Appendix III: Guidelines for Good Clinical Practices

Sponsor's role (possibly delegated to a subcontractor under the sponsor's responsibility)

- Regulatory obligations for the start-up, conduct and completion of a study;
- Preparation of documents (investigator's brochure, protocol, patient information and consent, case report forms, final report):
- Study medication;
- Monitoring of investigators;
- Data management;
- Management of adverse events;
- Filing and archiving;
- Systems audit and audit of data.

Investigator's role, clinical and functional investigation laboratory's role

- Sufficient availability;
- Expertise;
- Knowledge (of the study medication, protocol, main prerequisites);
- Sufficient, competent and well-informed team;
- Available equipment, satisfactory maintenance;
- Acceptance of monitoring;
- Acceptance of an audit and inspection;
- Proper storage of the study medication;
- Medical-record keeping for each patient
- Collection of consent;
- Compliance with the protocol;
- Monitoring of treatment.

Ethics committee or committee for the protection of persons

- Independence;
- Composition;
- Initial and continuing examination;
- Content of this written opinion;
- Members of the committee who took part.

International Conference on Harmonisation

Harmonisation of a certain number of European, US and Japanese rules has been formalized in the setting of the International Conference on Harmonisation. The texts produced in this setting, the rules of "good clinical practices" include the following:

- First, the protection of persons who are subjects in studies, generally summarized in national laws and thus becoming obligations;
- Second, recommendations relating to the quality of data and the credibility of conclusions that can be drawn from them: a breach of these conditions can result in the refusal to consider the results of an official dossier, in particular, for registration of a new (drug) treatment or a new modality for use of a treatment:
- The sponsor (manufacturer, licensee, "co-developer", contract research organization or even a sponsor-investigator);

- The clinical investigator, his team and clinical and functional investigation laboratories;
- The ethics committee or Institutional Review Board (IRB).

The consensus texts adopted by the International Conferences on Harmonisation (ICH) are important to take into account even outside of the setting for which they have been adopted (drug registration dossiers) in particular: minimal pre-clinical studies, especially on toxicology, necessary to ensure patient safety, the statistical principles to be complied with and writing the final report.

European Union

In the European Union, the directive involving "approximation of the laws, regulatory and administrative provisions of the Member States relative to the implementation of good clinical practices in the conduct of clinical trials on medicinal products for human use" harmonizes the level of requirement of Member States, while leaving to the latter the care to define its modalities of application (national languages, contacts, forms to use, etc.), and in certain cases to adopt additional measures of protection (In particular: oral consent in the presence of a witness for participating subjects unable to write, the dividing up of certain items to submit either to the ethics committee, or to the regulatory authority, modalities for formulation of the ethics committee's opinion, possible exceptions to supplying study products free of cost).

Thus transposition of this directive into national law in the Member-States reveals a certain number of differences, since it must take into account national specific components: systems of legislation, sensitivities, working methods and the organization of health-care systems.

USA

In the USA, for all trials subject to regulations of the Food and Drug Administration (FDA), it is necessary to apply the rules on the protection of persons, including informed consent, and submission to an Ethics Committee or Institutional Review Board (IRB). Furthermore, if the trial involves a new product or a new indication, an exemption for unapproved use (Investigational New Drug Exemption) must be obtained after submission of a file of pre-requisites. Such authorization confers the following obligations on the sponsor: choosing qualified investigators who are not banned from clinical trials, proper monitoring of them, use of investigational products in their facilities only, reporting of serious adverse events, information provided to the FDA of any significant risk, and of any investigator who does not comply with requirements, periodic reports, and archiving. Certain obligations are negotiable – beforehand only – to obtain a waiver. In the event of a hazard or doubt on proper conduct of the study, the latter can be temporarily subject to a clinical hold or even termination. The investigator agrees in writing (form 1572) to comply with the rules on the protection of persons participating in the trial, to monitor use of the studied medications, to collect adequate and correct data on the subjects in the trial, and to submit the project and its amendments to the ethics committee or IRB.