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 Health Products Regulatory Authority (HPRA) national scientific and regulatory advice is to support the development of new or existing human medicinal products. The objective of the advice is to serve as a guide to the applicant but it is not intended to substitute the applicant's responsibilities in the development of its medicinal product.

Scientific advice may be provided at any time before or after the authorisation of a medicinal product. It may cover questions related to the pharmaceutical quality, the design and conduct of non-clinical investigations and clinical trials, as well as regulatory advice. National scientific and regulatory advice can be provided to industry and other interested parties such as academic institutions and clinical trial investigators.

2 OVERVIEW

National scientific and regulatory advice is provided at the discretion of the HPRA. Upon receipt of a complete application for advice, requests are considered based on the availability of experts and departmental capacity and accepted or refused as appropriate.

National scientific and regulatory advice may also be requested by the HPRA, prior to the submission of applications, which routinely encounter difficulties and for which prior engagement is likely to facilitate a smoother assessment stage. A non-exhaustive list of these applications is provided in section 2.5.

National scientific and regulatory advice can never be a substitute for a complete application for marketing authorisation (MA) and the advice provided has no bearing on the final assessment of the HPRA and/or the Committee for Medicinal Products for Human Use (CHMP) at the European Medicines Agency (EMA).

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.

The scope of the advice is the list of questions to be provided by the applicant in relation to the human medicinal product development programme. The questions should be justified by the fact that they are either not covered by the relevant guidelines, or that specific aspects of these guidelines require interpretation.

It is not in the scope to provide a pre-assessment of data intended for a variation or marketing authorisation. Questions that are prospective and concern the future development of a medicinal product are preferred.

Advice can be requested in quality, nonclinical, clinical and regulatory areas.

Advice can be given in the format of a meeting (standard advice) or a written procedure (swift advice).

2.1 Quality advice

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

- chemical drug substances and medicinal products, including herbal products, 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
- inhalation products
- advanced therapies
- bioanalytical methods (for biological products)

2.2 Nonclinical advice

We provide national scientific and regulatory advice on the nonclinical (toxicological and pharmacological) development of products. Regulatory advice relating to environmental risk assessment (ERA) can also be provided, but it is not in the scope of national scientific and regulatory advice to provide technical advice on environmental risk assessment studies.

2.3 Clinical advice

We provide national scientific and regulatory advice on the clinical development of medicinal products.

Clinical advice is generally sought by pharmaceutical companies for national and decentralised medicines and by academic institutions during their research programmes.

It is not in the scope to provide a pre-assessment of data intended for a variation or marketing authorisation.

Advice prior to a marketing authorisation application or variation is focused on questions related to planning and conduct of a concrete, forthcoming application. Possible topics are the legal basis of the application; the dossier presentation (structure, content); and procedural aspects, as well as the draft labelling.

2.4 Regulatory advice

Regulatory advice may also be requested on issues such as:

- a change to the method of sale and supply of authorised medicines
- proposed labelling for product ranges

- significant changes to product information (SmPC), labelling or package leaflets (e.g. multilingual labelling)
- advertising or post-authorisation regulatory advice relating to a product range
- legal basis of marketing authorisation applications

Please also consult our Guide to Reclassification (Switching) of Legal Supply Status for Human Medicinal Products at www.hpra.ie in advance of any request for regulatory advice on a change to the method of sale and supply of authorised medicines.

2.5 Scenarios where national scientific and regulatory advice may be recommended by the HPRA

National scientific and regulatory advice may be recommended by the HPRA, for new application types where assessment challenges during the procedure are envisaged. Successful follow up of the advice given at this stage should enable applicants to submit applications of appropriate standards which are in conformity with the legal and regulatory requirements, which will facilitate assessment and impact timeline procedure positively.

National scientific and regulatory advice is strongly encouraged in particular for the following application types:

- Switches to the legal supply status or reclassification of a medicine.
- Marketing authorisation applications via a national application route.
- Marketing authorisations applications with an intended Article 10a, well-established use (WEU) legal basis.

For further details on when national scientific and regulatory advice may be recommended for switches to the legal supply status or reclassification of a medicine, please see our Guide to Reclassification (Switching) of Legal Supply Status for Human Medicinal Products.

2.6 General points in relation to all types of advice

Advice may not be given in certain circumstances (this list is not exhaustive):

- if a company has already obtained CHMP advice on the same issues
- when the rapporteur and co-rapporteur for an MA request have already been designated by the CHMP
- for concerns raised during assessment of any MA application or other procedures, etc.
- for qualification of biomarkers or other qualification opinions

Advice may be given in the format of a meeting (standard advice) or a written procedure (swift advice). The ultimate decision on the format of the advice will be decided by the HPRA 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 format will be followed.

3 MAKING A REQUEST FOR NATIONAL SCIENTIFIC AND REGULATORY ADVICE

3.1 Submitting a Request

To make a request, download the National Scientific and Regulatory Advice application form and briefing document from our website at www.hpra.ie and fill in the required details.

In the application form, you can request either a meeting (standard advice) or written procedure (swift advice). You can propose dates for a meeting within the form. In general, meetings are organised within two months from acceptance of the request although delays may arise due to availability.

In the briefing document, a brief overview and list of questions must be provided. The overview should contain details of the medicinal product, the development programme overview and/or marketing history. If additional supportive documents are needed, they can be submitted separately. The list of questions is necessary for the validation of the request. Only questions which have been put forward in the list are subject to the advice procedure. There is no limit to the number of questions that can be asked; however where a meeting is proposed, its duration will be no longer than 90 minutes and the applicant should ensure there is sufficient time for discussion. The meeting should focus on the key questions that were submitted in the initial request.

Submit the completed application form along with your briefing document to scientificadvice@hpra.ie.

3.2 Accepting/Rejecting a Request

Insufficient information or the lack of an appropriate justification for the request may lead to rejection of the application. The ultimate decision on the format of the advice (standard or swift) will be decided by the HPRA 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 format will be followed.

When a standard advice request is accepted, a meeting date will be agreed. The full briefing documents must be received at least 30 days before a meeting. For swift scientific advice, the full briefing documents can be submitted as soon as your request is accepted (see section 4 below).

When a swift advice request is accepted, the full briefing documents should be submitted as soon as possible (within seven days) after notification that the request for NSA is accepted, and the validation period will begin when these are received.

Changes to the list of questions can be submitted to scientificadvice@hpra.ie up to 30 days prior to a meeting and for the swift advice procedure, before validation, however a significant increase in number or complexity is not envisaged. If the changes to the list of questions are significant and the assessor(s) assigned to the case must be revised, your national scientific and

regulatory advice case may be delayed while capacity is revised. Please highlight in the email if an updated version of the list of questions is included.

4 DOCUMENTATION PROVIDED BEFORE THE MEETING

In addition to the information provided with the application form, the following full briefing documentation must be provided:

- background information (limited to essential information and no longer than 100 pages)
- disease/targeted population/indication
- the applicant's position and justification for each question
- investigator's brochure if relevant
- list of applicant attendees

For standard advice, the full briefing documentation must be provided electronically to scientificadvice@hpra.ie at least 30 days before the meeting.

For swift advice, the full briefing documentation must be provided to scientificadvice@hpra.ie within seven days of notification that your request has been accepted. When your full briefing documentation is received, your case can be validated and begin.

5 THE ADVICE

Standard advice meetings will be 90 minutes long and will be chaired by HPRA staff.

At the start of the meeting the applicant will be asked to provide a brief presentation of the product and topics to be discussed.

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

Written responses to the applicant's questions will be provided by the HPRA within 30 days of the meeting.

For swift advice, no meeting will take place and the written responses to the applicant's questions will be provided by the HPRA within 30 days of validation of the accepted swift advice case.

If the applicant requires any subsequent clarifications, these are limited to the issues discussed and must be sent within two weeks after receipt of the written advice by email to scientificadvice@hpra.ie. The HPRA will provide clarification within 14 days for standard advice and within seven days for swift advice.

6 FEES

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 at www.hpra.ie).

Fee code 240 also applies to swift advice.

Fee Code	Type
240	When advice is requested in a single area of quality or nonclinical development.
246	When advice is requested in the clinical development section only.
247	When advice is requested in two sections from nonclinical, 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:

Email: 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