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

March 2014

Guidance Note

The Review Panel

1 - Legislation provides that an applicant who disagrees with a proposal or decision of the licensing authority may choose to make a representation about the proposal or decision by submitting a request for a review of the proposal or decision pursuant to the relevant sections of the Human Medicines Regulations 2012 (HMR 2012).

2 - Schedule 5 of HMR 2012 sets out the procedure to be followed by the applicant should they wish to submit the proposal or, as the case may be, the decision to review upon oral representation

3 - To fulfil the function of the 'reviewers' the licensing authority is required by legislation to appoint a panel of at least two people (the "reviewers") to conduct the review.

The purpose of the guidance note

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.

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.

Terms of reference

6 - Where an applicant for marketing authorisation, clinical trials authorisation, herbal registration, homeopathic certificate of registration or a licence for manufacturing or wholesale dealing disagrees with the decision or proposal of the licensing authority, is eligible in the relevant legislation and wishes their case to be submitted to review upon oral representation, the Panel will, upon the applicant's request, carry out an independent review of the decision or proposal and prepare a report.

7 - In the course of carrying out its independent review 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 hearing
- produce a report containing its findings based on any evidence or expert information presented to it and the results of any further enquiries it makes
- provide its report to the licensing authority and a copy of its report to the applicant

8 - The licensing authority will always take into account the findings contained in the Independent Review Report when it makes its final licensing decision and may take into account any recommendations of the Panel. The Licensing authority must notify the applicant of its decision

9 - The chair 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.

10 - The Panel will produce an Annual Report which will include summaries of its Independent Reviews which will be published on its web page.

Legal background

11 - In this guidance note the following meanings apply:-

'Applicant' refers to an applicant for marketing authorisation, clinical trials authorisation, herbal registration, homeopathic certificate of registration or a licence for manufacturing or wholesale dealing. An applicant may also be a licence holder who is subject to a notice of suspension, revocation or variation of his licence and who seeks reinstatement of his licence. This Guidance Note deals with medicines for human use only. The Panel does not deal with devices.

'Licensing authority' means the authority established by legislation which is responsible for all licensing decisions concerning medicines for human use. Part 1, section 6 of the Human Medicines Regulations 2012 provides that the UK authority responsible for such licensing decisions is a body of Ministers. In practice the Ministers, being the Secretary of State for Health and the Minister for Health, Social Services and Public Safety in Northern Ireland, acting through the regulatory arm of Medicine Healthcare Products Regulatory Agency as their executive agency. In this Guidance Note 'licensing authority' refers to the licensing authority function of the MHRA. The MHRA also has non-licensing authority functions.

'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 licences for manufacturing and wholesale dealing, proposals to suspend revoke or vary such licences, marketing authorisations, clinical trials authorisations, herbal registrations and homoeopathic certificates of registration.

12 - Reference should always be made to the relevant legislation for specific detail of these procedures.

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

14 - In limited circumstances it is possible for an applicant for marketing authorisation, clinical trials authorisation, herbal registration or homeopathic certificate of registration 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.

15 - The procedure for dealing with disputes differs for manufacturing and wholesale dealing licences. There is no 'appropriate committee' stage. 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 notify the licensing authority they wish the licensing authority to submit the proposal to review upon oral representations. The procedure is set out in Schedule 5 of the Human Medicines Regulations 2012 as described in this guidance document.

16 - Following any request by the applicant for the licensing authority to submit the proposal to review upon oral representations.pursuant to any of the above legislative provisions, the Panel will conduct an independent review.

17 - The procedure for the Panel's review is based on the procedure under Schedule 5 of the Human Medicines Regulations 2012. In addition to the Panel's review procedure provided below, reference should always be made to the relevant legislation.

The independent review procedure

18 - 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.

19 - 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.

20 - The Panel will always:

- offer the applicant and the licensing authority an oral hearing;
- receive written representations from the applicant and the licensing authority;
- consider all evidence submitted to it, subject to the exception in paragraph 21 below; and
- write a report containing its findings which will be provided to the applicant and the licensing authority.

21 - The Panel will not consider previously undisclosed new data derived from scientific studies on the product in question. Under these circumstances, any hearing will be adjourned indefinitely and the review process suspended until such time as the marketing or other application is resubmitted, based on the new data, and has been considered afresh by the licensing authority.

Preparation for the independent review

22 - If an applicant wishes to request an independent review of a decision of the licensing authority in pursuance of the legislation above, it must give notice of its request in writing to the licensing authority within 28 days of the date of the decision notice or in the case of a proposed suspension, revocation or variation of a licence, no later than the date of the proposed suspension, revocation or variation. The applicant may apply in writing to the licensing authority for an extension of time for submission of a request of an independent review.

23 - For the avoidance of doubt, any application for a “person appointed” hearing or a review by the “Regulation of Medicines Review Panel” will be treated as an application for an independent review.

24 - Upon receiving the written request the licensing authority will inform the Secretariat of the Panel 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 the Secretariat of the Panel.

25 - The applicant and licensing authority will be notified that they have 3 months from the date of the request for an independent review to provide the Secretariat of the Panel with a written summary of the oral representations they intend to make at the review hearing, with copies of any documents upon which it is intended to rely in support of those representations. An extension of this time limit may be granted by the Panel, up to a maximum period of 6 months from the date of the request for an independent review.

26 - Additional written representations or documents may not be submitted by either party once the time limits stipulated above have expired, except with the permission of the Panel.

27 - If upon the expiry of 6 months from the date of the request for an independent review an applicant has failed to provide documentation in support of its request to be heard, the Panel may treat the request for an independent review as having been withdrawn by the applicant.

28 - 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 the witnesses to attend the full hearing.

29 - 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.

30 - The Panel may call for further information from either the applicant or licensing authority, either prior to or following the hearing.

31 - Unless otherwise specified by the Panel, the applicant and licensing authority need to provide the following information to the Secretariat of the Panel:

- All documentation in English or translated into English

- The names of any witnesses it is intended to call at the hearing, not less than 7 days prior to the hearing

- In the case of the applicant:

(i) all documentation from the application for marketing authorisation, clinical trials or other purpose, upon which it is proposed to rely at the hearing, and

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

- In the case of the licensing authority

(iii) the decision of the licensing authority

(iv) 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,

(v) copies of all relevant guidelines,

(vi) all documentation from the application for marketing authorisation, clinical trials or other purpose, upon which it is proposed to rely at the hearing, and

(vii) any other material in support of the licensing authority's case

- At least 10 hard copies of any supporting material, i.e. the information listed above as (i) to (vii), at least 10 working days before the date of the hearing
- One electronic copy of the above. These are to provided as a single indexed and paginated PDF document.
- The estimated time of any presentations if likely to last longer than 30 minutes, bearing in mind that the timetable for the hearing may under those circumstances need to be changed.

32 - 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.

33 - Further, in connection with manufacturing of medicinal products and wholesale dealing licences, the Panel may at the applicant's request, or with his consent, carry out an inspection of premises to which the licence relates. Reasonable notice will be given for any such inspection.

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

- Give at least 28 days' notice of the date, time and place of the hearing to the applicant and licensing authority

- Prepare a numbered and indexed bundle of all documents submitted for the hearing

- Send numbered and indexed bundles of documents to the applicant and the licensing authority at least 14 days before the date of the hearing.

- Ensure the Panel has indexed and numbered bundles, all the documentation submitted by the applicant and licensing authority and any other information relevant to the hearing such as site inspection information.

- Provide the applicant and the licensing authority with a template for exchanging any administrative information required by the Panel to conduct the review.

- Provide the names of the Panel members

Procedure at the hearing

35 - The Panel shall determine the procedure at the hearing.

36 - 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.

37 - The applicant and the licensing authority may appear themselves or be represented, call witnesses and address the Panel.

38 - The hearing shall be held in public if the applicant requests it.

39 - Other than that which is disclosed in the course of a public hearing, all hearing and independent review information shall, for reasons of commercial sensitivity, remain

confidential, subject to the application of the Freedom of Information Act 2000.

40 - The hearing will be recorded and transcripts provided to the applicant and licensing authority following the hearing.

41 - 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

42 - After the hearing the applicant and licensing authority will receive copies of the transcript and may correct errors and clarify any points they wish.

43 - 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.

44 - The Secretariat of the Panel will send copies of all post-hearing questions asked and replies received, to the applicant and licensing authority for their final written comments, if any.

45 - The Panel will write a report, which will include its findings, conclusions and any recommendations, with its reasons.

46 - The Panel will present its report to the licensing authority and provide a copy to the applicant. The licensing authority will then take the Panel's report into account and decide whether to confirm or alter its decision.

47 - If the hearing has been held in public, the report of the Panel will be published in full. An anonymised summary report containing all matters of public interest will be published on the Medicines and Healthcare Products Regulatory Agency website. (www.mhra.gov.uk)

Fees for a Regulation of Medicines Review Panel hearing

48 - The fee payable by an applicant who gives notice of a request for an independent review is £10,000, this being payable at the time the notice is given.

49 - 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

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

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

Review Panel Secretariat

51 - 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.

52 - Please note that the Secretariat makes requests for documentation and receives documentation from the applicant and licensing authority only as set out in this procedure.

53 - 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.

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

Contact details:

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