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NOTE FOR GUIDANCE ON THE INCLUSION OF APPENDICES TO CLINICAL STUDY REPORTS IN MARKETING AUTHORISATION APPLICATIONS

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NOTE FOR GUIDANCE ON THE INCLUSION OF APPENDICES TO CLINICAL STUDY REPORTS IN MARKETING AUTHORISATION APPLICATIONS

This note for guidance provides clarification on which appendices to clinical study reports should be systematically included in Marketing Authorisation Applications and which may be made available on request of the competent authorities.

1. INTRODUCTION

The Note for Guidance on Structure and Content of Clinical Study Reports (CPMP/ICH/137/95), describes in section 16 the appendices to a clinical study report. The Directive 2001/83/EC in Annex I section 5.2(e) sets out that: *"The particulars of clinical trials referred to above shall be forwarded to the competent authorities. However, in agreement with the competent authorities, the applicant may omit part of this information. Complete documentation shall be provided forthwith upon request."*

It is indicated in CPMP/ICH/137/95, that in writing the clinical study report a modular approach should be taken, i.e. that the report should consist of a core report, giving the necessary information to assess the results of the trial and of the appendices, containing additional information. The list of appendices includes a lot of information that may not be necessary for evaluation on a routine basis. Certain of the appendices should be submitted systematically with each report and others should be available on request. In order to provide a default guidance and "agreement with the competent authorities" the following list has been established, as the minimum required. This list should be supplemented where appropriate according to the nature of the study, indication and product; if there is a doubt these cases should be discussed with the competent authority (ies). They may be provided on paper or CD-ROM or both.

A copy of the complete report, including all appendices, should be available on request at the time of the application. When requested, the appendices should be provided to the authorities within 48 hours. The appendices, which are not listed below, should be set up in such a way, that they could be separated from the main report without impairment of the understanding of the report.

2. INCLUSION OF APPENDICES IN CLINICAL STUDY REPORTS SUBMITTED IN MARKETING AUTHORISATION APPLICATIONS

The following appendices are those that are required to be submitted, in the initial application dossier with each clinical study report. The numbering and text are taken from the Note for Guidance (CPMP/ICH/137/95) and clarification added in italics where applicable:

16.1 Study Information

16.1.1 Protocol and protocol amendments

16.1.2 Sample case report form (unique pages only) *(including sample patient diary card or equivalent data collection tools).*

16.1.3 List of IECs or IRBs – representative written information for patient and sample consent forms (*the written information for patient and sample consent forms can be the template developed for the study and need not be those from individual sites)*

16.1.4 List and description of investigators and other important participants in the study *(including e.g. CROs, central laboratories etc if not listed elsewhere in the report such as in*

*the text under section "6 Investigators and study administrative structure or section "9.6 Data Quality Assurance". The manufacturer of the investigational medicinal product should be indicated in section "9.4 Treatment".)**

16.1.5 Signatures of principal or coordinating investigator(s)

16.1.7 Randomisation scheme and codes (patient identification and treatment assigned)

16.1.8 Audit certificates (if available)

16.1.9 Documentation of statistical methods *(if not provided in the body of the report)*

16.1.10 Documentation of inter-laboratory standardisation methods and quality assurance procedures if used *(for pivotal studies where these represent study end-points and otherwise on request)*

16.1.11 Publications based on the study

16.1.12 Important publications referenced in the report*(s) (this can be once per dossier where the same publications are referenced in multiple clinical study reports (CTD 5.3.7)*

16.2 Patient Data Listings

16.2.2 Protocol Deviations

16.2.7 Adverse event listings (each patient) *(All SAEs, all AEs on request)*

16.3 Case Report Forms

16.3.1 The narrative texts in section 12.3.2 should include information on deaths and withdrawals due to serious adverse events. CIOMS reports (or equivalent) and CRFs should be available on request.

*There should be a clear tabulation provided, by investigator site of the number of patients recruited by each site, including a listing of the patient study numbers/codes enrolled at each site. This tabulation should enable the name and address of each investigator and the number of patients recruited by each site to be clearly linked. This may, for instance, be in 16.1.4 or in the body of the report most usually in section "10. Study patients".