Overview of responses received from Interested Parties and EMEA Recommendations on the New Framework for Scientific Advice & Protocol Assistance

1. Background

A 2-month public consultation on the New Framework for Scientific Advice & Protocol Assistance was launched on 22 September 2005. The New Framework for Scientific Advice & Protocol Assistance sets out initiatives described into five broad Q&A.

There were 12 responses to the New Framework for Scientific Advice & Protocol Assistance. The type of responses varied, with some short general comments, some short contributions and some extensive responses.

The respondents were also varied. There were individual responses from pharmaceutical companies and from pharmaceutical industry associations.

Organisations which commented on the New Framework for Scientific Advice & Protocol Assistance are as follows:
1. EFPIA: European Federation of Pharmaceutical Industries and Associations
2. AESGP: Association of the European Self-Medication Industry
3. BIA: BioIndustry Association
4. EBE: Emerging Biopharmaceutical Enterprises
5. IPFA : International Plasma Fractionation Association (NL)
6. Proneuron Biotechnologies, Inc. (Israel)
7. Eli Lilly and Company Limited (UK)
8. GE Healthcare Limited (UK)
9. GlaxoSmithKline (UK)
10. Merck Sharp & Dohme (BE)
11. Pierre Fabre Médicament (FR)
12. UCB-Group (BE)

Main responses and EMEA answers are grouped according to the Q&A topics 1 to 5 outlined in the New Framework for Scientific Advice & Protocol Assistance (EMEA/267187/2005). Changes introduced to the New Framework for Scientific Advice & Protocol Assistance are highlighted for each Q&A topic.

All EMEA Scientific Advice & Protocol Assistance guidance documents and SOPs will be reviewed to include changes suggested by interested parties. SOPs will also be made directly available on the EMEA website.
### 2. Responses from Interested Parties and EMEA Answers on the New Framework for Scientific Advice & Protocol Assistance

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<th>Interested parties responses on:</th>
<th>EMEA answers</th>
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| Q&A 1: How does the new Regulation impact on the scope of scientific advice and protocol assistance? | All aspects on this proposal were welcomed in the contributions. There were mostly requests for clarification on other provisions that may be addressed through EMEA Scientific Advice.  

**Clarification on what is “specific types of medicinal products and therapies” and “Broad and more general advice”**  
- The scope of scientific advice is broadened to encompass new types of scientific advice requests. For instance a company’s request for scientific advice on “specific types of medicinal products and therapies” may not be product specific, may refer to a class of medicinal products, the use of scales in a therapeutic indication or the use of new expression systems. A sponsor may also request at earlier timepoints of a development program advice on product or non-product specific scientific questions and/or include topics which may cover several indications (“Broad and more general advice”). For these new types of advice the EMEA strongly recommends to have scientific advice pre-submission meetings *(added in New SA Procedure).*  

**Clarification on the acceptability of SA relating to interpretation of applicable guidelines.**  
- Such requests will be accepted.  

**Clarification on the prospective nature of SA, differences with pre-evaluation of data to support a MAA application and advice on filing strategy:**  
- Scientific advice is prospective in nature. This should allow providing input on developments, which can be amended after SAWP/CHMP advice.  
- Scientific advice focuses on development strategies rather than pre-evaluation of data to support a MA application.  
- Scientific advice is different from feedback on ‘filing strategy’ for completed development programmes and assessment of maturity level of MAAs. This will be a matter for MAA-presubmission.  
- PharmacoVigilance and EU-Risk Management Plans may be the subject of SA requests. At any stage, but in particular during the pre-authorisation phase, a sponsor may request scientific advice on the need, development or content of an EU-RMS, in particular on the interpretation and implementation of the EU guideline on risk management systems for medicinal products for human use *(EMEA/CHMP/96268/2005).*  

**Clarifications requested on inclusion of additional types of SA that may be addressed by the EMEA/SAWP in view of revised legislation**  
- The applicants may request advice on whether a specific medicinal product being developed for a specific therapeutic indication falls within one of the categories set out in Article 2 and fulfils the condition laid down in Article 4(1)(c) of Commission Regulation (EC) No 507/2006 of 29 March 2006 on conditional marketing authorisation for medicinal products for human use defined in Regulation (EC) No 726/2004 *(added in New SA Procedure).*  
- The applicant may request advice about the justification for applying for a marketing authorisation under exceptional circumstances *(added in New Scientific Advice Procedure).* |
- The applicant may also request advice on acceptability of the development programme for future MAA under exceptional circumstances (Guideline on procedures for the granting of a marketing authorisation under exceptional circumstances, pursuant to article 14(8) of Regulation (EC) no 726/2004 EMEA/357981/2005). ‘Inability to provide comprehensive data’ should be discussed as early as possible during development. The applicant is encouraged to seek SA on the limitations imposed by the ‘rarity of the disease’, or ‘the impossibility to collect comprehensive information in the present state of scientific knowledge’ (added in New SA Procedure).

- An applicant may also request SA when designing trials to assess safety and efficacy in a new indication: 1) in accordance with Article 14(11) of Regulation (EC) No 726/2004 or Article 10(1) fourth subparagraph of Directive 2001/83/EC; and 2) for a well established substance in accordance with Article 10(5) of Directive 2001/83/EC as amended as by Directive 2004/27/EC (added in New SA Procedure).

- SA requests relating to paediatric developments questions are accepted for scientific advice (added in New Scientific Advice Procedure). However, the review of Paediatric Investigation Plans (PIP) will be exclusively within the remit of the Paediatric Committee, as defined in the current draft of the Regulation on medicinal products for paediatric use. During the review of the PIP by the Paediatric Committee, specific questions on paediatric development may be referred to the SAWP. Links between the Paediatric Committee and the SAWP will be established.

**Request on the need for fast advice on a single draft nonclinical and clinical protocol at certain time points of a development program (e.g. before launching a phase III study)**

- The 40-day procedure should accommodate the need for such advice in most cases. SA in this context cannot substitute for “clinical trial authorisation” which is within the responsibility of National Competent Authorities.

**Clarification requested on prioritisation of SA requests depending on the scope of advice**

- The SAWP will not prioritise the list of SA requests depending on the scope of the requests (amended wording in SA New SA Procedure).
The proposals were partly supported by respondents. There were mainly concerns on the planning phase, its benefits, and its impact on the overall timelines; clarifications on systematic or optional pre-submission meetings and on the “clarification phase”.

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<th>Clarifications on the planning phase, its organisational aspects, and pre-submission meetings</th>
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<td>- The pre-submission meetings remain optional. However, they are strongly recommended in particular for first-time users of the SA procedure, for Protocol assistance, for SMEs, for SA on “specific types of medicinal products and therapies”, and “broad and more general advice” (added in New SA Procedure). The presubmission meeting should be viewed as an opportunity for early interaction and dialogue with coordinators and experts, on scientific and procedural matters ahead of the collegial formal review by the SAWP.</td>
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<td>- The planning phase will allow early nomination of coordinators and identification of best expertise including patients’ representatives and individual academic experts for product specific type of requests. Expertise identified in the initial planning phase will be involved during the subsequent formal review by SAWP. The company will be informed of the names of coordinators and experts appointed.</td>
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<td>- For the planning phase, template letters will be included on the EMEA website, for applicants to send notifications and request a presubmission meeting more efficiently: the notification letter will include basic information needed to appoint coordinators (e.g. product, indication, scope of advice). The information needed ahead of the presubmission meeting will include a draft of the request, and may consist of a more limited package than the final documentation. Deadlines for submitting these documents will be published on the EMEA website.</td>
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<td>- If no presubmission meeting is taking place, the SA requests will be have to be submitted slightly earlier (amended in New SA Procedure).</td>
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<td>- The “list of issues” (renamed “List of Comments”) raised at the presubmission meeting by the EMEA will be reflected in the final request submitted by the company to EMEA for validation. The List of Comments will improve validation of SA requests, flag issues identified at the presubmission meeting to the SAWP.</td>
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<td>- The planning phase will also allow identification of requests for which expertise is particularly needed (added in New SA Procedure).</td>
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<td>- Regulatory aspects can also be addressed during the pre-submission meeting.</td>
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<th>Clarification on overall timings and duration of procedure of SA</th>
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<td>- The SA procedure is shortened from ~ 100 days to <del>70 days; the finalisation of advice immediately after discussion meetings (</del> 70 days) and the direct finalisation of some advice in 40 days will drastically decrease the timelines.</td>
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<th>Comments on the clarification phase and suggestion for expedited processing of clarifications</th>
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<td>- The sending of an “early draft” of the letter after adoption at the SAWP was a pilot phase in 2004-2005 (“clarification phase”). Experience showed that it is more valuable to consolidate the involvement of CHMP by formalising the peer review. This is expected to decrease the need for clarification and leave more time</td>
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to applicants to seek clarification at a later stage if at all needed. Finally, the removal of the clarification phase is considered as a positive measure by some respondents if a process for expedited review of clarifications is put in place. Therefore an expedited process will be implemented to provide clarifications immediately after the SAWP meeting.

**Clarification on the procedure for nomination of coordinators among SAWP**
- Appointed coordinators will continue to be nominated among SAWP members; nominations will be based on their preferences and availability, and equal opportunity among all SAWP members.
- For follow-up requests, to maintain consistency, one of the initial 2 coordinators nominated will normally be retained (*added* in New SA Procedure).

**Clarification on the involvement of WPs and SAGs**
- Links with WPs and SAGs will be established for the involvement of additional expertise.
Interested parties responses on “Q&A 3: How will the new framework increase transparency and communication with stakeholders?”

The proposals were supported by respondents. There were specific requests for more dialogue with coordinators and more transparency e.g. publication of SAWP membership, consultation of interested parties for Standard Q&A documents and preparation of workshops and think tank meetings.

Comments on Discussion Meetings (DM)
- The SAWP meetings are extended to 3 days; this will allow for increased dialogue through an increased number of discussion meetings with industry.
- In case of SAWP’s disagreement with the company’s development plans, the company will be invited to a discussion meeting (added in New SA Procedure).
- Preliminary oral conclusions will be outlined at the end of the discussion meetings, pending formal adoption of advice in the plenary SAWP/CHMP meetings (added in New SA Procedure).

Clarifications on organisational aspects of DM
- The Discussion meetings will take place during SAWP meetings to allow experts to attend (added in New Scientific Advice Procedure). This will also allow SAWP’s widest contribution to the discussion.

Clarifications on publication of SAWP membership
- The composition of SAWP will be made public on the EMEA website.

Clarifications on interaction with EMEA/coordinators
- Experience and industry feedback has shown that the EMEA product manager (PM) is the preferred contact person for the company for all scientific and procedural matters. To increase transparency, the EMEA should be involved or informed of any direct interaction that may happen between the company and the Co-ordinators.
- An alternate company contact point will be allowed for increased communication throughout the procedure. The new EMEA guidance will be amended accordingly.

Clarifications on the “Standard Q/A documents”; Request to prepare Standard Q&A documents in consultation with interested parties and concern about release of confidential information.
- “Standard Q/A documents” are complementary to guidelines and can be developed in shorter timeframes e.g. in areas where repeated SA has been provided. These will be released following appropriate consultation and will not include confidential information.

Requests for industry contribution to workshops and think tank meeting
- Planned workshops and think tank meetings will be included in the EMEA Annual Workprogramme and announced on EMEA website. Possible participation of industry will be specified. Learned societies will be consulted in workshops or think-tank meetings (amended in New SA Procedure).

Comments on procedures for involvement of patients’ representatives in SA and check of conflict of interests
- Existing procedures for checking conflicts of interest will be amended to take account of specificities. These will be made available on the EMEA website.

Comment on the need to release draft reports/letters
- Acknowledging the needs and constraints in releasing draft
reports/letters, the above-mentioned recommendations to increase transparency and communication will be developed to address the request for earlier access to information.

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<th>Q&amp;A 4: What will be the impact of the new definition of a follow-up scientific advice or protocol assistance request?</th>
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<td>This proposal has wide support. There were specific requests for shorter timeframes and need for continuity in nomination of coordinators of FU requests.</td>
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<td><strong>Request for a shorter timeframes for FU requests</strong></td>
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<td>- The 40-day procedure should accommodate the provision of such advice in most FU requests.</td>
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<tr>
<td><strong>Request on the procedure for nomination of coordinators for FU requests</strong></td>
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<tr>
<td>- For follow-up requests one of the initial 2 coordinators nominated will be proposed (added in New SA Procedure).</td>
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<th>Q&amp;A 5: How will the new Scientific Advice Working Party be organised in the new scientific advice and protocol assistance framework?</th>
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<td>The proposals were supported by respondents. In particular the Peer Review was considered a good approach. There were specific concerns on the impact of SA workload on consistency of advice, and requests to include the Parallel advice with the FDA provision in the new SA procedure.</td>
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<tr>
<td><strong>Request to include the Parallel advice with the FDA and clarifications requested on the procedure</strong></td>
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<tr>
<td>- The Parallel advice with the FDA is included in the new procedure. A new SOP will be developed to describe and streamline the practical steps in requesting Parallel advice with the FDA (added in New Scientific Advice Procedure).</td>
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<td><strong>Comment on the impact of workload on consistency of advice</strong></td>
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<td>- The extended SAWP membership, the introduction of tracking and of Peer Review systems will increase the consistency and quality of advice.</td>
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<td>- A SOP on Peer Review will be developed to describe the process for successive reviews throughout the procedure by SAWP members, EMEA scientific administrators (from several units and sectors) and CHMP/COMP members.</td>
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<td>- Questionnaires will be launched in collaboration with trade associations with a view to gain feedback and continuously improve scientific advice.</td>
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<td><strong>Comments on the lack of clarity of secretariat role</strong></td>
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<td>- The role of the secretariat will be clarified in the SOPs to be published on EMEA website</td>
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**Acronyms used**
- CHMP: Committee for Medicinal Products for Human Use
- COMP: Committee for Orphan Medicinal Products
- FDA: Food and Drug Administration
- FU: Follow-up
- MAA: Marketing authorisation application
- MB: Management Board
- PM: Product Manager
- SA: Scientific Advice
- SAG: Scientific Advisory Groups
- SME: Small and medium size enterprise
- SAWP; Scientific Advice Working Party
- SOP: Standard Operating Procedure