Support for ATMPs development in Spain: the (central) role of the Spanish Medicines Agency (AEMPS)

Marcos Timón

AEMPS
Biological Products, Advanced Therapies and Biotechnology

MINISTERIO DE SANIDAD

agencia española de medicamentos y productos sanitarios

Molecular Therapy vol. 20 no. 3 march 2012

Clinical Development of Advanced Therapy Medicinal Products in Europe: Evidence That Regulators Must Be Proactive

Romaldas Maciulaitis[1,2], Lucia D'Apote[3], Andrew Buchanan[3], Laura Pioppo[3,4] and Christian K Schneider[1,5,6]

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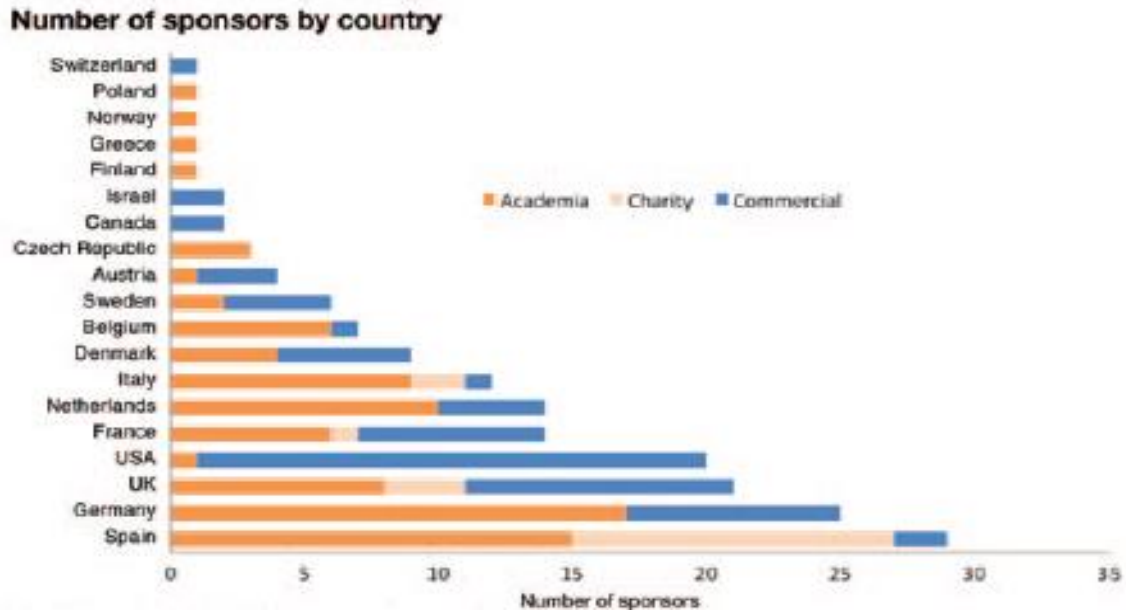

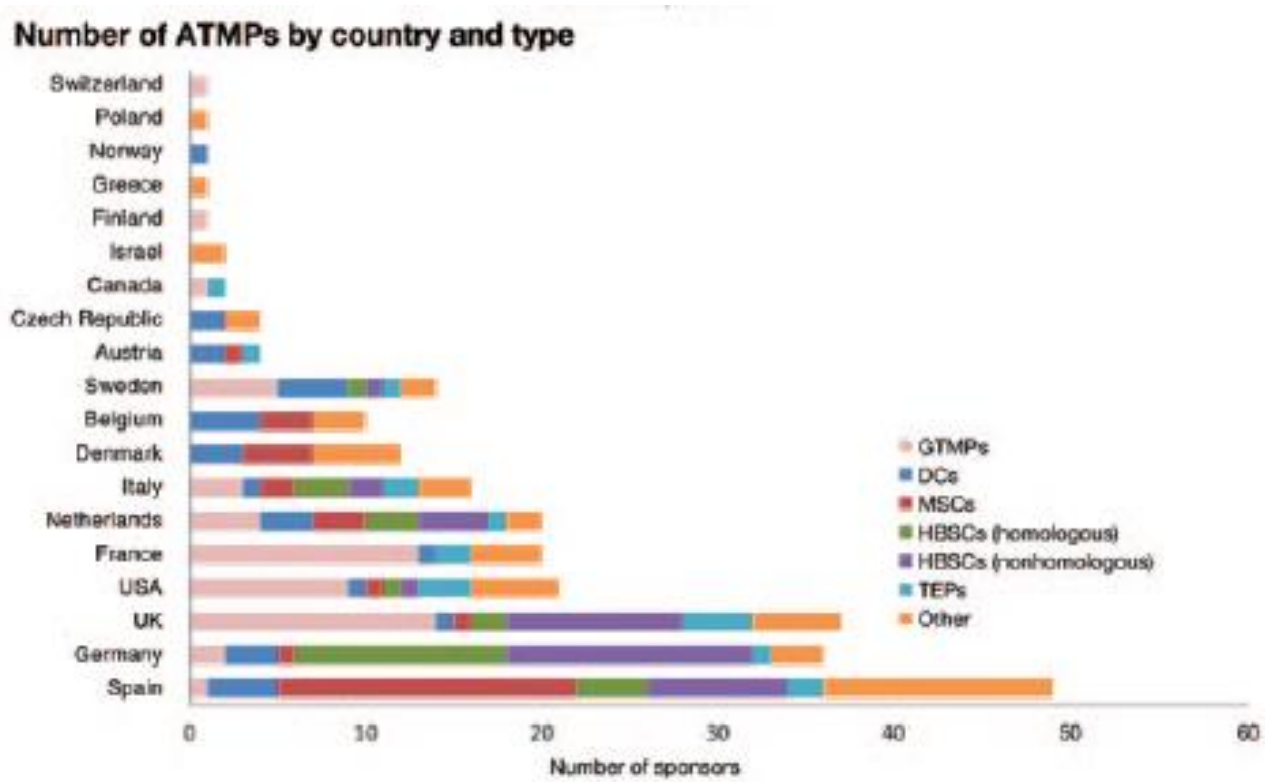

Clinical Development and Commercialization of Advanced Therapy Medicinal Products in the European Union: How Are the Product Pipeline and Regulatory Framework Evolving?

Tomáš Boráň,[1,†] Margarida Menezes-Ferreira,[2,†] Ilona Reischl,[3,†] Patrick Celis,[4] Nicolas Ferry,[5] Bernd Gänsbacher,[6] Hartmut Krafft,[7] Michele Lipucci di Paola,[8] Dariusz Sladowski,[9] and Paula Salmikangas[10,*]

HUMAN GENE THERAPY CLINICAL DEVELOPMENT, VOLUME 28 NUMBER 3
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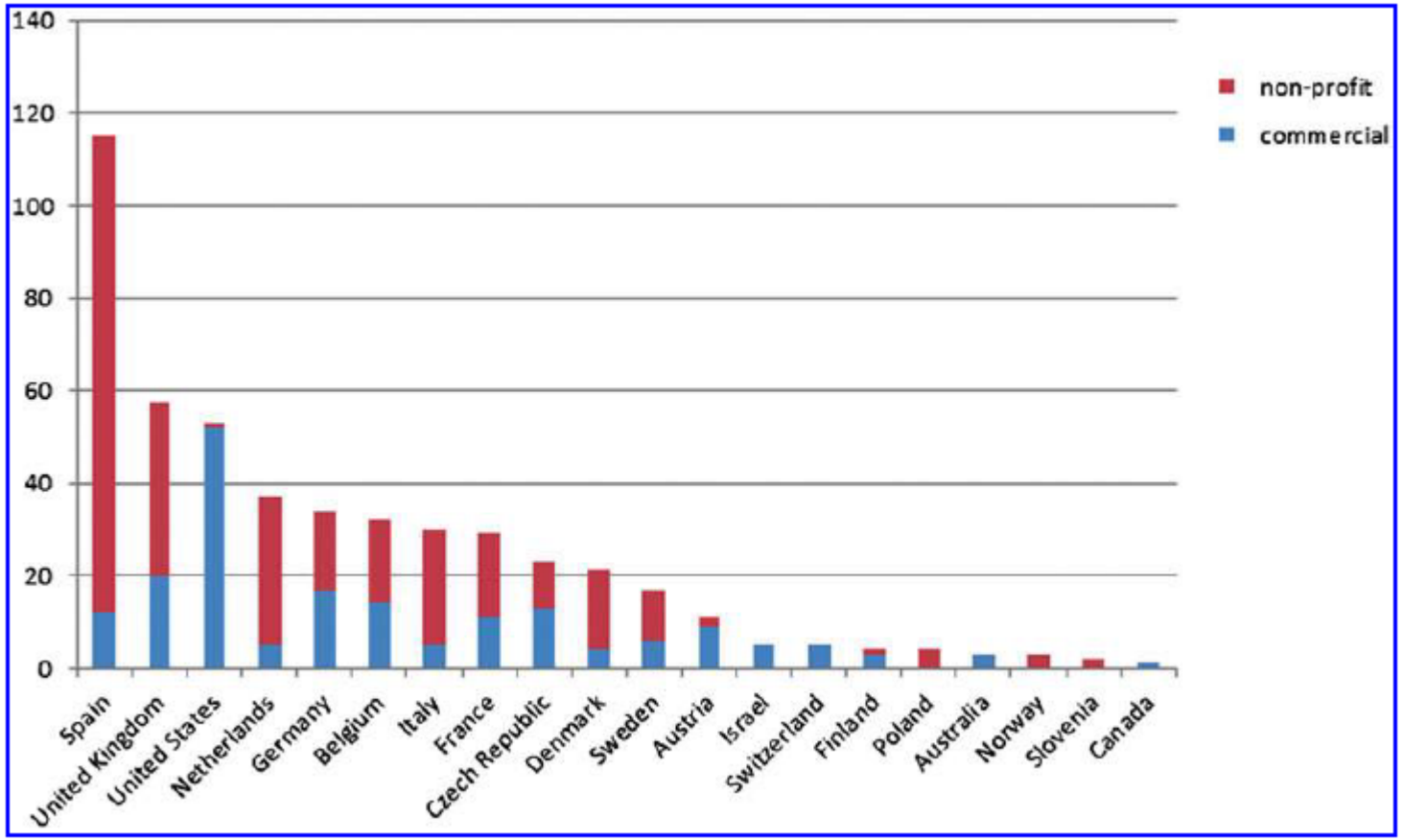
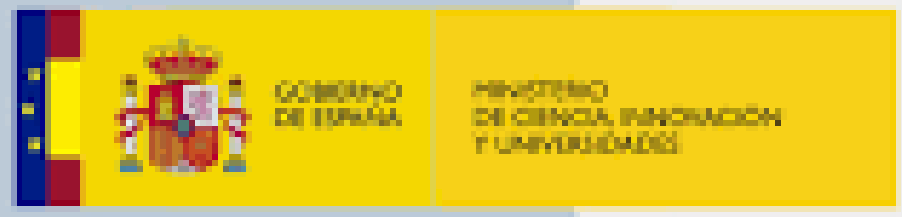
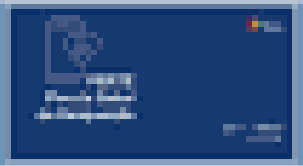


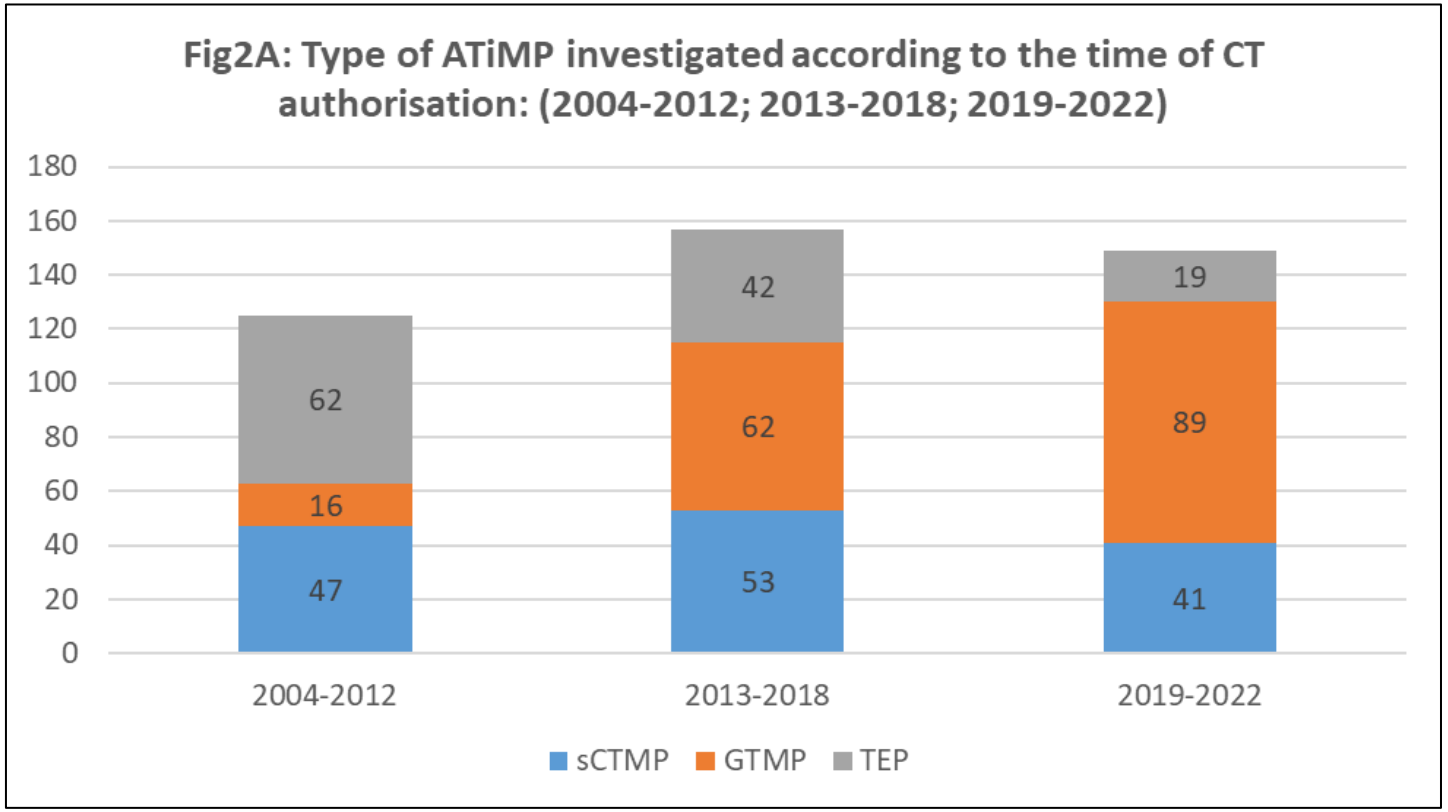
Empresa	[redacted]	Localidad	Comunidad Autónoma
BANC DE SANG I TEIXITS		Barcelona	CATALUÑA
CENTRO DE INVESTIGACIÓN BIOMÉDICA NAVARRABIOMED (CELLMA)		Pamplona	NAVARRA
CIEMAT		Madrid	MADRID
CLÍNICA UNIVERSIDAD DE NAVARRA		Pamplona	NAVARRA
Fundación Marqués de Valdecilla, Unidad de Terapia Celular / UTC		Santander	CANTABRIA
HOSPITAL CLÍNIC DE BARCELONA		Barcelona	CATALUÑA
HOSPITAL C.U. VIRGEN DE LA ARRIXACA (HCUVA)		El Palmar	MURCIA
HOSPITAL GREGORIO MARAÑON		Madrid	MADRID
HOSPITAL SANT JOAN DE DÉU		Esplugues de Llobregat	CATALUÑA
HOSPITAL UNIVERSITARIO CENTRAL DE ASTURIAS		Oviedo	ASTURIAS
HOSPITAL UNIVERSITARIO LA PAZ		Madrid	MADRID
HOSPITAL UNIVERSITARIO PUERTA DE HIERRO DE MAJADAHONDA		Majadahonda	MADRID
HOSPITAL UNIVERSITARIO Y POLITÉCNICO LA FÉ		VALENCIA	VALENCIA
INSTITUTO DE BIOLOGÍA Y GENÉTICA MOLECULAR (IBGM)		Valladolid	CASTILLA Y LEÓN
INSTITUTO DE INVESTIGACIÓN BIOMEDICA DEL HOSPITAL DE LA SANTA CREU I SANT PAU		Barceloba	CATALUÑA
SERVICIO ANDALUZ DE SALUD		Sevilla	ANDALUCÍA
UB-FARMATEC		Barcelona	CATALUÑA
Unidad de Fabricación de Medicamentos de Terapia Avanzada del Hospital Infantil Universitario Niño Jesús (UFMTA-HIUNJ)		Madrid	MADRID
UNIDAD DE PRODUCCIÓN DE TERAPIA CELULAR DEL HOSPITAL RAMÓN Y CAJAL		Madrid	MADRID
UNIDAD DE TERAPIAS AVANZADAS DEL CENTRO VASCO DE TRANSFUSIÓN Y TEJIDOS HUMANOS (CVTTH)		Galdakao	PAÍS VASCO

CONSORCIO ESTATAL EN RED DE TERAPIAS AVANZADAS (CERTERA)





Clinical Trials with ATMPs in Spain



Estévez Álamo J, Timón M, Sánchez Afán de Rivera I, Iriarte Torres B, Serrano Castro MA. Clinical Trials on Advanced Therapy Investigational Medicinal Products in Spain (2004-2022): Experience and Challenges for the Future. *Adv Exp Med Biol* 2023;1430:23-39.

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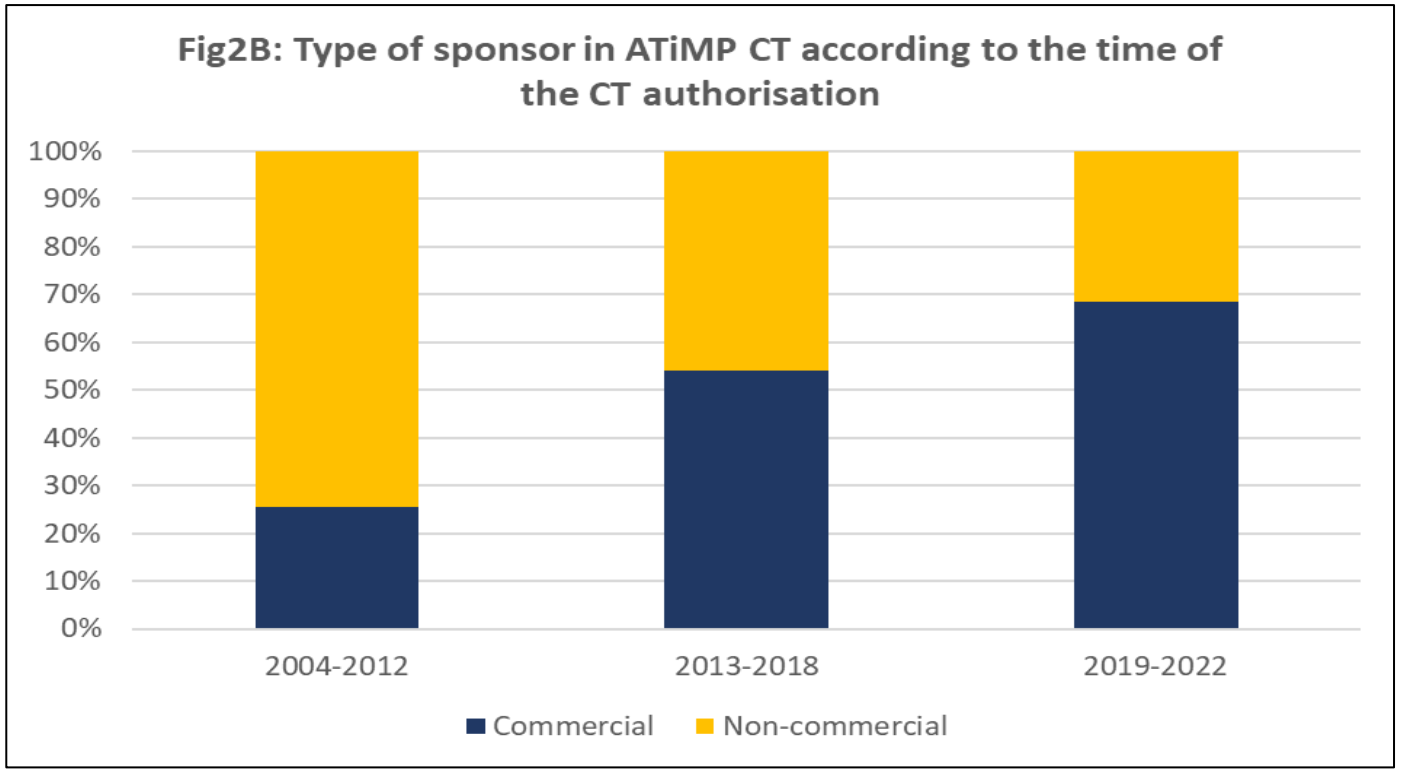
Clinical Trials with ATMPs in Spain



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1 National Support for Cell and Gene Therapies in Spain

Oficina de Innovación

innov_spain@aemps.es

Asesorías científicas Nacionales

ascina@aemps.es

Innovation Office

- Email: innov_spain@aemps.es
- Applicants

- **Tax free**
- **Informal report**

ACN

- Email: ascina@aemps.es
- Applicants

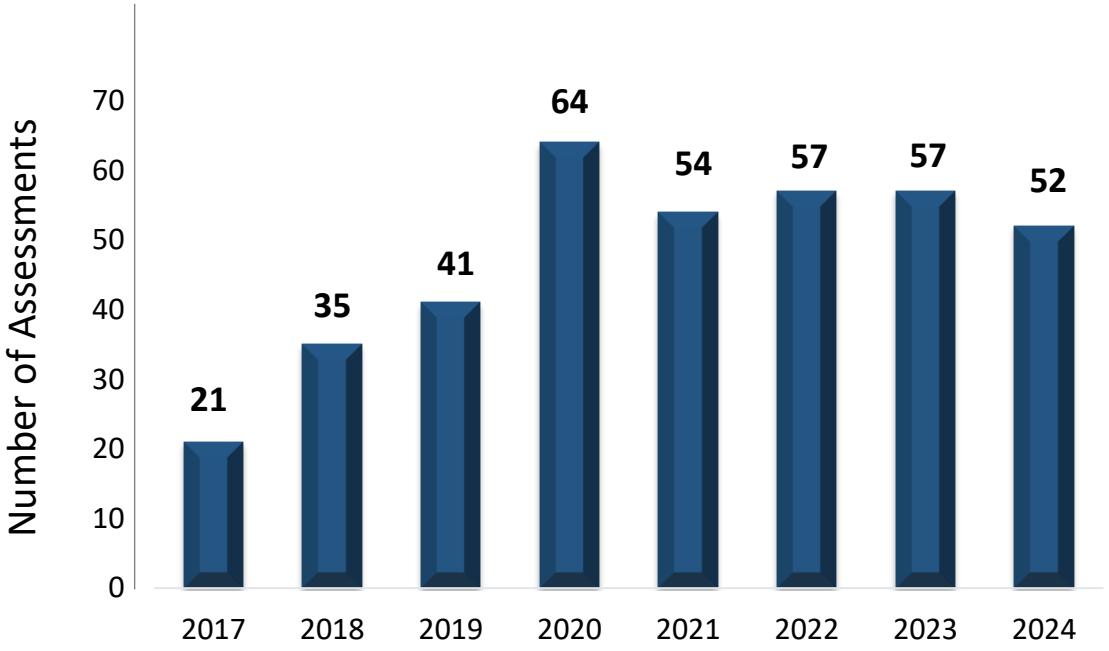
- **Subject to aTax**
- **Formal report**

Same assessors

Number of assessments

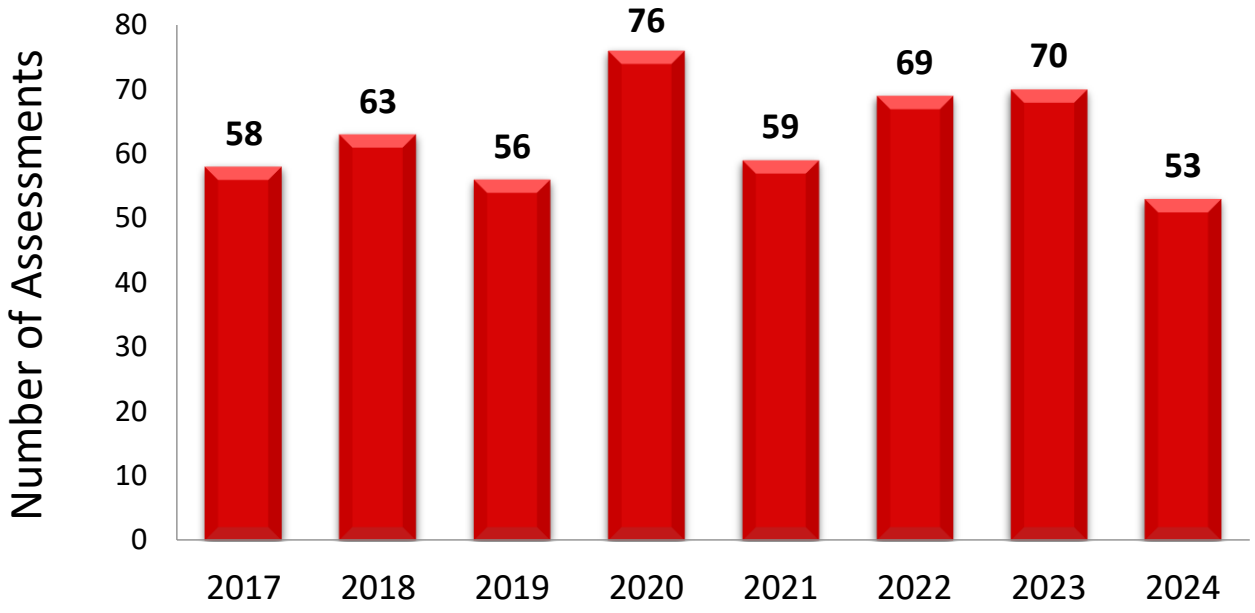
Oficina de Innovación

innov_spain@aemps.es

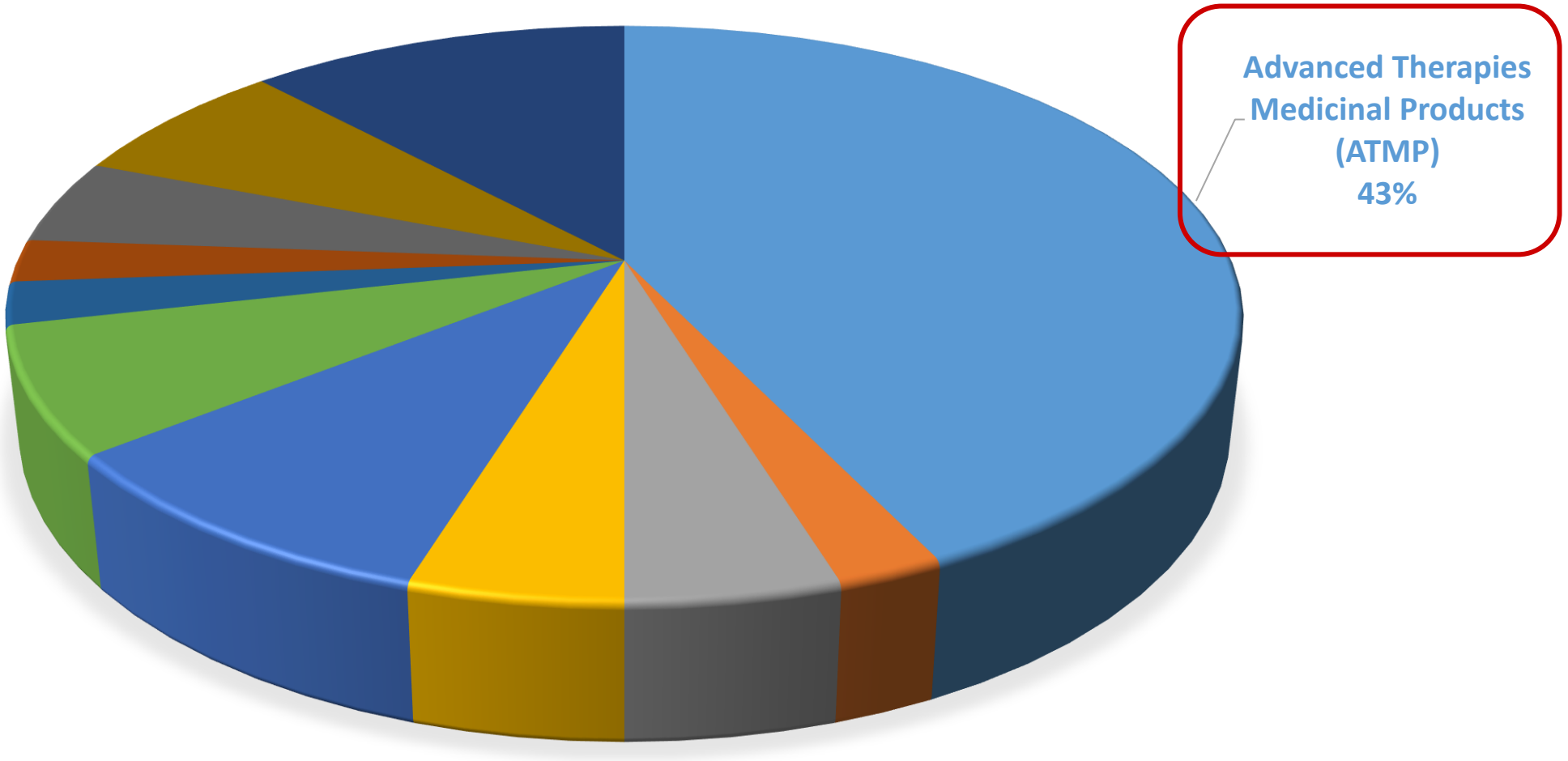


Asesorías científicas Nacionales

ascina@aemps.es



National assessments in Spain (2024)



Additional Support for Cell and Gene Therapies

MINISTERIO DE SANIDAD | agencia española de medicamentos y productos sanitarios | AGENCIA ESPAÑOLA DE MEDICAMENTOS Y PRODUCTOS SANITARIOS

La AEMPS pone en marcha un procedimiento de evaluación acelerada de ensayos clínicos

Fecha de publicación: 20 de mayo de 2024

- Accelerated assessment (Fast track) of Clinical Trials with ATMPs
- Maximum assessment time: 26 days
- Authorisation time: 31 days

Requirements:

-FIH with ATMPs

-For highly debilitating or life-threatening diseases with unmet medical need

-CT via CTIS to be carried out only in Spain

Extended since September 25 to all biologicals for oncology and rare diseases

“Hospital Exemption” in Spain: Authorization of use

BOLETÍN OFICIAL DEL ESTADO

Núm. 144 Sábado 14 de junio de 2014 Sec. I. Pág. 45068

I. DISPOSICIONES GENERALES

MINISTERIO DE SANIDAD, SERVICIOS SOCIALES E IGUALDAD

6277 *Real Decreto 477/2014, de 13 de junio, por el que se regula la autorización de medicamentos de terapia avanzada de fabricación no industrial.*

Regulation (EC) 1394/2007

Article 28

Amendments to Directive 2001/83/EC

2. in Article 3, the following point shall be added:

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.

Manufacturing of these products shall be **authorised by the competent authority** of the Member State. Member States shall ensure that national **traceability** and **pharmacovigilance** requirements as well as the specific quality **standards** referred to in this paragraph are **equivalent** to those provided for at Community level in respect of advanced therapy medicinal products for which authorisation is required pursuant to **Regulation (EC) No 726/2004** of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (*).

“HOSPITAL EXEMPTION” IN SPAIN: AUTHORIZATION OF USE

Real Decreto 477/2014

- Specific “authorizations of use” will be granted to each hospital
- Is not a marketing autorization
- The medicinal product can only be used within the authorized institution
- Manufacturing can be outsourced
- Authorization listed on public database at AEMPS
- Authorization valid for 3 years, subject to renewal

"HOSPITAL EXEMPTION" IN SPAIN: AUTHORIZATION OF USE

Real Decreto 477/2014

The authorization holder is responsible for:

- ❑ Assuring quality, safety and efficacy, as for other authorized ATMP
- ❑ Traceability
- ❑ Pharmacovigilance
- ❑ Annual report

Regulation 1394/2007, Directive 2009/120/CE and other relevant Directives and guidelines concerning ATMP have to be taken into consideration

This procedure is different from a clinical trial or compassionate use

"HOSPITAL EXEMPTION" IN SPAIN: AUTHORIZATION OF USE

Quality: RBA

Guideline on the risk-based approach EMA/CAT/CPWP/686637/2011

- ✓ Good product definition (characterisation)
- ✓ Good quality starting materials
- ✓ Aseptic manufacturing process
- ✓ Process and product consistency
- ✓ Establish a feasible control system (in-process control, release, stability…)
- ✓ Appropriate and sensitive qualified analytical methods
- ✓ GMP compliance

"HOSPITAL EXEMPTION" IN SPAIN: AUTHORIZATION OF USE

Safety and Efficacy

- ❑ Results of clinical trials according to clinical trial legislation and complying with "good clinical practices"
- ❑ Compassionate use data may be used as support
- ❑ "Consolidated use" data can be used as support if quality, safety and efficacy requirements are fulfilled

Traceability

- ❑ The holder of the authorization of use have to establish a system that allows the traceability of each product and each raw material (according to Regulation 1394/2007).
- ❑ The following Directives should be taken in consideration:
  - ❖ Directive 2004/23/CE (Tissues and Cells))
  - ❖ Directive 2002/98/CE (Human Blood Cells)

Pharmacovigilance

- ❑ Description of the pharmacovigilance system
- ❑ Qualified person responsible for pharmacovigilance
- ❑ Appropriate pharmacovigilance system allowing the detection and communication of adverse reactions.

ATMPs approved under HE in Spain

Nombre	Titular de la autorización de uso	Fecha autorización de uso	Ficha técnica	Prospecto	Material de prevención de riesgos
NC1- Suspensión celular en plasma autólogo 100-300×106 células – Hospital Universitario Puerta de Hierro Majadahonda, 1 jeringa precargada	Hospital Universitario Puerta de Hierro Majadahonda	29-01-2019	Ficha técnica	Prospecto	
ARI-0001 Dispersión para perfusión que contiene 0,1-1×10^6 células/kg – Hospital Clínic de Barcelona	Hospital Clínic de Barcelona	01-02-2021	Ficha técnica	Prospecto	
CEMTROCELL 50.000 células/microlitro – Suspención para implantación	Clínica Cemtro S.A.	31-10-2023	Ficha técnica	Prospecto	
Piel humana obtenida por ingeniería de tejidos 1,0-1,5 x 106 / 1,5-3,0 x 106 / lámina apósito impregnado	Hospital Universitario Virgen del Rocio – Sevilla	06-06-2024	Ficha técnica	Prospecto	
ARI0002H 13,5-720 X 10^e6 Células dispersión para perfusión	Hospital Clínic de Barcelona	08-08-2024	Ficha técnica	Prospecto	

https://www.aemps.gob.es/medicamentos-de-uso-humano/medicamentos-de-fabricacion-no-industrial/terapias-avanzadas/listado-de-autorizacion-de-uso/

Thank you!