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France - Trial Period for Medical Use of Cannabis-Based Products

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France is finally moving forward on the medical use of cannabis. At the end of 2019, Law No. 2019-1446 indicated that French law would allow for a trial for medical use of cannabis-based products. The decree and implementing ministerial order [*arrêté*] establishing the parameters of the trial were released last week.

In a nutshell, for a two-year period, France is authorizing the use of certain cannabis-based medicinal products in relation to certain therapeutic indications and clinical situations, for maximum 3,000 patients (Trial). The objective is to see, in real world conditions, if medical use of cannabis is an option for the future.

Stringent conditions apply to every element of the Trial: the cannabis-based products, the patients and the healthcare professionals participating to the Trial, and the suppliers and distributors of the cannabis-based products. A national register will be set up to collect the Trial data.

Although cannabis-based medicinal products included in the Trial must be provided for free for the duration of the Trial, it is expected that many of the products in the trial will be among the first to be authorized for marketing in France (should France decide to accept medical use of cannabis).

The Trial will start on 31 March 2021 at the latest. Companies interested in supplying cannabis-based medicinal products for the French trial must submit their application and product samples to the French Medicines Agency by 24 November 2020. This period is very short given the information and documents to be provided with the application and the obligations imposed on suppliers.

A. LEGAL BACKGROUND

In France, cannabis is classified as a narcotic, and Article R 5132-82 of the Public Health Code prohibits the production, manufacture, transport, importation, exportation, holding, offer, transfer, purchase and use of:

- cannabis, its plant and its resin; products that contain them or are obtained from them;
- tetrahydrocannabinols, except delta 9-tetrahydrocannabinol, their esters, ethers, salts as well as the salts of derivatives and products containing them.

However, exceptions may be granted for purposes of:

- research and control, as well as for the manufacturing of derivatives authorized by the French Medicines Agency (ANSM);
- cultivation, importation, exportation and industrial and commercial use of varieties of cannabis without narcotic properties or of products containing such varieties as may be authorized by a ministerial *arrêté*;
- manufacturing, transport, importation, exportation, holding, offer, transfer, purchase or use of medicinal products containing one of the substances mentioned above that have been granted a marketing authorization in France.

Last year, Article 43 of Law No. 2019-1446 provided that, for a trial period of two years, medical use of cannabis may be authorized, in the form of products that meet pharmaceutical standards, for certain therapeutic indications or clinical situations refractory to authorized and available treatments. The implementation conditions of the Trial had to be defined by a decree.

That decree - Decree No. 2020-1230 on a trial for medical use of cannabis (Decree) – and its implementing ministerial *arrêté* (Order)[1] were adopted on 7 and 16 October respectively.

The Order includes an annex that sets out the specifications for the supply and distribution free of charge of cannabis-based medicinal products for patients who participate to the trial (Specifications). In addition, the French Medicines Agency has published documents to assist companies applying to participate in the Trial. We will not explain the Specifications and ANSM's instructions in detail in this client alert.

B. LEGAL REGIME FOR MARCH 31, 2021 TRIAL OF CANNABIS-BASED MEDICINAL PRODUCTS

1. Duration of the Trial

A trial on medical use of cannabis in the form of medicinal products is authorized for a period of two years starting from the prescription for the first patient or on 31 March 2021, whichever the latest (Trial Period).

2. Trial Products

The products to be used for the Trial (Trial Products) are subject to the legal regime of narcotic drugs set forth in the Public Health Code. They must conform to reference documents for medicinal products to guarantee their quality, safety and therapeutic use. As such, they must be manufactured in accordance with good manufacturing practices (GMP) or any equivalent reference document recognized at international level.

Their characteristics, i.e. the composition (concentration in THC and CBD), pharmaceutical form, quality, leaflet, and labeling, are defined in the Specifications.

- Trial Products are finished medicinal products containing delta-9-tétrahydrocannabinol (THC) and cannabidiol (CBD) dosed in accordance with ratio margins specified in Part I of the Specifications.
- They may only take the following pharmaceutical forms:
  - inhalation by vaporization such as dried flower tops or granules containing THC and CBD;

  - oral form (capsules or equivalent form) made from extracts solubilized in an oil matrix containing THC and CBD;
  - oral or sublingual form made from extracts solubilized in an oil matrix containing THC and CBD.
- A vaporization device, which qualifies as a medical device, must be used for inhaled forms.

3. Trial Indications and Clinical Situations

Medical use of cannabis is only authorized for certain therapeutic indications or clinical situations refractory to authorized and available treatments (Trial Indications/Clinical Situations). The list of Trial Indications/Clinical Situations is set by the Order and includes:

- neuropathic pains refractory to available therapies (medication or not);
- certain forms of pharmaco-resistant epilepsy;
- certain rebel symptoms in oncology linked to cancer or anti-cancer treatment;
- palliative situations;
- painful spasticity of sclerosis or other NCS pathologies.

Trial Products are prescribed in case of insufficient relief or bad tolerance to available therapies (medication or else).

4. Trial Patients

The Trial applies to maximum 3,000 patients, and the ANSM will define the number of patients treated for each Trial Indication/Clinical Situation, based on medical needs.

For the duration of the Trial, Trial Patients (or their relative or caretakers) are authorized to obtain and use the Trial Products and to detain and transport them for their personal treatment.

At the time of prescription, (i) Trial Patients must be informed on the particular precautions of use, potential side effects, contra-indications and effects on driving or use of certain machines of the Trial Products, and (ii) a written document with this information must be handed out to them.

5. Trial Doctors, Pharmacists and Hospitals

The Trial Products are initially prescribed by doctors who volunteered to participate in the Trial, have received a specific training therefor and work in hospitals where the Trial Indications/Clinical Situations are treated. However, the prescription may be renewed by any doctor who has received the specific training for the Trial.

The Trial Products may only be dispensed by pharmacists who volunteered to participle in the Trial.

The conditions for voluntary participation of doctors and pharmacists will be set by ministerial *arrêté*. The mandatory prior training is meant to educate about cannabis for medical use and competences necessary to prescribe and dispense the Trial Products. The learning objectives and practical conditions of the training as well as the technical conditions for the training center will be defined by ministerial *arrêté*.

The list of Trial Hospitals will be set by the ANSM based upon their expertise and patient needs.

6. Trial Companies

Trial Products are supplied by manufacturers to French *exploitants*[2] that then distribute them to Trial Pharmacies. They must be provided for free to Trial Patients.

Specific conditions of importation, storage, distribution and control of the Trial Products (including traceability, batch follow-up and recall) are defined in the Specifications. However, cultivation of cannabis in France remains prohibited, even for purposes of the Trial.[3]

Importation and storage conditions of Trial Products, including traceability, follow-up and recall of the batches, are subject to the rules on narcotic medicinal products (Art. R 5132-74 and following) and good distribution practice (Art. L. 5121-5).

The Specifications indicate that two suppliers will be selected for each pharmaceutical form of the Trial Products: a main supplier and a secondary supplier, in case the first supplier defaults.

The supplier must be a legal entity set up to manufacture or cultivate medical cannabis. It need not be established in France, but it must enter into a partnership agreement with a French *exploitant*, which will take charge of wholesale distribution (free of charge), information, pharmacovigilance, batch follow-up and recall of the Trial Products in France. Distribution of the Trial Products occurs under the conditions set out in the Specifications. Importantly, the partnership agreement should include an order process that ensures a high traceability of the product flow and the fulfillment of orders made by pharmacies.

7. National Trial Register

An electronic national follow-up register will be implemented (in accordance with data privacy law) and run by the ANSM in order to ensure patient follow-up, including the security of the medicinal product circuit, pharmacovigilance and addictovigilance, as well as the follow-up of the Trial for study and additional analysis purposes. The conditions for the implementation and operation of the register will be set by ministerial *arrêté*.

The register will be filled in by the Trial Doctors and Pharmacists with the Trial Patient's consent, and an inscription certificate will be given to the Trial Patient.

C. IMPLEMENTATION BY THE FRENCH MEDICINES AGENCY

The ANSM has published documents on its website to help companies apply to participate to in the Trial, including:

- web pages with detailed explanations of the conditions of participation and selection;
- the Specifications;
- a Framework for Technical Response;
- a statement of partnership with a French *exploitant;*
- a statement about a later submission of missing documents;
- a Q&A on medical use of cannabis.

The relevant dates for the applications are as follows:

- 18 November to ask questions relating to the application;
- 24 November to submit the application and the samples;
- 15 December to submit the last supporting documents, in particular the *exploitant*'s authorizations relating to the import of the Trial Products.

Applications, which must be in French language, contain two parts:

- **Admissibility**: the application is admissible if the following compliance criteria are met:
  - Requirements for the actors: presentation of all the actors of the supply chain, from the producer of the raw material to the distributor, including transformers and intermediaries.
  - Requirements for the production of raw materials and finished products: detailed production method and identification of the production sites.
  - Requirements for finished products: complete description of each form of medical cannabis the supplier wants to supply (e.g., production, transformation, control process, characteristics, and varieties).
  - Samples: the supplier must provide the samples listed in Part II of the Specifications. The samples must conform to the technical specifications in Part II of the Specifications. Each form and, as the case may be, the vaporization device are provided in the original commercial packaging and with an information sticker. The supplier may also provide a patient leaflet indicating the optimal conditions of use.

    The ANSM will make a quality control of the Trial Product within three months following the selection.

    Note: Insofar as medical cannabis is a narcotic medicinal product, an authorization to import narcotics issued by the ANSM and an authorization to export narcotics issued by the competent authority of the country of storage must be obtained before importing the samples.

  Part II of the Specifications and the Framework for Technical Response define the expected answers.
- **Selection**: the application must meet selection criteria
  - Criteria linked to the finished products
  - Criteria linked to the production of raw materials and finished products
  - Criteria linked to the good supply of the Trial Products

  The criteria are detailed in the Framework for Technical Response, which also explains the expected content of the application and the documents to be annexed to the application.

The new French rules are complex, especially the requirements for becoming a supplier of Trial Products. King & Spalding lawyers may help you navigate through this new legal regime and prepare applications to supply cannabis-based medicinal products in France.

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[1] *Arrêté* of 6 October 2020 setting the specifications for cannabis-based medicinal products used during the trial period set forth at Article 43 of Law N° 2019-1446 of 24 December 2019 of financing of social security for year 2020, conditions of their availability as well as the therapeutic indications or clinical situations in which they will be used.
[2] An "*exploitant*" is the French company in charge of wholesale distribution, pharmacovigilance, information, control of advertising, storage, and batch follow-up and recall for the French territory.
[3] A case relating to CBD is pending before the European Court of Justice. A French Court asked the ECJ if Regulations No 1307/2013 and No 1308/2013, and the principle of the free movement of goods mean that the limitations on the cultivation, industrialization and marketing of hemp solely to fiber and seeds, impose a restriction that is not in accordance with EU law. A decision is expected in November 2020.