



## Answer JID

Dear Editor,

The Aix-Marseille University Ethics and Scientific Integrity Unit has been mandated by the President of the University to investigate the scientific publications of the IHU Méditerranée Infection teams and to respond to requests from publishers.

In the first part of this document, we will outline the various legislative requirements.

In the second part, we will provide you with the elements relating to our investigations concerning the two articles to which we believe your requests are connected.

## I French Laws

### **1. French Laws and Requirements for Research with Human Participants (2002–2006)**

During this period, **research involving human subjects in France** was governed primarily by:

#### **Loi Huriet-Sérusclat (Law No. 88-1138 of December 20, 1988)**

- This was the foundational law for biomedical research in France.
- It introduced mandatory ethical review and informed consent for research involving human participants.
- Codified in the **Code de la santé publique (CSP), Articles L.1121-1 to L.1126-9** (later renumbered).

#### **Key Requirements:**

- **Prospective research involving human participants** required **favorable opinion from a Comité Consultatif de Protection des Personnes (CCPPRB)**—the forerunner of the current **CPP (Comité de Protection des Personnes)**.
- **Informed consent** had to be freely given, specific, and written.
- A **sponsor (promoteur)** was responsible for ensuring compliance.

#### **References:**

- **Loi n°88-1138 du 20 décembre 1988** relative à la protection des personnes dans la recherche biomédicale
- **Décret n°90-872 du 28 septembre 1990**, implementing provisions of the law
- **CSP Articles L.1121-1 and following** (codified versions)

## 2. French Laws and Requirements for Use of Excess Blood Samples in Research (2019–2021)

For this period, research using **residual or surplus biological samples** from clinical care is governed by:

### Code de la santé publique (CSP) – Title on Biomedical Research and Biological Resources

- Primarily:
  - **Articles L.1243-3 to L.1243-5** (biological samples and collections)
  - **Articles L.1121-1 to L.1126-12** (research involving humans)
  - **Articles R.1121-1 to R.1126-34** (implementing decrees)

### Collection and Use of Residual Samples:

- If **samples are collected during routine care** and used **secondarily for research**, this falls under:
  - **Research not involving human participants directly** (*non-interventional*, e.g., retrospective studies)
  - **Loi Jardé** (Law No. 2012-300), as amended by **Ordonnance n°2016-800 du 16 juin 2016**

### Key Requirements (2019–2021):

- Use of **leftover clinical samples** for research:
  - May not require CPP approval **if anonymized** or used in a **non-interventional context**.
  - Otherwise, requires **ethical approval** and **participant information with non-opposition** (opt-out).
- **Informed consent or non-opposition** depending on sample use and identifiability.
- If samples are stored in a **biobank**, it must be declared or authorized by the **Ministry of Research or Health**, per **CSP Article L.1243-3**.

### References:

- **Loi n°2012-300 du 5 mars 2012** (known as the *Loi Jardé*)
- **Ordonnance n°2016-800 du 16 juin 2016** (modernizing legal framework)
- **CSP Articles:**
  - **L.1121-1 to L.1126-12** (human subject research)
  - **L.1243-3 and following** (biological sample use)
- **Arrêté du 12 avril 2018** on biobank declarations

## **II Articles**

### *1) Oral ivermectin in the treatment of body lice*

The above-mentioned study, published in your journal entitled "*Oral ivermectin in the treatment of body lice*" was published in 2006, 19 years ago. At that time, the French law governing biomedical research was the Huriet Sérusclat Law 1988 which was replaced by the Public Health Law on August 9, 2004 (transposing European law in France) whose implementing decree was published in September 2006.

So, the conditions of the Huriet Sérusclat law were in force on the date of the article. At this time CPP was not yet created but the approval of the CPPRB was needed.

**This study published in your journal respects the regulatory framework of the time.**

This study was promoted by our university hospital (AP-HM) which, under the Huriet law, has the legal obligation to present the protocol to CPPRB for its opinion. This opinion was submitted on 5 January 2004 under No. 04/08 and received a favorable opinion on 2 July 2004 (Annex 1) and this is indicated in the text of the article.

### *2) Monocytes and Macrophages, Targets of Severe Acute Respiratory Syndrome Coronavirus 2: The Clue for Coronavirus Disease 2019 Immunoparalysis*

Regarding the study published on August 2, 2021 entitled "Monocytes and Macrophages, Targets of Severe Acute Respiratory Syndrome Coronavirus 2: The Clue for Coronavirus Disease 2019 Immunoparalysis"

This study was carried out in 2021 under the so-called Jardé law, which replaced the public health law in 2012 and has been in force since 2016.

This study was promoted by the Mediterranean Infection Foundation under IDRCB No. 2020-A00756-33 and in this context received a favorable opinion from CPP No. 20027-60604 on April 30, 2020 (Annex 2). The CPP categorized the study as a RIPH 2.

**There are therefore no regulatory problems in this study either.**

However, as you can see, the paragraph describing the conduct of the study is incorrect and needs to be corrected, as it is not a retrospective study but a prospective study authorized by the CPP.

In this respect, we request a correction including the following paragraph: "This study was promoted by the Mediterranean Infection Foundation under IDRCB No. 2020-A00756-33 and in this context received a favorable opinion from CPP No. 20027-60604 on April 30, 2020"

We remain at your disposal for any further request.

**Ethics and Scientific Integrity Unit of Aix-Marseille University**