HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Guide for
National Scientific and Regulatory Advice

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This guide does not purport to be an interpretation of law and/or regulations and is for guidance purposes only.

CONTENTS

1 INTRODUCTION

The aim of providing HPRA national scientific or regulatory advice is to assist applicants in the development of new or existing human medicinal products by taking into account the current knowledge of a given condition, targeted patient population, existing treatment modalities and specificities of the product being developed. The HPRA can provide national advice to industry and other interested parties such as academic institutions and investigators intending to make an application for a marketing authorisation or a clinical trial investigation.

The advice is provided on request from a company or non-commercial body and may be in relation to scientific development, clinical trial application(s), regulatory advice or a combination of these. Discussion of the appropriate regulatory requirements and existing guidelines may be considered in the advice. The aim of the advice is to serve as a guide to the applicant but is not intended to substitute the applicant's responsibilities in the development of its medicinal product.

Advisory meetings are optional. If the applicant requests a meeting, the HPRA considers the request, and accepts or refuses it as appropriate.

In general, the advice given is based on the documentation provided by the applicant in light of current relevant scientific knowledge and without prejudice to evolving developments in the scientific field. Advice will be given in good faith, however, if circumstances change over time, an alternative approach to that previously advised may become more appropriate. Therefore, any advice provided is not binding for the applicant or for the HPRA.

2 OVERVIEW

Scientific advice and protocol assistance meetings are organised in order to provide responses to specific questions pertaining to medicinal products in development in the field of medicine (see sections 2.1 and 2.2).

Advice will be given in quality, pre-clinical and clinical areas. The range of advice areas covered may be expanded further over time.

2.1 Quality advice

The HPRA will provide national scientific and regulatory advice on quality aspects of product development for the following areas:

- chemical drug substances and medicinal products, including oligonucleotides and oligopeptides
- biological drug substances and drug products, including biosimilars and antibody-drug conjugates
- drug device combinations
- continuous manufacturing / process analytical technology / real time release / Quality by Design
- advanced therapies
- bioanalytical methods

2.2 Pre-clinical advice

The HPRA will provide national scientific and regulatory advice on the pre-clinical (toxicological and pharmacological) development of products. The applicant may pose questions on any issue relating to pre-clinical development with the exception of Environmental Risk Assessments (ERAs) as they are outside the remit of the HPRA.

2.3 Clinical advice

The HPRA will provide national scientific and regulatory advice on the clinical development of medicinal products over a broad range of therapeutic areas, including:

- respiratory medicine,
- rheumatology,
- obstetrics and gynaecology including fertility,
- dermatology (common conditions),)
- anti-infective products
- vaccines
- disorders of haemostasis and thrombosis
- heparins and low molecular weight heparins
- cardiovascular diseases
- radiopharmaceuticals,
- common allergic conditions
- indications for Botulinum neurotoxins,
- common ophthalmological conditions
- common endocrinological and gastrointestinal conditions,
- generic medicines and biosimilars in the above therapeutic areas.
- advanced therapies in certain clinical indications
- biostatistics
- pharmacokinetics

For protocol assistance, questions related to the demonstration of significant benefit within the scope of an orphan drug designation can also be discussed.

2.4 Regulatory advice

Regulatory advice may also be requested on non-specific issues such as:

- a change to the method of sale and supply ~~to~~of authorised medicines~~,~~
- proposed labelling for product ranges
- significant changes to product information (SmPC~~)~~), labelling or package leaflets ~~or advertising,~~(e.g. multilingual labelling)
- advertising or post-authorisation regulatory advice relating to a product range~~.~~

2.5 General points in relation to all types of advice

~~National~~If an EMA advice request is being planned by a company, national scientific and regulatory advice may be useful for applicants in identifying the most important points to discuss at the EMA~~, if an EMA advice request is planned by a company~~.

It is not in the scope of scientific and regulatory advice to provide a pre-assessment of data; however, the appropriateness and completeness of an MA file before submission may be discussed.

~~For statistical questions the advice will be provided in writing only.~~

Advice will not be given in certain circumstances as outlined in the examples below for illustration (this list is not ~~exclusive~~exhaustive):

- ~~If~~if a company has already obtained ~~the~~ CHMP advice on the same issues
- ~~When~~when the rapporteur and co-rapporteur for an MA request have already been designated by the CHMP
- ~~For~~for concerns raised during assessment of any MA request, VHP application or other procedures, etc.
- ~~If~~if products or therapeutic areas are outside the scope of this ~~advice document~~guide
- ~~Biomarkers~~for qualification of ~~Qualification~~biomarkers or other qualification opinions
- ~~Advanced therapies~~
- ~~Blood products~~
- ~~Quality aspects of vaccine development~~

3 MAKING A REQUEST FOR NATIONAL SCIENTIFIC AND REGULATORY ADVICE

You can request scientific and regulatory advice from the HPRA by ~~using~~submitting the National Scientific and Regulatory Advice application form which can be downloaded from our website www.hpra.ie.

Using the form, applicants should propose dates for a meeting. In general, meetings are organised within two months ~~after~~from receipt of the request~~.~~ although delays may arise due to the availability of experts, etc. If a delay is expected the applicant will be advised of its duration. ~~Delays may arise due to the availability of experts etc.~~

A draft list of questions in broad outline must be supplied with the application. Questions may relate to pre-clinical, clinical or quality development. The questions asked by a company should be as clear as possible, and should clarify the company's position on the question. All relevant documentation must be received at least 30 days before the meeting and should be submitted electronically to scientificadvice@hpra.ie.

Following review of the questions, the HPRA will inform the applicant whether a meeting is considered appropriate or not and whether any specific questions will not be discussed.

~~Within~~The HPRA will issue written advice within 20 working days following the meeting ~~the HPRA will issue written advice~~.

4 DOCUMENTATION PROVIDED BEFORE THE MEETING

In addition to the documentation and information provided with the application form, the following briefing documentation must be provided electronically to scientificadvice@hpra.ie at least 30 days before the meeting:

- ~~Background~~background information (limited to essential information and no longer than 100 pages~~).)~~
- ~~Disease~~disease/targeted population/indication
- ~~Final~~final proposed list of questions
- ~~For~~for each question the applicant's position and justification
- ~~Investigator's~~investigator's brochure if relevant~~.~~

There is no limit to the number of questions that can be asked by the applicant~~,~~; however, there are only 90 minutes available for the meeting. The applicant should ensure there is sufficient time for discussion; the ~~questions~~meeting should focus on the key questions for the applicant.

5 MEETING

The meeting will be ~~of~~ 90 minutes ~~duration,~~long and will be held in the offices of the HPRA. If necessary, experts may join by teleconference. The meeting will be chaired by HPRA staff.

At the start of the meeting the applicant will be asked to provide a brief introduction and overview of the product or topic to be discussed.

The applicant records brief minutes of the meeting and is requested to send them to the HPRA within ~~1~~one week following the meeting. The HPRA may comment on the recorded minutes prior to finalisation of the written advice.

The HPRA will provide written responses to the applicant's questions within 30 days following the meeting.

Any subsequent clarification requests are limited to the issues discussed and must be sent within two weeks after receipt of the written advice by e-mail to scientificadvice@hpra.ie. The HPRA will provide clarification within 14 days.

6 FEES

An applicant can request national scientific and regulatory advice at any stage of product development in preclinical, quality and clinical sections. The following fee codes apply (please refer also to the HPRA Guide to Fees and the HPRA Fee Application Form for Human Products on our website www.hpra.ie~~.~~).

Fee Code	Type
240	When advice is requested in a single area of quality or preclinical development
246	When advice is requested in the clinical development section only.
247	When advice is requested in two sections from preclinical, quality or clinical in any combination
248	When advice is requested in all three sections

7 CONTACT DETAILS

For further information or guidance, please contact:

E-mail: scientificadvice@hpra.ie

Human Products Authorisation and Registration
Health Products Regulatory Authority
Kevin O'Malley House
Earlsfort Terrace
Dublin 2
D02 XP77
Tel: +353-1-6764971
Fax: +353-1-6767836