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Can We Have European Anti-D Plasma Collection Programmes?

European Committee on Blood Transfusion (CD-P-TS) - Report

Richard Forde, EDQM

IPFA / EBA Symposium – February 2026

EDQM and CD-P-TS

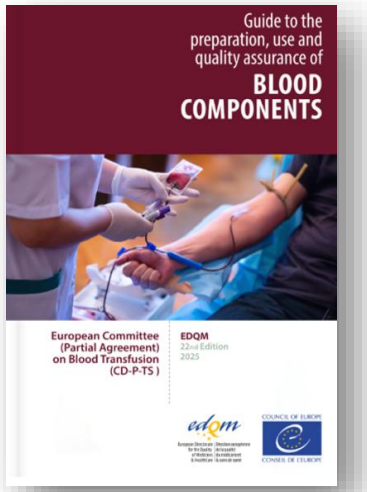
European Committee on Blood Transfusion (CD-P-TS)

VNRBD

Mutual assistance

Protection of donors & recipients

1. Developing legal instruments, technical standards, policies



Working Groups

2. Monitoring data and best practices

3. Operational activities supporting BEs implementing technical standards & EU legislation

Funded by the European Union and the Council of Europe

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CD-P-TS and anti-D Immunoglobulin

2010 – Position paper on the development of monoclonal anti-D antibodies

2014 - Report on anti-D alloimmunisation, immunoprophylaxis practices, and the status of European self-sufficiency in anti-D immunoglobulin (anti-D Ig)

2023 - Working group on anti-D Ig with the aim to raise awareness on the lack of anti-D plasma collection in Europe

Webinar Series

- Collection of anti-D plasma
- The production of plasma-derived anti-D Ig products
- The development and use of alternative and complimentary anti-D products

Presentations and Recordings available https://www.edqm.eu/en/latest-e-learning-resources

2024 - CD-P-TS / European Blood Alliance (EBA) - joint survey to assess the current status and prospects for initiating or resuming anti-D plasma collection across Europe.

Status of European anti-D plasma collection

Near total absence of anti-D plasma collection in Europe

CD-P-TS and EBA joint survey (October 2024)

Confirmed near-total absence of anti-D plasma collection in Europe

Only limited collection being performed (Poland, Ukraine – Biopharma Plasma)

Encouraging willingness to (re)start programmes

Several Member States expressed interest in initiating or resuming collection

Countries with previous programmes showed greater readiness to restart

Key challenges Identified

Donor identification, recruitment and retention
Financial and operational constraints
Regulatory and organisational complexity

Declining number of immunised donors, the potential need to immunise new donors, need for high titres, and the feasibility of collecting small batches of anti-D plasma for fractionation.

Green indicates countries that would be willing to start (or restart) anti-D plasma collection, while orange indicates the countries that would not.

Vulnerability in Anti-D Ig Supply

- Anti-D IgG is a critical medicine with no recombinant or EMA/FDA approved monoclonal alternatives
- Supply depends entirely on plasma from immunised donors
- Anti-D plasma collection has nearly completely ceased in Europe, limiting supply resilience
- Europe accounts for largest share of global anti-D use – yet relies almost completely on plasma collected in the USA
- Recent shortages (2023–2025) raise concerns on the vulnerability of supply[1]
- Global supply is highly concentrated, with ~85% authorised products produced by three manufacturers[2]
- Worldwide, only 50% of women in need receive anti-D prophylaxis[3]

1. U.S. Food & Drug Administration. CBER-Regulated Products: Current Shortages. Cited 2025 Nov 11. Available from https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/cber-regulated-products-current-shortages.
2. Patrick Robert, Marketing Research Bureau, EDQM Anti D Webinar Series 2023
3. Pegoraro V, Urbinati D, Visser GHA, DiRenzo GC, Zipursky A, Stotler BA, et al. (2020)Hemolytic disease of the fetus and newborn due toRh(D) incompatibility: A preventable disease that still produces significant morbidity and mortality in children. PLoS ONE 15(7): e0235807. https://doi.org/10.1371/journal.pone.0235807

Strengthening anti-D Ig Supply in Europe

Securing sustainable Anti-D Ig supply is a public health priority.

A coordinated European approach is needed, including;

- Develop a European roadmap to (re)establish anti-D plasma collection, including donor screening, immunisation, and collection protocols
- Establish a European plasma pooling model to enable efficient and sustainable manufacture
- Secure dedicated financial and policy support from European member states and European institutions
- Optimise clinical use through wider implementation of foetal RhD genotyping and appropriate dosing strategies
- Support research and development of sustainable alternatives to plasma-derived anti-D Ig

Coordinated Actions

European Medicines Agency (EMA) and the Heads of Medicines Agencies (HMA), through the Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG)

Recommendations to address vulnerabilities in the Anti-D IgG supply chain (June 2025)[4]

Member States
Create action plans to secure the supply of anti-D Ig

European Commission
Identify policy measures, support member state efforts

Plasma Industry
Fractionation manufacturing capacity, R&D alternatives, collaboration

EDQM of the Council of Europe, through the European Committee on Blood Transfusion (CD-P-TS)

Anti D - Technical Report (Publication Feb 2026)

Complements the MSSG recommendations by providing technical context to support their implementation.

Scientific, technical, regulatory, and operational considerations to support the development of European anti-D plasma collection programmes.

Aims to inform and support the (re) establishment of coordinated, sustainable anti-D plasma collection efforts across European member states.

1. **Shared Blueprint – anti D Plasma Collection**
2. **European Pooling Model?**

4. European Medicines Agency. Recommendations of the Executive Steering Group on Shortages and Safety of Medicinal Products to address anti-D immunoglobulin supply chain vulnerabilities. EMA/135603/2025, 23 June 2025.

Fundamentals

anti D Plasma Donors

RhD negative

- Naive donors immunised with RhD-positive RBCs
- Previously immunised during pregnancy or transfusion
- Rare natural anti-D carriers

Identification, Recruitment and Retention

Immunisation

Need for immunisation

- anti-D Ig level >45 IU/ml (~1:512 titre)
- Variable response to D antigen
- Annual restimulation via IV RhD-positive RBCs

Regulatory, safety, legal and ethical aspects

Fractionation

Isolation and purification of IgG

- Viral inactivation/removal
- Pooling anti-D plasma (>250 L, typically >3000 L)

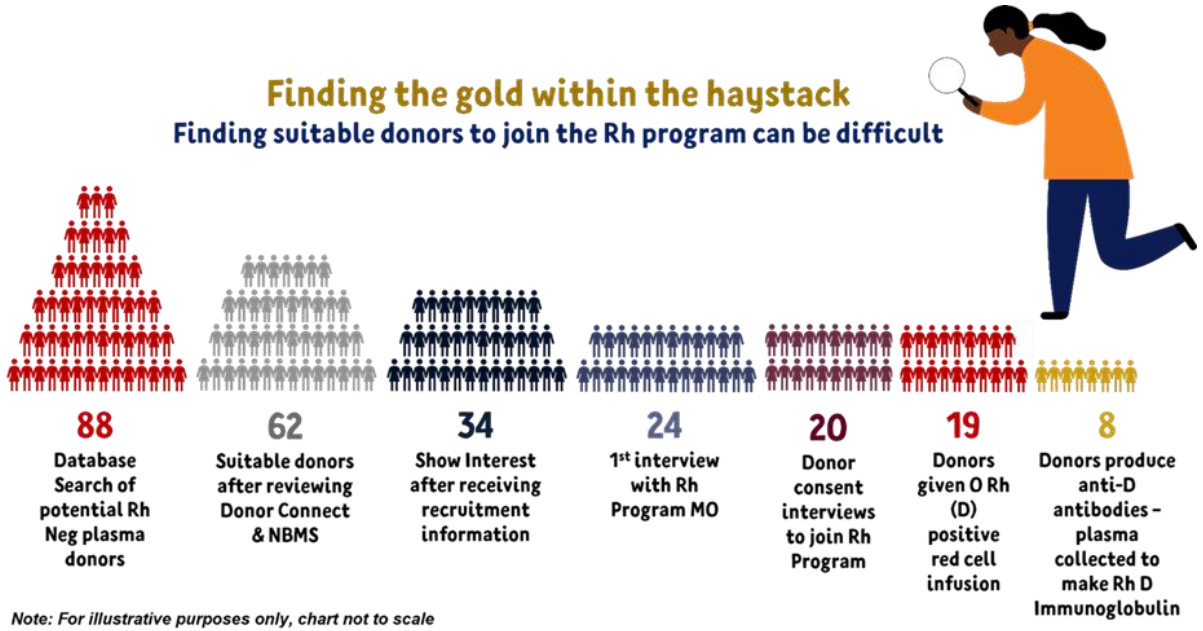
Larger pools allow cost-effective production

Reference Models

National self-sufficiency achieved and sustained since 1969

Near elimination of HDFN-related mortality - from 1.1/1000 births (1960's) to ~0.01/1000

Combination of naturally immunised and deliberately immunised donors



Currently maintained with ~172 active donors (~200 required for stability)

Supports ~48,000 RhD-negative pregnancies annually.

~50% of immunised donors reach required antibody levels (≥45 IU/mL)

Continuous recruitment required (~7% permanently deferred annually)

Non-invasive prenatal testing (NIPT) and targeted prophylaxis implemented 2025 - potential reduction in demand for Anti D Ig by 28%

5. Von Wiellgh K (Australian Red Cross Lifeblood). The Rh programme in Australia. Presentation at EDQM webinar series Anti-D Immunoglobulin: Exploring collection, production and alternatives. European Directorate for the Quality of Medicines & HealthCare, Council of Europe, 2023.

Reference Models

- Collection of anti-D plasma and production of Anti Ig – Ceased in 2020.
- Structured national donor programme (~300 immunised donors).
- Donors: mostly women immunised during pregnancy, some immunised naive donors and rare naturally occurring anti-D donors
- Immunisation used to maintain high antibody levels (~1:512 titre) with regular booster immunisations (matched for compatibility)

Research

- Demonstrated potential advantages of pregnancy-derived anti-D antibodies (enhanced functional activity of low fucosylated anti-D antibodies)[7]
- Predictive donor modelling to enable personalised boosting and improved donor management[8]
- Yield optimisation possible by prioritising high-responding donors (HLA DRB1*1501) and tailoring donation schedules
- Strong donor motivation and willingness to participate when approached[9]

Estimating Anti D Ig Needs

~16,000 RhD neg women – RhD pos children each year

~ 32,000 vials needed/year

~ 1,066 donations/year required

~ 200 active donors needed

~ 27 new donors/year required

~ 57 RhD alloimmunisation cases/year (potential donors?)

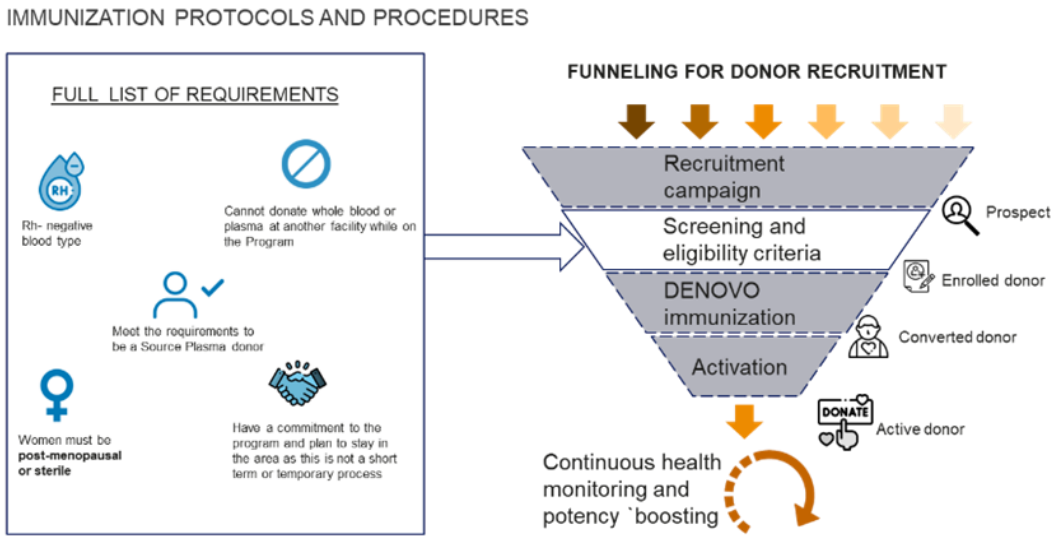
6. Van der Schoot E (Sanquin). Hyper-immunisation of Anti-D donors: The Dutch experience. Presentation at EDQM webinar series Anti-D Immunoglobulin: Exploring collection, production and alternatives, European Directorate for the Quality of Medicines & HealthCare, Council of Europe. 2023.
7. Kapur R, Della Valle L, Verhagen OJHM et al. .Prophylactic anti-D preparations display variable decreases in Fc-fucosylation of anti-D. Transfusion 2015;55(3):553–62. https://doi.org/10.1111/trf.12880
8. de Vos AS, van der Schoot CE, Rizopoulos D et al. Predicting anti-RhD titers in donors: Boostering response and decline rates are personal. PLoS One 2018;26(13):e0196382. https://doi.org/10.1371/journal.pone.0196382.
9. Slootweg YM, Koelewijn JM, de Kort WL et al. Facilitators and barriers for RhD-immunized women to become and remain anti-D donors. Transfusion 2018;58(4):960–8. https://doi.org/10.1111/trf.14490.

Reference Models

KEDPLASMA
UNITED STATES
a Kedrion Biopharma company

- Dedicated anti-D plasma collection centres within a network of 70 plasma centres (5 specialised centres)
- **DENOVO** programme - immunisation of Rh-negative donors to ensure sustainable supply

- Structured immunisation and high-frequency donation model
- Donors can donate plasma up to twice weekly (up to 104 donations/year)
- Controlled immunisation using RhD-positive red blood cells
- Centralised donor monitoring and potency management ensure consistent antibody production



- COVID-19 = 25 % reduction in active donors
- Limited eligible donor pool (Rh-negative only ~15% of population; additional eligibility criteria)
- Variable donor response: only ~30–35% of immunised donors develop sufficiently high antibody levels
- Long stabilisation period (up to 12 months) required before donors reach optimal production levels

10. Horton CA (Kedrion). KedPlasma – the hyper-immunization of Anti-D donors in the US: From Kedrion perspective. Presentation at EDQM webinar series Anti-D Immunoglobulin: Exploring collection, production and alternatives, European Directorate for the Quality of Medicines & HealthCare, Council of Europe. 2023

Can we have European Anti D Plasma Collection?

Reference models demonstrate feasibility

Donors

Anti-D plasma supply can be sustained with relatively small, well-managed donor pools

Continuous donor recruitment and specialised donor management are essential for sustainability

Long-term donor retention and engagement are critical success factors

Immunisation

Immunisation programmes are necessary due to declining availability of naturally immunised donors

Only a proportion of donors develop high and stable antibody levels, requiring careful selection and monitoring

Programmes must operate under strict ethical oversight, ensuring donor safety and informed consent

Fractionation

Scalability and economic viability must be ensured through structured programme design

Cross-border cooperation and plasma pooling may be an option to optimise efficiency and supply resilience

Strong collaboration between plasma collectors and manufacturers is essential to ensure production continuity

Existing and previous programmes provide the basis for a shared blueprint

Shared Blueprint – anti-D Plasma Collection

Shared "blueprint" outlining best practices for donor recruitment, safe immunisation strategies, donor care and safety monitoring, drawing on experience from existing and previous anti-D programmes as reference models.

Programme Governance and Objectives
anti D Ig needs, Programme leadership and resourcing

anti-D Plasma Donor Identification, Recruitment, Selection

anti-D Plasma Donor Interview, Testing and Monitoring

Immunisation and Monitoring
Red cell donor matching, immunisation, monitoring

Yield Optimisation and Programme Efficiency
Ab level-based collection

Donor Retention and Support
Structured donor panels, motivational strategies

Sustainability and Innovation
Continuous donor recruitment, research and innovation

Optimal and Alternative Approaches
Foetal genotyping, dosing, alternatives

European Pooling Model?

Strengthens European **supply security** by reducing reliance on external sources and improving long-term resilience

Enables **efficient manufacturing** through larger pooled volumes and optimised antibody levels

Improves **cost-effectiveness and feasibility,** especially for small and medium-sized countries

Efficiency of scale. A joint effort could help overcome the inefficiencies of fragmented national or local programmes producing low-volume batches that fall below the viable processing thresholds.

Knowledge sharing would be greatly enhanced, enabling participating countries to benefit from shared expertise, infrastructure, and innovation, particularly in areas such as donor management, predictive modelling, and plasma collection strategies.

Requires coordinated European framework with standardised protocols, regulatory alignment, and shared governance

Standardised methods for validating RBCs for immunisation, donor safety, plasma collection protocols, and potency testing

Shared coordination between anti-D plasma collectors and manufacturers to ensure scalability, traceability, and product consistency.

Resourcing and Funding – National / EU funding (e.g. EU4Health, Critical Medicines Act)

Summary

- Anti-D Ig is a critical medicine whose shortages could cause serious harm or pose significant risks to patients

- Europe is almost completely dependant on anti D plasma collected in the US, creating a supply vulnerability and risk to long-term supply resilience.

- Anti-D plasma collection programmes are largely absent or limited in Europe, but there is clear interest and potential in several countries to establish or restart programmes

- A coordinated European approach is needed

    - pooled plasma collection, can offer a realistic and sustainable solution, enabling efficiency of scale, strengthening supply chain, and improving resilience.
    - Implementation will require a Roadmap, including a shared blueprint on donor recruitment strategies, standardised technical protocols, regulatory alignment
    - sustainable governance and funding mechanisms.

- Optimise clinical use through wider implementation of foetal RhD genotyping and appropriate dosing strategies. Support research and development of sustainable alternatives to plasma-derived anti-D Ig

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Thank You

https://www.edqm.eu/en/blood-plasma-supply-continuity

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