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Hospital Exemption and Human Tissue–Cell Governance in the European Union: Regulatory Heterogeneity, Legal Certainty and Unequal Patient Access across 27 Member States

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Review Article

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Abstract

The European Union (EU) Hospital Exemption (HE) permits certain non-routinely prepared advanced therapy medicinal products (ATMPs) to be manufactured and administered without centralized marketing authorization, subject to stringent national conditions. The exemption intersects with-but does not replace-rules for the donation, procurement, testing, handling and traceability of human tissues and cells. Aim of this review is to characterize HE heterogeneity across the EU-27, distinguish demonstrable transposition failures from regulatory variation and insufficient transparency, and examine implications for equitable access to biological starting materials and advanced therapies. For this, doctrinal and comparative documentary analysis of EU primary legislation, a Court of Justice judgment, European Commission/HaDEA reports, published comparative research and 27 author-supplied national regulatory profiles were reviewed. Claims were graded as adjudicated infringement, documented national divergence, plausible implementation risk or unverified assertion. The 2025 EU HE study and comparative literature demonstrate markedly different national authorization architectures, definitions and controls. Heterogeneity can create unequal practical opportunities to obtain lawful HE treatment, but causal patient-level disparities and intentional non-compliance have not been demonstrated. Regulation (EU) 2024/1938 offers an opportunity to strengthen the SoHO–ATMP interface from August 2027, provided Member States implement coherent oversight and transparent procedures.

Keywords: Hospital exemption; Advanced therapy medicinal products; Directive 2004/23/EC; Regulation (EU) 2024/1938; tissue and cell legislation; Access to treatment; EU-27; health equity; Regulatory fragmentation

Introduction

The regulation of ATMPs is an unusually demanding test of European legal integration. Products derived from living cells, tissues or genetic modification can involve a donor, a procurement establishment, one or more testing laboratories, a processing or manufacturing site, a hospital and a physician, each operating under partially distinct legal duties. Centralized authorization under Regulation (EC) No 1394/2007 is the ordinary market pathway. Article 28 of that Regulation inserted Article 3(7) into Directive 2001/83/EC, establishing a limited HE for products prepared non-routinely to specific quality standards and used within the same Member State, in a hospital, under the exclusive professional responsibility of a medical practitioner, in response to an individual prescription [1,2].

The resulting framework is not a simple derogation from patient protection. National manufacturing authorization, quality requirements, traceability and pharmacovigilance remain necessary. At the same time, Directive 2004/23/EC and its implementing directives establish safeguards for human tissues and cells, including procurement, testing, processing, storage, distribution and vigilance [3-5]. These rules may attach to the starting materials even where downstream manufacture is subject to ATMP-specific regulation. The legal question is therefore not merely whether a Member State recognizes HE, but whether the full chain of regulated activities can be lawfully and predictably completed.

Prior comparative studies have described important differences in national HE practice, including interpretations of "non-routine", the availability of published authorization information, the identity of eligible institutions and approaches to clinical evidence [6,7]. The European Commission's 2025 study provides a more contemporary comparative baseline and national annex for 19 Member States [8]. The present review adds a distinct legal-certainty and distributive-justice perspective: can the design or opacity of national procedures make otherwise potentially eligible patients and their clinical teams unable to obtain access to lawful procurement, processing or treatment?

Research Questions and Methodology

We address four questions: (i) which HE differences are supported by national instruments or comparative reports; (ii) which alleged tissue-and-cell defects constitute established violations rather than uncertainty; (iii) how can differences in the regulatory interface affect access to biological samples and HE therapies; and (iv) what changes may follow from Regulation (EU) 2024/1938?

Sources comprise the EU legal instruments [1-5,9], CJEU Case C-29/14 [9], the Commission/HaDEA 2025 HE study and its Member State annex [8], published comparative scholarship [6,7], and Greek governmental consultation material [10] . The profiles are treated as research dossiers, not as independent proof of regulatory breaches. Their characterizations are explicitly differentiated from verified EU-level findings. This is a narrative comparative legal review, not a systematic review, audit of national inspection files, or an empirical analysis of individual patient outcomes.

Evidence hierarchy: Level A, final judicial infringement finding; Level B, verified statutory or administrative instrument; Level C, comparative study describing procedural divergence; Level D, documentary uncertainty or plausible compliance risk; Level E, allegation lacking adequate supporting primary evidence. A missing public register is not proof that no authorization exists; absence of an HE route does not automatically establish breach of Directive 2004/23/EC, whose subject matter is different.

Normative Framework: Two Connected but Distinct Regulatory Pathways

Hospital Exemption Under ATMP Law

Article 3(7) of Directive 2001/83/EC requires a non-routine product made according to specific quality standards, used in a hospital in the same Member State, under a medical practitioner's exclusive professional responsibility and for an individual patient pursuant to an individual prescription. Manufacturing must be authorized by the national competent authority; national traceability, pharmacovigilance and quality standards must be equivalent to those for centrally authorized ATMPs [1,2]. EU legislation leaves national authorities substantial administrative design space, which can generate different evidentiary burdens, processing times, authorization periods and interpretations of routine versus exceptional manufacture.

Directive 2004/23/EC and Implementing Instruments

Directive 2004/23/EC lays down quality and safety standards for human tissues and cells intended for human application. Directive 2006/17/EC provides technical rules for donation, procurement and testing, while Directive 2006/86/EC addresses traceability, reporting of serious adverse reactions/events and technical processing and coding obligations [3-5]. The relevant legal obligations depend on the material, activity and stage of the chain; it would be legally unsound to assert that every cell-based ATMP is governed identically by every provision of the tissue directive throughout manufacture. A precise compliance analysis must map the hand-off from procurement/testing to ATMP manufacture and then hospital use.

The Soho Transition

Regulation (EU) 2024/1938 expressly identifies divergence created by the choices left to Member States under the former blood and tissue/cell directives and seeks a more coherent, transparent and sustainable framework [10, recital 5]. It repeals Directives 2002/98/EC and 2004/23/EC with effect from 7 August 2027; most provisions apply from that date, with exceptions and transition rules [10, article 85-87]. The Regulation directly applies, but national authorities still require institutional readiness, supervision, enforcement and operational interfaces with ATMP legislation. As of October 2026, failure to perform a future duty that is not yet applicable cannot ordinarily be called a present infringement.

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Comparative Heterogeneity in HE Across the EU

The 2025 Commission/HaDEA study covers HE implementation from the ATMP Regulation's entry into force through January 2025 and includes in-depth information for 19 Member States [8]. It documents the need for more consistent data collection on authorizations, safety and efficacy. Earlier multi-country research also reports variability in the interpretation of HE conditions, quality oversight, utilization and public transparency [6]. These differences have regulatory significance even where they are lawful: patients in otherwise similar clinical circumstances may confront different procedural feasibility, institutional access and timing.

Heterogeneity in the Regulation and Interpretation of Hospital Exemption Across EU Member States

Regulatory dimension	Documented pattern	Possible access or oversight consequence
Eligible institutions	National frameworks may restrict which hospital or establishment can apply	Patients may need referral to a qualifying center; private/public distinctions can matter
Meaning of "non-routine"	Variable national operational interpretations	Different feasibility for repeated individualized manufacture
Authorization design	Different procedures, scope, duration and evidence expectations	Unpredictable lead times and investment decisions
Transparency	Uneven publication of routes and authorized products	Clinicians and patients may struggle to identify a lawful pathway
Tissue/ATMP interface	Distinct authorities may supervise procurement and manufacture	Potential delays in material transfer and fragmented accountability
Clinical oversight	Manufacturing consent and clinical treatment decisions may be separated	Need for explicit responsibility and outcome-monitoring mechanisms

Table 1: Variability in the Interpretation of Hospital Exemption Requirements Across EU Member States.

Illustrative national contrasts follow. Germany has a dedicated HE provision in §4b of the Arzneimittelgesetz and a specialized federal authority, the Paul-Ehrlich-Institut. France uses a distinct national category for occasionally prepared ATMPs. Spain operates an authorization mechanism under Royal Decree 477/2014 and has public examples of hospital-based ATMP authorization. Italy's 16 January 2015 ministerial decree structures a more institution-specific pathway. The Netherlands and Nordic states have adopted other interpretations and operational models. These are examples of differentiated legal architecture, not findings that any of those states breached tissue-and-cell law [6-8,11-14].

EU-27 Documentary Assessment

Table 2 identifies the principal research question raised by each national dossier. It is deliberately a verification register rather than a list of proven violations. "Operationally uncertain" refers to the visibility of an HE-specific procedure in the reviewed material, not to the existence of tissue-and-cell legislation generally.

Country-Specific Questions Identified During Primary Source Verification of EU Member State National Dossiers

Member State	Priority question for primary-source verification
Austria	Interface between medicines and tissue-establishment controls
Belgium	Authorization duration, scope and transparency
Bulgaria	Public visibility of dedicated HE procedure
Croatia	Competent-authority coordination
Cyprus	Dedicated HE route not clearly established in dossier; tissue law identified
Czechia	National HE authorization conditions
Denmark	Balancing clinical innovation and HE safeguards

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Estonia	Reported recent changes and practical implementation
Finland	Authorization continuity and public reporting
France	MTI-PP categorization and institutional eligibility
Germany	§4b AMG and oversight at tissue/ATMP boundary
Greece	2026 HE primary law and status of secondary implementation
Hungary	Competent-authority and procedural clarity
Ireland	HE procedural accessibility and public guidance
Italy	Institutional eligibility and non-repetitive preparation
Latvia	Recent national HE developments and enforcement
Lithuania	Authorization and quality control interface
Luxembourg	Limited publicly identified dedicated HE route
Malta	Small-state capacity and HE procedural visibility
Netherlands	Individualized/non-routine interpretation
Poland	Historical CJEU tissue transposition breach; present HE manufacturing/clinical boundary
Portugal	Public procedural guidance and oversight
Romania	Dedicated HE route not clearly established in dossier
Slovakia	Operational guidance and tissue/ATMP hand-off
Slovenia	Small-market operational capacity
Spain	Royal Decree 477/2014 and hospital authorization
Sweden	Authorization scope, duration and follow-up

Table 2: Overview of Questions Identified During Review and Primary Source Verification of National Dossiers.

The register should not be read as asserting that all 27 Member States have defective legislation. An infringement inventory requires an article-by-article legal crosswalk, dated consolidated national instruments, competent-authority records, and-where relevant-Commission infringement correspondence or judgments. The 2025 study's in-depth country sample is 19 rather than 27 Member States [8].

Poland: Established Historical Infringement and the Limits of Inference

The strongest direct judicial evidence concerns Commission v Poland, Case C-29/14, judgment of 11 June 2015. The Court held that Poland failed to fulfil its obligations under Article 31 of Directive 2004/23/EC and specified provisions of Directives 2006/17/EC and 2006/86/EC because national transposition excluded reproductive cells and foetal and embryonic tissues [9, paras 43-51]. The Court rejected the proposition that a mixture of general provisions and non-binding professional rules could provide the specificity, precision and binding force required for transposition. It emphasized the legal certainty of individuals and the high level of public-health protection pursued by the directives.

This precedent is highly relevant to HE governance as a general principle: Member States cannot cure a substantive omission from mandatory tissue/cell coverage merely by invoking dispersed or non-binding practices. Yet the judgment concerned specified reproductive and developmental materials; it did not adjudicate Polish oncology HE manufacturing, current enforcement in 2026 or the legality of any particular patient treatment. Those propositions must not be conflated.

The Polish dossier identifies a formal ATMP-HE manufacturing-consent route under the Pharmaceutical Law, particularly Articles 38a and 38aa, supervised by the Chief Pharmaceutical Inspector. It also notes a distinction between authorization of manufacture and the physician's clinical decision. This separation raises a legitimate governance question: how are donor qualification, batch quality, patient selection, informed consent, clinical follow-up and adverse-event reporting joined into a continuous accountability chain? It does not by itself prove a gap in law. Verification requires the current consolidated Polish statutes, inspectorate practice, inspection findings and any relevant treatment-specific decisions.

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The unresolved legal question is therefore narrow but consequential: are the safeguards and precise allocation of responsibilities required by applicable EU law implemented and enforced for each relevant tissue/cell and ATMP activity? A historical finding of infringement warrants heightened scrutiny, not an automatic presumption of persistent illegality or intentional obstruction.

Greece: Late Explicit HE Codification and Legal-Certainty Questions

Greek governmental consultation material for Article 32 of the 2026 legislative reform explicitly identified the need to set conditions for the production and administration of ATMPs under HE and to avoid interpretive divergence and an insufficiently regulated parallel supply system [10]. The Greek national dossier reports that Law 5302/2026 (Government Gazette A 78/20 May 2026) inserted Article 8B into Legislative Decree 96/1973, establishing an express statutory basis for HE. This is a material legal development and precludes a simple present-tense assertion that Greece has no HE legislation.

The principal research issue concerns operationalization: what secondary measures specify facility eligibility, manufacturing authorization, inspection, traceability, adverse-event reporting, clinical accountability and the interface with tissue establishments? Does an applicant have a clear, reviewable route to obtain an authorization, and can a hospital access compliant biological starting materials without legally unnecessary barriers? If a mandatory procedure is absent in practice, a failure-to-act or legal-certainty question may arise, but that conclusion requires the operative statutory texts, ministerial decisions, authority guidance and concrete evidence of administrative conduct.

Directive 2004/23/EC transposition must be assessed separately from HE implementation. The presence of a delayed or incomplete HE-specific mechanism does not establish that Greece failed to transpose the tissue directive. Equally, formal tissue legislation does not prove that its rules are effectively applied at the SoHO–ATMP interface. Whether the combined system unlawfully frustrates EU objectives remains an open, testable legal question-not an established finding of intentional infringement.

Legal Consequences and Patient-Equity Implications

Potential EU-Law Consequences

If a Member State fails to transpose a directive correctly or fails to fulfil enforceable EU obligations, the Commission may investigate and, where appropriate, bring infringement proceedings under Article 258 TFEU. Following an adverse judgment, continued non-compliance can engage Article 260 TFEU. Other possible routes, depending on facts and national law, include judicial review of administrative refusals, preliminary references under Article 267 TFEU, and claims for state liability where the demanding conditions established by EU case law are met. No particular remedy or damages entitlement can be presumed from HE heterogeneity alone.

Biological Material Access and Cross-Border Inequity

The patient-facing problem is best framed as a pathway dependency. Access to a personalized cell-based therapy may require a compliant donation/procurement route, reliable testing, lawful transfer to a qualified manufacturing site, authorization of non-routine manufacture, and an eligible hospital willing to administer the product. A failure or ambiguity at any link can prevent treatment even when scientific capability exists. Cross-border procurement and transfer can introduce additional practical and legal complexity, while HE itself is constrained by its same-Member-State manufacturing/use condition. This can disproportionately affect patients in smaller markets or those without access to specialized hospitals.

Three inequities should be distinguished. Procedural inequity arises when similarly situated patients face different waiting periods or approval complexity. Institutional inequity arises when only certain hospitals can act as HE sponsors or recipients. Informational inequity arises when patients and physicians cannot readily identify lawful routes or publicly documented outcomes. These are plausible consequences of heterogeneity, not measured differences in treatment outcomes. Demonstrating unfairness empirically would require linked data on eligible patients, applications, refusals, processing times, travel, costs, outcomes and socioeconomic status.

Intentional Obstruction: Evidentiary Threshold

A finding that officials or governments intentionally compromise HE requires evidence of knowledge, purpose and conduct, such as contemporaneous correspondence, repeated refusals despite clear binding obligations, documented selective treatment, or authoritative investigative findings. Neither the existence of restrictive national choices nor the absence of published HE activity establishes intention. A journal manuscript should therefore state a research hypothesis about potentially avoidable administrative obstruction, not allege deliberate wrongdoing without evidence.

Regulation (EU) 2024/1938: Opportunities and Unresolved Boundaries

The SoHO Regulation responds directly to the regulatory fragmentation identified in recital 5 [15]. Its direct applicability should reduce some divergence in upstream

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human-material quality and safety rules, clarify competent-authority responsibilities and support more consistent information exchange and oversight. For ATMP developers, the crucial interface is between activities that remain within SoHO supervision and activities governed by medicinal-product law. Traceability must not be interrupted by the transfer of material into ATMP manufacture, and overlapping authority should not become a regulatory vacuum.

Nevertheless, the SoHO Regulation does not itself eliminate the HE discretion embedded in ATMP law. Member States will still differ in hospital capacity, reimbursement, staffing, inspection resources and operational HE procedures. Harmonization of tissue/cell safety should therefore be evaluated separately from harmonization of access to HE-ATMPs. A 2027–2029 evaluation agenda should track authorization decisions, time to decision, permitted products, adverse-event systems, cross-border material movements, and patient access while respecting confidentiality.

Comparative Interpretation of Non-Routine Manufacture

The phrase "non-routine basis" is central to the hospital exemption but does not itself prescribe a uniform numerical ceiling on patients, batches, annual production, or repeated manufacture. Member States have consequently developed divergent techniques for operationalizing the same Union-law standard. A qualitative approach asks whether manufacture is individualized, exceptional and clinically justified; a quantitative approach can supplement that analysis with thresholds or production-frequency indicators. Neither approach is necessarily unlawful, but each has distributional consequences. A restrictive interpretation may reduce access for patients with rare conditions in institutions lacking routine industrial manufacturing capacity. An excessively permissive interpretation risks transforming an exceptional route into a substitute for ordinary marketing authorization and the evidence-generating obligations associated with it.

The 2025 Commission-supported HE study identified particularly explicit national approaches in Belgium, Germany, Estonia and the Netherlands, and it also reported significant differences in authorization duration. Those findings should be read against the text of Article 3(7) of Directive 2001/83/EC, which does not create an unlimited national discretion. National criteria must remain consistent with the exception's individual-prescription, hospital-use and quality-protection requirements. In a future EU-27 assessment, each authority should be asked to provide the operative definition, any quantitative guidance, a sample of anonymized decisions and the legal basis for refusing or limiting repetitive production.

A doctrinally defensible infringement argument would require more than proof that one state authorizes more products than another. It would require evidence that the state's operative rule or decision practice is incompatible with a binding Union requirement, for example by systematically dispensing with individualized prescriptions or equivalent quality safeguards. Conversely, an excessively restrictive domestic rule could raise proportionality or legal-certainty questions where it effectively defeats a route that EU law contemplates, although the HE provision does not confer an unconditional individual entitlement to treatment.

Authorization Architecture, Timelines and Administrative Capacity

The administrative architecture of HE determines how easily a hospital, academic manufacturer or specialist clinician can translate a clinical concept into a lawful treatment. The 2025 study reported national application-review periods ranging from approximately 14 days in Denmark to 210 days in Spain. Such figures are descriptive and cannot be treated as directly comparable measures of regulatory efficiency without accounting for dossier completeness, application category, clock stops, and the complexity of the product. Nonetheless, a variation of this magnitude makes administrative time a legitimate object of comparative study.

Some systems distinguish establishment or manufacturing authorization from product or clinical-use authorization; others combine these decisions or allocate them to separate authorities. France and Italy were identified in the Commission-supported study as examples in which separate authorizations may be required. Dual review can create valuable independent checks, but also increases the risk of duplicated requests, inconsistent decisions and unallocated responsibility. A high-quality comparison must identify the responsible authority, legal decision deadline, formal opportunity for scientific advice, fees, review criteria, appeals and publication of final decisions.

For patients, administrative predictability is not merely a convenience. A person with rapidly progressive disease may have a clinically meaningful therapeutic window shorter than the time required to clarify the competent authority or obtain a manufacturing consent. The relevant equity problem is therefore an interaction among law, institutional expertise, financing and disease progression. It should be investigated empirically through application-to-decision intervals, reasons for withdrawal, incomplete applications, and time from consent to administration. The absence of such data prevents a defensible conclusion that a particular national law caused a specified patient to lose treatment access.

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Scope and Legal Classification at the Soho–ATMP Boundary

A biological material does not enter a single regulatory category for its entire life cycle merely because its eventual destination is an ATMP. The collection and testing of human cells can engage tissue-and-cell rules; substantial manipulation, non-homologous use or other product characteristics can bring the manufactured intervention within the ATMP framework. The classification exercise must be performed on the actual product and process, not on marketing terminology such as "stem-cell treatment," "regenerative preparation" or "personalized immunotherapy."

This boundary is particularly sensitive where institutions procure tissue or cells under a healthcare authorization and later transfer material to a pharmaceutical manufacturer. The legal crosswalk should specify which actor verifies donor eligibility, which establishment documents consent and testing, when custody transfers, which quality system applies to transport, and who maintains identifiers sufficient for bidirectional traceability. A tissue-establishment license is not a substitute for an HE manufacturing authorization, and an HE authorization cannot retrospectively cure an unlawful procurement. A national framework that leaves those responsibilities unallocated can generate practical uncertainty even where each statute, viewed alone, appears formally complete.

Comparative legal research should avoid assuming that every cell product is covered by every provision of Directive 2004/23/EC at every manufacturing stage. The applicable instrument depends on the regulated activity and product classification. This qualification is essential in evaluating alleged infringements: the first question is whether the disputed material and activity fall within the specific obligation invoked. Only then should the researcher assess transposition, enforcement and any available legal remedy.

Traceability, Serious Adverse Events and Long-Term Follow-Up

Traceability links patient safety to legal accountability. For a cell-derived ATMP, the ability to reconstruct donor origin, procurement conditions, testing results, intermediate processing, transport, manufacture, batch release and administration may be essential to investigating contamination, misidentification or delayed adverse effects. Directive 2004/23/EC and Directive 2006/86/EC impose specific duties within their scope, while HE also entails national requirements on traceability and pharmacovigilance equivalent to those for centrally authorized ATMPs.

A regulatory gap can arise where different competent authorities oversee adjacent stages without an agreed hand-off protocol. For example, a serious event initially detected by a hospital may require communication with the manufacturer and with the tissue establishment; the event may also be reportable under more than one system. A paper-based legal review should therefore ask whether national instruments identify a primary reporting actor, deadlines, cross-notification duties, record-retention rules and a process for reconciling multiple identifiers. The existence of a vigilance provision is not equivalent to proof that cross-sector reports are made reliably.

The European Blood Alliance's 2025 position paper highlights the need for more consistent collection of HE outcomes and a clearer ATMP–SoHO boundary. This is important because a lack of public outcome reporting can impair learning without necessarily constituting a violation of an existing publication duty. The proposed post-2027 assessment should distinguish mandatory reporting from desirable transparency, examine the practical interoperability of registries and prioritize adverse-event investigation across the whole donation-to-recipient chain.

The Meaning of Unequal Access in EU Health Law

Cross-national inequality in access to HE therapies should not be equated automatically with unlawful discrimination. Member States retain important responsibilities for organizing and financing health services, and HE is a conditional exemption from centralized marketing authorization rather than a Union-wide guarantee that a particular investigational product will be provided. Nevertheless, the principles of legal certainty, proportionality, non-discrimination where applicable and effective judicial protection provide a relevant normative framework for examining arbitrary or opaque administrative obstacles.

A useful analytical model separates four access dimensions: legal eligibility, institutional availability, affordability and timely clinical opportunity. Legal eligibility concerns whether a compliant route exists and is intelligible. Institutional availability concerns whether qualified establishments and specialists can use that route. Affordability includes the funding of procurement, manufacture and hospitalization. Timeliness concerns whether administrative review can be completed while treatment remains clinically appropriate. A patient may be formally eligible yet practically excluded because no hospital has the capacity to manufacture or procure the product.

The claim of unfairness is strongest where comparably situated patients face materially different opportunities

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because public authorities apply unexplained criteria or fail to establish a legally required procedure. It is weaker where the difference reflects transparent, lawful national healthcare choices or the absence of a clinically validated product. Future empirical studies should compare standardized patient scenarios across jurisdictions, controlling for diagnosis, urgency, hospital capability and reimbursement. Such work would make distributive claims measurable rather than rhetorical.

Biological Samples, Donor Consent and Cross-Border Constraints

Access to biological samples is a distinct regulatory issue from access to finished ATMPs. Tissue and cell procurement requires attention to donor consent, testing, eligibility, confidentiality, processing and transport. The applicable requirements may change when material is imported, exported or transferred between establishments. Meanwhile, Article 3(7) requires the exempt ATMP to be used in a hospital within the same Member State in which it is prepared. The geographic constraint on HE treatment must not be confused with a universal prohibition on cross-border movement of all biological starting materials.

The practical concern is that a hospital may be unable to obtain compliant cells because the identity of an authorized procurement establishment, import procedure or responsible authority is unclear. Conversely, allowing unregulated procurement would undermine the safety rationale of the Union framework. Legal reform should therefore seek transparent, proportionate pathways rather than blanket deregulation. A robust national guidance document would specify the material's classification, donor and consent requirements, permitted transfers, documentation at release, and responsibility for deviations discovered after the material has moved.

Claims that national regulatory omissions caused unfair exclusion from samples should be supported by documentary case histories: the applicant's request, the authority's response, the legal provision invoked, the sample type and its intended use. Without such records, the manuscript can identify a credible access mechanism but should not allege that a named state intentionally withheld biological materials.

Poland: Doctrinal Significance of Commission V Poland

The Court of Justice's judgment in Case C-29/14 supplies a particularly instructive standard for national implementation. Poland's principal transposing statute excluded reproductive cells and foetal and embryonic tissues. The government argued that other legal provisions and professional practices nevertheless ensured adequate protection. The Court rejected that position because the combination of measures did not provide the binding specificity, precision and clarity required by the directives and by legal certainty. The judgment also highlights the Member State's duty to identify transposition measures clearly in its communications with the Commission.

The case should be characterized accurately. It establishes a historical failure to fulfil obligations concerning specified categories of tissues and cells; it does not itself establish that Poland's present ATMP hospital exemption route is unlawful. Nor does it establish an infringement involving oncology-derived circulating tumour cells or every autologous preparation. A modern claim would need to identify the current consolidated statute, the material in question, the applicable procurement and manufacturing stages, and a contemporary administrative practice inconsistent with EU law.

The case nevertheless has broader analytical force. If a national system relies on dispersed guidance, professional custom or informal permissions to regulate a mandatory safety obligation, the Court's legal-certainty reasoning may be relevant. A properly framed research hypothesis is whether the current division between pharmaceutical inspection, tissue establishment oversight and hospital clinical governance creates similarly indeterminate obligations in specific applications. That hypothesis should be tested, not treated as a proven continuation of the 2015 infringement.

Greece: Distinguishing Legislative Reform from Implementation

Greece's May 2026 statutory reform is a temporal break that comparative scholarship must not obscure. Pre-reform reports can establish that a dedicated HE framework was not identified at the earlier observation date, but cannot by themselves prove that the same legal position persists after Law 5302/2026. An accurate October 2026 manuscript must identify the new statutory text, the delegated rulemaking powers and any subsequently issued implementing measures, while recording where a measure has not been independently verified.

The legally salient issue is whether the framework is operational in practice. Relevant questions include the authority responsible for manufacturing consent; authorization and inspection standards for public and private facilities; documentation for individual prescriptions; interaction with national tissue and cell establishment authorizations; traceability and vigilance duties; and access to administrative review. A hospital that cannot identify the

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procedure for an otherwise lawful application may encounter a legal-certainty problem even if Parliament has enacted an enabling clause.

Whether such a problem amounts to infringement of Directive 2004/23/EC is a separate inquiry. A deficient HE procedure is not automatically a failure to transpose tissue legislation. The researcher must establish that a specific obligation under the tissue-and-cell acquis is missing, incorrectly implemented or inadequately enforced in a manner attributable to the state. Evidence of intentional obstruction would require still more: contemporaneous documents, repeated disregard of clear duties or other reliable proof of intent. In the absence of such evidence, the article should pose a testable question concerning possible breach and practical patient disadvantage rather than assert deliberate misconduct.

Cross-Country Typology: Established Frameworks and Evidentiary Gaps

The comparative landscape is better represented as a typology than as a binary ranking of compliant and non-compliant states. One group has longstanding, identifiable national HE provisions and regulatory procedures, although these may differ considerably in scope and operation. Germany, France, Italy and Spain exemplify this group. Another group has explicit frameworks but different levels of observed use, guidance or administrative maturity. A third group is insufficiently documented in the public comparative literature to permit confident claims about current HE availability. The categories describe the strength of the reviewed evidence and do not grade the legality of the underlying tissue legislation.

The 2025 study reported national rules in 19 of the 27 Member States for the period examined and identified 110 approved HE-ATMPs between 2008 and January 2025, with 62 products then available. These counts are highly informative but should not be converted into a conclusion that the other eight Member States had violated EU law. A state may have no eligible products or limited clinical activity; an exemption does not compel the development of a treatment. Equally, the presence of numerous approved products does not independently prove adequate inspection or outcome monitoring.

A useful future country matrix would record: the official HE legal basis; current competent authority; authorization type; definition of non-routine; duration and renewal; applicable manufacturing standards; tissue-establishment interface; published inspections; vigilance obligations; and public decision data. For each entry, researchers should retain the date of the instrument and grade the underlying evidence. Such a matrix could support comparative inference without falsely assigning infringements based on silence in secondary reports.

The 2027 Soho Transition and Regulatory Continuity

Regulation (EU) 2024/1938 responds in part to the limitations of the older directive-based framework, including fragmented implementation and the need for more coherent oversight. It is directly applicable, but direct applicability is not the same as operational self-execution: competent authorities must be designated and equipped, regulated entities need processes and information systems, and interfaces with ATMP rules must be clarified. The general application date is 7 August 2027, with exceptions and transitional provisions. This chronology matters because a claim of present breach cannot ordinarily rest on a duty that has not yet become applicable.

For HE manufacturers, the transition should trigger a process map from SoHO donation and collection through the point at which ATMP-specific manufacturing rules govern. Authorities should publish guidance on mixed activities, classification disputes, establishment responsibilities, donor protection, import and export controls, and reporting. Hospitals and academic facilities may need additional quality-management and information-system resources. The reform should also be evaluated for possible unintended access costs, particularly in small Member States with few specialized establishments.

The new framework should not be presented as automatically harmonizing the HE exemption itself. The latter remains anchored in ATMP law and national authorization decisions. Harmonization of upstream SoHO quality and safety can reduce one source of uncertainty while leaving divergent national HE eligibility, reimbursement, manufacturing capacity and clinical-evidence expectations largely intact. A post-2027 research agenda should measure these distinct dimensions rather than infer convergence solely from the replacement of the directive.

Possible Legal Remedies and Thresholds of Proof

A regulatory dispute can involve several distinct legal pathways. A person or institution may seek an administrative decision and challenge it under national law, potentially invoking relevant Union provisions where applicable. National courts may refer questions on interpretation of EU law to the Court of Justice under Article 267 TFEU. The European Commission may investigate an alleged Member State failure and, where warranted, pursue infringement

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proceedings under Article 258 TFEU. These routes have different standing rules, remedies and evidentiary thresholds.

A defensible allegation of incorrect transposition should identify the directive article, the transposition deadline, the national implementing provision and the precise mismatch. An allegation of defective application should instead provide a decision, inspection finding or pattern of administrative conduct. A complaint about opacity should establish whether EU or national law actually requires publication of the missing information. Finally, a claim that an omission deprived patients of access should document causation rather than merely juxtapose differing national treatment volumes.

Intentional infringement is an especially demanding allegation. Evidence that officials knew of a clear obligation and deliberately circumvented it may be relevant, but delay, ambiguity or inconsistent practice alone does not demonstrate intent. Peer-reviewed legal scholarship can examine plausible systemic incentives or governance failures without imputing unlawful motives to named public authorities. This evidentiary restraint strengthens, rather than weakens, a critique of avoidable legal uncertainty.

Research Design for an EU-27 Verification Audit

To move from narrative review to a reproducible comparative legal study, the next stage should use a registered extraction protocol and two independent reviewers per jurisdiction. Each reviewer would extract the current consolidated legal texts and date-stamped competent-authority guidance in the original language, identify the relevant EU article, and code whether the obligation is fully implemented, partially implemented, disputed or not assessable. Disagreements should be resolved by a jurisdiction-qualified legal reviewer and the resolution documented.

Administrative evidence should be collected separately: number of HE applications and authorizations, median processing time, rejected or withdrawn applications, inspections, serious adverse event reports and published enforcement measures. These data require careful denominator selection and should not be treated as equivalent across states without adjustment for population, disease burden, research infrastructure and product mix. A targeted patient-access module could examine hypothetical standardized cases, including an autologous cell therapy, an allogeneic tissue-engineered product and an individualized gene-modified therapy.

The final audit should publish a machine-readable legal crosswalk, source URLs, access dates, translation method, uncertainty notes and a clear distinction between binding law and guidance. This would permit readers to reproduce country-level findings and update them after the SoHO Regulation begins applying. The current manuscript offers a structured doctrinal foundation but does not claim that such an audit has already been completed.

Recommendations

First, competent authorities should publish consolidated HE legal bases, application requirements, timelines, authorized institutions and appeal routes. Second, Member States should publish a crosswalk showing which regulator is responsible at each stage from procurement through clinical administration. Third, EU and national institutions should develop a common minimal dataset on HE activity and outcomes, including denials and reasons for delay. Fourth, the transition to Regulation (EU) 2024/1938 should be supported by documented inspections and practical guidance for the SoHO–ATMP boundary. Fifth, independent patient-access research should quantify unmet demand and determine whether legal uncertainty, rather than capacity or clinical suitability, explains unequal access.

Limitations

The analysis combines verified EU-level legal material with country dossiers of variable evidentiary depth. It has not reviewed every current national consolidated act or inspected individual administrative files; national dossiers sometimes report an absence of public guidance rather than a proven legal omission. The 2025 HE study's principal in-depth sample comprises 19 Member States. We cannot infer intentional infringement, systematic denial of biological samples, or causal patient harm without further primary evidence. Changes after the stated cut-off are not assessed. These limits are material to the interpretation of the EU-27 register.

Conclusion

Hospital Exemption across the EU is characterized by meaningful heterogeneity in authorization architecture, interpretation, transparency and institutional feasibility. The tissue-and-cell acquis supplies essential safeguards for biological starting materials but is not synonymous with the HE regime. Poland illustrates the strict legal certainty standard through a historically adjudicated transposition failure, while Greece illustrates the challenge of converting express 2026 statutory recognition into a fully accessible operational pathway. The legal question of whether any present administrative deficiency amounts to an EU-law infringement must remain open until supported by the relevant primary records. The normative concern is

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nonetheless substantial: uncertainty in procurement, manufacture and hospital authorization may translate into unequal practical access to advanced therapies. Regulation (EU) 2024/1938 creates a timely opportunity to improve upstream coherence, but patient equity requires transparency, accountable oversight and evidence of real-world access.

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