The New French Law Applicable to Trials Involving Human Subjects: Clarifications for a More Efficient Framework

BY CHRISTOPHE FICHET

After long-running parliamentary discussions initiated in January 2009, France adopted a new law on trials involving human subjects (Law No. 2012-300, also called “Loi Jardé”) on March 5, 2012.

This act should be implemented once the application decrees and ministerial decisions are published in the Official Gazette of the French Republic, on Aug. 1 at the latest.

Trials involving human subjects were first regulated by the “Huriet-Sérusclat” Law of Dec. 20, 1988, on “the protection of persons who submit to clinical trials,” and subsequently over the following years through several laws, including the Law of July 29, 1994, “regarding the respect of the human body” and the Law of March 4, 2002, “regarding the rights of patients.”

This legal framework was completed with the Law of Aug. 9, 2004, “regarding Public Health Policy,”1 which implemented the regulatory requirements set forth by the European Union Clinical Trials Directive 2001/20/EC. However, the Law of 2004 increased the administrative constraints for the sponsors of trials involving human subjects. For example, the simplified procedure introduced for trials on routine care2 proved to be rather complicated in practice. In addition, the Law of 2004 did not provide a specific regulatory framework for noninterventional (also called “observational”) trials, which had increased remarkably over the last 10 years.

As a consequence, it became necessary to clarify the rules, as Member of Parliament Olivier Jardé stated in his report submitted to the French National Assembly (“Assemblée Nationale”) in 2010. The Loi Jardé aims at improving a legal framework that was “uselessly complex, often dissuasive and yet in some respects incomplete,” according to his report.3

The Loi Jardé provides a unique framework for trials involving human subjects. It reconciles two goals,

---

1 Enforced with the corresponding application decree No. 2006-477 of April 26, 2006.
2 Routine care, as defined in the Law of 2004 regarding Public Health, consists “(i) in acts, combinations of acts, or (ii) in preventive, diagnostic, or treatment medical strategies that are frequent in practice, meaning that they benefit from a professional consensus with respect to their indications.”
namely (i) facilitating trials, and (ii) guaranteeing patients’ protection from any risk arising from trials. Specifically, the Loi Jarde defines three categories of trials involving human subjects, depending on the level of risk incurred.4

1. Definition of three categories of trials depending on the level of risk

Whereas the Law of 2004 distinguished between trials with direct therapeutic purposes and trials devoid of therapeutic purposes, the Loi Jarde makes a distinction based on the level of risk of the intervention and has defined in this respect three categories of trials:

i. Intervventional Trials with Therapeutic Risks which do not constitute the patient’s usual care;

ii. Risk-Limited Interventional Trials which do not involve medicinal products; trials falling within this category will be listed progressively by decisions of the French Ministry of Health after the notice of the French Agency for Safety of Health Products (“Agence Française de Sécurité Sanitaire des Produits de Santé” (AFSSAPS), now “Agence Nationale de Sécurité du Médicament et des Produits de Santé” (ANSM)); and

iii. Non-Interventional Trials without specific risks for the patient, involving observing treatments over a long period. Such trials were not regulated until now.

2. Modification of the rules applying to the information, the consent, and the protection of the patients

The Loi Jarde establishes a general obligation to disclose to the patient any relevant information regarding a trial.5 Pursuant to Article L.1122-1 of the French Public Health Code (“Code de la Santé Publique”), “the person whose participation is solicited is informed of his/her right to be provided with, during or after the trial, information concerning his/her health, held by the investigator or, where appropriate, by the doctor or the qualified person representing him/her” and a trial cannot be performed on a person without his/her free and informed consent.

The Loi Jarde sets forth different rules applying to the consent of the patients according to the type of trial. Whereas a written consent of the patient is requested for interventional trials with therapeutic risks, such consent must be only a “free, informed, and express consent” in the case of risk-limited interventional trials. Regarding noninterventional trials, the patient is informed of the objectives, methodology, and duration of the trial and can refuse to submit to it (an “opt-out” type of consent). It should be noted that the Loi Jarde allows exemptions from these rules in the case of life-threatening emergencies; in such cases, trials can be performed without the formal consent of patients, under the control of an ethics committee.7

Moreover, the Loi Jarde no longer requires the patient to be registered with a social security (Sécurité Sociale) regime to participate in a trial. This amendment was designed to facilitate observational trials on emerging diseases or involving migrant populations.8 Thus, nonregistered patients now can be involved in noninterventional trials. A specific approval of an ethics committee (“comités de protection des personnes” (CPP)) is, however, required for any interventional trial. The relevant ethics committee must ground its authorization on at least one of the following two criteria: (i) “Whether the resulting benefits justify the risks taken by patients,” or (ii) “justification of such trial in light of the expected benefits for other individuals in the same legal situation. In that case, there should be no predictable risk and constraints of such trial shall be minimal.”

3. Reinforcement of the relevant health authorities’ prerogatives

The Loi Jarde creates a National Commission for Trials Involving Human Subjects (“Commission Nationale des Recherches Impliquant La Personne Humaine”) supervised by the French Ministry of Health. This commission aims at ensuring “the coordination, harmonization and assessment of practices” of the ethics committees to which the Loi Jarde confers larger prerogatives. This commission also is the appeal body in case of a dispute arising out of an ethics committee’s decision.

Under the Law of 2004, protocols for trials covered by Article L.1121-1 of the French Public Health Code had to obtain a prior favorable opinion from an ethics committee, as well as the authorization of the ANSM. The Loi Jarde maintains these requirements for protocols for interventional trials with therapeutic risks, whereas protocols for risk-limited interventional trials and noninterventional trials will only have to obtain a favorable opinion from an ethics committee.9 When the relevant ethics committee has justifiable doubts on the qualification of a trial under the three categories defined by the Loi Jarde, it can request the opinion of the ANSM.

The relevant ethics committee gives its opinion on the conditions of validity of the trial, regarding in particular its scientific relevance, the protection of participants, the adequation between the objectives and means used, and the qualifications of the investigator.10 Whereas sponsors previously could choose the committees, the Loi Jarde now establishes their random appointment by the new National Commission for Trials Involving Human Subjects (“Commission Nationale des Recherches Impliquant La Personne Humaine”),11 which ensures their independence. However, the sponsor can request that the National Commission appoint another committee before the commission gives its decision. In any case, if the protocol is refused by the appointed committee, sponsors can ask the National Commission to submit it to another committee for a second review.12

To ensure the proper functioning of the ethics committees, good practice guidelines are to be published by

6 Pursuant to the European Directive 2001/20/EC, an investigator is “a doctor or a person following a profession agreed in the Member State for investigations because of the scientific background and the experience in patient care it requires (...).”
9 With the exception of noninterventional trials on cosmetic or alimentary products pursuant to Article L.1121-16-2 of the French Public Health Code.
11 This measure should be implemented by July 2014.
the ANSM. The Loi Jardé also provides for the creation of a national register for trials involving human subjects. Furthermore, the French State can be held liable if an ethics committee is at fault.

4. Data Protection issues

Pursuant to the French Data Protection Act (Law 78-17 of Jan. 6, 1978, as amended), the French Data Protection Agency (“Commission Nationale de l’Informatique et des Libertés” (CNIL)) and the Advisory Committee on Data Protection (“Commission Consultative sur le Traitement de l’Information en Matière de Recherche dans le Domaine de la Santé” (CCTIRS)) are in charge of controlling the collection, processing, and transfer of personal data within the context of trials.

The Law of 2004 provided that the CCTIRS had to review the protocols for trials before they could be authorized by the CNIL. Pursuant to the Loi Jardé, only protocols for interventional trials are still subject to this procedure.

Regarding the methodology for notification of protocols, the CNIL had established a simplified declaration procedure by issuing a “methodology of reference,” namely the MR-001, “for the processing of personal data in the context of clinical trials.” Pursuant to this declaration procedure, a sponsor had to address a mere commitment to comply to the CNIL, as long as the protocol for the trial fitted with this methodology of reference. However, the CNIL has not yet made any amendment to reflect the changes of the Loi Jardé.

5. Applicable Liability Regime

Since the Law of 2004 came into effect, patients subject to clinical trials are largely protected. In this respect, Article L.1121-10 of the French Public Health Code establishing the no-fault liability regime has been extended by the Loi Jardé to all the categories of trials involving human subjects.

In addition, the Loi Jardé now expressly designates the sponsor as the “person responsible for the trial,” holding him/her liable if the trial causes damage to a patient. Thus, the sponsor must indemnify the harmful consequences resulting from the trial, unless he/she proves he/she was not at fault.

Furthermore, it should be noted that the French National Office of Compensation for Medical Accidents, Iatrogenic Disorders and Nosocomial Infection (“Office national d’indemnisation des accidents médicaux, des affections iatrogènes et des infections nosocomiales” (ONIAM)) remains competent to compensate the victim if the sponsor’s fault is rejected.

***

The Loi Jardé aims at providing a clearer and more precise legal framework for trials involving human subjects, ensuring security and predictability for both the pharmaceutical industry and the patients.

Within the context of current debates at the European level to amend EU Directive 2001/20/CE,13 this framework could however be modified in the following months to reflect the revisions imposed by the European Commission.14,15

---

13 John Dalli, the European Commissioner in charge of Health and Consumer Policy, expressed his wish to replace the Directive with a European Regulation.
15 The author thanks Orianne Pasco, articling student, Sciences Po Paris, for her kind assistance and collaboration.