# ATMP treatment under the Hospital Exemption

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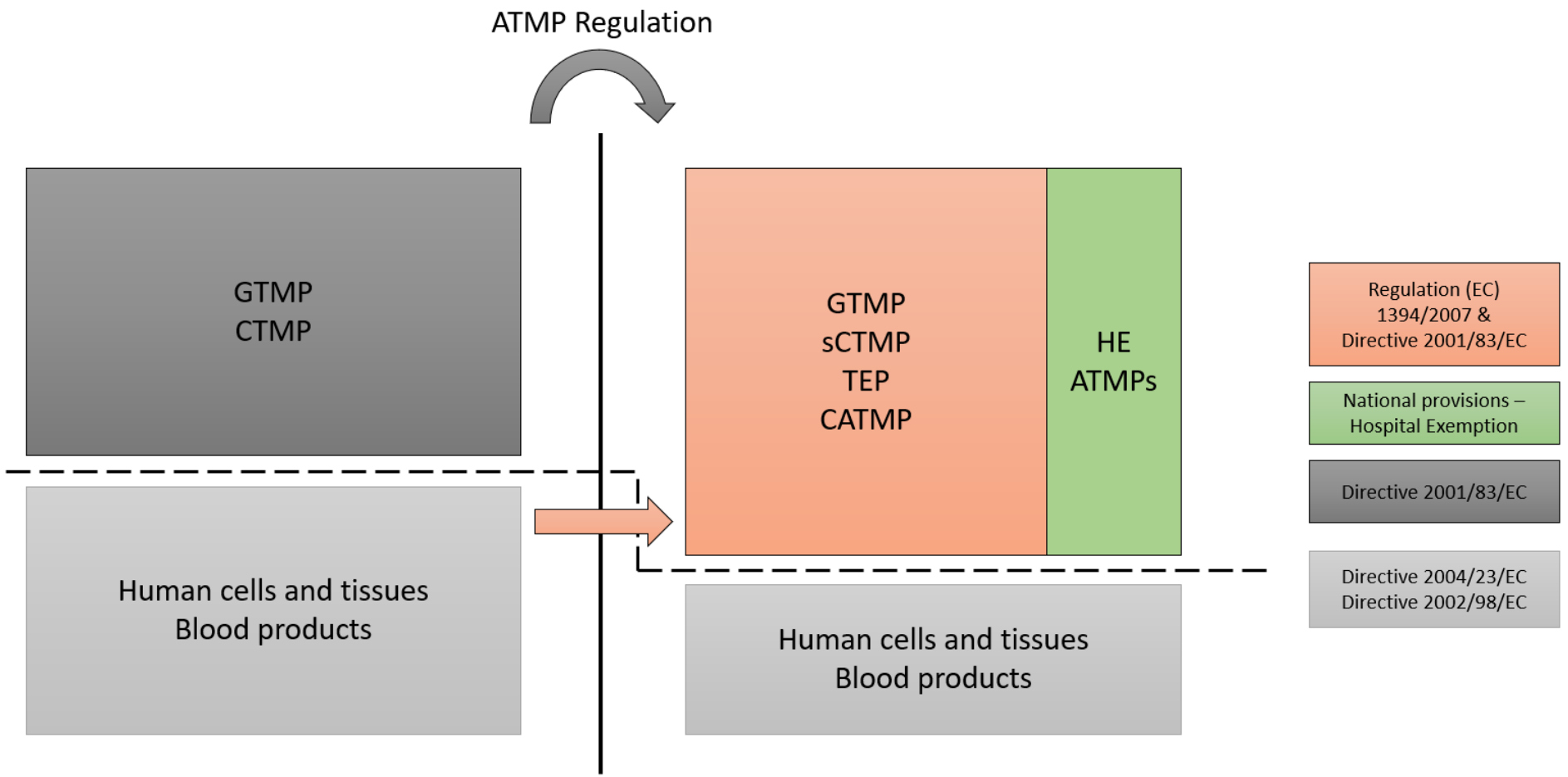
# ATMP definitions and legislation



# Hospital Exemption (HE): Article 28(2)

"Any advanced therapy medicinal product, as defined in Regulation (EC) No 1394/2007, which is prepared on a *non-routine basis* according to specific quality standards, and used within the same Member State in a hospital under the exclusive professional responsibility of a medical practitioner, in order to comply with an *individual medical prescription for a custom-made product for an individual patient*."

# National provisions

Table 2. Variable and additional national provisions for the Hospital Exemption, per selected country.

| | AT | BE | FI | FR | DE | IT | NL | ES | UK |
|---|---|---|---|---|---|---|---|---|---|
| **Scope** | | | | | | | | | |
| Nonroutine/custom-made product | Nondefined | Guidance | Guidance | Nondefined | Guidance | Nondefined | Guidance | Nondefined | Guidance |
| Number of patients | Nondefined | Nondefined | Nondefined | Nondefined | Nondefined | Nondefined | 10/50 patients | Nondefined | Nondefined |
| Duration of license | Nondefined | 1 year | Nondefined | 5 years | Nondefined | Nondefined | 1 year | 3–5 years | Nondefined |
| Annual reporting | Required | Required | Required | Required | Required | Required | Required | Required | Required |
| **Eligibility** | | | | | | | | | |
| Eligible license holders | Hospitals | All | All | All | All | Public institutes | All | Hospitals | All |
| Restricted when licensed products are available | No | Yes | Yes | Yes† | No | Yes | Yes | No | No |
| Medical need considerations‡ | Yes | Yes | Yes | Yes† | No | Yes | Yes | No | No |
| **Data entry requirements** | | | | | | | | | |
| Manufacturing & quality | Required | Required | Required | Required | Required | Required | Required | Required | Required |
| Clinical | Not required | Required | Not required | Not required | Required | Not required | Required | Required | Not required |
| **Process standards** | | | | | | | | | |
| GMP compliance | Required | Required | Required | Not required§ | Required | Required | Required | Required | Required |

†When clinical data are not available.
‡Refers to whether the competent authority considers medical need justifications in their decision making for authorization.
§Not required for non-pharmaceutical establishments only.
AT: Austria; BE: Belgium; DE: Germany; ES: Spain; FI: Finland; FR: France; IT: Italy; NL: Netherlands; UK: United Kingdom.

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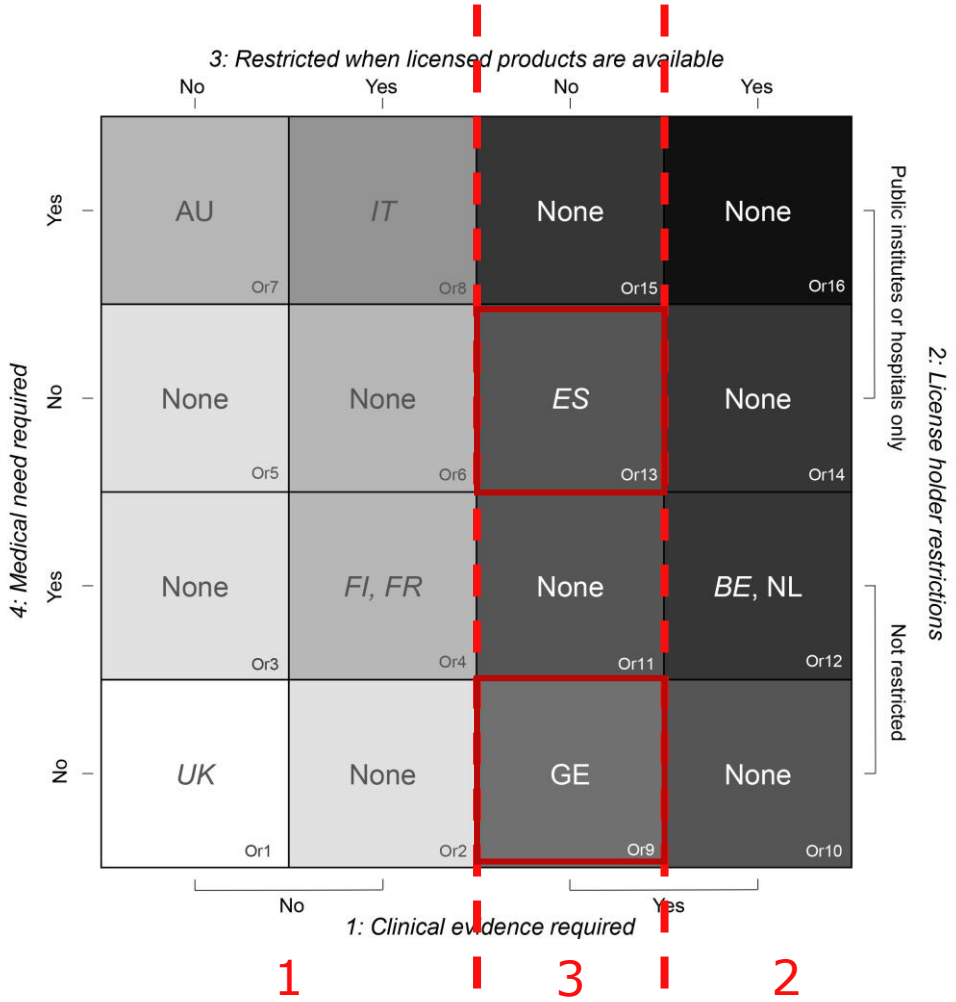
# Intended use by authority

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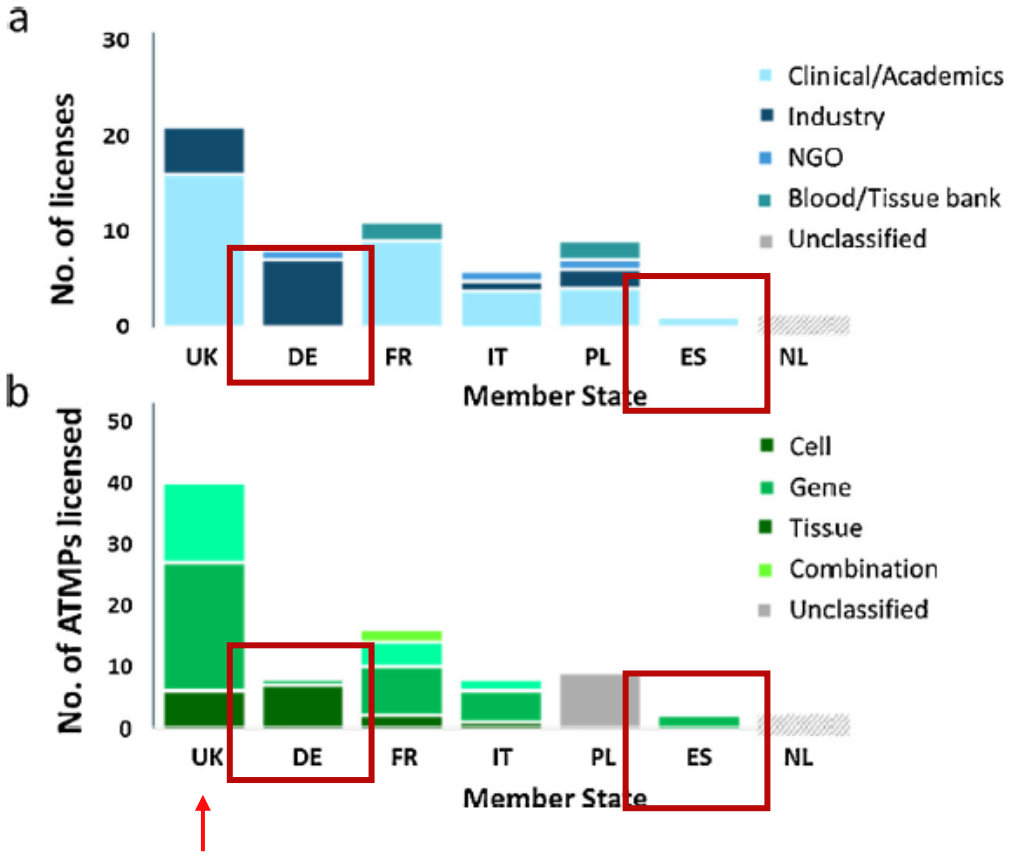
1. Exemption situations (unmet medical need)
2. Exemption situations; with evidence of benefit/risk
3. National authorisation; enables innovation – HE as stepping stone towards centralised registration

# National HE use for manufacturing




Specials scheme

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**Table 2**
Scope and scale of manufactured ATMPs under exemption pathways by public facilities, per country.

| Regulatory pathway | Hospital exemption | | | | |
|---|---|---|---|---|---|
| Country | FI (n = 1) | DE (n = 3) | IT (n = 2) | NL (n = 6) | Total HE (n = 12) |
| ATMP subtype | | | | | |
| Somatic cell therapy medicinal product | 0 | 3 | 2 | 6 | 11 |
| Combination ATMP | 1 | 0 | 0 | 0 | 1 |
| Origin of cellular material | | | | | |
| Autologous | 1 | 1 | 0 | 2 | 4 |
| Allogeneic | 0 | 2 | 2 | 4 | 8 |
| (Proposed) active substance | | | | | |
| Lymphocytes | 0 | 1 | 0 | 1 | 2 |
| Hematopoietic stem cells | 0 | 1 | 0 | 1 | 2 |
| Mesenchymal stromal cells | 1 | 1 | 2 | 4 | 8 |
| Target disease/condition | | | | | |
| Immunology | 0 | 1 | 0 | 3 | 4 |
| Infection | 0 | 0 | 0 | 1 | 1 |
| Cardiovascular | 0 | 1 | 0 | 1 | 2 |
| Hematology/oncology | 0 | 1 | 1 | 1 | 3 |
| Musculoskeletal | 1 | 0 | 0 | 0 | 1 |
| Unknown | 0 | 0 | 1 | 0 | 1 |
| Scale of manufacturing | | | | | |
| 0–10 batches | 1 | 0 | 2 | 3 | 6 |
| 10–50 batches | 0 | 1 | 0 | 2 | 3 |
| 50–200 batches | 0 | 0 | 0 | 1 | 1 |
| More than 200 batches | 0 | 2 | 0 | 0 | 2 |
| Unknown | 0 | 0 | 0 | 0 | 0 |

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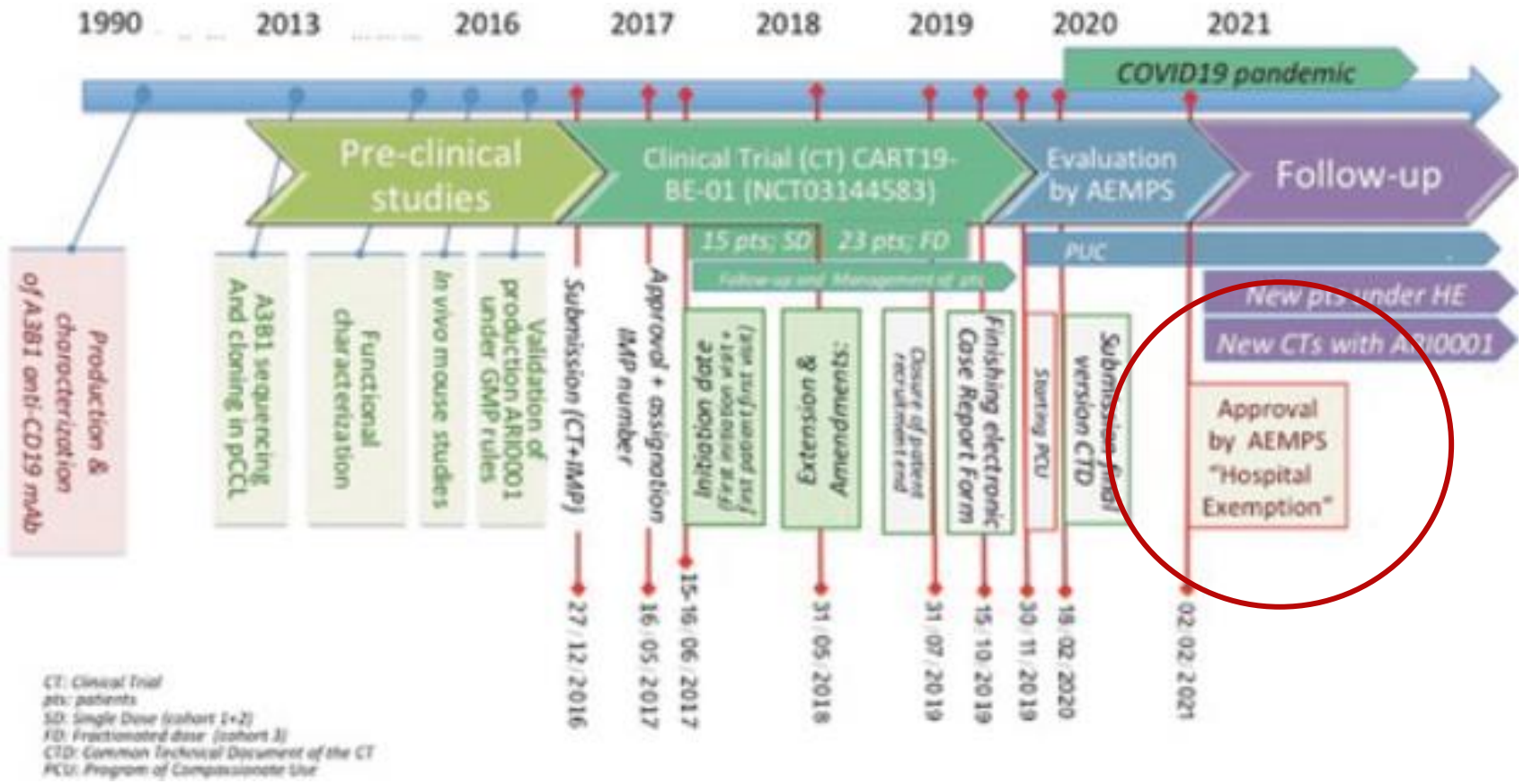
# CAR-T authorization in Spain - HE

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# CAR-T authorization in Europe

| | | | | | Authorization | Access |
|---|---|---|---|---|---|---|
| Kymriah® | Pharma | FMC63 | ALL ≤25 years old and DLBCL | 13.4 m ALL<br>11.9 m DLBCL | EU | ? |
| Yescarta® | Pharma | FMC63 | DLBCL | 25.8 m DLBCL | EU | ? |
| Tecartus® | Pharma | FMC63 | MCL | 18.2 m MCL | EU | ? |
| Breyanzi® | Pharma | FMC63 | DLBCL | 21.1 m DLBCL | EU | ? |
| ARI-0001® | Acad | A3B1 | ALL ≥25 years old | 20.2 m ALL | ES | ES |
| Abecma® | Pharma | anti-BCMA scFv | Multiple Myeloma | 21.4 m MM | EU | ? |


> Tension academic and commercial competitiveness; affects national vs. EU access

Adapted from Juan et al Hum Gene Ther 2021

european-union.europa.eu

# Patient access to ATMPs in NL

1. Exemption situations; with evidence of safety or positive benefit/risk profile; Hospital Exemption
2. Development to the market through centralised EMA registration; ATMP regulation & Directive 2001/83/EC

3. Academic innovations (added clinical benefits, transcending the scale of exemption situations, possible limited commercial value); regulatory gap to enable access to current ATMPs that are in later phases of development

# Solutions to guarantee patient access

1. Use of Hospital Exemption for national authorization (such as in Spain) as a stepping stone towards centralized marketing authorization for academic innovations
   - ➢ How to ensure that this pathway is complementary?

2. Support academic developments to enter the centralized marketing authorization pathway, with regulatory space for compassionate use under the Hospital Exemption


KWF