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From: [redacted]
Sent: 15 December 2018 10:01
To: EO-PresubmissionConsultation
Subject: Comments Ombudsman Inquiry on EMA pre-submission activities
Attachments: Ombudsman_Response to Public consultation_LBI HTA_2018_final.pdf

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Hello !
I send you my/our answers to the „Inquiry on EMA pre-submission activities".
Best
Claudia Wild

Priv. Doz. Dr. phil Claudia Wild
Director
Ludwig Boltzmann Institute for Health Technology Assessment

Garnisongasse 7/20, 1090 Vienna
Tel: +43 (0) 1 236[redacted]
Web: http://hta.lbg.ac.at

How the European Medicines Agency engages with medicine producers before they apply for authorisations to market their medicines in the EU - Invitation to comment within the European Ombudsman's inquiry OI/7/2017/KR

Intention of pre-submission activities: "Scientific advice (SA)" – provided by the European Medicines Agency - has been introduced is to give advice to a developer on the appropriate tests and studies in the development of a medicine in order to facilitate the development and availability of high-quality, effective and acceptably safe medicines, for the benefit of patients. SA helps to ensure that no major objections regarding the design of the tests are likely to be raised during evaluation of the marketing-authorization (MA) application. Following EMA's advice increases the probability of a positive outcome.

Process of pre-submission activities: EMA gives SA by answering questions posed by medicine developers. The advice is given in the light of the current scientific knowledge, based on the documentation provided by the medicine developer. SA focuses on development strategies rather than pre-evaluation of data to support a MA application. SA is not legally binding neither for EMA nor the medicine developer.

https://www.ema.europa.eu/en/human-regulatory/research-development/scientific-advice-protocol-assistance

Answers to the questions raised by the European Ombudsman:

1.) It may happen that EMA staff members and experts who participate in pre-submission activities will be involved in the subsequent scientific evaluation and/or marketing authorisation procedure for the same medicine. To what extent is this a matter of concern, if at all? Are there specific pre-submission activities of particular concern in this regard? How should EMA manage such situations?

Answer: EMA is a public body, but financed to 90% by private sources:

"For 2018, the total budget of the European Medicines Agency (EMA) amounts to €337.8 million. Around 90% of the Agency's budget derives from fees and charges, 7% from the European Union (EU) contribution for public-health issues and 3% from other sources.

Of the total budget in 2018:

- approximately €304.5 million will come from fees and charges levied for regulatory services;
- approximately €22.4 million is expected in income from the EU, mainly to support the policies for orphan and pediatric medicines, advanced therapies and micro, small and medium-sized enterprises".

https://www.ema.europa.eu/en/about-us/how-we-work/governance-documents/funding

For Scientific Advice for Human Medicines the Fees are from € 43,000 to € 86,100.

https://www.ema.europa.eu/en/human-regulatory/overview/fees-payable-european-medicines-agency

Payments from industry are perceived in light of severe Conflict of Interests (CoI) and are perceived – ever more often – as a major issue in healthcare, most often discussed as influence on health care providers (clinicians, physicians), less often publicly discussed on influence on regulator by the medicine developers.

Since 90% of EMA´s income is derived by pharma industry´s fees, of which fees for SA is part, serious risks for conflicts of interests exist. The fact that a public agency is financed by industry is perceived by some as "severe system failure". This "system failure" can only be handled with maximal transparency.

To manage such CoI it is important to clearly name both EMA staff (which would be persons employed by EMA) and experts (which could be medical experts but also assessors from the national regulatory agencies which actually provide both the SA and the assessment for MA). To manage the CoI all information on SA between regulator (scientific advisor) and medicine developer should be publicly available:

- SA given for which medicine, fees paid, regulator-experts involved
- MA provided for which medicine, fees paid, regulator-experts involved

2.) Should EMA allow experts from national authorities, who have previously provided scientific advice at national level on a particular medicine, to be involved in EMA's scientific evaluation of the same medicine?

Answer (See above): NO !

3.) What precautionary measures should EMA take to ensure that information and views provided by its staff members and experts in the context of pre-submission activities are not, in practice, considered as a "binding" pre-evaluation of data used to support a subsequent application for authorization?

Answer: All SA should be open to the public: Most of the content of SAs is dealing with general topics such as patient groups, comparator, relevant outcomes, study designs that can easily be shared and ev. lead to a reduction of the workload (but also income) derived by SA. With public SA the public ("public citizen", consumer advocacy, etc.) can track the process and results of SA and of MA.

4.) Is the way in which EMA engages with medicine developers in pre-submission activities sufficiently transparent?
If you believe that greater transparency in pre-submission activities is necessary, how might greater transparency affect: i. EMA's operations (for example the efficiency of its procedures, or its ability to engage with medicine developers) and ii. medicine developers?

Answer: NO, there is no transparency under the explanation of "confidential information". See answer above: BUT there is little "confidential information" in SA, but more general exchange on specific patient groups, comparator, relevant outcomes, study designs that could be of value for more than one drug developer.

Greater transparency would affect EMA´s operations by i. increasing efficiency (see answer to 6.), ii. by proving that there is little "confidential information" in SA and iii. by leading to greater credibility of EMA´s operations.

5.) Is there a need, in particular, to enhance the transparency of scientific advice EMA provides to medicine developers? Would it, in your opinion, be useful or harmful, for example, if EMA:
- disclosed the names of the officials and experts involved in the procedures;

- disclosed the questions posed in scientific advice procedures; and/or
- made public comprehensive information on the advice given.
If you have other suggestions, for example regarding the timing of the publishing of information on scientific advice, please give details and the reasons for your suggestions.

Answer: NO, it is of utmost necessity to disclose

- names of the officials and experts involved in the procedures
- the questions posed in scientific advice procedures
- comprehensive information on the advice given
- AND: to open the SA to (registered NGOs) public citizens/ civil society

6.) What would the advantages and disadvantages be of making scientific advice, given to one medicine developer, available to all medicine developers?

Answer: Two advantages can be foreseen

- One advantage of public SA would be that the suggested changes in the development programme by one original applicant for the SA will eventually lead to changes by other medicine developers and thus enhance the overall quality of drug development.
- Additional, the reduction of the workload for all involved would be a major advantage.

7.) Should EMA be limited to providing scientific advice only on questions not already addressed in its clinical efficacy and safety guidelines[4]?

Answer: YES

8.) Any other suggestions on how EMA can improve its pre-submission activities? If so, please be as specific as possible.

Answer: All answers provided above are also valid for "Early Dialogues (ED)" between HTA-agencies and medicine developer and for "joint SA & ED": full transparency and publicity is needed.

Priv. Doz. Dr. phil. Claudia Wild, Director
Ludwig Boltzmann Institute for Health Technology Assessment (LBI-HTA)
Garnisongasse 7/20, 1090 Vienna
Tel: +43 (0) 1 236[redacted]
Web: http://hta.lbg.ac.at