

## ANNEX I

### APPLICATION DOSSIER FOR THE INITIAL APPLICATION

#### E. INVESTIGATOR'S BROCHURE (IB)

25. An IB, which has been prepared in accordance with the state of scientific knowledge and international guidance, shall be submitted.
26. The purpose of the IB is to provide the investigators and others involved in the clinical trial with information to facilitate their understanding of the rationale for, and their compliance with, key features of the protocol, such as the dose, dose frequency/interval, methods of administration, and safety monitoring procedures.
27. The information in the IB shall be presented in a concise, simple, objective, balanced and non-promotional form that enables a clinician or investigator to understand it and make an unbiased risk-benefit assessment of the appropriateness of the proposed clinical trial. It shall be prepared from all available information and evidence that supports the rationale for the proposed clinical trial and the safe use of the investigational medicinal product in the clinical trial and be presented in the form of summaries.
28. If the investigational medicinal product is authorised, and is used in accordance with the terms of the marketing authorisation, the approved summary of product characteristics (SmPC) shall be the IB. If the conditions of use in the clinical trial differ from those authorised, the SmPC shall be supplemented with a summary of relevant non-clinical and clinical data that support the use of the investigational medicinal product in the clinical trial. Where the investigational medicinal product is identified in the protocol only by its active substance, the sponsor shall select one SmPC as equivalent to the IB for all medicinal products that contain that active substance and are used at any clinical trial site.
29. For a multinational clinical trial where the medicinal product to be used in each Member State concerned is authorised at national level, and the SmPC varies among Member States concerned, the sponsor shall choose one SmPC for the whole clinical trial. This SmPC shall be the one best suited to ensure patient safety.
30. If the IB is not an SmPC, it shall contain a clearly identifiable section called the 'Reference Safety Information' (RSI). In accordance with paragraphs 10 and 11 of Annex III, the RSI shall contain product information on the investigational medicinal product and on how to determine what adverse reactions are to be considered as expected adverse reactions, and on the frequency and nature of those adverse reactions.

**Changes to legislation:**

There are currently no known outstanding effects for the Regulation (EU) No 536/2014 of the European Parliament and of the Council, Division E..