

# **Quality Assurance of extended half-life products**

Dr Ian Jennings  
Scientific Programme Manager  
UK NEQAS for Blood Coagulation

# Monitoring Treatment in Haemophilia

Pre-treatment




Post-treatment



asma containing  
patient FVIII

Plasma containing  
FVIII concentrate  
= drug monitoring  
assay



# EQA for treatment monitoring of FVIII and IX

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- Evaluate ability of lab to measure FVIII and FIX
  - Performance assessment
- Compare results with peer groups and other methods

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- Detects method/reagent changes
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- Post licence surveillance

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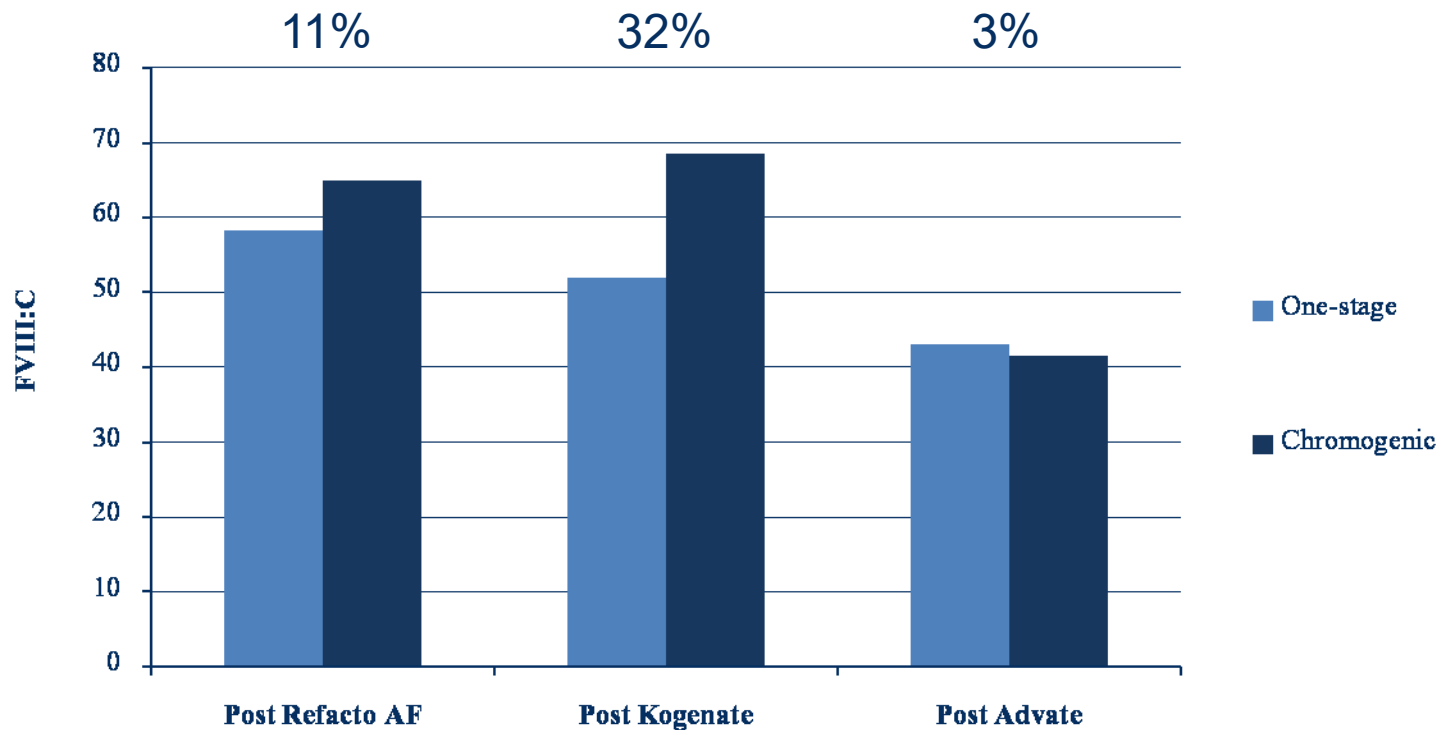
- Multicentre: wide range of routine reagents/methods evaluated
- Detects method/reagent changes
- Can educate laboratories about how their method compares
- Post licence surveillance

- Disadvantages

- Require large volumes of plasma
  - Spiked samples - commutability

# Standard Half Life Products – Data from EQA exercises

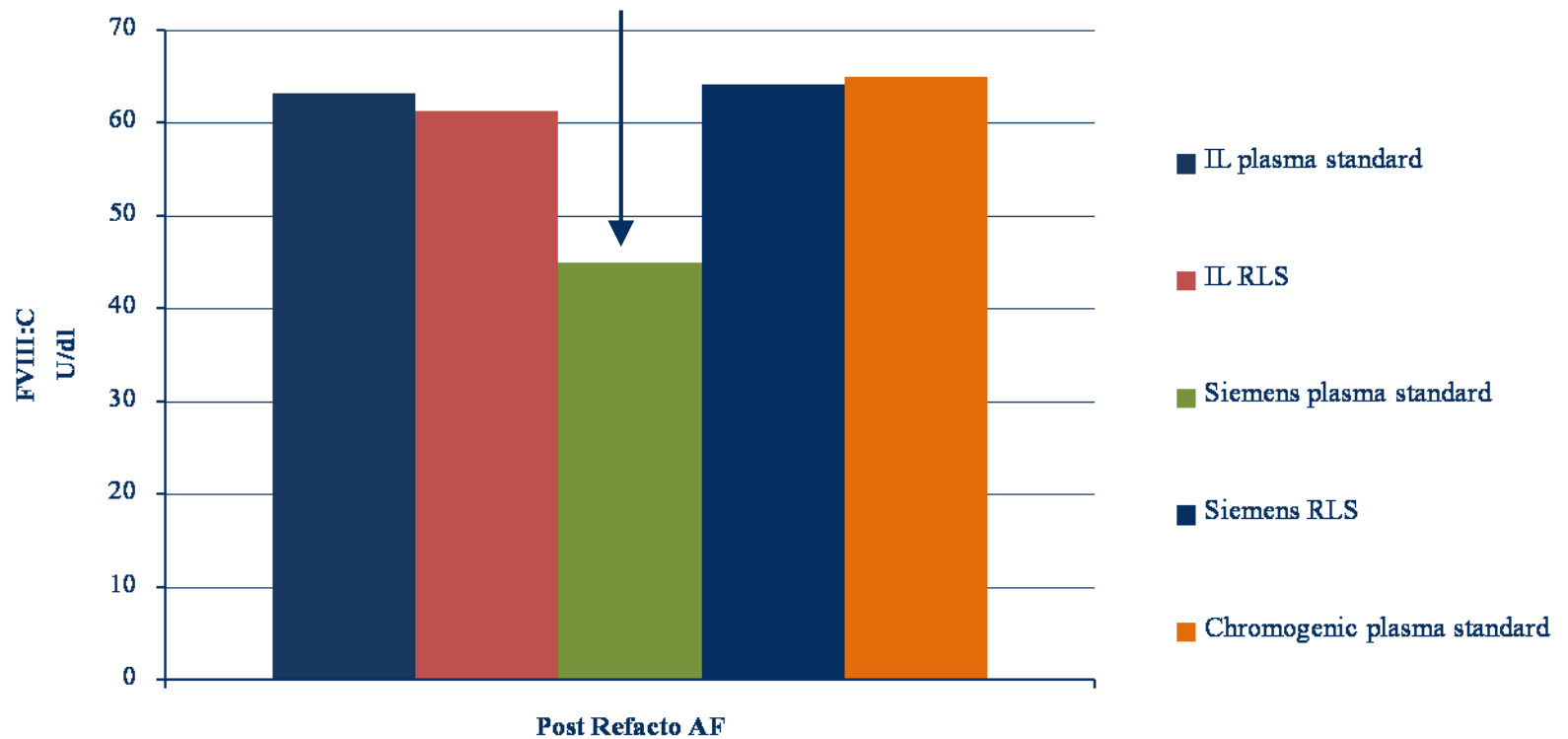
One-stage (n=46) and chromogenic (n=10) assays (plasma standards) – UK NEQAS (BC) data



# POST REFACTO AF<sup>®</sup> SAMPLE: USE OF RLS



Siemens reagents/plasma standard



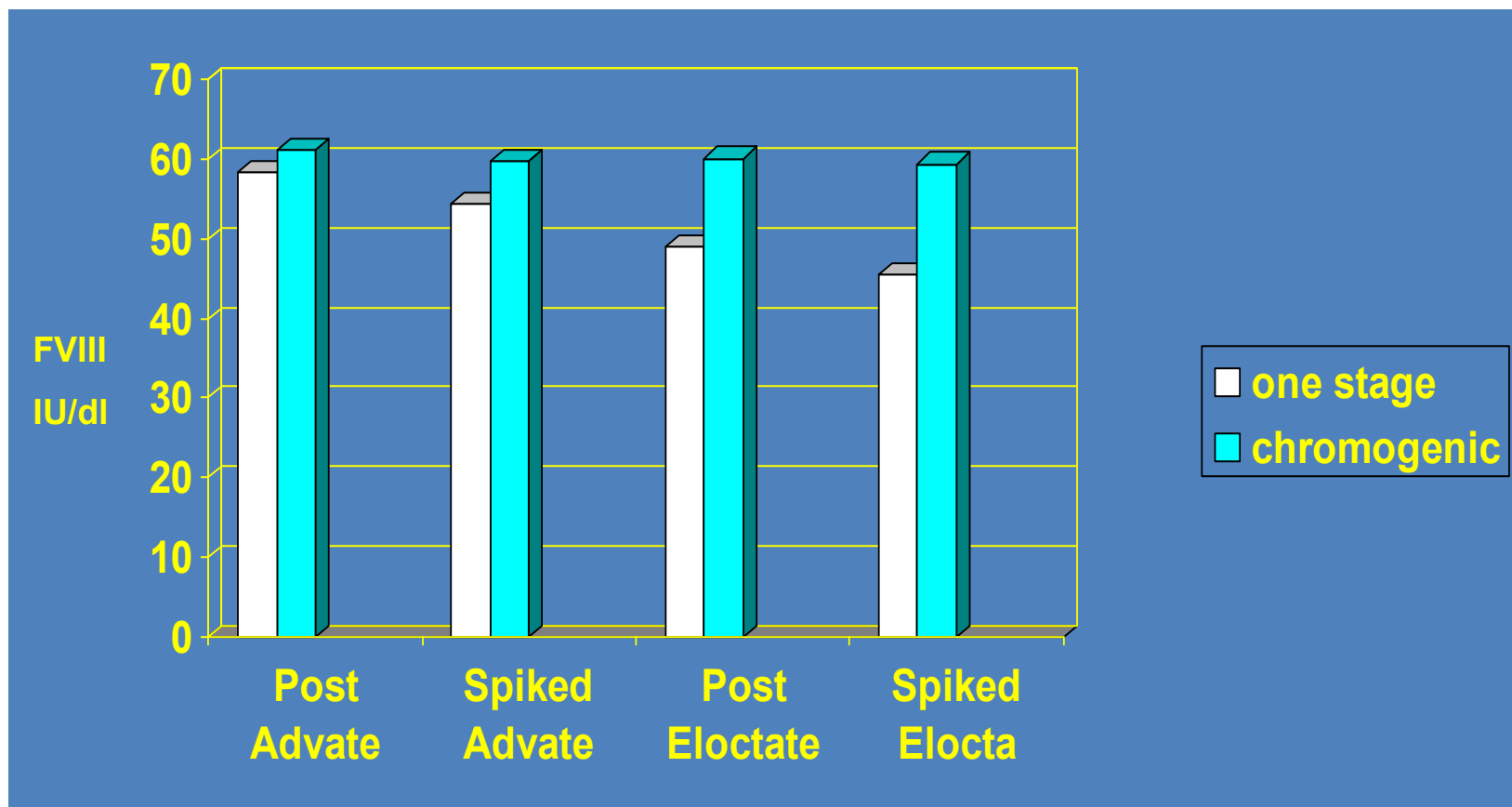
# Extended half-life products

Name	Manufacturer	Technology	Half-life in hours
<b>Factor VIII products</b>			
Elocta	Biogen/SOBI	Fc fusion	18.8–19.0
Adynovate	Baxalta	Pegylation	14.3–16.0
BAY 94–9027	Bayer	Pegylation	18.2
Afstyla	CSL Behring	Single chain FVIII	14.5
N8–GP	NovoNordisk	Pegylation	19.0
<b>Factor IX products</b>			
Aprolix	Biogen/SOBI	Fc fusion	57.6–82.1
Idelvion	CSL Behring	Albumin fusion	91.6–94.8
N9–GP/Refixia	NovoNordisk	Pegylation	93–96



# One stage and Chromogenic assay

(usual locally used plasma standards)



UK NEQAS study 2016

# FIX exercise, 2018

**UK NEQAS**  
Blood Coagulation

**RCPAQAP**  
The Royal College of Pathologists of Australasia  
Quality Assurance Programs



**ECAT Foundation**

External quality Control for Assays and Tests  
*with a focus on Thrombosis and Haemostasis*

# FIX exercise, 2018



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with a focus on Thrombosis and Haemostasis

	Used by patients covered by your centre?			
	n	(%)		
Kogenate FS	58	50		
Helixate FS	40	34		
Refacto AF	57	49		
Advate	81	70		
Haemate P	50	43		
Xyntha	18	16		
Elocta/eloctate	51	44		
Afsytla	4	3		
Adynovate	12	10		
Other	Fahndi, Immunate, Octanate, Novoeight, Haemoctin, N8-GP, Nuwiq, Optivate, Voncento, Wilate, Wilfactin, Alphanate, 8Y, Klot Feiba, Biostate, BAY94-9027, Beriate, Kovaltry Factane, Obizur, Recombinate			

# FIX exercise, 2018



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	Used by patients covered by your centre?		Assay Method used	
	n	(%)	1-stage assay (%)	Chromogenic Assay (%)
Kogenate FS	58	50	86	14
Helixate FS	40	34	79	21
Refacto AF	57	49	68	32
Advate	81	70	84	16
Haemate P	50	43	85	15
Xyntha	18	16	94	6
Elocta/eloctate	51	44	61	39
Afsytla	4	3	50	50
Adynovate	12	10	50	50
Other	Fahndi, Immunate, Octanate, Novoeight, Haemoctin, N8-GP, Nuwiq, Optivate, Voncento, Wilate, Wilfactin, Alphanate, 8Y, Klot Feiba, Biostate, BAY94-9027, Beriate, Kovaltry Factane, Obizur, Recombinate			

# FIX exercise, 2018



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	Used by patients covered by your centre?			
	n	(%)		
Replinine	9	8		
Benefix	81	70		
Alprolix	34	29		
Idelvion	29	25		
Rixubis	5	4		
Other	Alphanine, Betafact, Haemonine, Aimafix, Immunine, Ixed, N9-GP, Octanine Monofix Berinin, Nanofix, Novoseven			

# FIX exercise, 2018



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with a focus on Thrombosis and Haemostasis

	Used by patients covered by your centre?		Assay Method used	
	n	(%)	1-stage assay (%)	Chromogenic Assay (%)
Replinine	9	8	88	12
Benefix	81	70	99	1
Alprolix	34	29	86	14
Idelvion	29	25	84	16
Rixubis	5	4	100	0
Other	Alphanine, Betafact, Haemonine, Aimafix, Immunine, Ixed, N9-GP, Octanine Monofix Berinin, Nanofix, Novoseven			

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***When you receive a sample in the laboratory for FVIII or FIX measurement do you receive information about whether the sample is a diagnostic sample, or a pre- or post-treatment sample?***

Always (48%) Sometimes (45%) Never (7%)

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***When you receive a sample in the laboratory for FVIII or FIX measurement do you receive information about whether the sample is a diagnostic sample, or a pre- or post-treatment sample?***

Always (48%) Sometimes (45%) Never (7%)

***For post infusion monitoring, do you receive information about what product the patient is receiving?***

Always (32%) Sometimes (51%) Never (16%)



- EQA material:



+



Spiked samples prepared

Buffered and Lyophilised



Sent for testing



Data analysed



# FIX exercise, 2018

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External quality Control for Assays and Tests  
*with a focus on Thrombosis and Haemostasis*

- Benefix
  - Idelvion
  - Alprolix
  - Refixia/Rebinyn
- 
- 6 IU/dL, 60 IU/dL,
- 
- UK NEQAS (n=84)
  - ECAT (n=63)
  - RCPAQAP (n=18)
- 
- Total of 172 sets of results



# FIX exercise, 2018



**ECAT Foundation**  
External quality Control for Assays and Tests  
*with a focus on Thrombosis and Haemostasis*

Sample Code	Benefix S18:05	Benefix S18:06	Idelvion S18:07	Idelvion S18:08	Alprolix S18:09	Alprolix S18:10	Refixia S18:11	Refixia S18:12
Factor level (based on potency)	6.0 IU/dl	60 IU/dl	6.0 IU/dl	60 IU/dl	6.0 IU/dl	60 IU/dl	6.0 IU/dl	60 IU/dl
1-stage assay results (n=164)								
Median (IU/dL)	8.0	63.0	6.0	42.5	6.6	50.0	4.8	33.9

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Recovery (%)	133	105	100	71	110	83	81	57

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Range (IU/dL)	3.95-21	49-90	0.84-11.3	17.5-77	1.3-19	27-80	0.8-144.5	6.3-1060

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Chromogenic assay results (n=40)								
Median (IU/dL)	4.2	45.0	7.0	73.3	4.1	45.0	5.0	53.5

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Recovery (%)	70	75	116	122	69	75	83	89



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Range (IU/dL)	2.9-8	31-68	3-11.5	23-122	3-8.4	33-74.1	2-8.7	23-97

# FIX exercise, 2018

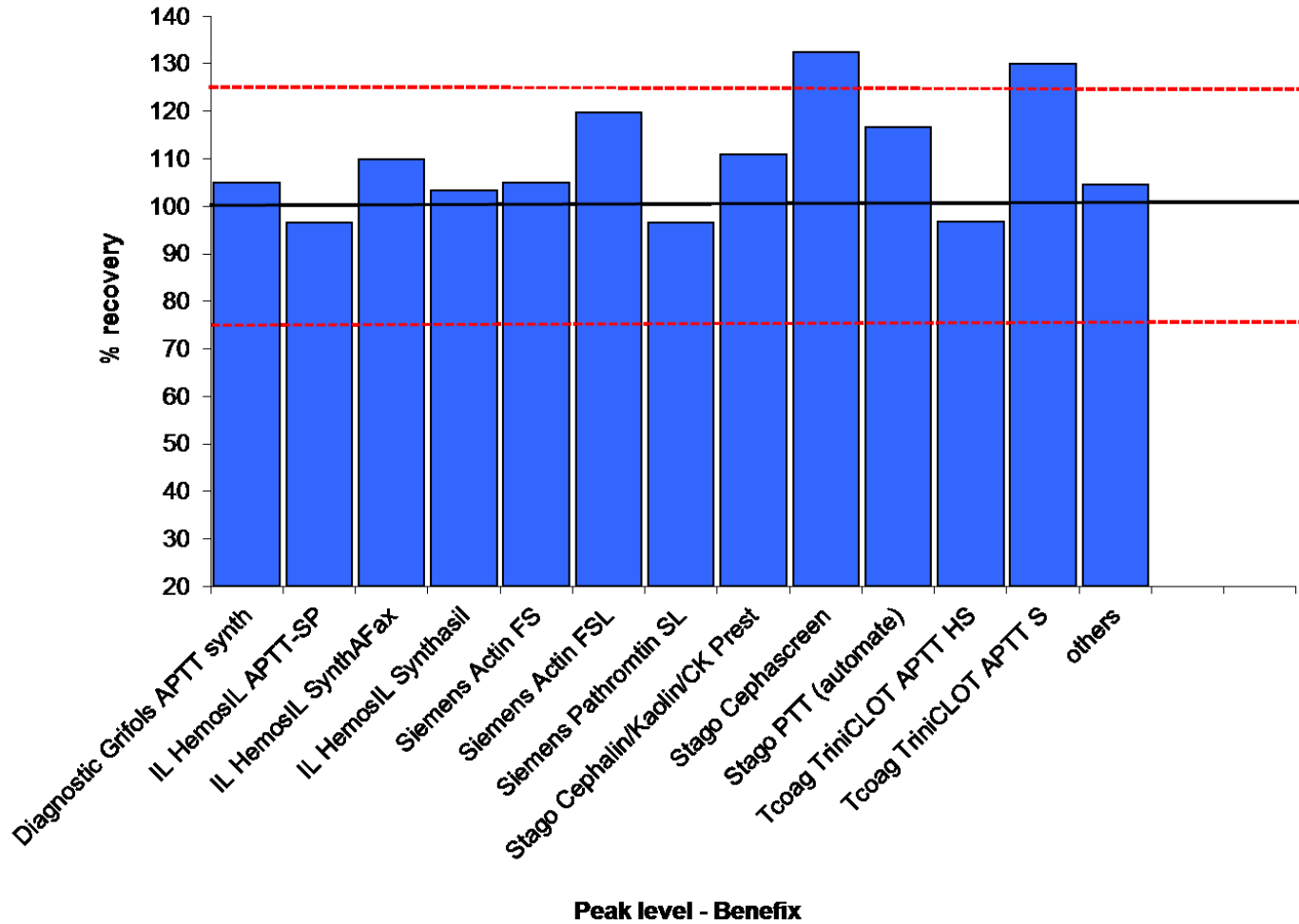


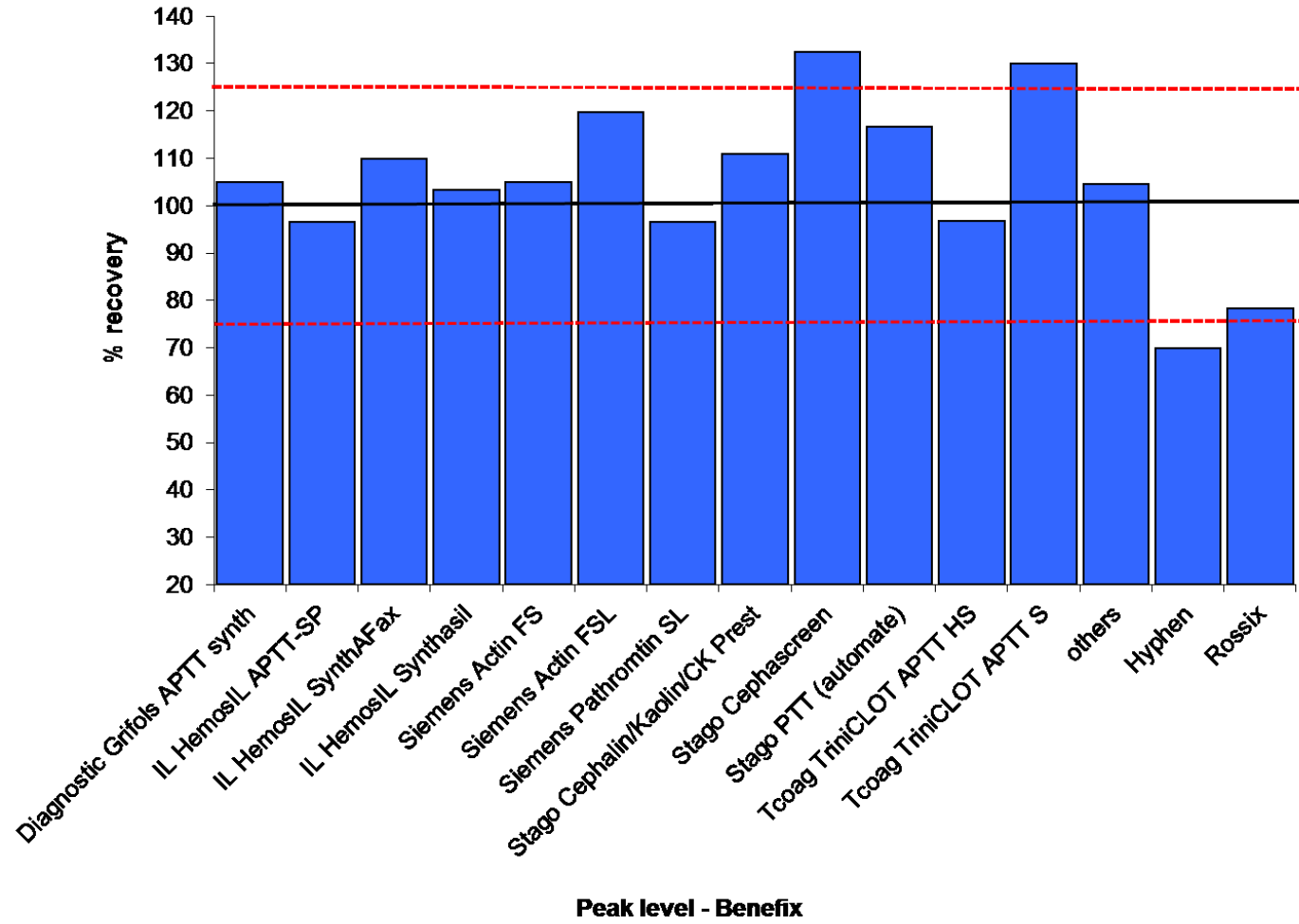
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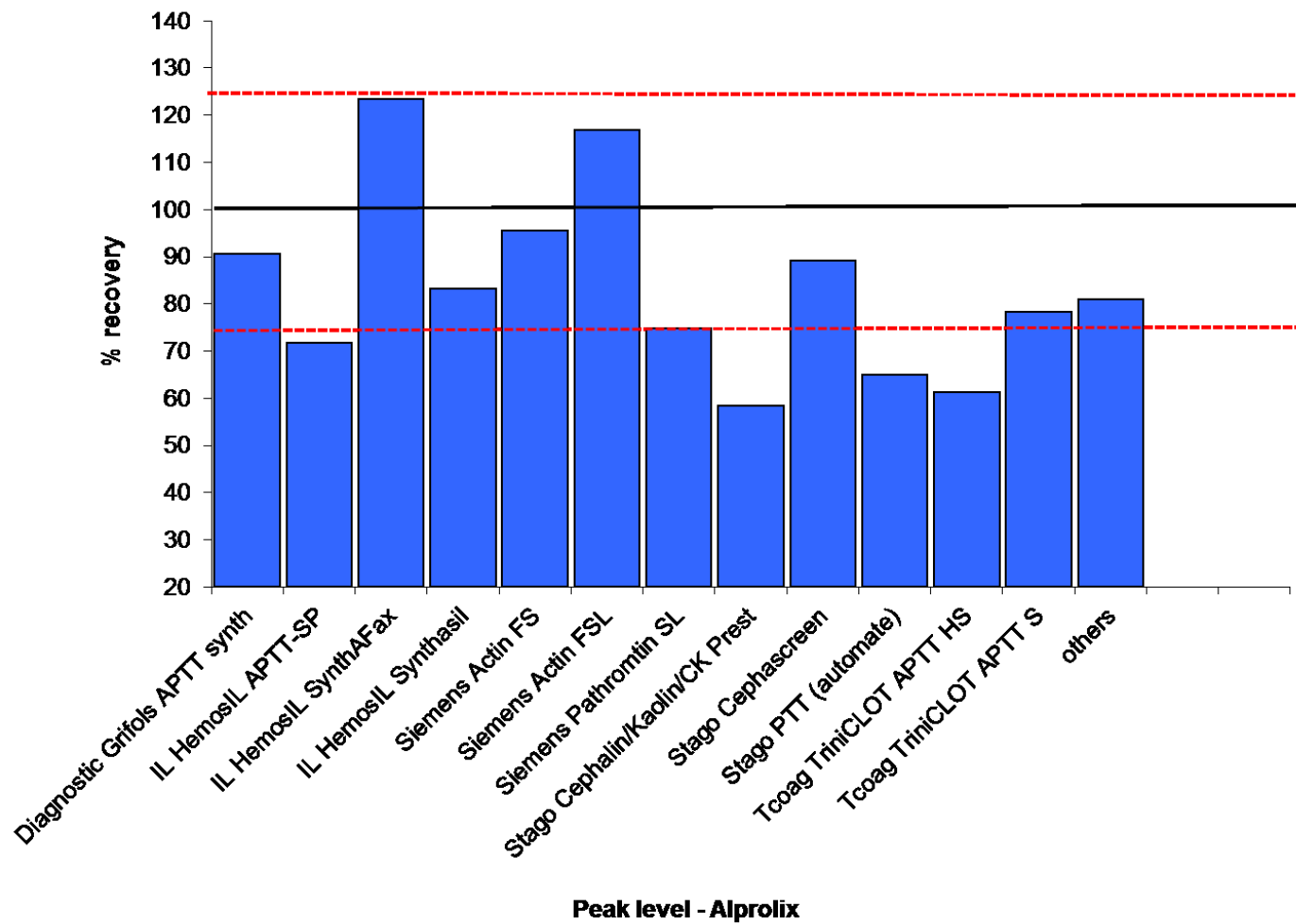
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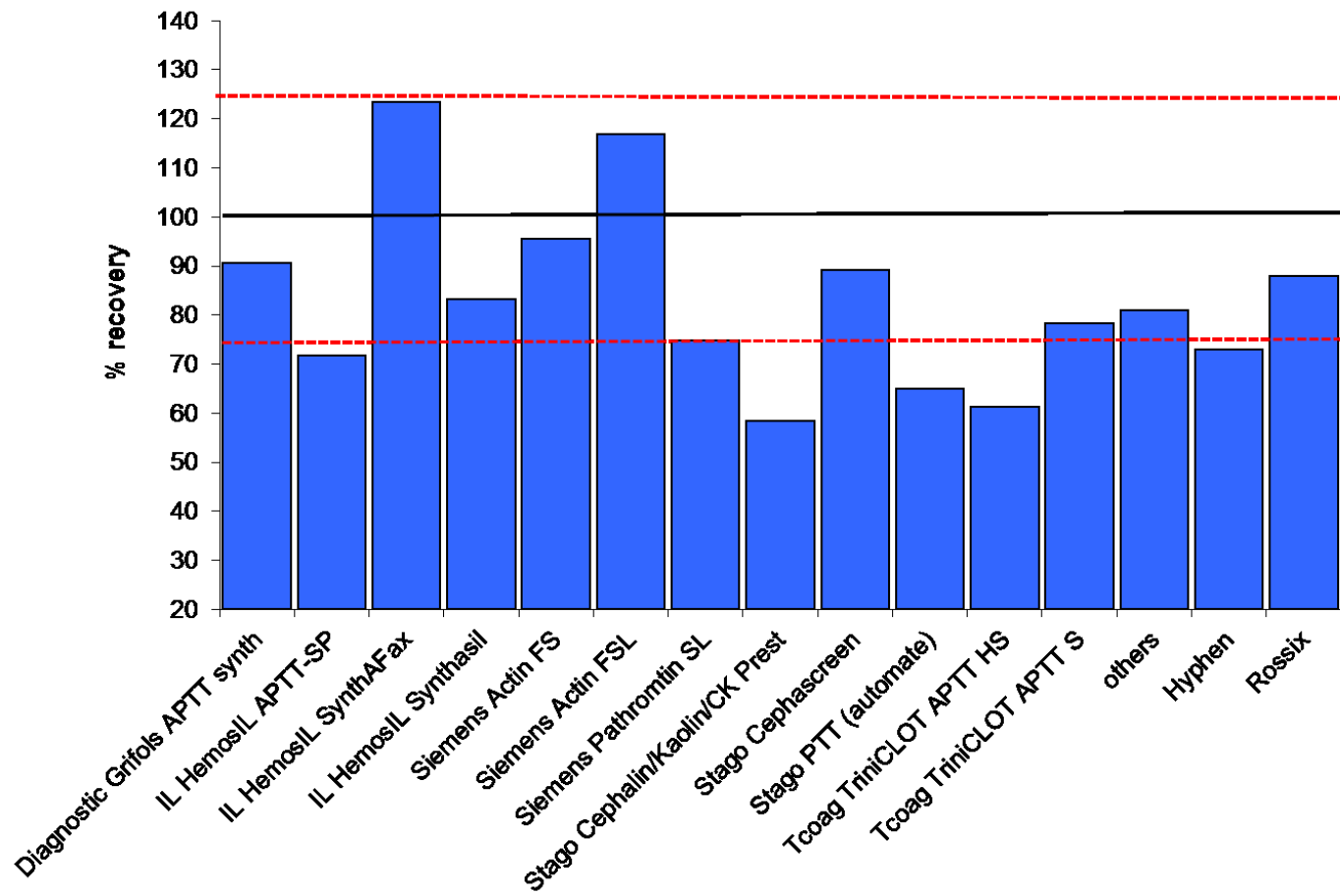
<b>APTT Reagent</b>	<b>UK NEQAS</b>	<b>RCPAQAP</b>	<b>ECAT</b>	<b>Total</b>
Diagnostic Grifols APTT synth	1	0	0	1
IL HemosIL APTT-SP	2	0	2	4
IL HemosIL SynthAFax	1	0	0	1
IL HemosIL Synthasil	38	4	26	68
Sekusiu Coagpia APTT-N	1	0	0	1
Siemens Actin FS	21	5	6	32
Siemens Actin FSL	1	1	3	5
Siemens Pathromtin SL	5	0	7	12
Stago Cephalin/Kaolin/CK Prest	8	0	6	14
Stago Cephascreen	1	0	3	4
Stago PTT (automate)	3	0	6	9
Stago PTT-LA	0	0	1	1
Tcoag TriniCLOT APTT HS	1	2	1	4
Tcoag TriniCLOT APTT S	0	4	0	4
others	1	1	2	4
<b>Total</b>	<b>84</b>	<b>17</b>	<b>63</b>	<b>164</b>

# Recovery of FIX against expected levels – median data from all results

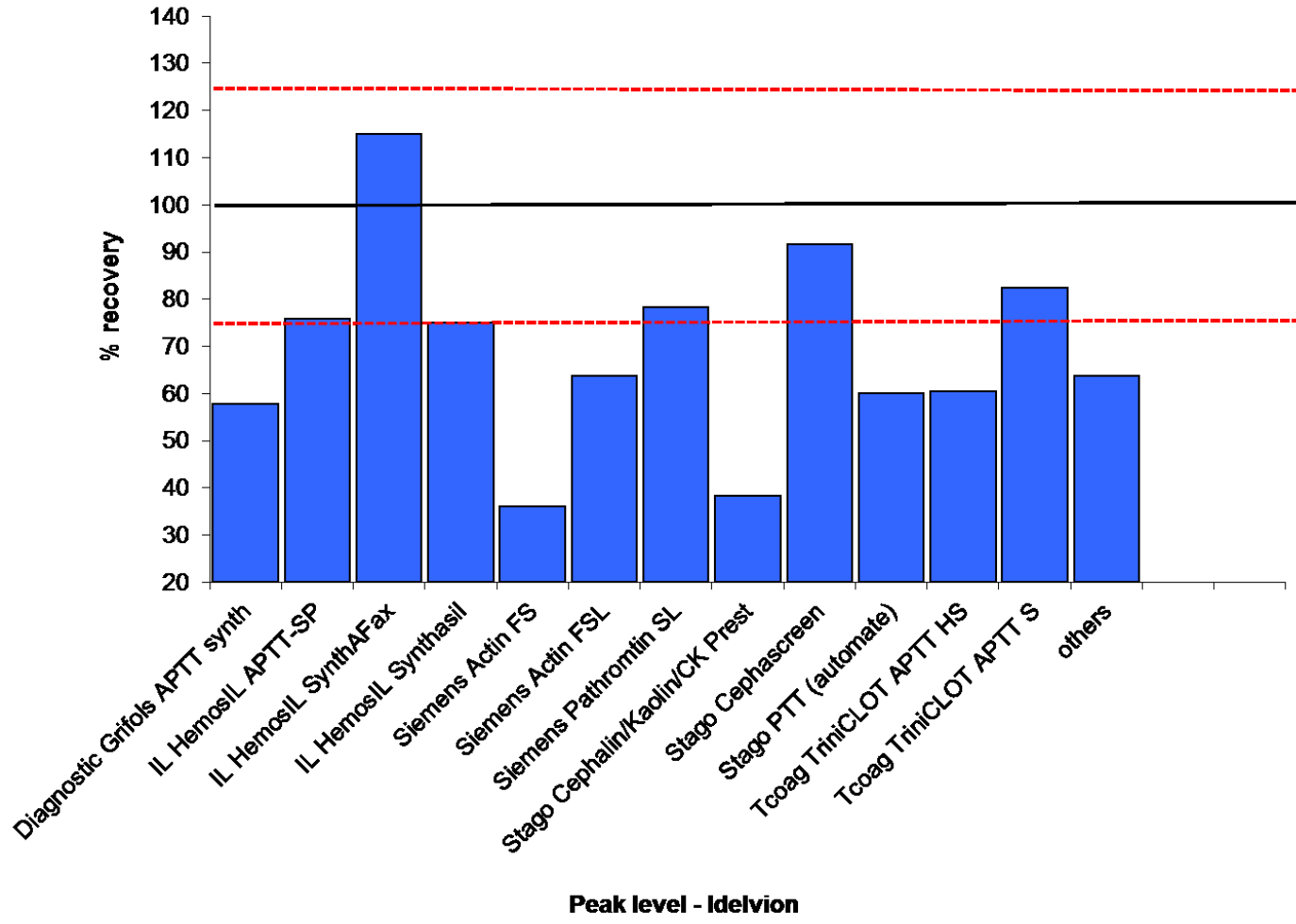




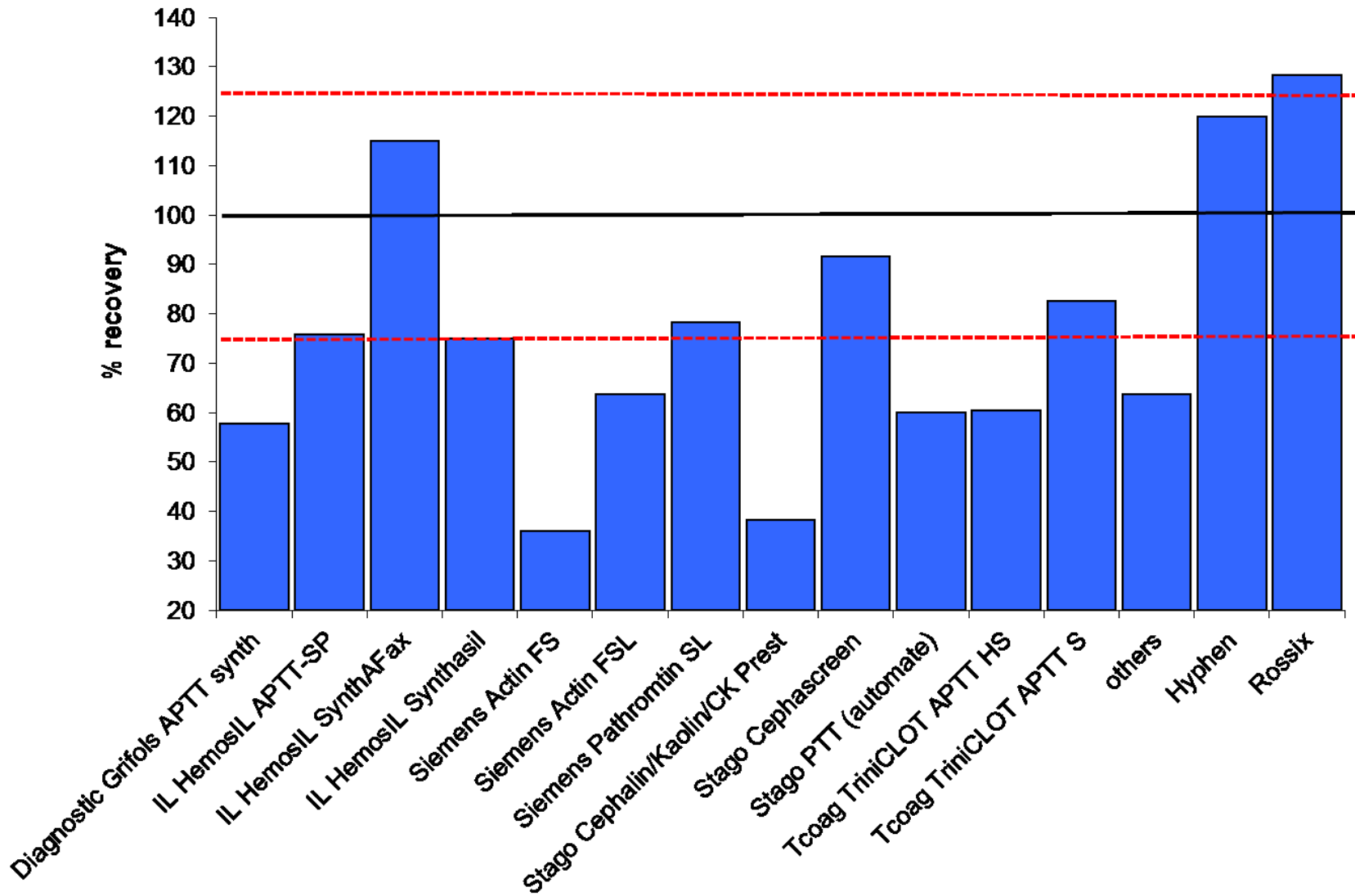




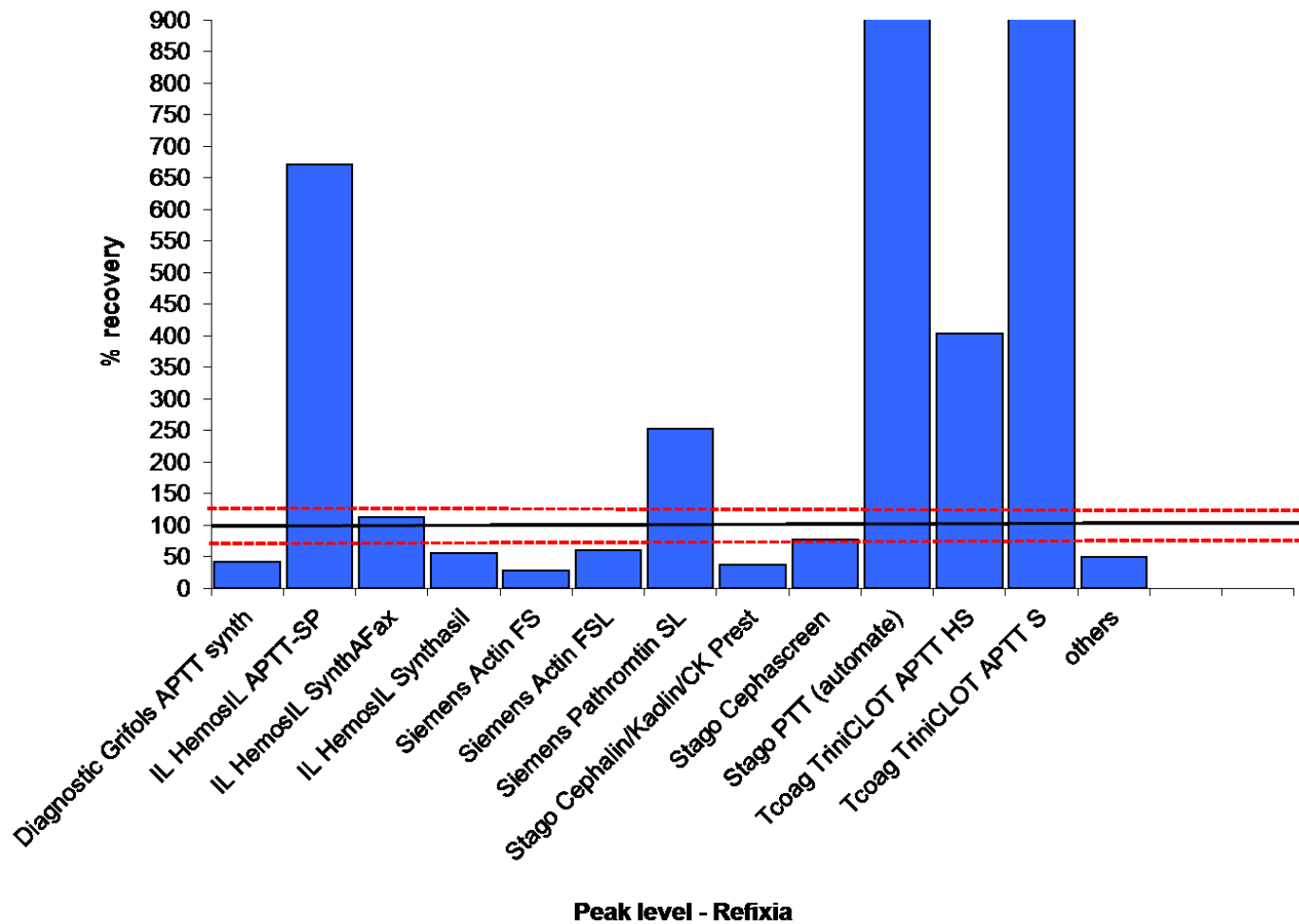
Peak level - Alprolix

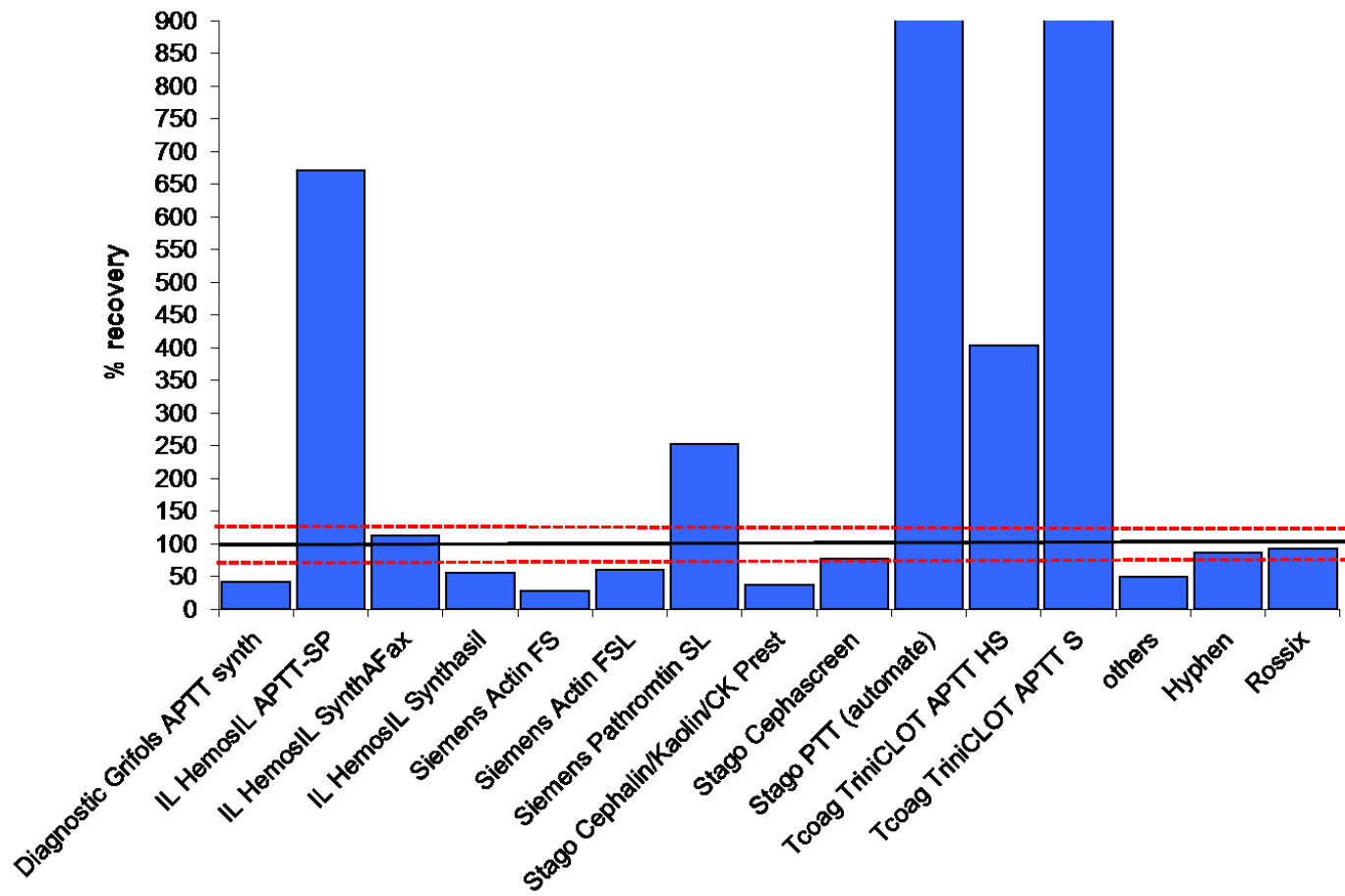






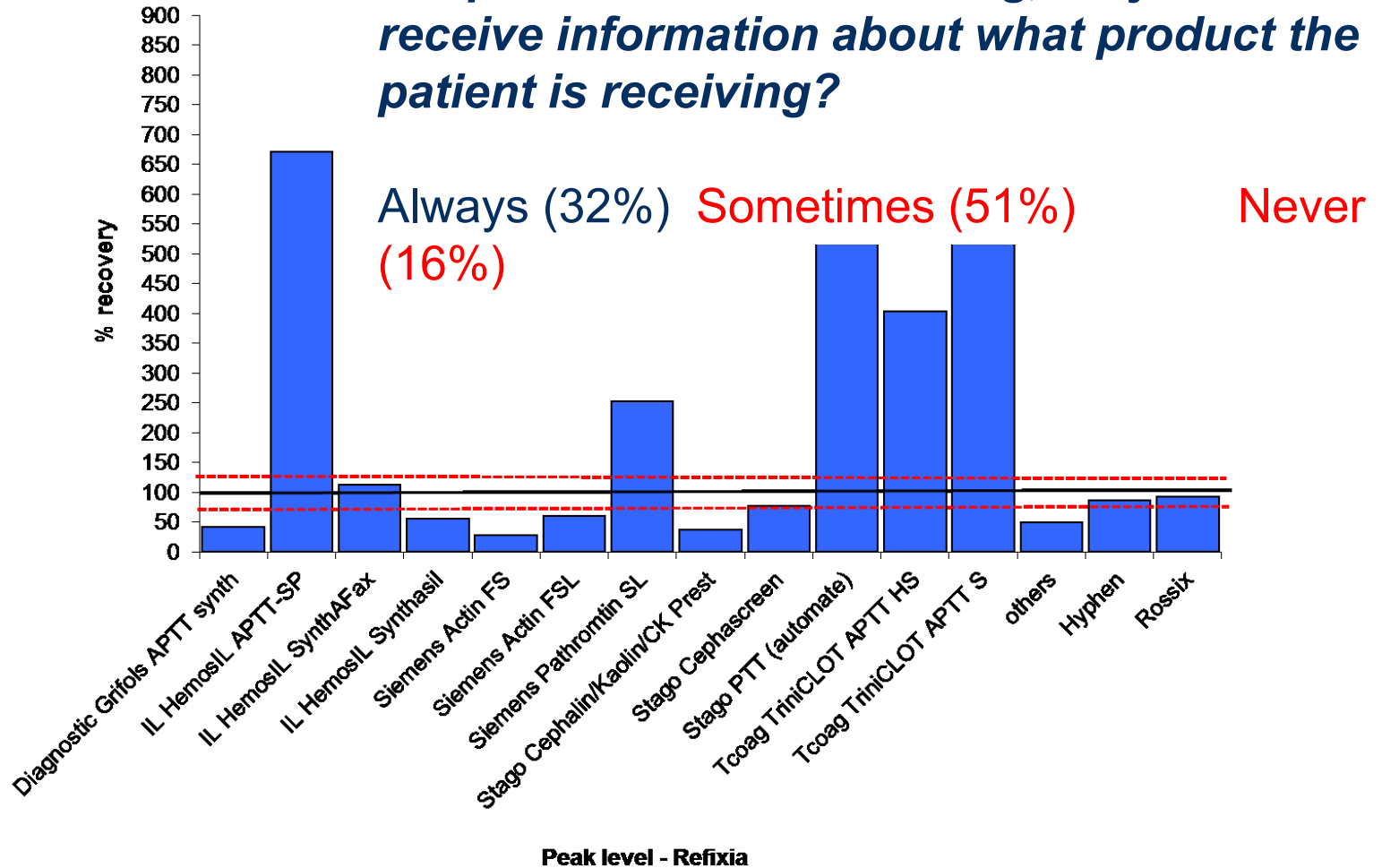
Peak level - Idelvion





Peak level - Refixia

**For post infusion monitoring, do you receive information about what product the patient is receiving?**



# EXTENDED HALF LIFE PRODUCTS: WHICH ASSAY?

Name	Technology	Chromogenic?	One-stage?
<b>Factor VIII products</b>			
Elocta	Fc fusion	Yes	<b>Yes</b>
Adynovate	Pegylation	Yes	<b>Yes</b>
Bay 94-9027	Pegylation	Yes	<b>Some</b>
Afstyla	Single-chain FVIII	Yes	<b>Some</b>
N8-GP	Pegylation	Yes	<b>Some</b>
<b>Factor IX products</b>			
Aprolix	Fc fusion	Yes	<b>Some</b>
Idelvion	Albumin fusion	No?	<b>Some</b>
N9-GP	Pegylation	Yes	<b>Some</b>

# Summary

- EHL products potentially offer improved treatment for many people with haemophilia
- Assays designed to measure native FVIII and FIX (in diagnostic samples and to monitor treatment) may not behave in the same way when plasma containing EHLs is tested
- It is vital laboratories are aware of what product the patient is receiving
- It is vital the laboratory understands how their assays behave with these EHLs
- EQA exercises can help with this, and highlight issues with individual lab performance in drug monitoring, as well as method-related issues.

# Acknowledgements



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- Piet Meijer, Angelique Nederlof
- Ros Bonnar, Nae Ali Pour
- Steve Kitchen, Di Kitchen, Tim Woods, Isobel Walker
  
- CSL Behring, Novo Nordisk, Pfizer, Sobi for donation of material for spiking and for unrestricted educational grants which supported this study