Independent Review Procedure

A guidance note to the procedure to be followed when an applicant or licence holder wishes to submit certain decisions and proposals made by the licensing authority to review upon oral representation

September 2024

Guidance Note

Introduction

1 - The Human Medicines Regulations 2012 ("the HMRs") provide that a holder of a licence who receives notification of a decision or proposal by the Licencing Authority under regulation 27(3)(b) of the HMRs, and an applicant for, or holder of, an authorisation, certificate or registration who receives notification of a decision or proposal by the Licencing Authority under Schedule 11, can request a review of the proposal or decision upon oral representations. There are other instances whereby such a review can be requested as well.

2 - The HMRs set out the process for requesting such a review including the appointment of a panel by the Licensing Authority to conduct an independent review of the decision or proposal being challenged ("the Panel").

3 - Schedule 5 of the HMRs sets out the procedure that the review should follow.

4 - This guidance note explains the purpose of and procedures associated with the Panel's independent review in order to assist applicants and the licensing authority with the review process. For the avoidance of doubt:

a. Whilst this guidance note makes reference to other regulations, paragraphs and Schedules of the HMRs insofar as they relate to Schedule 5, it is not intended to assist with any aspect of the HMRs except the procedure which a review under Schedule 5 should follow as well as the means by which such a review should be requested; and
b. This guidance note deals with medicines for human use only; it does not deal with medical devices.

5 - Although a general description is given of the provisions of the law and the way in which the Panel's review process operates in practice, this guidance note must not be considered as a substitute for reference to the relevant legislation. In particular, reference should be made to the relevant provisions of the HMRs for the details of the procedure; and the Applicant as well as the Licensing Authority should consider whether they need to take specialist legal advice.

6 - The guidance note is without prejudice to the powers of the Panel under Schedule 5 paragraphs 3(6) and 3(10) which allow the Panel to establish dates by which procedures under Schedule 5 must be completed; and to make other directions as they see fit for the conduct of a hearing. Further to that:

a. Some of the steps referred to in this guidance note are not referred to specifically in Schedule 5; and
b. The Applicant and Licensing Authority will be notified in advance of the Panel taking any steps that are additional or contrary to those set out in this guidance note.

7 - An Applicant usually has two opportunities to present its case:

(i) Where an Applicant is notified of a provisional opinion of the Licensing Authority and disagrees with that provisional opinion, the Applicant may make representations to the 'appropriate committee' which is advising the Licensing Authority. The Licensing

Authority is advised as to safety, quality and efficacy by a number of 'appropriate committees'. When an Applicant makes representations to one of these 'appropriate committees', the committee must report its findings and advice to the Licensing Authority, which must take their findings and advice into account before making its decision.

(ii) Where an Applicant disagrees with the decision of the Licensing Authority, having already made representations to the 'appropriate committee' under Schedule 11, the Applicant may request the Licensing Authority to submit the decision to review upon oral representations. It is at this stage that the Panel will conduct an independent review.

8 - In limited circumstances it is possible for an applicant for marketing authorisation, traditional herbal registration or certificate of registration, or where there is a proposal to decide that the orphan criteria are not met in relation to a medicinal product which is the subject of an application for the grant of a UK marketing authorisation, to ask for a review before the Panel even when the applicant has made no representations to the 'appropriate committee'. This is possible only where the Licensing Authority's decision is not in accordance with the advice of the appropriate committee or the appropriate committee has not been consulted or not given a provisional opinion.

9 - There is no 'appropriate committee' stage for licences such as manufacturing and wholesale dealing licences. Instead, following suspension, revocation or variation of a licence or notification of a proposal to suspend, revoke or vary a licence, the Applicant may ask to make written representations to the Licensing Authority with respect to the proposal, or the Applicant may notify the Licensing Authority they wish the Licensing Authority to submit the proposal to review upon oral representations.

Legal Background

10 – The key terms used in this guidance note (along with their meanings) are set out below. For the avoidance of doubt, these are not definitions under the HMRs but have been formulated for the purposes of this guidance note.

11 - '**Applicant'** includes:

a. the holder of a manufacturing or wholesale dealing licence;
b. the broker, where the licensing authority proposes to suspend or vary a broker's registration or remove a broker from the register;
c. the person with an active substance registration, where the licensing authority proposes to suspend or vary an active substance registration or remove a person from the active substance register;
d. the person on the list of persons who are entitled to supply medicinal products by information society services that is maintained on licensing authority's website, where the licensing authority proposes to suspend, vary or remove the person's entry on the list;
e. the applicant for, or holder of, a UK marketing authorisation, certificate of registration or traditional herbal registration, where (on the grounds of safety, quality or efficacy) the licensing authority notifies that applicant or holder of a decision related to the authorisation, certificate or registration (as the case may be), such as a decision on the grant, renewal, revocation, variation or suspension of the authorisation, certificate or registration, or a decision on the orphan criteria of a medicinal product which is the subject of a UK marketing authorisation application;
f. the applicant for, or holder of, a parallel import licence, where there is a proposal

notified to the applicant related to the licence and the proposal is **not** on the grounds of safety, quality or efficacy;

g. the applicant for a variation application, where the licensing authority notifies the applicant of the decision to refuse to grant the variation application;
h. the applicant for a traditional herbal registration, where the licensing authority refers the application for a traditional herbal registration to the appropriate committee.

12 - **'Licensing authority'** means the authority established by legislation (the HMRs) which is responsible for all licensing decisions concerning medicines for human use. Regulation 6 of the HMRs provides that the UK authority responsible for such licensing decisions is either or both of the Secretary of State for Health and/or the Minister for Health, Social Services and Public Safety. In practice they act through the regulatory arm of the Medicines and Healthcare products Regulatory Agency ("*the MHRA*") as their executive agency. In this guidance note 'Licensing Authority' refers to the licensing authority function of the MHRA. For the avoidance of doubt, the MHRA also has non-licensing authority functions.

13 - **'Decision',** for the purpose of this Guidance Note, has a broad definition and is used to mean any licensing decision of the Licensing Authority including the grant, renewal, suspension, revocation and variation of:

a. licences for manufacturing and wholesale dealing;
b. broker's registration;
c. an active substance registration;
d. a person's entry on the list of authorised sellers of medicinal products at a distance;
e. UK and GB marketing authorisations, traditional herbal registrations as well as certificates of registration;
f. paediatric investigation plans;
g. a proposal to decide that orphan criteria in a UKMA application are not met; and
h. a parallel import licence and the proposal is not on the grounds of safety, quality or efficacy.

14 - **"Day",** this means calendar day.

15 - Where the applicant disagrees with the decision or proposal of the Licensing Authority and requests from the Licensing Authority a review of that proposal or decision upon oral representations, the Panel will be appointed to carry out an independent review of the decision or proposal and prepare a report.

16 - The general procedure contained in Schedule 5 and adopted by the Panel in the course of carrying out its independent review is set below. The Panel will always:

- conduct it in such away as it considers necessary to ensure fairness;
- provide the Applicant and Licensing Authority with an opportunity to give oral evidence at a review hearing;
- consider the written representations received from the Applicant and the Licensing Authority along with all evidence before it;
- produce, within 60 days or notify the Applicant and Licensing Authority within this period if further period is noted, a report containing its findings based on any evidence or expert information presented to it (subject to the restrictions imposed by Schedule 5 paragraphs 3(4) and 3(9) of the HMRs) and the results of any further enquiries it makes ("*the Report*") which are dealt with at paragraphs 51-55 below; and
- provide the Report to the Licensing Authority and the Applicant

17 - The Licensing Authority must then take into account the Report when it makes its final decision and notify the applicant of that decision.

The Panel

18 – Under Schedule 5 paragraph 2 of the HMRs:

a. The Licensing Authority must appoint the Panel to conduct an independent review of the decision or proposal being challenged. The Panel must contain at least 2 persons. Generally (although not always), the Panel will consist of a chair who will sit at each Panel review with at least two other individuals from the Panel who have appropriate medical and/or scientific expertise. Depending on the subject matter of the hearing, specialists in a particular field may be called upon by the Panel to advise them further in any way, including attendance with the Panel at any site visit which may be necessary, and advising the Panel at the hearing.
b. A person must not be appointed to the Panel if, within a period of 1 year immediately preceding that time, the person has been a member of:
    i. The Commission;
    ii. An expert committee appointed by the Licensing Authority;
    iii. An expert advisory group;
    iv. The British Pharmacopoeia Commission or any of its sub committees;
    v. The Advisory Board on the Registration of Homeopathic Products formerly established under section 4 of the Medicines Act 1968; or
    vi. The Herbal Medicines Advisory Committee formerly established under Section 4 of the Medicines Act 1968.
c. A person appointed to the Panel must not be an officer or servant of a Minister of the Crown, the Scottish Minister, the Welsh Ministers or a Northern Ireland Minister.

The Independent Review Procedure

19 - The procedure contained in this guidance note is intended to ensure that the Panel is provided with all the information it needs in order to conduct a full independent review of the issues which are the subject of the Applicant's request. The Applicant will have the opportunity to set out in detail why it disagrees with the Licensing Authority's decision. The Licensing Authority will have the opportunity to set out in detail why it considers it was justified in reaching its decision.

20 - The procedure for dealing with any dispute or disagreement between an applicant and the licensing authority is broadly similar for marketing authorisation, herbal registration and certificates of registration, and is set out in the relevant legislation above.

21 - The Panel will conduct its review as it considers necessary for the purpose of fulfilling its function of ensuring thoroughness and fairness, and may call for additional information at any time during its review.

22 – As set out at Schedule 5 paragraph 3(4), in relation to a decision of the Licensing Authority under Part 1, 2 of 3 of Schedule 11, or a proposal of the Licensing Authority under paragraph 12 of Schedule 11, the Applicant's written representations and evidence must not be based

on any evidence or data that was not available to the Licensing Authority at the time that the decision or the proposal in question was notified to the Applicant by the Licensing Authority, unless the evidence is unfavourable regarding the safety, quality or efficacy of the product concerned. Further to that, as set out in Schedule 5 paragraph 3(9), the Panel must not take into account any evidence it thinks might have been unavailable to the Licensing Authority as aforementioned unless it is unfavourable regarding the safety, quality or efficacy of the product concerned. Therefore, in such situations, the Panel will not consider previously undisclosed new data that was not available to the Licensing Authority at the time of decision or proposal on the product in question was notified to the Applicant. Under these circumstances, any hearing may be adjourned for such period as the Panel may decide. Do note that the Applicant can submit new data under a new application to the Licensing Authority, which will be considered afresh by the Licensing Authority.

Preparation for the Independent Review

23 - If an applicant wishes to notify the Licensing Authority that they want the decision or proposal in question to be subject of a review upon oral representations they should send the Licensing Authority notification as detailed below ("*the Notification").*

a. For manufacturing and wholesale dealing licences, Notification should be given before the date upon which the Licensing Authority has informed the Applicant that its decision will take effect.
b. In all other cases, in accordance with Schedule 11 to the HMRs, the Notification must be given within the period of 28 days beginning with the day upon which decision of the Licensing Authority has been given, or such longer period as the Licensing Authority may allow. The applicant may apply in writing to the Licensing Authority for an extension of time.
c. A capital fee of £11,000 is payable by the person who gives notice (see further details in paragraph 56 below).

24 - Upon receiving the Notification, the Licensing Authority will inform the Secretariat of the Panel ("*the Secretariat*") that an independent review has been requested. All arrangements for and communications in connection with the review, including the hearing, will, from the date that a request for a hearing is received by the Secretariat, be dealt with by them.

25 - The Applicant must supply the Panel with a written summary of the oral representations and any documents that they wish to rely on before the end of the period of 3 months beginning from the date of the Notification.

26 - The Licensing Authority may also supply the Panel with a written summary of the oral representations and any documents that they wish to rely on within the same time period as the Applicant.

27 - An extension of this time limit may be granted by the Panel (with the Licensing Authority's agreement), up to a maximum period of 6 months from the date of the Notification.

28 – The Applicant ensures all written representations or documents are submitted within the time limits stipulated above, except with the permission of the Panel under Schedule 5 paragraph 3(3).

29 - Prior to fixing a hearing date, the Secretariat will send out a request for the Applicant and Licensing Authority to inform the Secretariat of any dates to avoid. The Secretariat will

consider any responses and will give at least 28 days' notice of the date, time and place of the hearing to the Applicant and Licensing Authority. For the avoidance of doubt, whilst the Panel will take into account any dates to avoid, if necessary, they can fix a hearing on those dates.

30 - If the Applicant fails to comply with the time limits set out at paragraphs 25 and 27 above, or other time limit set by the Panel in accordance with Schedule 5 Paragraph 3(6), the Applicant may not appear before the Panel.

31 - If the Applicant fails to provide documentation in support of its request upon the expiry of 6 months from the date of the Notification, the Panel may treat the request for an independent review as withdrawn by the Applicant.

32 - The Panel may, if it considers it necessary, ask the Applicant and Licensing Authority to attend a pre-hearing meeting with the Panel in order to clarify the main issues, the written evidence to be submitted and discuss any witnesses that may be called to attend the full hearing.

33 - The Applicant and Licensing Authority should ensure that they provide the Panel with all the evidence needed to support their respective cases, in advance of the hearing.

34 - The Panel may call for further information from either the Applicant or Licensing Authority, either prior to or following the hearing.

35 - Unless otherwise specified by the Panel, the Applicant and Licensing Authority need to provide the following information to the Secretariat:

- All documentation in English;
- The names of any witnesses it is intended to call at the hearing, not less than 10 days prior to the hearing;
- The Applicant and Licensing Authority should provide an electronic copy of the documents set out below in the form of a single indexed and paginated WORD and PDF document.

  (a) In the case of the Applicant:

  (i) all documentation from the application, including presentation materials, upon which it is proposed to rely at the hearing (where appropriate);

  (ii) a written skeleton summary of the argument to be made at the hearing; and

  (iii) any other material in support of the applicant's case.

  (b) In the case of the Licensing Authority

  (i) the decision of the Licensing Authority being challenged;

  (ii) the full written advice of the Committee on Human Medicines and/or all other appropriate committees which have already considered the application, including assessment reports (where appropriate);

  (iii) copies of all relevant guidelines;

(iv) all documentation from the application, including presentation materials, upon which it is proposed to rely at the hearing;

(v) a written skeleton summary of the argument to be made at the hearing; and

(vi) any other material in support of the Licensing Authority's case.

- Both the Applicant and the Licensing Authority should provide the estimated time of any presentations, especially if they are likely to last longer than 30 minutes, bearing in mind that the timetable for the hearing may under those circumstances need to be changed.

- Amendments on any submitted materials should be provided to the Secretariat at least 7 days before the date of the hearing.

36 - Where, in connection with manufacturing of medicinal products and wholesale dealing licences, a premises inspection report has been prepared by a duly authorised person, the applicant must provide not less than 7 days' notice of any fact disputed in the report and the duly authorised person must attend the hearing in order to be questioned by the applicant and the Panel about any facts in the report.

37 - Further, in connection with manufacturing of medicinal products and wholesale dealing licences, the Panel may at the applicant's request, or on its own initiative, carry out an inspection of premises to which the licence relates. Reasonable notice will be given for any such inspection and any permission required from the Applicant shall not be unreasonably refused.

38 - Prior to the hearing the Secretariat of the Panel will:

- Send all written summaries of oral representations and supporting documents to the Panel;

- Send written summaries referred to at paragraphs 25-27 above to the Applicant and the Licensing Authority at least 28 days before the date of the hearing;

- Ensure the Panel has the bundles referred to at paragraphs 25-27 and 33-36 above prior to the hearing;

- Send any additional materials submitted to the Applicant and Licensing Authority least 7 days before the date of the hearing;

- Provide the Applicant and the Licensing Authority with a template for exchanging any administrative information required by the Panel to conduct the review; and

- Provide the names of the Panel members to the Applicant and Licensing Authority.

39 - The hearing must be held in public if the Applicant requests it under Schedule 5 paragraph 4(2). The Panel would be grateful if the Applicant would inform them of such a request as soon possible.

40 - Where a public hearing was requested by the Applicant, the Applicant should notify the Secretariat well in advance if they decide for a closed hearing instead.

Procedure at the Hearing

41 – Prior to the hearing, the Panel shall determine the directions for the conduct of the hearing.

42 - The Panel may, if it thinks fit, postpone or adjourn any hearing, and if it postpones or adjourns make any directions necessary for the adjourned or postponed hearing.

43 - The Applicant and the Licensing Authority may appear themselves or be represented, call witnesses and address the Panel.

44 - The hearing will be recorded and transcripts provided to the Applicant and Licensing Authority following the hearing for the purpose of report-writing only.

45 - If the Applicant fails to appear at the hearing, the Panel may conduct the review on the basis of the Applicant's written summary of the oral representations and supporting documents submitted in accordance with paragraphs 25-27 above.

46 – Subject to the hearing having been held in public, all information disclosed in the course of the hearing along with the contents of the hearing transcripts shall, for reasons of commercial sensitivity, remain confidential, subject to the application of the Freedom of Information Act 2000.

47 - The following information and advice is provided for the benefit of the Applicant and Licensing Authority:

- The Applicant and Licensing Authority should ensure that those representing them at the hearing are fully conversant with the subject matter of the dispute and have the competence to address in detail all relevant legal, scientific and technical issues.

- At the hearing, the Chair will provide the Applicant and the Licensing Authority with a full opportunity to present their cases and respond to the Panel's questions.

- Those making presentations should be aware that the Panel will be familiar with the documentation. The Panel advises that the most effective presentations will be concise and to the point, addressing the disputed issues in the decision notice and highlighting the key points relied upon.

After the Hearing

48 - After the hearing the Applicant and Licensing Authority will receive electronic copies of the transcript and may correct errors and clarify any points they wish.

49 - The Panel may call for further information, comment or clarification from the Licensing Authority and the Applicant concerning any matters arising from the hearing, in connection with which it may set a post-hearing time scale for reply.

50 - The Secretariat of the Panel will send electronic copies of all post-hearing questions asked and replies received, to the Applicant and Licensing Authority for their final written comments, if any.

51 - The Panel will write the Report, which will include its findings, conclusions and any recommendations, with its reasons.

52 - The Panel will provide a report to the Applicant and Licensing Authority by the end of 60 days after the hearing, or notify within that timeframe as to when the Report will be available.

53 - The Panel will present its report to the Licensing Authority and provide a copy to the Applicant. The Licensing Authority will then take the Report into account and decide whether to:

a. Proceed with its proposal, for example, to revoke, vary or suspend the authorisation or the persons entry into the list, depending on what the case may be;
b. Confirm or alter its decision to refuse, grant or review an application.

54 - An anonymised summary of all matters of public interest will be published in the Review Panel Annual Report on the Review Panel website. (https://www.gov.uk/government/groups/the-review-panel-mhra)

55 - If the hearing has been held in public, the report of the Panel will be published in full.

Fees for a Regulation of Medicines Review Panel hearing

56 - The fee payable by an Applicant who gives notice of a request for an independent review is £11,000, this being payable at the time the notice is given (Part 12 of The Medicines (Products for Human Use) (Fees) Regulations 2016).

57 - The Licensing Authority will refund to the Applicant:

- 60% of that fee if the Applicant withdraws before a Panel has been appointed to consider the case.

58 – The Licensing Authority will consider refunding up to:

- 100% of the fee if the outcome of the hearing is positive for the Applicant and the original advice is overturned.

59 - If the application is withdrawn after the Panel has been appointed, no refund will be applicable.

Review Panel Secretariat

60 - Administrative support to the Panel is provided by a secretariat of MHRA staff selected on a case-by-case basis to ensure they have at no time been involved with any of the processes or any decision-making connected with the product considered for review.

61 - Please note that the Secretariat makes requests for documentation and receives documentation from the Applicant and Licensing Authority only as set out in this guidance note.

62 - The Secretariat is not able to assist the Applicant or Licensing Authority with any administrative tasks or with opinions as to the relevance of material provided.

63 - The Secretariat will pass enquiries concerning possible hearings or related correspondence on to the Chair of the Panel.

64 - The Secretariat handles administrative matters for the Review Panel only and is not involved in the final licensing decision.

Contact details:

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