

## BACKGROUND

Chimeric Antigen Receptor T cells (CAR-T cells) are Advanced Therapy Medicinal Products (ATMP) and are more specifically considered as genetically modified organisms (GMO). They need strict requirements and specific authorizations for their use. The CAR-T cells YESCARTA® and KYMRIAH® are classified as Class 1 GMO and they are indicated in hematologic malignancies.

## AIM

→ This work presents the building of the preliminary file required for the submission of the pharmaceutical project to the French Health Authorities.

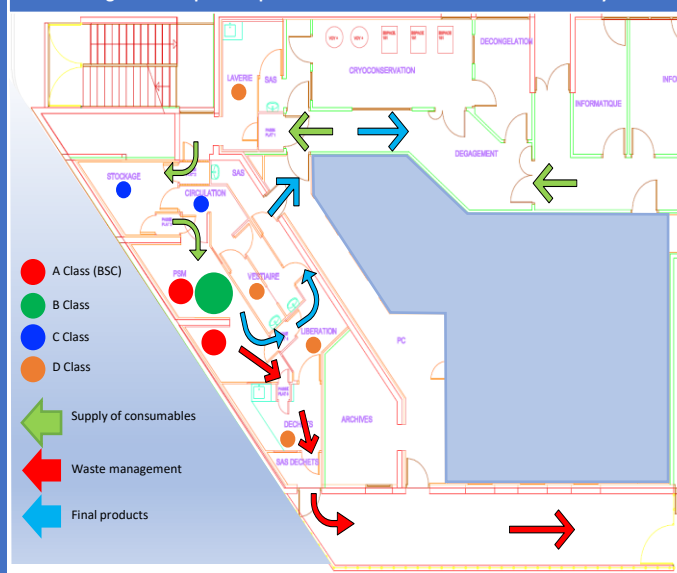
**Figure 1:** List of requirements specified in the « Arrêté du 8 août 2019 modifiant l'arrêté du 28 mars 2019 » for the specific use of CAR T cells.

**Figure 2:** The plans of the premises have been thought out to respect the principle of « forward march ». The biosafety cabinet (BSC) is located in the cleanroom (low pressure room). Thanks to these layouts, the handling of Class 2 GMO is possible.

**Figure 3:** The risk assessment was built using 2 methods. An Ishikawa diagram was firstly applied to each pharmaceutical stage of the CAR T cells circuit, in order to identify the main failure modes. The FMECA method then allowed us to assess the risks and their criticality.

Figure 1 : Requirements for the CAR T cells use
Authorization to perform hematopoietic stem cell transplants
Authorization to collect cells by apheresis for therapeutic purposes
Organization of the cells processing for the future manufacturing by the pharmaceutical establishment
Organization of hemato-oncology consultation meetings in the establishment
Approval for the contained use of Class 1 and 2 GMO by the Haut Conseil de Biotechnologie (HCB)
Specific pharmacy authorization for the reconstitution of ATMP / already carrying out this activity
Teams trainings for the different stages of the CAR T cell circuit and the patients monitoring
Access to a certified hemato-oncology Intensive Care Unit (ICU)
24/7 Presence of medical staff specialized in Anesthesiology-Resuscitation activity
Access to a certified neurology ward
Access to Magnetic Resonance Imaging (MRI) with the 24/7 presence of a radiologist on duty
Immediate and permanent coordination between hemato-oncologists, resuscitators and neurologists trained in the administration of CAR-T Cells
Direct and easy availability of Tocilizumab
Declaration to the Regional Health Agency (ARS) as a user center of CAR T cells

Figure 2 : Map of the premises dedicated to the CAR T cells activity



## METHOD

Literature review

Users Feedbacks

Ishikawa diagram

FMECA

## RESULTS

## CONCLUSION

This work will be part of the territory shared medical project and will require a real multidisciplinary coordination. It represents a challenge for both medical and pharmaceutical teams in order to offer optimal care to patients suffering from hematologic malignancies.

Figure 3 : Risk Analysis

### Ishikawa diagramm :

- Risks assessment and their potential causes for each step →
- Classification of causes : Material, Medium, Method, Labour, raw Materials

Reception

Storage

Prescription +  
Pharmaceutical  
validation

Preparation +  
Thawing

Libération

Delivery

Waste

### FMECA

- 2nd risks assessment
- Failures detection
- Optimization of circuit reliability
- Evaluation of the risks criticality