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From: [redacted]
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To: EO-PresubmissionConsultation
Subject: Comments Ombudsman Inquiry on EMA pre-submission activities
Attachments: EuropaBio response to EU Ombudsman inquiry on EMA pre-submission activities.pdf

Follow Up Flag: ema17
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Dear Madam/Sir,
Please find attached the response of EuropaBio, the European Association for Bioindustries, to the public consultation regarding the Ombudsman Inquiry on EMA pre-submission activities.
I remain at your disposal in case of any questions.
Best regards,
Violeta

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Strategic inquiry into pre-submission activities organised by the European Medicines Agency (OI/7/2017/KR)

Response by EuropaBio

EuropaBio represents 77 corporate/associate members and bioregions, as well as 15 national biotechnology associations, in total representing over 1800 biotech SMEs. Together, we represent an innovative and dynamic European biotechnology industry which is committed to the socially responsible use of biotech to improve quality of life, to prevent, diagnose, treat and cure diseases.

The development of life-enhancing and life-saving medicines is a complex endeavour which involves both regulators and innovative businesses and relies on a strong, efficient and responsible interaction process between both parties. For a medicine to reach the patient in the best conditions, a sophisticated regulatory path where the responsible health authority and the medicine developer interact with each other on a continuous basis is required. These interactions are not only intended to inform or strengthen the regulators' understanding and scrutiny of the development of a new medicine, but they also contribute to shaping new regulatory standards in fields where science is moving fast and where the EU needs to play a key role to remain competitive on the world stage. For example, in the area of advanced therapy medicinal products (ATMPs), new manufacturing and trial models have contributed to closer collaboration and collective learning in the early phase. Therefore, pre-submission and pre-authorisation exchanges, including scientific advices, are indispensable for timely and efficient medicine development.

The pre-submission activities organised by the European Medicines Agency (EMA) benefit both the EMA, the medicine developer and the patients. They help to ensure that the new medicine research programme, development plan and clinical studies are well designed to meet their purpose and safeguard study participants. This is also why the practice of pre-submission activities has become standard in the world.

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?

EuropaBio is of the opinion that this cannot be a matter of concern as long as the EMA continues to pursue the high standards we see today of transparency, firm policy against conflicts of interest and clear differentiation between scientific advice and evaluation process.

The scientific evaluation of new medicines is an inclusive and orderly process which involves rapporteurs and co-rapporteurs, the Committee for Medicinal Products for Human Use (CHMP) and all EU Member States. As such, it disperses both the responsibility and accountability of the people involved, so that no one single staff member or expert can have a final say.

EuropaBio strongly believes that if such a robust system is not trusted by the public, it is not the system that should be changed, but the public perception of its contribution. This is a shared responsibility of all actors involved in medicine development - medicine developers and regulators alike.

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?

As long as the responsibility and accountability for new medicines evaluation remain dispersed over the different actors mentioned above, EuropaBio not only finds no reasons for the exclusion of experts from national authorities, but also sees the potential of enhancing both the efficiency and the excellence of the evaluation process as some national experts have the specialised expertise in certain disease areas. With the increasing number of submissions in very specialised fields, it became difficult to find always experts with the right level of expertise. Therefore, approaches involving multi-national teams are worth considering in the future.

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?

EuropaBio would like to stress that none of our member companies take the view that their participation in the EMA pre-submission activities guarantees success for a subsequent application for authorisation. The Scientific Advice (SA) provided by the EMA staff members and experts is not legally binding for either side.

In this context, it is important to understand that the SA is optional, and it does not provide for pre-evaluation of data used to support a subsequent application for authorisation. SA generally considers early data (from non-clinical, Phase1/2 clinical studies) and helps to inform a CHMP view on the data package that they consider should be generated in future studies to enable a future benefit-risk assessment by the regulators.

Specifically, in areas of rapid technological development (such as gene-editing-based technologies) where EuropaBio member companies are very active, precedents are few and guidance does not exist. Therefore, the EMA process for providing SA is invaluable to ensure that the right experiments are done and to decrease waste due to unnecessary pre-clinical or clinical testing.

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?

EuropaBio is firmly convinced that the way in which EMA engages with medicine developers in pre-submission activities is sufficiently transparent. It also ensures the protection of legitimate private and public interests. The EMA Guidance on pre-submission activities, which is available online, navigates these interactions. Further transparency is secured by the EMA policy on access to documents.

EuropaBio supports the current EMA policy to disclose the details from the SA interaction after the grant of the marketing authorisation of the medicine in question. When a developer has engaged with the EMA and once the authorisation process is complete for the product for which early advice was sought, the details of this early interaction can be disclosed.

Specific product-related information cannot be disclosed to undermine the protection of commercial interests and the developers' intellectual property. If this standard rule of law is weakened, medicine developers would turn to non-EU regulatory jurisdictions for SA.

It is EuropaBio's view that if a regime of transparency beyond the rules existing today that would potentially undermine competitiveness is implemented, the EU will miss out on taking the forefront in developing the currently most scientifically sophisticated cell and gene therapies, to the detriment of EU patients and the EU-based biotechnology industry.

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.

Regarding the suggestion to disclose the names of the officials and experts involved in the procedures, EuropaBio does not see how such a practice would lead to any use which benefits the access of patients to new medicines which is the ultimate goal of the system. More public exposure of the EMA staff and experts should not interfere with their independence and the effective fulfilment of their work responsibilities.

Regarding the suggestion to disclose the questions posed in SA procedures, EuropaBio evaluates that this can be done only after the grant of the marketing authorisation. Pre-marketing authorisation disclosure would amount to disclosing details about the medicine development plan which is confidential business information.

Regarding the suggestion to make public comprehensive information on the advice given, EuropaBio is convinced that, first, this would be difficult from a legal point of view as most of the information would be regarded as confidential business information, and second and if the aforementioned rule of law is discarded, this will lead medicine developers to seek SA outside the EU where sensitive product-related information is kept confidential. A lack of EU SA would have a detrimental effect on medicine developers' decisions on whether to conduct clinical studies in the EU and could impact when, and if, products are submitted in the EU for marketing authorisation.

Instead, as it is done already today, general learnings about scientific advances should be communicated in the regular publicly available guidance documents of the EMA and further discussed in scientific fora with the involvement of society at large, including patients' organisations.

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

EuropaBio reiterates that the SA cannot but involve information about the development plan which is seen as confidential business information and if such is disclosed, this will distort the fair competition climate in the EU, thus resulting in medicine developers seeking SA outside the EU and undermining the ecosystem for the EU-based biotechnology industry.

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

It is the understanding of EuropaBio that it is exactly questions addressed in the EMA's clinical efficacy and safety guidelines that form the most part of the SA provided by the EMA with a focus on the interpretation and application of these guidelines to the specific product being developed by the medicine developer. While the EMA guidance documents give direction to the medicine developer, the specifications of a

particular product and completeness of the data package which accompanies it can only be dealt with in a dedicated exchange on that very product and its dataset. The clinical efficacy and safety guidelines will never provide a sufficient scientific level of detail.

At the same time, questions which are not addressed in the existing EMA guidelines remain important to discuss in order to keep regulatory guidance up to the latest scientific advancements and innovative methodologies for e.g. trial design, statistics, measuring minimal residual disease, etc. This is ever more relevant for the area of ATMPs.

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

EuropaBio sees a direct correlation between the advance of science and the need to enhance regulatory processes, including regarding the EMA's pre-submission activities. For example, the speed at which promising ATMPs are being developed should be matched by more efficiencies in the EMA's pre-submission activities to avoid administrative delay in areas of unmet medical needs. This would require both broader (including e.g. from patients, Health Technology Assessment bodies and payers) and better-organised involvement of scientific expertise (not only between the different EMA scientific committees, but also between the EMA and the EU Member States' national authorities).

EuropaBio would also welcome the organisation of teleconferences as a new type of pre-submission activities as these would provide faster advice on the studies required during development. Faster advice would positively impact on the ability of medicines developers to deliver clinical trials in the EU and speed up time to availability of medicines in the EU.

EuropaBio also sees opportunities for both the EMA staff and experts and the medicine developers to prepare better for the face-to-face pre-submission interactions if e.g. a draft of the EMA considerations was communicated to the medicine developer before the actual meeting.