Agence nationale de sécurité du médicament et des produits de santé

Information

Authorisation of clinical trials on medicinal products: the ANSM sets the goal of processing half of the applications by the end of 2018 in the framework of the pilot phase of the European regulation

On 17 October 2017 in the presence of executives from the Department of Health (French Ministry of Social Affairs and Health) and a representative of the European Medicines Agency, the ANSM brought together academic and industrial sponsors of clinical trials and ethics committees (ECs) to assess the pilot phase preparing for the application of the European regulation on clinical trials on medicinal products. This experimental phase, which began two years ago, is significant in terms of patients' access to innovative medicinal products and the attractiveness of France for conducting clinical research in Europe.

European regulation on clinical trials on medicinal products[1] notably provides for:

- the implementation of a rapid, centralised, and coordinated review of clinical trial authorisation applications, as well as their modifications, whenever the trial is conducted in at least one European Union member state. This regulation introduces a single submission process for authorisation applications made by the clinical trial sponsor on a European portal that will group together all of the information and data relating to this trial and be partially accessible to the public
- a two-part scientific and ethical examination completed within a set period of time:
    - part I: a coordinated review between the member states concerned, leading to a single conclusion
    - part II: an ethical review by each member state concerned, leading to a national conclusion
- the principle of tacit authorisation

The application of this regulation is dependent on the availability of the single European portal through which sponsors will be able to submit their clinical trial files. This European portal should be made operational in 2019 according to Noémie Manent (from the EMA), who presented its main technical features.

Assessment two years after the pilot phase

Since September 2015, the ANSM has been mobilising ECs and academic and industrial sponsors of clinical trials to prepare for the application[2] of this European regulation.

France was the first European country to implement an experimental procedure (the pilot phase) which initially operated with 21 voluntary ECs.
After the Jardé law[3] came into effect, 39 French ECs were included. Submitted files are assigned through a random selection process organised by the Ministry of Social Affairs and Health. Jean-Yves Lacoste (from the DGS) presented the information technology[4] (IT) that will promote discussions between sponsors and ECs, as well as between ECs and the ANSM on a national level. The national IT platform is expected to be operational in early 2018 and at that time sponsors will be able to submit their files through the platform.

[1] the European regulation on clinical trials on medicinal products for human use was published in the Official Journal of the European Union on 27 May 2014.
[2] Initially set to take effect in May 2016, enforcement shall only become effective when the single European portal is made available.
[3] Law no. 2012-300 of 5 March 2012 on research involving human subjects, as amended by Order no. 2016-800 of 16 June 2016 and its Enforcement Decree no. 2016-1537 of 16/11/ 2016 on research involving human subjects (O.J. 17/11/2016)
[4] Article D. 1123-34 of the Public Health Code provides for the secretary of the National Commission for Research Involving Human Subjects (CNRIPH) implementing an IT system with a secure storage space

The two-year assessment of the pilot phase that was presented during the meeting confirms the advances seen during previous six-month assessments, such as support for the change, constructive discussions between stakeholders, the increase in the number of files submitted in the framework of the pilot phase, and the integration of the new organisation linked to the implementation of the Jardé law[3].

By 28 September 2017, 260 files were submitted and 210 were processed in the framework of the pilot phase, accounting for 14.2% of the files submitted to the ANSM. The 50 unprocessed files were either not admissible or were unable to be processed in the time frame by the EC concerned. Close to half of the files processed concerned oncology and haematology medicinal products. 33 different academic sponsors (for 97 submitted files) and 40 different industrial sponsors (for 113 submitted files) participated in the pilot phase.

Of the 193 applications processed by 28 September 2017, 127 were granted an authorisation by the ANSM and a favourable opinion from the EC concerned. The average time for processing was 68.9 days. The two-year quantitative assessment presented during the meeting can be consulted here.

http://www.ansm.sante.fr/var/ansm_site/storage/original/application/4f4caf13ab033f56623891aa7c63cc85.pdf

Two-year quantitative assessment (from 28/09/15 to 28/09/17)

- Number of files **submitted** as part of the pilot phase: **260**
- Number of files **processed** as part of the pilot phase: **210***

	1st experimental phase 14 months	**2nd experimental phase 10 months (application of the Jardé law)**	**Total**
Period	14 months	10 months	24 months
No. of files submitted	148	112	260
No. of files processed	123	87	210
	8.8 per month	8.7 per month	

* Accounts for **14.2%** of files submitted to the ANSM

→ 210 files submitted by 28 September 2017

Files submitted	Sponsor type		Trial type					Trials involving research centres	
	academic	industrial	Phase 1	Phase 2	Phase 3	Phase 4	NS*	national	international
6 months (51 files)	18	33	15	13	17	6	0	19	32
12 months (112 files)	50	62	24	28	53	7	0	52	60
18 months (152 files)	66	86	31	42	68	10	1	67	85
24 months (201 files)	97	113	40	56	98	14	2	96	114

→ 193 clinical trial authorisation (CTA) applications closed by 28 September 2017

Closed out files	Sponsor type		Trial type					Trials involving research centres	
	academic	industrial	Phase 1	Phase 2	Phase 3	Phase 4	NS*	national	international
6 months (26 files)	11	15	8	7	7	4	0	12	14
12 months (89 files)	39	50	18	22	42	7	0	39	50
18 months (128 files)	56	72	24	35	60	8	1	58	70

24 months (193 files)	88	105	34	54	89	14	2	88	105

The informational and discussion meeting organised by the ANSM helped all stakeholders take stock two years after the launch of the pilot phase and highlight the advances made, but also helped identify difficulties and measures to take to be ready when the European regulation takes effect.

The round table dedicated to feedback from stakeholders revealed persistent difficulties for clinical trials overall and the general willingness to fix them and take actions that could improve how the system operates. Pierre-Henri Bertoye (president of the CNRIPH[4]) explained how the CNRIPH's work with the ministry would help harmonise the operations and working methods of ECs. The time frames, which were negatively affected by introducing random selection process for all ECs, should be improved through a couple of actions: working groups established by the CNRIPH and digital tools for improving monitoring the evolution of files.
For its part, the ANSM has implemented an action plan in order to reduce these time frames while ensuring that the safety of participants in trials, which are bothpriorities. A unit dedicated to early clinical trials opened on December the 18th..

One goal : 50% of files in the pilot phase by the end of 2018

All stakeholders deemed that the pilot phase is a preferred tool for working on the time frame for authorising clinical trials. Nevertheless, the percent of files currently submitted in this framework (14.2%) is insufficient for France to be well-prepared with the European regulation within two years. The goal suggested by the ANSM of having 50% of files submitted in the framework of the pilot phase by the end of 2018 was collectively shared. This goal is achievable according to ECs and something that "should only be encouraged" according to industrial sponsors who say that there is no risk in entering this phase and only improvements can be expected. For their part, academic sponsors state that they are "convinced of the usefulness of the pilot phase for preparing for European deadlines".

Further reading

- *Practical Information Guide for Applicants : Clinical Drug Trials submitted within the Pilot Phase to ANSM (French National Agency for Medicines and Health Products Safety) and the CPP (French Ethics Committee) AEC_DOC008A V06 (07/08/2017) (838 ko)*
  http://ansm.sante.fr/content/download/78617/996267/version/14/file/AEC_DOC008A_AECMED_GUIDE_PHASE_PILOTE_+v06_20170804.pdf