



London, 23 January 2007
Doc. Ref. SOP/H/3043

**COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE
(CHMP)**

**SOP ON HARMONISATION OF EUROPEAN BREAKPOINTS ANTIMICROBIAL
SUSCEPTIBILITY TESTING SET BY EMEA/CHMP AND EUCAST**

ADOPTION BY CHMP FOR RELEASE FOR CONSULTATION	22 January 2007
END OF CONSULTATION (DEADLINE FOR COMMENTS)	31 March 2007

Comments should be provided using this [template](#) to Bo.Aronsson@emea.europa.eu

Fax +44 20 7418 8613

The proposed SOP will replace current SOP/H/3043 Harmonisation of European Breakpoints set by EMEA/CHMP and EUCAST, first published 15/02/05.

Title: Harmonisation of European Breakpoints Antimicrobial Susceptibility Testing set by EMEA/CHMP and EUCAST		
CONSULTATION (PUBLIC)		Document no.: SOP/H/3043
Lead Author	Approver	Effective Date:
Name: Bo Aronsson	Name: Xavier Luria	Review Date:
Signature:	Signature:	Supersedes: SOP/H/3043 (14-FEB-05)
Date:	Date:	

1. Purpose

To describe the interaction between EMEA/CHMP and EUCAST in the process of setting harmonised European breakpoints for antimicrobial susceptibility testing.

2. Scope

This SOP applies to Product Team Leaders in the Human Pre-Authorisation Unit, (Co)Rapporteurs and Clinical/Non-Clinical Experts involved in the assessment of microbiological data and the setting of susceptibility breakpoints for antibacterial agents intended for systemic use. It also applies to relevant members of EUCAST. The feasibility of the procedure for individual applications depends on the agreement with the applicant (Annex 1).

This SOP primarily describes the procedure for new marketing authorisation applications. However, in principle it also applies to:

- Variations of existing marketing authorisations that might potentially impact on the information on breakpoints in the SPC - (e.g. extension of indications, new dosage recommendation) (see further annex 2).
- Revision of susceptibility test breakpoints during the post-authorisation period, should information come to light indicating that re-consideration might be appropriate.

3. Responsibilities

It is the responsibility of the EMEA and the EUCAST to ensure that this procedure is adhered to within their own remits. The responsibility for the execution of a particular part of this procedure is identified in the right-hand column in section **9. Procedure**.

4. Changes since last revision

In Section 2 – Scope - and Annex 2: inclusion of activities during the post-authorisation phase.
In Section 9 - Procedure: clarification in the process (steps 1, 4.3, 5, 8 and 9).

5. Documents needed for this SOP

Form on an “Agreement between EMEA and applicant to allow the EMEA expert information sharing during the EUCAST Steering Committee meeting” (Annex 1).

Public declaration of interest and confidentiality undertaking of EMEA scientific committees’ members and experts.

6. Related documents

“Clarifications on the EUCAST process” (Annex 2).

7. Definitions

BSAC - British Society for Antimicrobial Chemotherapy

CA-SFM - Comité de l'Antibiogramme de la Société Française de Microbiologie

CHMP - Committee for Medicinal Products for Human Use

CLSI (previously NCCLS) – Clinical Laboratory Standards Institute, USA

DIN - Deutsches Institute for Normung

DM&P - Document Management and Publishing

EFPIA - European Federation of Pharmaceutical Industries Associations

EMA - European Medicines Agency

EUCAST - European Committee on Antimicrobial Susceptibility Testing

ISO/CEN - International Organization for Standardization/European Committee for Standardization

MAA - Marketing Authorisation Application

MAH – Marketing Authorisation Holder

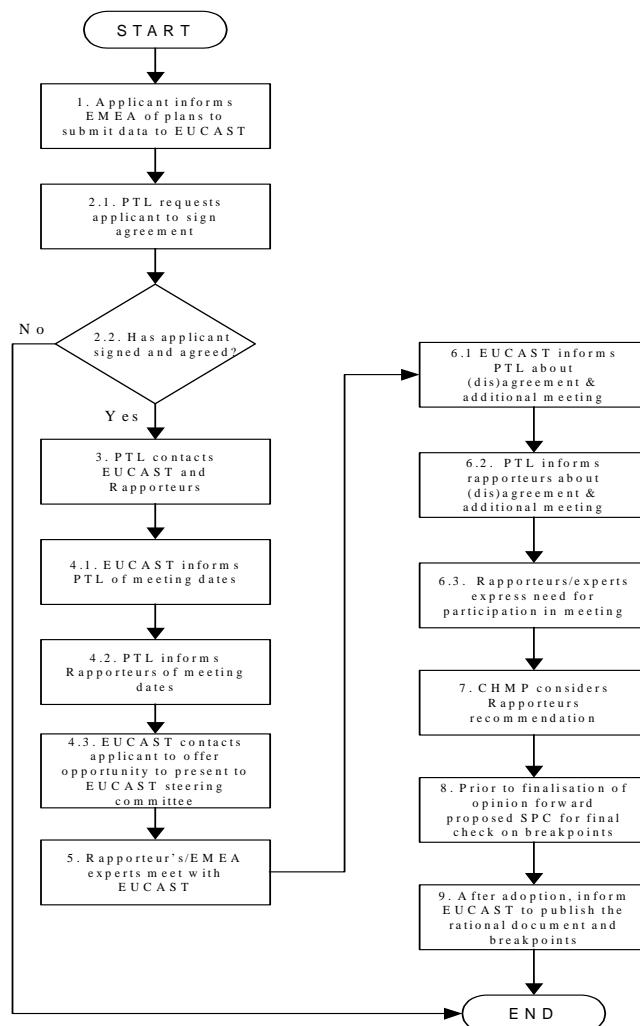
NCCLS (now CLSI) - National Committee on Clinical Laboratory Standards

PTL - Product Team Leader

SPC - Summary of Product Characteristics

SRGA - The Swedish Reference Group of Antibiotics

8. Process Map(s)/ Flow Chart(s)



9. Procedure

Step	Action	Responsibility
1.	<p>During pre-submission meeting at the EMEA or upon receipt of information on intention to submit a MAA:</p> <p>Ask applicant for any plans to submit data to EUCAST in relation with:</p> <ul style="list-style-type: none"> - The timing of the submission to EUCAST (at or before the marketing authorisation application). - Whether the content will be as defined by EUCAST (www.eucast.org) 	PTL
2.	During pre-submission meeting at the EMEA or at the time of receipt of the MAA:	
2.1	Fill in form (Annex 1) and request applicant to sign agreement between the EMEA and applicant to allow active participation of CHMP Rapporteur/Experts in EUCAST Steering Committee meetings thus enabling the possibility of discussing data from the CHMP assessment.	PTL
2.2	<p>If the agreement in step 2.1 is denied by the applicant, the process ends here.</p> <p>If the agreement is accepted by the applicant proceed to step 3.</p>	PTL
3.	<p>After agreement with the applicant on submission of data to both EMEA and EUCAST and planned date of submission and after a signature has been obtained on form (Annex 1):</p> <p>Contact the EUCAST chairman and scientific secretary (emails on the EUCAST web-site www.eucast.org) and CHMP appointed Rapporteurs and inform about agreement and planned submission date.</p>	PTL
4.	Upon confirmation of the EMEA/CHMP participation:	
4.1	Inform EMEA PTL about the meetings dates of the EUCAST Steering Committee.	EUCAST chairman
4.2	Inform the (Co) Rapporteurs about the dates.	PTL
4.3	<p>Upon receipt of the documentation, contact the applicant to offer opportunity to present the compound to the EUCAST Steering Committee (in the open part of the discussion).</p> <p>(All correspondence between EUCAST and applicant to be copied to PTL.)</p>	EUCAST chairman
5.	<p>Upon finalisation of the initial assessment (or during first clock stop in the centralised procedure in order to coincide with the scheduled EUCAST meetings):</p> <p>Meet with EUCAST Steering Committee:</p> <ul style="list-style-type: none"> - To present the status and issues raised during the initial review as regards possibly approvable indications and relevant pathogens (only the breakpoints for the pathogens relevant to the final list of indication(s) will be included in the SPC). - To discuss the data to reach a preliminary agreement on breakpoints. - To participate in the discussions with both EUCAST and the applicant, as appropriate 	Rapporteurs' experts and EMEA Expert

Step	Action	Responsibility
6.	Upon receipt of comments from National breakpoint committees to EUCAST, prior to Day 150 of the Centralised procedure	
6.1	Inform the EMEA PTL about: <ul style="list-style-type: none"> - European agreement or disagreement on breakpoints. - any planned additional EUCAST meeting with the applicant if this is considered to be necessary 	EUCAST chairman
6.2	Inform (Co) Rapporteurs about this agreement/disagreement and/or planned additional meeting.	PTL
6.3	(Co)Rapporteurs and EMEA experts to express the need for their participation in such an additional meeting.	(Co)Rapporteurs / CHMP experts and EMEA expert
7.	Upon receipt of final position from EUCAST, consider Rapporteurs' recommendation on breakpoints.	CHMP
8.	Prior to the finalisation of the Opinion, to communicate the proposed SPC to EUCAST for final check on the set breakpoints (within hours).	PTL
9	Once final Opinion has been adopted by CHMP, inform EUCAST in order for EUCAST to publish the rational document and breakpoints table on their website.	PTL

10. Records

Hardcopies of reports generated by this SOP will be archived in the Product Master File. The electronic versions will be saved in the relevant product folder in EDMS.

Annex 1

Agreement between the EMEA and the Applicant for the marketing authorisation for <product name> to allow the EMEA expert information sharing during the EUCAST Steering Committee meeting.

<Company name> hereby agrees that the EMEA expert is entitled to discuss any scientific issues related to the assessment of our product <product name> in the EUCAST Steering Committee meeting aimed at proposing tentative breakpoints for this antimicrobial agent. Therefore any scientific data that comes out of the regulatory assessment of the dossier can be brought forward by the EMEA expert and included in that discussion.

<Place>

<Date>

<Name and Signature of company representative>

Annex 2

Clarifications on the EUCAST process in association with Centralised Applications as agreed between EMEA/CHMP, EUCAST and EFPIA.

- For a centralised submission, bridging studies to the methods used by Member States (e.g. BSAC, CA-SFM, DIN or SRGA) will not be required.
- EUCAST will accept data generated with CLSI (previously NCCLS) methodology and/or in the future an agreed ISO/CEN methodology. However, it would be useful to consult/inform EUCAST prior to initiating the studies.
- The applicant may want to set provisional breakpoints before Phase III of the clinical development programme. It may be helpful for applicants to also consult with EUCAST at that time. If an applicant goes to EMEA/CHMP for scientific advice on provisional breakpoints and has already consulted with EUCAST, the CHMP would take the EUCAST response in to account in their advice.
- EUCAST will use the same form regarding conflict of interest (Declaration of Interest) that is used by EMEA/CHMP. This covers consultancies, limits for personal and institutional gain.
- Each of the steering committee members of EUCAST will sign a confidentiality agreement and the chairmen of national breakpoint committees will garner the signatures of their respective committee members at the soonest possibility (the ensuing national committee meeting).
- Any scientific issues raised by EUCAST during the review will be posed directly to the applicant and the applicant will respond directly to EUCAST. However, all communications between EUCAST and applicant will be copied to the EMEA PTL/CHMP Rapporteurs. The applicant will also be kept informed by the EMEA of any interaction between the EUCAST and the CHMP during the review.
- As will be agreed between the applicant and EUCAST, the applicant will be able to attend the EUCAST Steering Committee meeting(s) to present the data requesting a breakpoint.
- For any proposed changes to the product information in conjunction with, for example, variations to add one or more indication(s) or to amend the dose recommendations in any way the MAH should consider whether there could be a need to add new and/or amend existing breakpoint recommendations. It is recommended that the matter should be discussed between EUCAST and the MAH before filing such application for variation. Because of the limited procedural timing for assessing variation, EUCAST should be requested to consider new or revised breakpoints before filing. In this way the new breakpoints should be available before CHMP reaches an opinion.
- When a need to add/amend breakpoints is identified only during the assessment process, EUCAST should be notified as soon as possible with the aim of obtaining recommendations before the procedure is finalised. The arrangements between the MAH, Rapporteurs, EMEA/CHMP and EUCAST and the timeframes may have to be determined on a case-by-case basis.
- A proposal for a review of existing breakpoints may be triggered by the Rapporteurs, any CHMP member, the MAH or by EUCAST. For example, the request for review could be generated as a result of information provided in response to a follow-up measure or at any time when scientific data justify such an update.

- Even if a proposed new indication or new dose is not thought to have an impact on the breakpoints, EUCAST will be informed by the MAH and/or EMEA about the change since EUCAST's breakpoints rational document available on the EUCAST website might need to be updated.
- At least at the time of renewal, EUCAST could be consulted to see if it is considered that there could be a need for revision.