# Consultation on « Hospital Exemption » status

For CELL*for*CURE, the main difficulty in the application of the ATMPs regulation is linked to the exemption status.

As a **general and preliminary remark**, in the unique perspective of benefit for patient and public health, the hospital exemption status should be considered very cautiously and really limited to very specific cases (e.g. pathologies with very few numbers of patients).

1) **Regarding the definition,** "for individual patients" should be clarified to avoid any ambiguity. This definition should not overlap the field of autologous therapies which could be considered in a wrong way as therapy for individual patients. Indeed, some autologous therapy may be addressed to a large population and requires to be considered as classical ATMP in order to be available for all patients.

2) The **exemption status could generate a second and parallel medicinal product status which may question** :
   - **The Quality of products**

   It is not clear if GMP is mandatory: indeed some referential different from GMP seem to be soon in force in some countries, (e.g. in France). "GMP like" rules will necessary lead to lower quality of products than standard GMP.
   - **The Safety:**

   **T**he risk is to authorize a large number of hospital exemptions corresponding to the same type or to very similar products, each site being authorized nationally based on proper manufacturing technology. This situation could question the safety issues as:
     - the multiplicity of the production sites using similar but slightly different manufacturing processes is a less safe situation compared to a limited number of manufacturing sites with a unique standard manufacturing technology for which audits and inspections are more frequent…,
     - the processes elaborated for a very low number of patients are always performed in less closed systems (increased risk of contamination) with less automated solutions (decrease of robustness and reproducibility).
   - **A lack of efficacy evidence.**

   Authorizing a large number of Hospital exemptions acting as local sponsors, reduces by nature the size of cohorts for clinical trials. Therefore, evidence of efficacy will really be more difficult to establish compared to data obtained with a large size cohort. Furthermore it appears that in some EU countries, clinical trial is not necessary for hospital exemption.
   - t**he access to the therapy is not ensured for patient**

   The access of patient to relevant therapy is a fundamental right. However, critical limitation of this access could be due for example to supply-chain and distribution insufficiency and production capacity limitations related to small capacity facilities. This could seriously constrain the availability of ATMPs by exemption for European patients.

3) A **negative signal for industry and investors to invest in R&D.**

The multiplicity of exemption is a negative signal to be provided to industry and investors. A large number of exemptions for a given pathology correspond de facto to a fragmentation of the market. Consequently, such pathology appears less attractive for investment from companies and private investors. There is then a risk to impair R&D investments in the field.

As a minimum incentive, a solution could be, that when a market authorization for an ATMP is granted for a given indication, all exemptions in the 27 MSs should be stopped for the same indication, meaning that even if the population appears to be limited in one country, within 27 MS this targeted population should be on line with a medium/important production capacity for classical ATMP. Thus, the objective for public health authorities is to target in one safe authorization the 27 MS, giving preference to develop safe classical ATMPs.