

ANNEX I

APPLICATION DOSSIER FOR THE INITIAL APPLICATION
G. INVESTIGATIONAL MEDICINAL PRODUCT DOSSIER (IMPD)1.1. **Data relating to the investigational medicinal product***Introduction*

37. Regarding data, the IMPD may be replaced by other documentation which may be submitted alone or with a simplified IMPD. The details of this 'simplified IMPD' are set out in section 1.2 'Simplified IMPD by referring to other documentation'.
38. Each section of the IMPD shall be prefaced with a detailed table of contents and a glossary of terms.
39. The information in the IMPD shall be concise. The IMPD must not be unnecessarily voluminous. It is preferable to present data in tabular form accompanied by a brief narrative highlighting the main salient points.

Quality data

40. Quality data shall be submitted in a logical structure such as that of Module 3 of the ICH Common Technical Document format.

Non-clinical pharmacology and toxicology data

41. The IMPD shall also contain summaries of non-clinical pharmacology and toxicology data for any investigational medicinal product used in the clinical trial in accordance with international guidance. It shall contain a reference list of studies conducted and appropriate literature references. Wherever appropriate, it is preferable to present data in tabular form accompanied by a brief narrative highlighting the main salient points. The summaries of the studies conducted shall allow an assessment of the adequacy of the study and whether the study has been conducted according to an acceptable protocol.
42. Non-clinical pharmacology and toxicology data shall be submitted in a logical structure, such as that of Module 4 of the ICH Common Technical Document format.
43. The IMPD shall provide a critical analysis of the data, including justification for omissions of data, and an assessment of the safety of the product in the context of the proposed clinical trial rather than a mere factual summary of the studies conducted.
44. The IMPD shall contain a statement of the good laboratory practice status or equivalent standards, as referred to in Article 25(3).
45. The test material used in toxicity studies shall be representative of that of the clinical trial use in terms of qualitative and quantitative impurity profiles. The preparation of the test material shall be subject to the controls necessary to ensure this and thus support the validity of the study.

Data from previous clinical trials and human experience

46. Data from previous clinical trials and human experience shall be submitted in a logical structure, such as that of Module 5 of the ICH Common Technical Document format.
47. This section shall provide summaries of all available data from previous clinical trials and human experience with the investigational medicinal products.

It shall also contain a statement of the compliance with good clinical practice of those previous clinical trials, as well as a reference to the public entry referred to in Article 25(6).

Overall risk and benefit assessment

48. This section shall provide a brief integrated summary that critically analyses the non-clinical and clinical data in relation to the potential risks and benefits of the investigational medicinal product in the proposed clinical trial unless this information is already provided in the protocol. In the latter case, it shall cross-refer to the relevant section in the protocol. The text shall identify any studies that were terminated prematurely and discuss the reasons. Any evaluation of foreseeable risks and anticipated benefits for studies on minors or incapacitated adults shall take account of the specific provisions set out in this Regulation.
49. Where appropriate, safety margins shall be discussed in terms of relative systemic exposure to the investigational medicinal product, preferably based on 'area under the curve' (AUC) data, or peak concentration (C_{\max}) data, whichever is considered more relevant, rather than in terms of applied dose. The clinical relevance of any findings in the non-clinical and clinical studies along with any recommendations for further monitoring of effects and safety in the clinical trials shall also be discussed.