ACCREDITATION OF PHASE I UNITS AND PROTECTION OF THE SUBJECTS PARTICIPATING IN CLINICAL TRIALS IN FRANCE

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REGULATION OF CLINICAL TRIALS IN FRANCE

- HURIET - SERUSCLAT LAW 1988 covers:
  - Accreditation of CPU
  - Protection of the subjects participating in clinical trials (volunteers national file)
  - Process to be followed to initiate a study (Afssaps information and CPPRB review & consultative approval)

- PUBLIC HEALTH LAW, MAR 2006 & APPLICATION DECREE 26 AUG 2006
  - Main changes
    - Authorization of clinical trials by AFSSAPS
    - & mandatory Approval by CPP (Committee for the protection of person)
    - Accreditation revisited
→ Biomedical Research with and without therapeutic benefit
→ Mandatory supervision of a physician (MD) with an appropriate experience. Investigator should be a medical doctor.
→ Authorization of clinical pharmacology sites in which trials are conducted with special attention to subject’s safety
→ Scientific value: pre-clinical prerequisites, benefit-risk ratio, reference to GCP, GMP like procedures
→ Protection of the subjects participating in the research, with special attention to patients in emergency care, children, incapacitated adults
→ Mandatory insurance to guarantee the sponsor’s liability
→ Possible inspections by AFSSAPS
Since 1988 in France=> accreditation/authorisation of Phase I units

Inspection by a physician and a pharmacist representing the Health Authority in the Region:

→ Accreditation for 5 years which may be withdrawn

→ If authorisation not used (no study conducted) within one year => is cancelled
Contract with an intensive care and emergency unit near the accredited place is mandatory. However, no requirement for the Clinical Pharmacology Unit (CPU) to be in a hospital.

Contract with a (clinical) pharmacologist

Need to ensure archiving and confidentiality of data

Need for a Quality assurance system
AUTHORISATION REQUIREMENTS: STAFF

- Qualification of staff
- Appropriate training (SOPs and protocol-specific)
- Mandatory supervision of a physician (MD) with an appropriate experience. Investigator should be a medical doctor.
- Manufacturing authorization granted for packaging and labeling provided the site has a pharmacist with at least 1 year of experience.
AUTHORISATION REQUIREMENTS: STAFF

- Appropriate medical and paramedical supervision of the subjects throughout the study
- **24 hours medical supervision** (with paramedical staff during night if needed) when subjects are hospitalised in the unit
- For outpatient study, need to provide a (mobile) phone number of an on-duty physician available 24 hours a day for emergencies or SAE or any question.
- Clinical facilities allowing supervision of hospitalised subjects (wards with central control area and/or video surveillance system ..)

- Monitoring (vital signs & ECG) and resuscitation equipment (defibrillator, O2 ...) allowing emergency treatment if needed

- Emergency trolleys whose content & equipment validated by an emergency physician

- Mandatory maintenance
AUTHORISATION REQUIREMENTS: EMERGENCY

- Mandatory contract with an emergency/ intensive care unit close to the facility to allow immediate transfer of the subject if necessary. Transfer training may be planned. Mandatory information of the emergency/ resuscitation unit of the protocols (summary, dates etc).
- Emergency training of CPU medical & paramedical staff
- Antidotes, if available, in emergency trolleys.
- SOP or SPI to deal with risk-benefit and expected AEs or SAEs of protocols as well as instructions in the protocol about these risks and their management.
Supplying, packaging and labelling operations of investigational medicinal products (IMP) and the corresponding storage operations are carried out by a site pharmacist.

Release of IMP by the pharmacist of the Phase I unit is not necessary. No need for a QP in the Phase 1 unit.

The QP of the pharmaceutical company must not certify the activities conducted by the Phase I unit pharmacist.
Possibility for Phase I unit pharmacist to order the comparative/reference drugs if not provided by the sponsor

Pharmacy accreditation is for all the experimental drugs used in studies as well as reference products and other products necessary for the research

Type of studies

→ First Administration in human (Dose Escalation)
→ Drug-Drug Interaction
→ Bioequivalence
- **National Volunteers Database** managed by the Health Authority through secure Internet line
- Contains exclusion period (to be defined by the investigator for each protocol) and indemnity earned in the previous year
- Prevents concomitant or close participation in several clinical trials
- Allows check maximal indemnity per year (4500 €).
- Prevents volunteer professionalism
CONCLUSION

- Phase 1 Clinical Pharmacology Units are accredited in France since 20 years.
- This regulation did not produce detrimental effects on Phase 1 business in France. It increased CROs’ professionalism and standardized/improved subjects safety.
- Subjects safety recently reinforced by EMEA/CHMP Guideline on Strategies to Identify and Mitigate Risks for First-in-human Clinical Trials with Investigational Medicinal Products (Jul 2007) issued after the Te Genero case.