Belgium

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


There have also been three Royal Decrees about the application of the law.

All these documents and some other information can be found on the website of the Federal Agency for Medicines and Health Products (FAMHP) (www.fagg-afmps.be): go to “medicines”, then to “human use”, then to “research and development”.

There is also a regulation on medical devices which is the transposition of the European Directive.

No other legislation is involved for other clinical research projects.
**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 Royal Decree of 27 September 1994 made RECs compulsory for every hospital or group of hospitals. This law also defined the RECs aims, composition & function, closely following the code of deontology of the “Ordre des Médecins”.

On 7 May 2004 the Law relating to Experimentation on Humans came into force, which for the first time endows RECs with a legal status. It covers all types of medical experimentation, not just clinical trials. Up until September 1 2006 (in fact until December 31 2006), the ethics committees of all hospitals could evaluate protocols of experiments in humans.

At this moment, only fully recognised ethics committees can give a single opinion. 38 ethics committees have this complete recognition until the 31st of March, 2012.

Only ethics committees having given:

1. At least 20 opinions on protocols of multicentre experiments on average per year.
2. At least 5 single advices for experiments on average per year.

have the full recognition. The recognition has a validity of 3 years, and is based on the average of 3 years.

Only these 38 fully recognized committees can give the single opinion in multicentre studies and in single centre studies. The other hospital committees (approximately 170 committees) can give a local advice for multicentre studies, in which they evaluate the competence of the local investigator, the infrastructure of the research site and the informed consent documents.

Within the 38 recognised committees, some have priority and should give the single advice if they participate: those of the 7 university hospitals; for oncology trials also by the ethics committee of the Bordet Institute for Cancer; and for paediatric trials also by the Reine Fabiola Paediatric Hospital.

The list of the committees fully recognized from April 1, 2009 on (based on their activity in 2006-2007-2008) is available on the above mentioned website of the Medicines Agency.

Apart from the hospital committees, the responsible minister can recognize a few other committees, mainly those of medical schools and those of the two scientific organizations (French speaking and Flemish speaking) of general practitioners: they do not have at this moment the full recognition mentioned above.
There is also a central Consultative Committee for Bioethics, officially installed in 1996, which formulates opinion & informs the public, acting only on a consultative basis, and not involved in the evaluation of clinical trial protocols.

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

The sponsor submits the application to the competent authority (the Federal Agency for Medicines and Health Products: FAMHP). The authority has in principle 28 days (with the possibility of one clock-stop of maximum one month for questions), 15 (fifteen) days for phase 1 trials. The approval by the competent authority is a silent one: if there is no answer within the 28 days, the experiment can start. The website for the authority is at www.fagg-afmps.be.

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

The investigator submits the application to the ethics committee(s) of the research sites, which has (have) in principle 28 days to respond (with the possibility of one clock-stop for questions), 15 (fifteen) days for phase 1 trials. The ethics committee has to give a written reply. See item 2 for the choice of the ethics committee.

**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?

There is no single website that provides this information.

The website of the Federal Agency for Medicines and Health Products (which is the competent authority for Belgium) is at www.fagg-afmps.be.

The website of the Consultative Committee for Bioethics is at http://www.health.fgov.be/bioeth/.
**Question 7:** Is there a procedural interaction between the national or local competent authority and the (research) ethics committee during the approval process?

No, except that the research ethics committee has to send a copy of its letter to the investigator with the decision (with approval or not) to the minister.

**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?

This is not defined. The trial cannot start until both instances have given a positive reaction.

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

There are currently about 215 committees. The majority are associated with hospitals and some are associated with non-hospital institutions. Until the 31st of March 2012, 38 of these research ethics committees have the full recognition. See item 2.

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

RECs charge fees for trials with a commercial sponsor as follows:

1. For interventional studies:
   - *Initial evaluation:* single opinion committee €1000; other committees €300 (local advice only).
   - *Amendments:* €250 to the ethics committee that gave the single advice.

2. For non-interventional studies:
   - *Initial evaluation:* single opinion committee €400; other committees €100 (local advice only).
   - *Amendments:* €100 to the ethics committee that gave the single advice.

The fees are fixed by the Royal Decree of July 15, 2004, but they are subject to an indexation each year. Correct fees can be found on the Agency’s website. The committees do not charge fees for academic (non-commercial) trials.

Moreover, the committees receive each year a certain amount of money from the competent authority (which has a direct fee of €2850 for initial dossiers and €250 for amendments): indeed, 75 % of the fees paid by commercial sponsors to the competent authority, should be redistributed to the ethics committees. This redistribution is done on the basis of the number of trial protocols evaluated by each committee.
**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 principal / coordinating investigator for the trial submits the single application for ethical review. This applies to both single-site and multi-site trials.

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

The single opinion is given by one of the above mentioned ethics committees: the choice is that of the investigator, but there are some restrictions (priority for certain ethics committees – see point 2).

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

8 to 15.

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

This is defined in the procedures of individual research ethics committees.

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

They are appointed by the direction of the hospital to which the committee is attached or by the direction of the non-hospital organisation to which a committee is attached.

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

The only regulatory measure is that the director of the hospital, the chief physician and the chief of the nursing department of the hospital to which the research ethics committee is attached, cannot be members of the committee.

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

The regulations state that the committees should send in a declaration of possible conflicts of interests for each member, and that members should state possible conflicts of interests for particular dossiers. Until now, no further specifications are available.

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

The regulations state that at least half of the members should be physicians; the presence of at least one physician not attached to the hospital, one lawyer, and one member of the nursing staff is required. Committees can, however, decide to include an ethicist, a member of the public etc.
**Question 19:** How do RECs obtain specialist expertise?

See Question 18. Additionally, the law states that in case of experiments with children, experiments with incompetent adults and experiments in emergency situations, at least two specialists in the respective matter should be consulted: either they are members of the committee, or outside experts.

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

None are laid down.

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

There are none.

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

15 calendar days for phase 1 studies, 28 days for other studies. One clock-stop for questions to the investigator is allowed. There are exceptions for protocols with GMO’s, biotech drugs, etc.

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

By the investigator to the research ethics committee; for a multicentre trial only to the single opinion committee.

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

This has not been defined.

**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?

This has not been defined.

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

This has not been defined.
Question 27: Is there an ongoing quality assurance process (e.g. audits, inspections, internal SOP) for (research) ethics committees in Belgium?

No.

Question 28: Is there an appeal mechanism?

No.

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

In a very disparate way and attempts are made to harmonize this.

Question 30: How are ‘substantial amendments’ defined?

As in the European guidance documents. No other definitions are specified.

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

A no-fault insurance is required.

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

This is covered by the insurance contract of the hospital or other organization to which the committee is attached.

Question 33: How is informed consent obtained from vulnerable subjects who are potentially to be involved in a clinical trial?

The regulations state that in trials with children, with incompetent adults and in emergency situations consent is given by the legal representative.

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

This is not yet known.

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?

This is not defined
**Question 36:** Do national regulations in Belgium allow research on healthy volunteer children (subjects under 16)?

Yes, this is described in the Law.

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

No payment other than expenses is allowed (art.7, 7° of the Law).

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

This is defined in the procedures of each research ethics committee.

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

No, the decisions, advisory comments and minutes are confidential.

**Question 40:** Is there any scope for Chairman’s actions in between meetings?

This is defined in the procedures of each research ethics committee.

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

This is defined in the procedures of each research ethics committee.

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

Not at this moment.

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

N/A

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

N/A

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