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Public online survey on Hospital Exemption

Fields marked with * are mandatory.

Introduction

Following the recent event **"Implementation of the Hospital Exemption in the EU and its Role in Boosting Innovation and Patient Access to Innovative Therapies"** held on 21 November 2024, we are launching this survey to gather public feedback on key takeaways related to the implementation of HE across Member States.

This survey aims to explore best practices identified during the event, validating their relevance and assessing their impact in different countries. The study focuses on practices that can support ATMP developers, foster innovation, and improve patient access.

We welcome opinions from diverse stakeholders, whether the practices are implemented in your country or not. The survey is designed to ensure that the final report reflects a comprehensive understanding of HE practices across Member States and provides meaningful insights for the ATMP community.

The aim of the survey is:

- To get feedback from participants of the event “Implementation of the Hospital Exemption in the EU and its Role in Boosting Innovation and Patient Access to Innovative Therapies” on the best practices regarding the current implementation of HE in the EU.
- To investigate whether there are other best practices that should be shared to support national regulators and ATMP developers.
- To understand the impact of these best practices on enabling patient access to ATMPs and boosting innovation around ATMPs.

The survey is anonymous; no personal or identifying information will be collected.

Deadline: 17 January 2025

Section 1: Profile

This section collects basic information to understand the diversity of perspectives contributing to the survey.

* Which country are you responding from?

- AT - Austria

- BE - Belgium
- BG - Bulgaria
- HR - Croatia
- CY - Cyprus
- CZ - Czechia
- DK - Denmark
- EE - Estonia
- FI - Finland
- FR - France
- DE - Germany
- EL - Greece
- HU - Hungary
- IE - Ireland
- IT - Italy
- LV - Latvia
- LT - Lithuania
- LU - Luxembourg
- MT - Malta
- NL - Netherlands
- (●) Other - Other
- PL - Poland
- PT - Portugal
- RO - Romania
- SK - Slovak Republic
- SI - Slovenia
- ES - Spain
- SE - Sweden

Please specify

* Which category best describes your organisation?

- Academia
- Non-profit research organisation
- Biotech SME (micro-small, or medium-sized enterprise)
- Large pharma company
- Scientific society
- Contract research organisation
- Contract manufacturing organisation
- National Competent Authority (NCA)
- Healthcare professional
- Patient organisation or advocacy group
- Healthcare provider (e.g., hospital, pharmacy)
- Funding body (Public payer or social health insurance)
- Regulatory/public authority (other than NCAs)
- Citizen/public

- [x] Other

Please specify

Trade association

* Are you directly involved in HE-related activities (e.g., research, development, regulation, use or reimbursement of HE products)?

- [ ] Yes
- [x] No

Section 2: Validation of best practices

This section explores best practices identified during the event, assessing their relevance and impact across Member States.

Best practice: Publication of HE approvals and nationwide registry of HE-ATMPs

Are there clear reporting mechanisms regarding the use of HE-ATMPs in your country?

- [ ] Yes
- [x] No

Why not?

To date practices and procedures for ATMP hospital exemption vary greatly across EU Member States and in some countries transparency is very limited. This has been highlighted in several publications including Hills et al Cytotherapy, Dec 2020 (DOI: 10.1016/j.jcyt.2020.08.011) and Coppens et al Regen Med., Aug 2020 (DOI: 10.2217/rme-2020-0008).

To what extent do you think having a registry of HE-ATMPs at national level is a best practice?

- [ ] 1: Not a good practice
- [ ] 2: Somewhat useful but not essential
- [ ] 3: Neutral/Neither good nor bad
- [ ] 4: A useful practice
- [x] 5: An essential best practice

Please specify

A publicly accessible registry that includes a list of products under the HE scheme will ensure transparency on its use across Member States as well as enable public scrutiny and assurance that the system is being used as intended by EU legislation. National registries must be consolidated or easily accessible at EU level.

Is information on HE-approvals published in your country?

- [ ] Yes

- [x] No

Why are the data are not/cannot be published in your country (e.g., national restrictions).

While information about HE-approvals is publicly available in some countries, to our knowledge it is not a standard practice across all EU countries. Even the national standards for HE-approvals can be opaque across Member StatesIt is unclear why information on HE-ATMPs is not published in some countries. At a minimum, basic information about the product and its intended use should be made available in the public interest and there should be increased on the specific approval standards and procedures.

Do you believe that clinical data registries, such as those maintained by the European Society for Blood and Marrow Transplantation (EBMT), could be a useful tool for collecting HE-related data, particularly considering the specific applications for HE presented during the event?

- [ ] Yes
- [ ] No
- [x] Not sure

Please elaborate on any additional information or support you would need to assess their usefulness.

- It is essential that data on the use, safety, efficacy and quality of the HE-ATMP, , as well as relevant patient follow-up data, are collected and reported by the HE-ATMP holder to the national competent authority. Many institutions likely to engage in HE ATMP manufacture and delivery may already have experience reporting data to EBMT so leveraging existing registry infrastructures such as those maintained by EBMT could be useful if the registry is fit for purpose and facilitate sharing of data at EU level.
- The ongoing safety of patients is a priority and therefore their follow-up in the long term is important, particularly in the event of any latent safety signals arising. Considering the expected low volume of patients receiving HE-ATMPs, special attention should be paid to ensure long-term follow-up periods are appropriately risk-based and reflect the level of evidence available including any known and/or potential risks associated with the product.
- Clinical data from HE-ATMPs and authorised ATMPs collected in the same database do not necessarily enable robust scientific comparison as appropriate methods for indirect comparisons need to be applied.
- In addition to clinical data in such registries, information on product quality issues related to HE-ATMPs should be collected and reported to a national competent authority even if they do not result in any immediately obvious impact on safety and efficacy. Learnings from product quality data on the manufacture of ATMPs under the hospital exemption setting would be useful for both regulators and developers and can only be analyzed and understood if reported.

Best practice: Consistency among reimbursement possibilities

To what extent do you think the same pricing and reimbursement rules should apply to HE-ATMP and centrally authorised ATMPs?

- [ ] 1: Not a good practice
- [ ] 2: Somewhat useful but not essential
- [x] 3: Neutral/Neither good nor bad
- [ ] 4: A useful practice
- [ ] 5: An essential best practice

Please specify

Appropriateness of applying the same pricing and reimbursement rules for HE-ATMP and centrally authorised ATMP depends on country-specific circumstances and scale of HE-ATMP production. We believe HE is best employed in exceptional circumstances where no alternative treatments can meet the needs of an individual patient as may be the case in some rare and ultra-rare diseases. Where this is the case, applying the same pricing and reimbursement rules would likely be inappropriate. However, we are aware of situations in some Member States where the scale of HE-ATMP production may reach a level where it would be appropriate to apply the same pricing and reimbursement rules including standards for comparative effectiveness evidence that could be addressed if appropriate clinical trials to support a centralised marketing authorisation were conducted. Each member state should comment publicly on how they would approach applying standard pricing and reimbursement rules to instances in which HE-ATMP production is likely to reach or has reached a level commensurate with what would be considered commercial scale, taking into account the prevalence and incidence of the disease.

Is national reimbursement of HE-ATMPs a possibility in your country?

- ○ Yes
- ○ No

Best practice: Pursuing Central Marketing Authorisation (CMA)

To what extent do you think pursuing a CMA as the end goal to HE-ATMPs is a best practice?

- ○ 1: Not a good practice
- ○ 2: Somewhat useful but not essential
- ○ 3: Neutral/Neither good nor bad
- ◉ 4: A useful practice
- ○ 5: An essential best practice

Please specify

Hospital Exemption is not intended as a pathway for development. It is an exception to the standard procedures for centralised marketing authorisation to enable patient access on a non-routine basis. HE should not be initiated with the intention of pursuing a centralised marketing authorisation at the outset. However, EU legislation should encourage HE-ATMPs with promising outcomes to pursue further development via well designed, regulated clinical trials and centralised marketing authorisation procedures for ATMPs when an appropriate threshold has been reached.

Would support mechanisms make the CMA process more accessible for HE-ATMP developers?

- ☐ EMA pilot for academic developers of ATMP
- ☐ EMA Innovation Task Force briefing meetings
- ☐ National Innovation meetings
- ☐ EMA Scientific Advice
- ☐ National Scientific Advice
- ☐ Simultaneous National Scientific Advice (SNSA)
- ☐ EMA Qualification of novel methodologies and biomarkers
- ☐ EMA Prime scheme
- ☐ CAT classification

- [ ] EMA Academia Briefing meetings
- [ ] Parallel EMA-HTA body scientific advice
- [ ] CAT certification
- [ ] EMA SME Office
- [ ] Orphan designation

Is a CMA pursued by ATMP developers after making a HE-ATMP available to patients in your country?

- ( ) Yes
- ( ) No

Section 3: Success stories of using HE

This section highlights real-world applications of HE to inspire discussion of its potential across Member States.

In Sweden, burn care provides an example of HE is being used for life-saving treatments (e.g., cultured autologous keratinocytes for severe burns). Are there similar cases in your country?

- ( ) Yes
- ( ) No

In Belgium, HE has been instrumental in boosting a spin-off company by facilitating early-stage innovation and product access. Are there examples in your country where HE has supported the development of spin-offs or similar initiatives?

- ( ) Yes
- ( ) No

In France, the new provision (II of Article L.4211-9-1) regulates the preparation, distribution, and administration of MTI-PP (HE-ATMP) within hospitals as part of the same medical intervention as the tissue or autologous cell collection. Are there examples in your country where a similar provision has facilitated patient access to advanced therapies or supported innovation in hospital settings?

- ( ) Yes
- ( ) No

Various Member States have notable examples of a non-profit or public organisation that holds manufacturing and distribution rights for an approved ATMP, showcasing the potential of public/non-profit ownership of ATMPs. How do you view public or non-profit ownership of ATMPs, and are there similar cases in your country?

- (•) Yes
- ( ) No

Please provide details of similar cases in your country and share your views on public/non-profit ownership of ATMPs.

Academia plays an important role in the research and development of ATMPs driving innovation in the field and we fully support efforts to assist academic (public) and non-profit developers, such as EMA's pilot programme, in meeting the expected regulatory standards set for these products. It is essential that EU legislation ensures a level playing field and that the same scientific and regulatory standards are applied consistently to similar products regardless of who produces them.

Section 4: Final comments

This section invites participants to share any additional thoughts or suggestions to ensure no important topics are overlooked.

Are there any additional aspects or insights related to the Hospital Exemption context that were not covered in this survey, or do you have any final comments or suggestions regarding HE practices?

While HE is an important option for patients who may have exhausted other treatment alternatives, availability of HE pathway and products must not become a disincentive to generate robust evidence and obtain a centralised marketing authorisation.
Hospital Exemption is not a route for routine product development but a regulatory mechanism to allow treatment of individual patients with urgent medical need, where no alternative option is available. Therefore, HE-ATMPs should not be positioned as representing an equivalent in terms of Quality, Safety and Efficacy standards to treatments with a marketing authorisation.
The scientific evidence supporting the use of products manufactured under a hospital exemption license is inherently limited compared to a product that has obtained a marketing authorisation. For example, it was noted in the presentation from Dr. Babs Fabriek on her experience as clinical assessor for MEB during November 21 workshop that “a meaningful assessment of safety (and efficacy) of treatment under HE remains challenging [as] low patient numbers preclude strong conclusions.” As another example, the definition of ‘non-routine’ provided for in German law indicates HE-ATMPs are manufactured and used on such a small scale that it is not to be expected that sufficient clinical experience can be gained to fully evaluate the medicinal product or have not yet been produced and applied in sufficient numbers so that the necessary knowledge for their comprehensive evaluation has not yet been obtained. In contrast, authorised ATMPs must provide comprehensive data and undergo a rigorous benefit-risk assessment.
Measures that would promote or lead to prioritisation of hospital exemption use based on affordability when an authorised alternative is available would represent an unacceptable risk for patients given the differences in scientific evidence available, as well as disincentivise further investment in innovation on ATMPs in Europe.
A harmonised interpretation of ‘non-routine basis’ that explicitly clarifies that ATMP hospital exemption can be granted in justified cases of medical necessity, specifically excluding economic considerations, and only in the absence of other solutions for the individual patient including an authorised medicinal product, a compassionate use programme referred to in Article 26 of [revised Regulation 726/2004] or under a clinical trial for which the patient is eligible [in the Union] would be an important guardrail for ensuring protection of public health and safety of individual patients.
The EU legislation lacks a definition of ‘non-routine’ which creates uncertainty regarding the role of the HE when a centrally authorised product becomes available. This uncertainty makes the EU regulatory framework less attractive than other regions for ATMP development. Furthermore, when the HE is used in a way which is different than what was intended, such as a parallel regulatory track to marketing authorisation, the HE risks to negatively impact the competitiveness of the EU regulatory framework and dilutes the practical effects of the marketing authorisation principle. This results in a distortion and fragmentation of the EU single market which must be avoided, both for patient safety reasons as well as to maintain Europe’s attractiveness for companies in the sector, and ultimately, to ensure that patients in Europe will continue to benefit from transformative therapies. Europe is already trailing behind Asia and the US in terms of the number of therapeutic developers, new clinical trials, and investment into the ATMP sector (see: EFPIA Report Assessing the clinical trial ecosystem in Europe: https://www.efpia.eu/media/3edpooqp/assessing-the-clinical-trial-ecosystem-in-europe.pdf, page 20; ARM Cell and Gene Therapy Sector Data - Q3 2024: https://alliancerm.org/data/) . Developers would be further disincentivised to invest in complex, costly and risky clinical development activities in Europe if they have had to compete with others that do not face the same requirements.

Thank you for your participation!

Thank you for taking the time to complete this survey. Your insights and perspectives will be carefully considered as part of the study team's efforts to compile the final report on Hospital Exemption (HE)

practices across Member States.

If you have any questions or additional input, please feel free to contact the study team at mrodes@predictby.com.

Thank you once again for your input!

Contact

Contact Form