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From: [redacted]
Sent: 21 January 2019 12:20
To: EO-PresubmissionConsultation
Subject: Comments Ombudsman Inquiry on EMA pre-submission activities
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Follow Up Flag: Follow up
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Dear madam or sir,

please find enclosed the comments from the German Pharmaceutical Industry Association regarding the Ombudsman inquiry on presubmission activities.

Kind regards

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Comments

To: European Ombudsman

From: Ginnow, Britta

CC: Kevin Rieger, BPI Brussles

Subject: Public Consultation

Date: 15.01.2019

Public Consultation: How 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

BPI thanks to have the opportunity to comment on the public consultation. We want to answer the eight questions as follows.

In general, pre-submission meetings between industry and the regulatory authorities are very valuable and are performed in an established, well-defined process where the necessary safeguards take place. The concept of pre-submission meetings is performed in every regulatory authority world-wide. The regulatory authorities have established rules for the pre-submission meetings and industry follows these rules. Any risks of bias or imbalance that could be assumed is managed accordingly by strict rules (e.g. policy for conflict of interests, briefing books).

It is a goal that clinical studies for the development of new and safe medicines are properly designed. Therefore, the concept of clinical studies is discussed in a pre-submission meeting in order to get the needed evidence for the marketing authorisation of a new product and to avoid useless studies where recruited patients won't get any benefit. The interaction between developers of medicinal products, which are often SMEs or academia and regulatory staff is of valuable importance to get an understanding of regulatory needs and to get an overview on the issues and topics regarding the risks and benefits of the product. Patient access to new medicines will be faster in the end.

For companies involved in developing innovative medicines, pre-submission guidance including scientific advice from a regulatory agency is an important part of development new medicines in order to ensure that medicinal products are developed in a way to meet the health authority requirements and to ensure the market access to effective, safe and high-quality medicines to patients.

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 authorization 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?**

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From BPI`s point of view, there is no concern at all. There are appropriate safeguards at EMA as well as for national Agencies in place which include a policy of conflict of interests and there are strict guidances on how to perform pre-submission meetings.

Furthermore there is a separation between the scientific advice meeting and the assessment of the data included in the dossier for a marketing authorisation. No single assessor is solely involved in the decision-making process for an authorization of a medicinal product proceeding form pre-submission activities. The final decision for a marketing authorization is taken by a Committee (CHMP) which include more members (approx. 30) as members were involved during a pre-submission meeting. The assessment is also supported by a wide range of external experts.

The assessment of a product in the centralized procedure (CP) is done by a Rapporteur and a Co-Rapporteur, but the CHMP Opinion is subject to a process including experts from all Member States. They have the possibility to assess the documentation and to express their statements. From our point of view, the process is very balanced and protects against any conflict of interests

From our point of view, there is no concern and EMA as well as other national authorities manage these procedures very well.

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 on the same medicine?**

   Yes, every assessor of a national authority is subject to a strict policy regarding conflict of interests and safeguards measures are established everywhere. It can be of an advantage if an expert has already scientific experience with a drug or has evaluated it already. The knowledge gained in the national area can be placed in EMA`s scientific evaluation and can be discussed. Using the same expertise in both stages leads to efficiencies and this should be promoted.

   Expertise from national authorities is very valuable as national authorities are specialized in particular therapeutic indications. So the German BfArM is an expert on neurological diseases and the Paul Ehrlich-Institute (PEI) has a well renowned expertise regarding biopharmaceuticalsThe assessors work very often as Rapporteurs/Co-Rapporteurs in a centralised procedure (CP).

   The development programs for new medicinal products become more complex as there are new innovative concepts on medical therapies. It becomes very challenging to find experts with the specialized knowledge, so experts from national Agencies should be appreciated.

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 authorisation?**

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The guidance provided by EMA ensure sufficiently that pre-submission activities are not regarded as a "binding" pre-evaluation of the proceeding application for a marketing authorization. The introduction on the Scientific Advice Chapter of the EMA webpage clearly mentions that scientific advice received from the Agency is not legally binding on the Agency or on the medicine developer with regard to any future marketing-authorization applications for the medicine concerned.

Furthermore it is stated that Medicine developers can request scientific advice from the EMA at any stage of development of a medicine, whether the medicine is eligible for the centralized authorization procedure or not. This shows that a scientific advice is a separate procedure not linked with the evaluation.

The Mandate, objectives and rules of procedures of the Scientific Advice Working Party (SAWP) emphasize that that the SAWP shall not be responsible for the pre-assessment of data that will be used to support future marketing authorization applications (see point 31).

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. EMAs operations (for example the efficiency of its procedures, or its ability to engage with medicine developers) and ii. Medicine developers?**

BPI is of the opinion that pre-submission activities are sufficient transparent. All pre-submission activities are supported by detailed guidance.

Transparency of EMA pre-submission activities must always be appropriate and in accordance to Regulation 1049/2001 the Agency must not disclose information where a disclosure would undermine the protection of commercial interests of a natural or legal person, including intellectual property (Article 4 No. 2). Pre-submission activities generally take place at an early stage of development and a disclosure of information would certainly undermine the intellectual property rights and commercial interest of the company. To injure that requirement would lead to the fact that companies would avoid a pre-submission meeting, like scientific advice in Europe, making the way for new medicinal products to patients unnecessarily longer

Kommentiert [SP1]: ???
To ignore the importance of respecting IP rights

When a company has sought for a scientific advice and the marketing authorisation was granted, the information on discussed issues during a scientific advice meeting can be found in EPAR.

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 advice given**

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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 you suggestions

According to BPI`s opinion, there is no need to enhance the transparency of scientific advice EMA provides to medicine developers. Results of the scientific advice discussions are already disclosed after the medicinal product has received the marketing authorization. They can be found in the respective EPAR. This is sufficient and appropriate.

Disclosing the names of the officials and experts involved in the single pre-submission activities would not be useful. There are already information on experts available on the EMA webpage like names, CV and the written declarations regarding conflict of interests of the CHMP members. There is already a high level of transparency and no need to establish a different approach for pre-submission activities. We are of the opinion that the existing approach of including experts in the pre-submission stage to provide scientific advice, and then conducting the assessment at a committee level, where the names, details and curriculum vitae of all committee members are available is appropriate.

Disclosing the questions posed in scientific advice procedures; and/or making public comprehensive information on advice given could jeopardise the aim of supplying European patients fast with needed medicinal products. Disclosing the questions posed could undermine the IP protection rights as these questions directly refer to the development plan for the medicinal product for which a marketing authorisation should be subsequently applied for. If these questions are disclosed prior granting the marketing authorisation, companies would avoid to seek/ask for scientific advice in Europe. This would, again, make the way for new medicinal products to patients unnecessarily longer.

Making the scientific advice outcomes publically available would offer all kind of information to other pharmaceutical companies for the development of generics/biosimilars.

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

BPI is strongly against pursuing this approach of making scientific advice available to all medicine developers for it leads directly to a decreased supply of therapy innovations for patients:

This approach undermines the commercial interests and intellectual property protection rights,

Furthermore, a pre-submission meeting like scientific advice refers to a specific medicinal product respectively to an active ingredient and to a specific therapeutic indication under development. Therefore the consultation for which a company seeks scientific advice has specific and target-oriented questions regarding the particular level of development. There is no advantage for other medicinal developers to have

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these information, because it rarely can be used for other development projects. Above that, a briefing book prepared for a scientific advice meeting contains confidential information on the medicinal product under development. To disclose these information, would have the effect that companies would stop seeking advice in Europe and would move to other areas where this information is confidentially kept. Research and development of new products in Europe would invariably fall behind other areas protecting these sensitive information.

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

   The EMA guidance on Scientific Advice states under point 3: “Scientific advice may be given on issues relating to interpretation and implementation of EU (draft) guidelines”. Guidance documents are a result of a concerted scientific view of EU experts of the working parties and represent the “state of the art”-knowledge on specific scientific topics to a specific point of time. Due to the reason that scientific progress moves on very fast and new developed medicinal products are very complex, there might be a need to interpretation of the guideline regarding the specific product or follow a justified approach divergent from current guidelines which should be discussed during a scientific advice meeting. Guidelines are “living documents” and during scientific discussions gaps in the guidelines may be identified. Guidelines may include new or revised requirements which are the results of scientific discussions between medicinal developers and regulatory staff. The “state of the art”-knowledge is enhanced on the scientific progress and from our point of view, both sides, regulators and medicinal developer benefit from the scientific discussion on issues relating to interpretation and implementation of EU (draft) guidelines.

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

   The system of pre-submission activities and the safeguard rules are appropriate