



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



HURIET-SERUSCLAT LAW ON BIOMEDICAL RESEARCH: GENERAL PRINCIPLES

- 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



ACCREDITATION OF PHASE I UNITS IN FRANCE

- 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 - Accreditation for 5 years which may be withdrawn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



AUTHORISATION REQUIREMENTS

- 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.



AUTHORISATION REQUIREMENTS : CPU

- 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. Transfert 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.



ACCREDITATION FOR PHARMACEUTICAL OPERATIONS

- 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



PHARMACIST IN ACCREDITED SITES

- 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 FILE USED BY ACCREDITED PHASE 1 UNITS

- **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 produced 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 caze.