France

**Question 1:** What laws or regulations apply to an application for conducting a clinical trial in France?

Code de santé publique, but different regulations according to the scope of the research. Loi 2004-806 du 09 août 2004, relative à la politique de santé publique. (The purpose of this particular review was to implement Directive 2001/20/EC).

Article L1121-1 of the law 2004-806 of August 9, 2004 defines the scope of the law as all biomedical research involving human beings, with the aim of increasing biological or medical knowledge. This law covers trials about medicines around all biomedical researches. It states an exception: when products are used in the usual way, without any supplementary diagnostic or surveillant measure, or when research aims at evaluating current clinical practice.

Decree of 26 April 2006.
Decision of 24 November 2006.

Law 78-17 of 1978, modified in relation to computer science, to databases and to data collection.

**Question 2:** Which government, legal or authoritative body or bodies is or are responsible for the establishment and/or accreditation of (research) ethics committees for IMPs, and for their supervision and quality? Are there different (research) ethics committees reviewing other projects?

The competent regional research ethics committees (CPPs) replace CCPPRBs.

The French Ministry of Health is responsible for the agreement of CPPs which nevertheless still remain independent committees. They have the task of evaluating biomedical protocols.
The process for evaluation of REC (CPP) is in progress. Biomedical research which are not concerned by the law 2004-806 don't need to be submitted to ethics committees.

Epidemiological studies are not considered as research studies, and are not covered by the law. They are covered by the law on bio-ethics and by the law 78-17 concerning databases and their exploitation.

Genetic studies are covered by the bioethics law of August 2004, with an important role of the newly created “Agence de biomédecine”.

There are no other RECs reviewing other projects.

**Question 3:** What is the process for achieving clinical trial authorisation from the competent authority in France?

**Question 4:** What is the process for obtaining ethical review of a clinical trial protocol by a competent (research) ethics committee in France?

*NB For France these two questions are most appropriately answered together.*

Clinical trial sponsors have to submit their protocols both to the competent regional ethics committee (CPP), and to the competent authority. These submissions can be either simultaneous or one after the other.

The authorisation to conduct a trial requires both the E.C. (CPP) approval and the competent authority authorization.

No clinical trial will ever start without a CPP approval. This committee evaluates the different parts of the protocol, in line with the requirements set out in the Directive. The CPP sends its written and argued advice within 35 days to the sponsor. This advice is also sent for information to the competent authority.

The CPP has 35 days from the reception of the protocol to give a written argued advice. Lack of advice after the deadline is considered as a refusal. If the CPP needs more information about the research, it can ask the sponsor only on time, the delay for advice sis 60 days.

The competent authority acknowledges receipt of the protocol and informs the sponsor of the date after which in the absence of any remark, the trial can begin (silent approval).

The competent authority is allowed to ask sponsors additional information or to have reservations. These questions are transmitted to the CPP.

The EFGCP Report on
The Procedure for the Ethical Review of Protocols for Clinical Research Projects in Europe
(Update: May 2011)

The French licensing authority is the Agence Française de Sécurité Sanitaire des Produits de Santé. Its website is at http://www.afssaps.fr.

**Question 5:** Is there a single organisation to which to apply for ethical review of a clinical trial for an investigational medicinal product, regardless of whether this is for a single site or multiple sites?

No.

**Question 6:** What is the website for the organisation that issues guidelines on the ethical review of a clinical trial for an investigational medicinal product?

The most useful website is at http://www.recherche-biomedicale.sante.gouv.fr.

**Question 7:** Is there a procedural interaction between the national or local competent authority and the (research) ethics committee during the approval process?

Yes but only to exchange information.

Interactions between the competent authority and the research ethics committee are constant during the approval procedure as the competent authority sends a copy to the CPP of all their questions and reservations.

**Question 8:** Does the application to the REC and to the competent authority have to be submitted in parallel, or, if not, in which order?

In parallel generally, if not, it is first to REC and then to CA.

**Question 9:** How many (research) ethics committees are there in France?

40 CPPs.

**Question 10:** How are RECs funded in France? Do they charge fees? If yes, what is their scale of fees?

The Ministry of Health offers allocations to the committees in relation to their activity.
**Question 11:** Who is responsible for submitting the request for ethical review to the competent (research) ethics committee for single-site and for multi-site clinical trials?

The sponsor.

**Question 12:** How is a “single opinion” achieved for multi-site studies?

The sponsor chooses a national coordinating investigator and then submits the protocol to a CPP of they investigator’s region: the advice of the CPP is valid for all sites.

**Question 13:** How many members serve on a REC?

28 members (14 occupants, 14 deputies).

**Question 14:** How many members constitute a quorum?

7.

**Question 15:** How are REC members appointed?

Members are appointed in each region by the prefect after spontaneous candidature.

**Question 16:** How is the independence of members ensured?

There is no control system but members have to declare their conflicts of interests.

**Question 17:** How are conflicts of interest of REC members avoided?

They have to make the declaration.

**Question 18:** What backgrounds and/or qualifications of members are actively sought?

There are 28 members per CPP divided into 2 colleges:

**College 1**

4 persons with qualification and great experience with biomedical research. Among these 4 persons: 2 or more must be medical doctors and one has to be well-versed in biostatistics or in epidemiology,
- 1 general practitioner,
- 1 hospital pharmacist and
- 1 Nurse
College 2

- 1 ethicist.
- 1 psychologist.
- 1 social worker.
- 2 lawyers.
- 2 representatives of patients associations.

No particular background in ethics is required. Half of the members of the committee mustn't belong to the biomedical research domain.

**Question 19: How do RECs obtain specialist expertise?**

Research ethics committees ask the advice of outside experts and specialists for paediatrics and for trials involving incapable adults. There is a national list of experts (members of the 40 CPP).

**Question 20: What are the training requirements for members of RECs?**

Training is not compulsory.

**Question 21: What training programmes are available for REC members in France?**

There is a national conference of the CPP’s which gives training during an annual meeting and workshops.

**Question 22: What are the timelines for the assessment of single- and multi-site studies?**

5 weeks.

**Question 23: How are substantial amendments submitted during the review process dealt with?**

In the same way as the original protocol.

**Question 24: How does a REC assess the suitability of investigators and of sites?**

- On the basis of the curriculum vitae of the investigators (physician, medical qualification, clinical research suitability, publication).
- On the basis of a specific document describing sites.
Question 25: How are the requirements for (research) ethics committees to review the contractual or financial arrangements in clinical trials for both investigators and hospitals handled?

At this moment, the research ethics committees do not look at these aspects.

Question 26: How are the requirements for (research) ethics committees to review the compensation arrangements for study subjects handled?

There is no uniform system but a subject cannot receive more than 4500 € for year. All persons included in clinical trials can be paid according to constraints, respected by the REC.

Question 27: Is there an ongoing quality assurance process (e.g. audits, inspections, internal SOP) for (research) ethics committees in France?

No.

Question 28: Is there an appeal mechanism?

Yes. This appeal can be done within 15 days after the first negative advice once only. The protocol is then submitted to another REC, the French Ministry of Health chooses the second REC.

Question 29: How do RECs deal with SUSAR reports and Annual Safety Reports?

RECs must be informed by the sponsor of every SUSAR in France, and by six-monthly report for other SUSAR. The Annual Safety Reports are examined by the REC.

Question 30: How are ‘substantial amendments’ defined?

Substantial amendments are defined as amendments that modify significantly any aspect of the research. Some of them concern only the REC or the CA or both.

Question 31: What are the indemnity insurance requirements for research projects?

Variable.

Question 32: What are the indemnity insurance requirements for (research) ethics committee members themselves?

These are not specified.
Question 33: How is informed consent obtained from vulnerable subjects who are potentially to be involved in a clinical trial?

There are specific dispositions for each category of vulnerable subjects.

Consent by the legal representative.

Question 34: How do RECs assess the progress and outcome of research projects that they have approved?

The REC must be informed by the sponsor at the beginning and at the end of the research. A summary of final report must be send to the REC and to the competent authority.

Question 35: How does the REC ensure reception of the Annual Safety Report and the Summary of the Final Report of a research project that it has approved?

Not yet defined.

Question 36: Do national regulations in France allow research on healthy volunteer children (subjects under 16)?

Yes.

Question 37: Do national regulations in France allow payment, (other than expenses), to children taking part in research?

No.

Question 38: Do RECs invite or allow a) applicants or b) observers to attend committee meetings?

The ethics committee meetings are generally closed but the chairman of the committee can invite a sponsor with investigator or not, for more information about a clinical trial or to respond to any questions of the reviewers. The sponsor can ask also to be received.

Question 39: Are the minutes of (research) ethics committee meetings made public?

The minutes are not public. The decisions are sent to the sponsor and competent authority. The negative decisions are sent to all French RECs.
**Question 40:** Is there any scope for Chairman’s actions in between meetings?

The actions of the chairman, the vice-chairman, and the secretary are specified.

**Question 41:** Do (research) ethics committees ever appoint subcommittees for any specific purpose?

No. Sometimes there is a sub-committee between two monthly plenary meetings for final opinion deadline.

**Question 42:** Is there a national policy on the registration of clinical trials before they start?

Yes, the public list of clinical trials on medicinal products, managed by AFSSAPS

**Question 43:** If the answer to Question 42 is ‘yes’, do (research) ethics committees have any role to play in reviewing such registration?

No.

**Question 44:** If the answer to Question 42 is ‘yes’, is this register of clinical trials made available to the public?


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