1. Introduction

The Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte, BfArM) offers applicants the opportunity to obtain scientific and procedural advice from the authority related to the development and licensing of medicinal products and medical devices which are in the remit of the Institute.

The following advice procedures are offered:

- **Advice during development** ("Scientific Advice")
- **Advice prior to application** ("Pre-submission Meeting")

Scientific Advice may be provided at any time before or after the initial authorisation of the medicinal product, and may cover questions related to the pharmaceutical quality (including biological and biotechnological aspects), the assessment of medical devices, the design and conduct of non-clinical investigations and clinical trials of medicinal products and medical devices (including biostatistics), as well as aspects related to pharmacovigilance and the risk management plan.

Pre-submission Meetings are focused on questions related to planning and conduct of a concrete, forthcoming marketing authorisation application (MAA); possible topics are the legal basis of the application, the dossier presentation (structure, content) and procedural aspects, as well as the draft labelling.

In addition to this, the Institute can be consulted with regard to questions and problems arising in the initial stages of an application for orphan drug status which are thus not yet in the remit of the respective scientific committee at the EMA.

Furthermore, the BfArM offers so called **Portfolio Meetings**; these meetings provide the opportunity for pharmaceutical companies to present an overview of different development projects to the BfArM.

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1 This version replaces the Guidance for Applicants dated January 24th, 2017.
In principle, advice service does not extend to advice decisions from completed procedures, applications, or ongoing legal proceedings.

2. Procedure for Scientific and Procedural Advice

Basis for the advice procedures by BfArM is laid out in Section 71c of the Administrative Procedure Act (VwVfG) in conjunction with Section 25 sentence 2 VwVfG. Further to be noted are the German Medicines Act (Arzneimittelgesetz, AMG), Act on Medical Devices (Medizinproduktegesetz, MPG), directly applicable EU legislation (e.g. regulations), the pharmacopoeia (DAB, HAB, Ph.Eur.), the guideline for the testing of drugs, notifications from the BfArM, the EU "Notice to Applicants", ICH/CHMP/EMA guidelines, “Points to Consider” documents etc. in their current version. Furthermore, drafts thereof which are in public consultation should be adequately considered, if they are relevant for the respective question.

The scope of the advice is the list of questions to be provided by the applicant in relation to the drug or medical device development program; the questions should be justified by the fact that they are either not covered by the mentioned legal texts, or that specific aspects of these legal texts require interpretation.

Advice through the BfArM needs to be applied for and is subject to fees; it may be provided at any time during product development before or after the initial authorisation. BfArM may provide advice either through direct dialogue or in writing.

In addition to the exact list of questions the applicant is requested to provide an up-to-date documentation tailored for the list of questions. When preparing the list of questions and the documentation it should be considered that it is not the BfArM's task to define the development programme for the applicant.

There will be no preliminary assessment of data in the light of a forthcoming MAA submission.
2.1 Application

The request for advice needs to be made in writing using the application form available on the BfArM website. The following application procedures are possible:

- **Standard procedure**
- **Procedure with supplemental submission**

The two application procedures differ with regard to the time of submission of the documentation. In case of the standard procedure the documentation needs to be submitted at the time of initial application together with the list of questions. In certain situations the applicant has the option to apply for a procedure with supplemental submission by providing a detailed list of questions but without the documentation. In this case a date for a meeting will be scheduled following validation of the application. The required documentation needs to be provided at least four weeks prior to the scheduled date. If the documentation will not be submitted in time or if it is considered to be inadequate for the advice procedure, the request for advice may be rejected. This rejection is subject to fees in accordance with the applicable fee ordinances.

The application should be provided as a hardcopy and in electronic form. An application consists of the following documents:

**Cover letter**

The cover letter should summarise the essential information regarding the requested advice procedure including the name and address of the applicant as well as the description of the product. It should be highlighted in the subject heading that the submission concerns a request for scientific or procedural advice. Enclosure to the cover letter is the application form. The application should be sent to the address indicated in section 4.

Applicants based outside the EU seeking advice should appoint a contact person in Germany or the EU.

**Application form**

Use of the application form is necessary to ensure that all relevant information for a valid request is provided at the time of initial submission. Sections A, B, C, and F are relevant for all requests. Section C1 has to be filled in case of Medicinal Products, section C2 is for medical devices. Section D is required for requests for Scientific Advice; section E is required for requests for a Pre-submission Meeting.
The following points should be considered:

A. Applicant
   - Name and address of the applicant, the legal representative, if applicable, including telephone number and e-mail address, as well as the billing address if different
   - BfArM exclusively advises pharmaceutical companies or sponsors of clinical trials. If the inquiry is submitted via a legal representative, a letter of authorisation from the applicant specific for this legal representative and for this procedure must be provided at the time of initial application

B. Type of procedure
   - Information about the type of advice procedure (Scientific Advice or Pre-submission Meeting), the application procedure (standard procedure or procedure with supplemental submission), as well as to whether an initial or a follow-up advice is requested
   - Information about the preferred procedural scenario (in writing or meeting) is optional
   - Consultations related to the planning of clinical trials may include, at the request of the applicant, experts from the Federal Joint Committee (G-BA)
   - Information about previous or applied for advice procedures
   - In case the applicant has received advice from other national authorities on the same subject, it would be appreciated if minutes of these meetings were brought to the attention of the BfArM

C. Details about the product
   - Information about the product, differentiation between medicinal product or medical device

C1. Details about the Medicinal Product
   - Information about the name of the active ingredient, the dosage form, and the route of administration
   - Details about the (planned) therapeutic indication and the ATC code
   - Details about approvals, rejections/revocations and (ongoing) applications in other EU member states may be of importance for classification of the application

C2. Details about the Medical Device
   - Information about the type of Medical Device
   - Details about the identification of the product and its nomenclature
   - Information on combination of the medical device with medicinal products, animal tissue or derivates rendered non-viable, as well
information on a combination of the medical device with human plasma or stable blood derivates
- Information on CE marking

D. Scope of the Scientific Advice
- Information regarding the topics of the question (multiple choice possible)
- Justification for the request
- Identification of clinical trials in which the applicant of the advice acts as sponsor, which are either on-going or applied for and are directly related to the development program to be discussed
- Identification of the studies using EudraCT or EUDAID number

E. Scope of the Pre-submission Meeting
- Information about the application type as well as about the role the BfArM should have in a European procedure
- Information about the planned submission date
- Information regarding the topics of the question (multiple choice possible)
- Justification for the request

F. Confirmation regarding payment of fees
- For a valid application confirmation must be given by marking the respective box with a cross

List of Questions
A concrete and precise list of questions has to be provided together with the request for advice. The template (Application Form Appendix) available on the BfArM website should be used. At the time of initial application the list of questions should be indicated as version 1 and should be provided as a Microsoft Word® document. The list of questions is absolutely necessary for the validation of the request and the decision regarding the procedural scenario, respectively. Only questions which have been put forward in the list are subject of the advice procedure. Since changes to the list of questions may require the involvement of different assessors from the Institute, it is necessary to contact the Unit “Advice, Innovation Office, Expert Panels” in advance. In case the changes are accepted a revised list of questions should be provided using the above-mentioned template; the versions should be numbered consecutively. The list of questions should be structured in accordance with the topics as per sections D and E of the application form. The goal is to discuss the presented concepts - and not to develop these during the course of a meeting.
For each question raised the applicant should state his position and provide a written summary below.

Up-to-date and relevant documents must be made available to the BfArM’s scientists in due time and always prior to the actual meeting date in order to ensure efficient advice by the Institute. If new data require an amendment of either the questions or the position/justification from the applicant, then it will be required to provide a new list of questions.

Documentation

The documentation submitted for an advice procedure should be sufficiently extensive to provide the necessary background information for BfArM’s to be involved units (max. 50 pages). The data should be presented in correspondence with the submitted list of questions and in a manner that allows BfArM’s scientists to answer the questions raised.

The data should be presented in concise and clear manner in order to ease access to the information and to support a discussion focused on the specific questions. The documentation should be single fold as hardcopy and electronically as PDF-file at the following time points:

- Standard procedure: simultaneously with the application
- Procedure with supplemental submission: at the latest 4 weeks prior to the scheduled meeting date

Summary of documents for application:

<table>
<thead>
<tr>
<th>Document</th>
<th>Paper Version</th>
<th>Electronic Version</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cover Letter</td>
<td>✔️</td>
<td>✔️</td>
</tr>
<tr>
<td>Application Form</td>
<td>✔️ (Signed Original)</td>
<td>✔️ (Word document)</td>
</tr>
<tr>
<td>List of Questions</td>
<td>✔️</td>
<td>✔️ (Word document)</td>
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<tr>
<td>Briefing Document</td>
<td>✔️</td>
<td>✔️ (pdf document per e-mail, EUDRALINK or CD-ROM)</td>
</tr>
<tr>
<td>List of Attendees</td>
<td>✔️</td>
<td>✔️ (Word document)</td>
</tr>
</tbody>
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2.2 Planning of the meeting

New requests are being validated regarding form and content. Insufficient information or the lack of an appropriate justification for the request may lead to rejection of the application. The procedural scenario (in writing or meeting) will be decided by the BfArM following review of the request in close collaboration with the internal experts to be involved. The applicant will be informed whether the application will be accepted and which procedural scenario will be followed. In case of an application with supplemental submission the acceptance is subject to the submission of the documentation in due time. For an advice meeting the meeting date will be agreed upon with the applicant following internal consultation of the experts to be involved.

Scheduling
As a rule it will be possible to conduct a meeting within a timeframe of 6 weeks to 5 months; this however, depends on the availability of the scientific units involved. Capacity constraints can lead in rare situations to longer waiting times.

List of participants
Prior to the meeting, BfArM expects a list of participants from the applicant. Positions/functions of the individual attendees should be listed. A draft of this list could be included in the initial application in order to ensure adequate participation of experts from the Institute. If the applicant makes changes to the list of participants during the planning phase, this should be communicated to the Unit “Advice, Innovation Office, Expert Panels”. The final list should be provided at least 1 week prior to the actual meeting date.

In this context it should be highlighted that the number of participants should be limited. A group size of 4 up to maximally 7 persons (if several different aspects are to be discussed) should not be exceeded by the applicant. It is recommended to name only those internal experts and external consultants (if applicable), who are familiar with the respective project and who can contribute to the discussion.

Technical aspects
Conference rooms are equipped with a multimedia projector, which can be hooked up to any laptop. If requested, BfArM can provide a laptop; however, this should be communicated to BfArM in advance.
2.3 Conduction of the meeting

**Advice meeting**

As a rule, two hours are scheduled for meetings for advice. The meeting is chaired by the BfArM. Following greetings and introduction of the participants, the applicant should give a short presentation outlining the issue and a problem statement (10-15 minutes). Generally, the list of questions is discussed after the presentation. However, in some cases it may be useful to discuss the questions directly in connection with the presentation. Deviations are either agreed upon during the meeting itself or are discussed and arranged in advance.

**Meeting Minutes**

The applicant provides the draft meeting minutes of the advice meeting. It should be borne in mind that not the name of the individual BfArM scientists should be indicated but simply "BfArM" should be stated.

The Federal Institute expects to receive the minutes within 5 working days after the meeting took place. The drafts are to be sent as Word documents via e-mail to the Unit “Advice, Innovation Office, Expert Panels”. The minutes are corrected if necessary and the final version is returned to the applicant within two weeks.

The minutes of the advice meetings reflect the respective scientific state of the art at the time of the discussion. More recent developments that can become known later are thus not reflected but do still have to be considered in any case. Taking recourse to the state of knowledge at the time of the advice with the aim of not implementing more recent findings into the company's own product development to the necessary extent is not possible.

**Written Advice**

Written advice will be provided by BfArM in cases in which the subject is limited to a specific problem of a particular scientific unit. Written advice can be requested by the applicant. Should BfArM consider a requested meeting to be unnecessary, the Institute may provide written advice instead. After the BfArM has received the complete documentation, the applicant can expect an answer within four to six weeks - depending on the complexity of the inquiry.
2.4 Fees

As a rule, the Institute's cost centre sends out an invoice after the advice procedure has been completed. The costs depend on the actual BfArM resources involved (human and other). The fees will be determined in accordance with the AMG-Fee or MPG-Fee Ordinances.

The BfArM does not charge any fees for Pre-submission Meetings regarding centralised European Procedures.

In case of withdrawal of the application or rejection of the application after initiation of processing fees will be charged in accordance with the AMG- and MPG-Fee Ordinances.

3. Portfolio Meetings

Portfolio Meetings provide the opportunity for pharmaceutical companies to present a brief overview of different (also early stage) development projects to the BfArM. Advice on specific aspects of individual development projects is not in the scope of Portfolio Meetings. However, the need for subsequent Scientific Advice may be the result of a Portfolio Meeting; this advice needs to be applied for separately.

Requests for a Portfolio Meeting should be sent without further formal requirements to the address indicated in section 5. In addition the documents should be sent electronically by e-mail to the address indicated in section 5.

The following should be subject to the request:

- Name and address of the pharmaceutical company and the contact person (including telephone/fax number and e-mail address)
- Tabular overview of the development projects with details about the active ingredients, the therapeutic indications as well as the development status, ordered by therapeutic areas
- List of participants from the applicant

Following validation of the request the BfArM decides whether a Portfolio Meeting will be arranged. In this case a meeting date will be arranged with the applicant; as a rule it will be possible to arrange for a meeting within six to eight weeks following receipt of the request. The duration of the meeting is two hours. Regarding the list of participants and the technical aspects, please refer to the information in section 2.2.
4. Contact

Bundesinstitut für Arzneimittel
und Medizinprodukte (BfArM)
Unit "Advice, Innovation Office, Expert Panels"
Kurt-Georg-Kiesinger-Allee 3

D - 53175 Bonn

In case of questions related to Scientific Advice procedures the following contact is provided:

E-Mail: advice@bfarm.de
Tel.: +49 (0) 228 99 307 3958