the development of the medicines and possibly increase efficiency, but the systematic involvement of the EMA all along the drug development could influence the final assessment of the product and open the door to possible conflicts of interest.

7. New and emerging science

New and emerging technologies raise high expectations with regard to their potential in diagnostics, drug development and delivery (ex. personalised treatments), preventive methods and other health-related applications (ex. regenerative medicine). However a wide range of legal and ethical regulatory challenges need to be addressed, including the distinction between therapeutic and non-therapeutic use. There is therefore an urgent need to adapt the legal/regulatory framework but also to develop *ad hoc* methodology for the safety assessment of such technologies.

More specifically, on nanotechnologies, a major problem is the lack of a clear definition of nanomedicine and the consequent uncertainty as to which regulatory provisions are applicable, also in term of consent, confidentiality and data protection. For example, given that nanomedicinal products may combine different mechanisms of action (pharmacological, mechanical, chemical etc) the distinction between medical product and medical devices may be blurred[6]. We believe that in those complex cases the product should be regulated as a medicinal product to guarantee the highest level of safety for the patient (this principle is applied also in the Advanced Therapy Regulation[7]).

It is also important to make a distinction between risks for the patients undergoing an application of nanomedicine (for example risk of toxic effects in a person involved in clinical trials because of possible accumulation of cross-effect in tissues and organs) and health related risks associated with the toxicological effects of nano-pollution.

Medicinal products containing nanoparticles have already been authorised both in the EU and in the US under the existing legal framework and standard processes have been used to assess their risk for the patient.

General health related risk of nanoparticles have already been examined by several competent authorities including the Scientific Committee on Emerging and Newly

6 Opinion on the ethical aspects of nanomedicines, n.21, January 2007.

7 Regulation of the European Parliament and of the council on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004.

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Identified Risks (SCENIHR) and the Scientific Committee on Consumer Products (SCCP) on behalf of the EU, as well as the UK's Royal Society and Council for Science and Technology. According to these bodies, there is not only an alarming lack of data regarding the safety of nanomaterials, but also - and perhaps more importantly – the current risk assessment methodologies used for nanomaterials are inappropriate and need to be revised. Despite the above concerns of these leading scientific bodies, insufficient measures have been taken thus far regarding the management of the risks related to the use of nanomaterials.
Prospective technology studies should also be performed: scenarios need to be elaborated about possible adverse events related to the use of nanotechnologies in medicine and responses should be prepared to deal with these events.

8. Pharmacovigilance

We are confident that the ongoing revision of the EU pharmacovigilance legislation will provide the Agency with more powers and more tools to better ensure patient safety, in particular with the creation of a stronger pharmacovigilance committee.
We also welcome that, in the context of the EMA transparency policy and with the forthcoming legislative framework, the EMA will proactively publish more pharmacovigilance information.

9. Health technolocy assessment (HTA)

HTA is a useful tool for decision makers in order to better ensure that consumers benefit from high quality, safe and efficient health care. HTA processes should be transparent and sensible. While it is vital that the EMA provides HTA bodies with all the relevant information and data to corroborate their decisions, HTA bodies should not be bound by the EMA decisions. This ensures a second level of scrutiny to safeguard public health and also contributes to an open and constructive dialogue between equivalent scientific bodies. The road map refers to the use of HTA for the access to market of novel medicines while we believe it should be used also to remove the 'old' inefficient ones.

10. Herbal and homeopathic medicines

The existing legislation on herbal medicines offers important benefits to consumers – including pre-marketing check of product quality and safety, necessary warning against incorrect or unsafe use, post-marketing surveillance - but indeed it is not fully exploited and is still not equally applied in all Member States.
In addition, the fact that it remains possible to market the same herb both as a medicine and as a food supplement creates confusion. In this respect, particularly for borderline products, we encourage the EMA to foster the collaboration with the European Food Safety Authority (EFSA).

We recommend including in the Road Map a reference to homeopathic medicines. According to European legislation, homeopathic medicines commercialised with therapeutic indications must obtain marketing authorisation but the different rules applied at national level create confusion for consumers. In this respect we believe that the process of harmonisation should be strengthened and that more experience with the registration procedures should be gained with more focus on the evidence regarding the safety and most of all the efficacy of these products.

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