MHRA
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

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Decision Cover Letter

Decision of the licensing authority to:

accept change(s) to the agreed paediatric investigation plan and to the deferral

MHRA-102467-PIP01-26-M01

Scope of the Application

Active Substance(s)

HUMAN FIBRINOGEN

Condition(s)

Treatment of congenital fibrinogen deficiency

Pharmaceutical Form(s)

Powder for solution for injection or infusion

Route(s) of Administration

INTRAVENOUS USE

Name / Corporate name of the PIP applicant

Grifols Worldwide Operations Limited

Basis for the Decision

Pursuant to the Human Medicines Regulations 2012, Grifols Worldwide Operations Limited submitted to the licensing authority on 14/04/2026 22:05 BST an application for a Modification

The procedure started on 15/04/2026 18:22 BST

1. The licensing authority, having assessed the application in accordance with the Human Medicines Regulations 2012, decides, as set out in the appended summary report:

to accept change(s) to the agreed paediatric investigation plan and to the deferral.

2. The measures and timelines of the paediatric investigation plan are set out in the Annex I.

This decision is forwarded to the applicant, together with its annex and appendix.

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Final Decision Letter

MHRA-102467-PIP01-26-M01

Of 20/04/2026 09:25 BST

On the adopted decision for HUMAN FIBRINOGEN (MHRA-102467-PIP01-26-M01) in accordance with the Human Medicines Regulations 2012.

The licensing authority, in accordance with the Human Medicines Regulations 2012, has adopted this decision:

Agreement on modification of a paediatric investigation plan (including modification of a waiver or deferral included in that paediatric investigation plan)

This decision applies to a Modification for HUMAN FIBRINOGEN, Powder for solution for injection or infusion , INTRAVENOUS USE .

This decision is addressed to Grifols Worldwide Operations Limited, Grange Castle Business Park, Dublin, Dublin, IRELAND, D22 R2X3

ANNEX I

1. Waiver

1.1 Condition:

Not applicable

2. Paediatric Investigation Plan:

2.1 Condition(s):

Treatment of congenital fibrinogen deficiency

2.2 Indication(s) targeted by the PIP:

Treatment of congenital fibrinogen deficiency

2.3 Subset(s) of the paediatric population concerned by the paediatric development:

The paediatric population from birth to less than 18 years of age

2.4 Pharmaceutical Form(s):

Powder for solution for injection or infusion

2.5 Studies:

Study Type	Number of Studies	Study Description
Quality Measures	0	Not applicable
Non-Clinical Studies	0	Not applicable
Clinical Studies	1	Study 1 (Study 984) Open-label, non-controlled PK/PD and safety and efficacy study: Part I: investigation of 14 day single-dose pharmacokinetics and pharmacodynamics of human fibrinogen concentrate in patients from birth to less than 18 years of age (and adults) with congenital fibrinogen deficiency (afibrinogenemia or severe hypofibrinogenemia). Part II: investigation of haemostatic efficacy and safety of single and/or repetitive intravenous infusions of human fibrinogen concentrate for on-demand prophylaxis and/or on-demand treatment of bleeding events in patients from birth to less than 18 years of age (and adults) with congenital fibrinogen deficiency (afibrinogenemia or severe hypofibrinogenemia).
Extrapolation, Modeling & Simulation Studies	2	Study 2 Semi-mechanistic population PK/PD model (Fibrinogen Antigen/ Fibrinogen Activity) with subsequent link to the surrogate of efficacy (maximum clot firmness) to support the dosing strategy and activity of human fibrinogen concentrate in patients from birth to less than 18 years of age with congenital fibrinogen

		deficiency (afibrinogenemia or severe hypofibrinogenemia). Study 3 Extrapolation study to support the understanding of dosing and efficacy of human fibrinogen concentrate in patients from birth to less than 18 years of age with congenital fibrinogen deficiency (afibrinogenemia or severe hypofibrinogenemia) using data obtained in part I and II of Study 984 (PIP study 1).
Other Studies	0	Not applicable
Other Measures	0	Not applicable

3. Follow-up, completion and deferral of a PIP:

Concerns on potential long term safety and efficacy issues in relation to paediatric use:	Yes
Date of completion of the paediatric investigation plan:	30/09/2020
Deferral of one or more studies contained in the paediatric investigation plan:	No