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ATMPs: exceptional manufacturing returns to the patient's bedside

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Introduction

Since the European Regulation (No. 1394/2007) on **Advanced Therapy Medicinal Products (ATMPs)**, only 30 ATMPs have obtained a marketing authorization in the European Union as at 30 September 2025, but most are still at the clinical trial stage.

❑ The European **Hospital Exemption (HE)** allows the use of certain ATMPs at the **national level** without formal central marketing authorization provided specific criteria are met: a non-routine basis preparation, a **medical prescription for an individual patient**, a use within the same Member State, in a hospital setting under the exclusive responsibility of a medical practitioner, a GMP compliant manufacturing, and compliance with traceability and pharmacovigilance requirements. It provides a practical solution for facilitating timely access to innovations stemming from national academic research and hospital initiatives.

❑ In France, the decree of **February 16, 2022**, has established a **sub-exemption** within the framework of HE, specifically designed to address the practical challenges only for ATMPs derived from **autologous cells or tissues** and not involving **any substantial manipulation**. It authorizes the manufacturing, distribution, and administration of these ATMPs, as part of the same medical procedure as the procurement of the autologous tissues or cells used in their composition, without requiring the manufacturing process to take place in a specially approved manufacturing facility (GMP classroom production), subject to prior validation by the French National Agency for Medicines and Health Products Safety (ANSM). By formalizing a legal framework for a so-called **“decentralized bedside” production**, the decree aligns regulations with the practical realities of personalized medicine, promotes a more agile organization of healthcare, and accelerates access to these ATMPs for patients.

❑ Within this new context, this poster presents the first French implementation of this new decree through the MICROPREP III clinical trial.

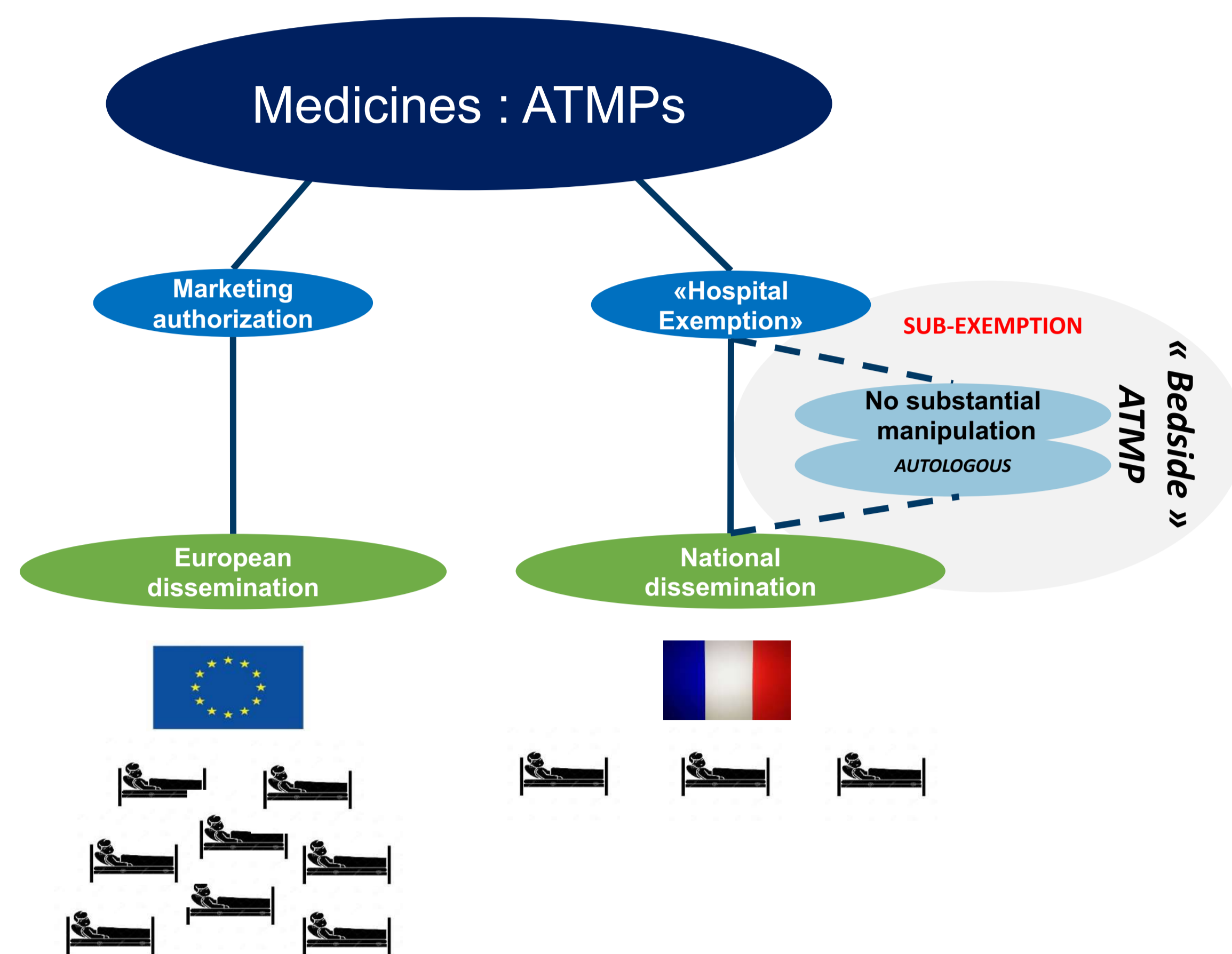


FIGURE 1 : Regulation frame for a national decentralized “bedside” sub-exemption ATMP manufacturing

New measures for a “decentralized bedside autologous hospital exemption ATMP manufacturing”

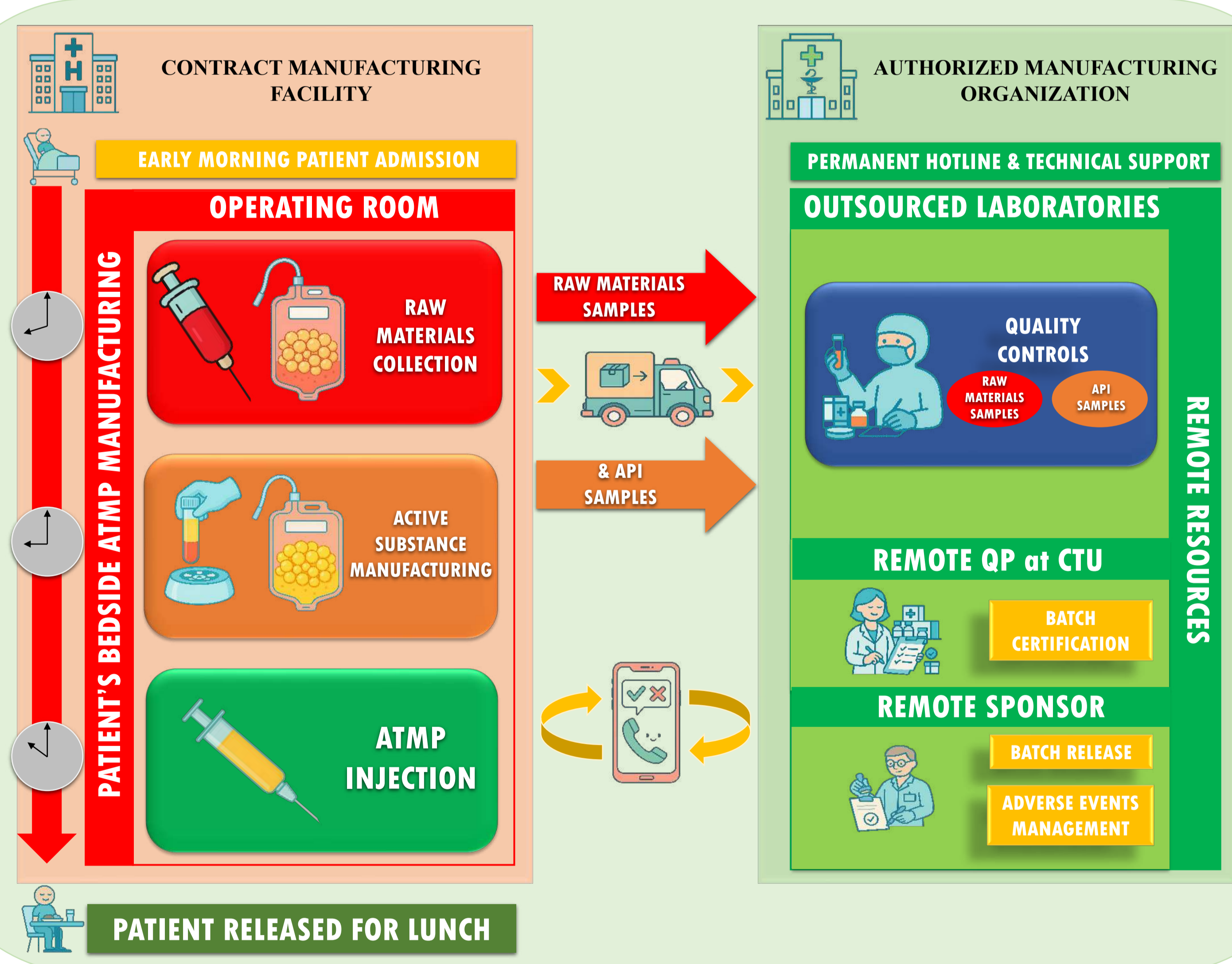


FIGURE 2 : MICROPREP III autologous “bedside” ATMP setup proposal

The First French therapeutic application of this innovative regulatory framework is addressed within the setup of **MICROPREP III clinical trial** (EudraCT No 2023-507683-40) authorized in May 2024.

❑ It is designed to evaluate in **180 patients** the efficacy of **intra-articular injections of autologous microfat**, optionally combined with **autologous platelet-rich plasma (PRP)**, as an adjunctive therapy for patients with **Knee osteoarthritis**.

❑ The application of the **single-step autologous ATMPs** exemption needed to implement new measures and agreements between clinicians and manufacturer to ensure compliance to GMP guidelines and ATMPs quality remaining under the responsibility of the authorized establishment despite delocalization (as mentioned in figure 2). The setup proposal by the national authorized manufacturing establishment consists in :

- ❑ Using directly the operating room for the harvesting-manufacturing-administration of the “single step manufactured autologous ATMP”
- ❑ Training and accrediting the medical staff
- ❑ Centralizing quality controls
- ❑ Centralizing the quality management at the authorized manufacturer level
- ❑ Establishing fluid communication and traceability

Expectations and Perspectives

❑ Changes to ATMP's remote management rules

- Responsibilities between the manufacturer and the delegated staff
- New relationship between the manufacturer and the physician
- New measures in the quality management system

⇒ **Formal contract is a mandatory step**

❑ Challenges are expected regarding the standardization of protocols, requirement of trained personnel, reproducibility from site to site...

❑ Reduced ATMP's production time should increase patient treatment capacity (see figure 3), and is expected to be more suitable to supply & demand.

❑ More affordable expected cost to the healthcare system for a single batch of autologous ATMP

✓ How will the manufacturer and sponsor manage the risk management plan ?

✓ Will other EU countries apply new tools and rules to accelerate decentralized manufacturing at the patient's bedside under the hospital exemption for autologous ATMP, and how?

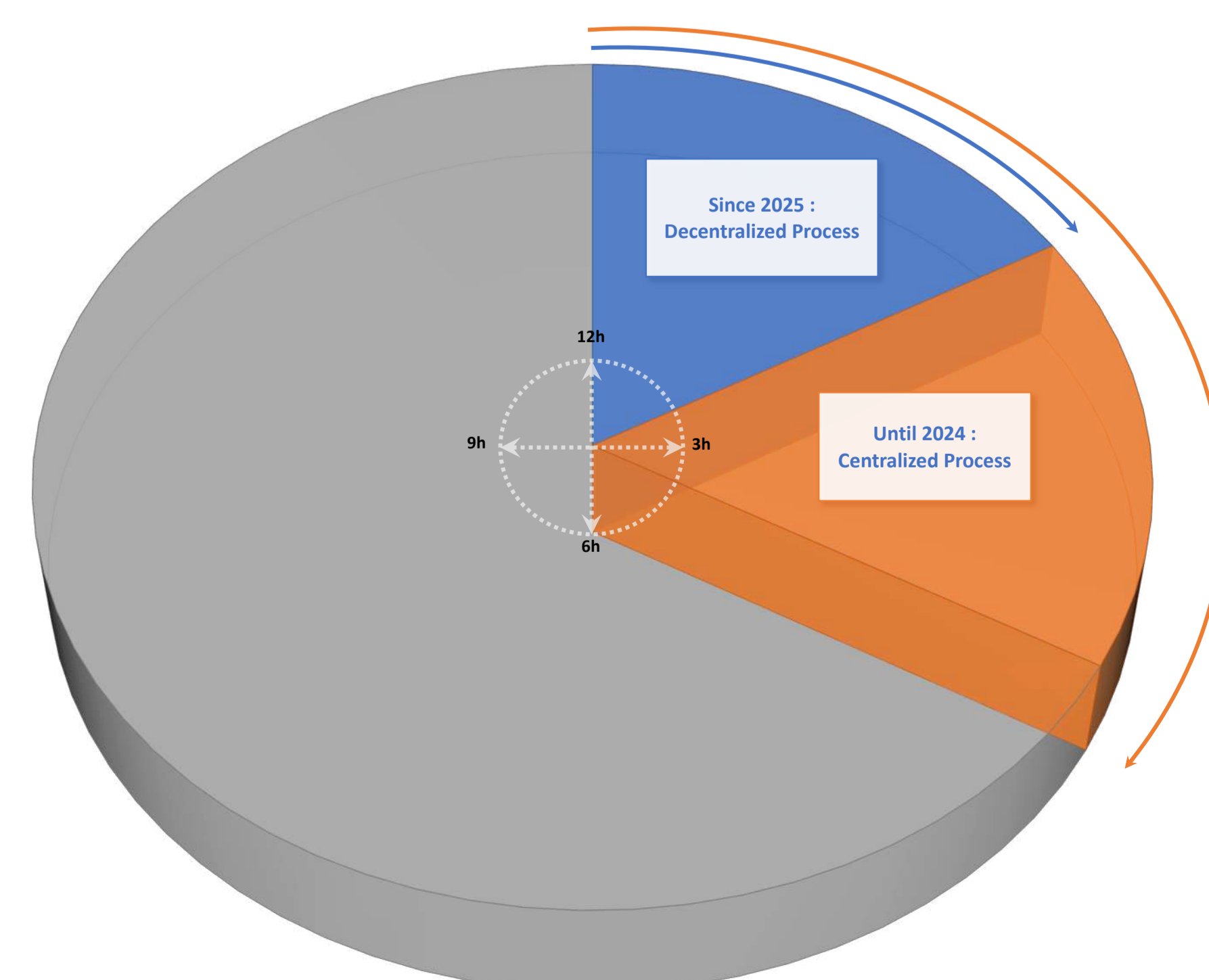


FIGURE 3 : Expected ATMP manufacturing time comparison from raw material collection to ATMP batch release between centralized process in GMP classroom (Internal data extracted from GMP ATMP batches in Marseille Cell Therapy Unit) and decentralized process in the case of the “bedside” operating room production planned for MICROPREP III clinical trial.