Introduction to Inhibitor Testing

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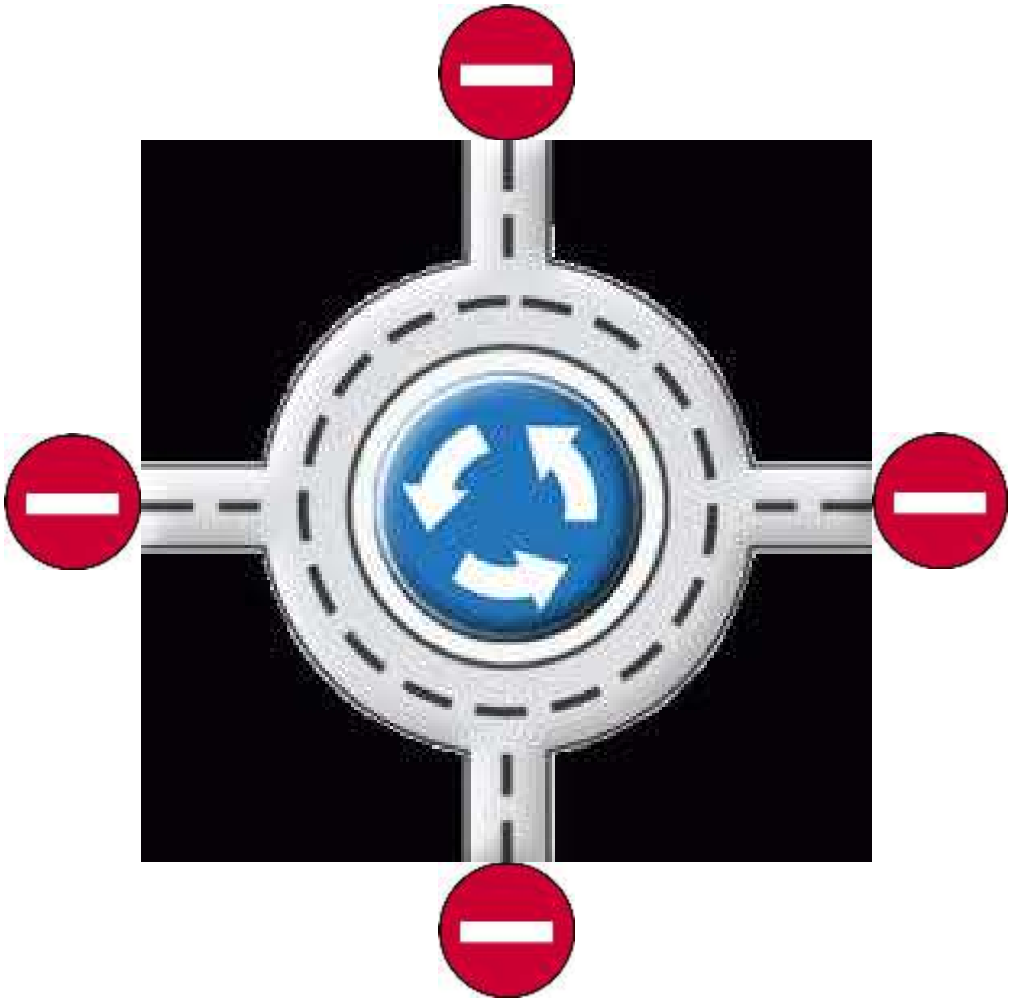
5th Anniversary of ECAT inhibitor lectures

- **2004**
  Factor VIII inhibitor testing: background, history and standards and pitfalls in the diagnosis of inhibitors
- **2006**
  Principles and Pitfalls in Inhibitor Testing
- **2010**
  Factor VIII Inhibitor Testing: The Way to Better Comparison of Results
- **2012**
  Factor VIII Inhibitor Testing: A Way to Comparable Test Results
- **2014**
  Introduction to Inhibitor Testing

5th Anniversary of ECAT inhibitor lectures



ECAT activities in factor VIII inhibitor testing

2005	Start of ECAT factor VIII inhibitor surveys
2008	ECAT workshop on Inhibitor detection and quantification
2009	Start of quality improvement cycle: extra survey with 51 laboratories
2009	ECAT /Radboud University international workshop on factor VIII inhibitor testing
2009	Extra ECAT survey with workshop participants
2009	Publication in Seminars in Thrombosis and Haemostasis on ECAT experience with factor VIII inhibitor surveys
2011	Extra ECAT survey with 51 laboratories
2011	Publication in Journal of Thrombosis and Haemostasis of results of workshop 2009
2012	Publication in Seminars in Thrombosis and Haemostasis of results of workshop 2008

Results Workshop 2009

	Pre-Workshop Survey		workshop	results		
Sample no. (nominal inhibitor activity)	51 laboratories	15 laboratories selected for the workshop	Session 1	Session 2	Session 3	Session 4
1 (1.6 U/ml)	2.32 (35.8%)	2.69 (42.6%)	2.97 (39.0%)	3.40 (40.7%)	1.94 (9.6%)	1.93 (7.6%)
2 (0.8 U/ml)	0.79 (49.0%)	1.02 (30.6%)	1.33 (69.1%)	1.18 (51.4%)	0.90 (14.1%)	0.94 (5.2%)
3 (1.4 U/ml)	0.97 (41.2%)	1.16 (38.6%)	1.17 (30.2%)	0.98 (34.6%)	1.18 (12.5%)	1.16 (6.4%)
4 (0.7 U/ml)	0.44 (69.5%)	0.59 (68.7%)	0.61 (45.2%)	0.50 (42.8%)	0.58 (14.7%)	0.50 (13.4%)
5 (2.0 U/ml)	1.74 (36.0%)	1.74 (37.1%)	2.34 (41.0%)	2.31 (35.7%)	2.32 (12.8%)	2.22 (12.0%)
6 (15.0 U/ml)	11.0 (35.8%)	11.5 (44.3%)	14.9 (41.3%)	17.0 (38.1%)	15.5 (19.1%)	14.6 (5.8%)
Mean CV	46.8	43.6	44.3	40.6	13.8	8.4

Results of Quality Improvement Cycle

	Pre-Workshop Survey (2009)		Workshop (2009)	results	Post-workshop survey (2010)	Standardized final survey 2012
Sample no. and nominal inhibitor activity	51 Laboratories	15 laboratories selected for the workshop	First Session	Last Session	13 Laboratories	22/51 Laboratories
1 1.6 BU/ml	2.3 (36%)	2.7 (43%)	3.0 (39%)	1.9 (8 %)	2.9 (41%)	2.7 (31%)
2 0.8 BU/ml	0.8 (49%)	1.0 (31%)	1.3 (69%)	0.9 (5%)	1.1 (88%)	0.7 (17%)
3 1.4 BU/ml	1.0 (41%)	1.2 (39%)	1.2 (30%)	1.2 (6%)	1.1 (31%)	1.0 (23%)
4 0.7 BU/ml	0.4 (70%)	0.6 (69%)	0.6 (45%)	0.5 (13%)	0.6 (61%)	0.5 (30%)
5 1.9 BU/ml	1.7 (36%)	1.7 (37%)	2.3 (41%)	2.2 (12%)	1.9 (31%)	1.8 (22%)
6 15.4 BU/ml	11.0 (36%)	11.5 (44%)	14.9 (41%)	14.6 (6%)	12.0 (36%)	12.4 (27%)
Mean CV	45%	44%	44%	8%	48%	25%

Did ECAT survey results improve?

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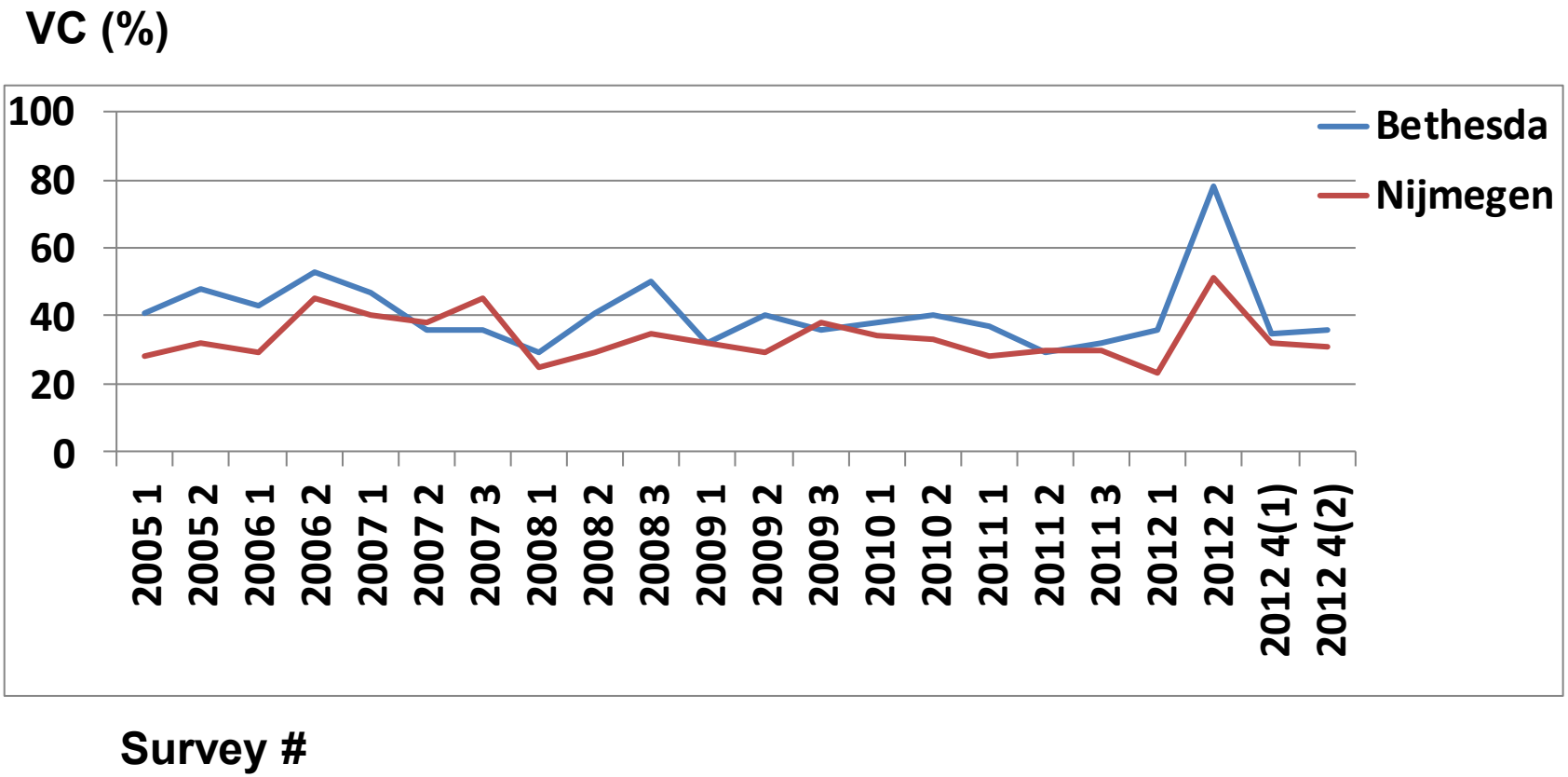
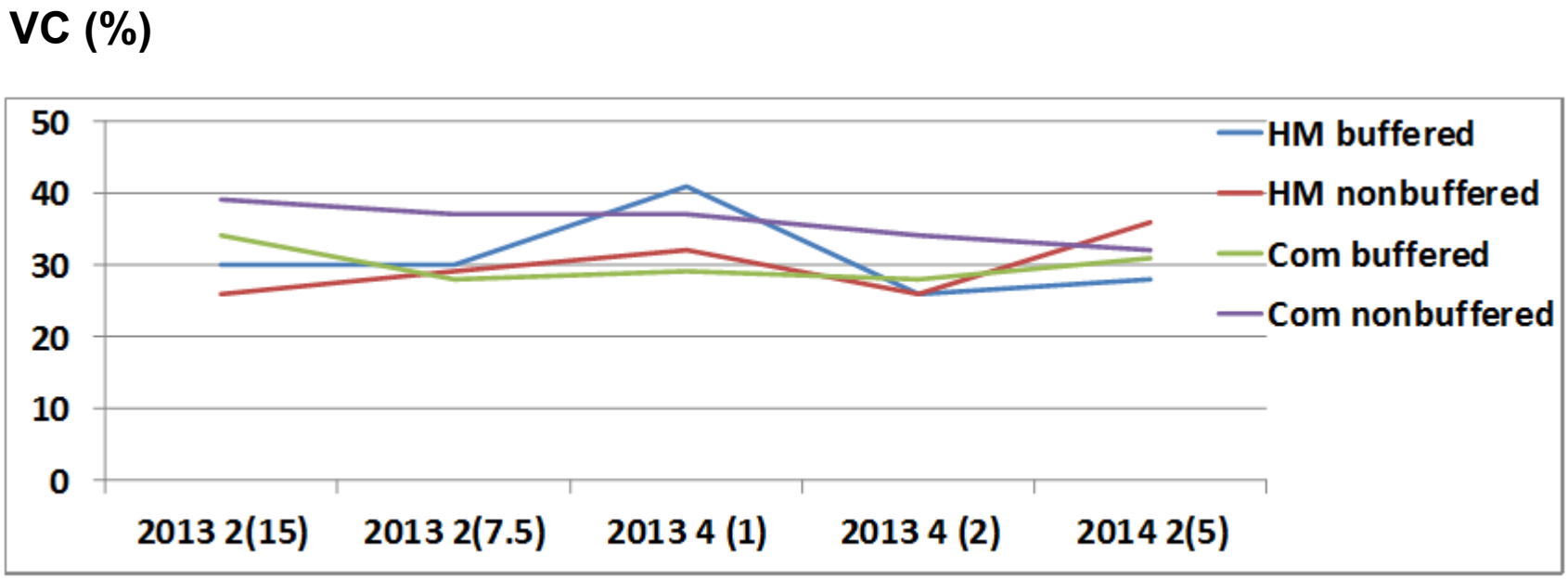
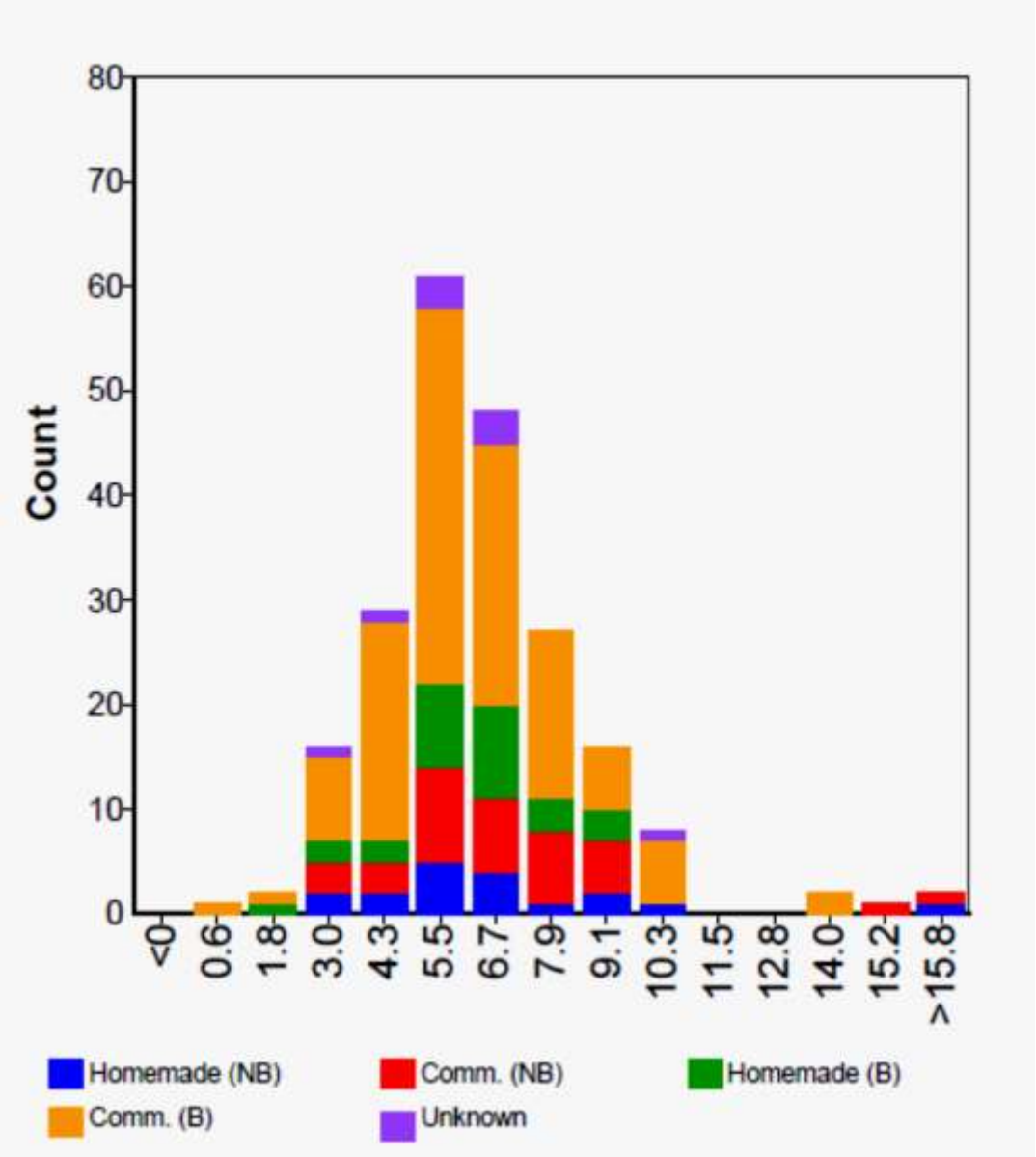


Did ECAT survey results improve?




Count
80
70
60
50
40
30
20
10
0
<0
0.6
1.8
3.0
4.3
5.5
6.7
7.9
9.1
10.3
11.5
12.8
14.0
15.2
>15.8
Homemade (NB)
Comm. (NB)
Homemade (B)
Comm. (B)
Unknown

	n	assigned value	CV (%)	range	your result	z-score
Total Group	206	7.1	31.5	1.4 - 34.0		
Home-made (non-buffered)	20	6.8	29.0	4.0 - 16.0		
Buffer	7	7.5		5.8 - 9.0		
Buffer + Albumin	2	7.1		4.0 - 10.2		
Factor VIII Deficient Plasma	3	7.1		5.4 - 16.0		
Heat-activated normal plasma	2	6.2		4.5 - 7.9		
Other	6	5.9		4.4 - 7.1		
Commercial (non-buffered)	43	8.3	37.2	3.6 - 34.0		
Buffer	25	8.5	34.3	3.7 - 34.0		
Factor VIII Deficient Plasma	7	7.1		3.6 - 12.5		
Heat-activated normal plasma	4	11.1		8.0 - 12.8		
Other	7	6.8		5.4 - 10.7		
Home-made (buffered)	30	6.7	30.4	3.2 - 13.0		
Buffer	7	6.0		4.3 - 9.0		
Buffer + Albumin	4	7.0		4.7 - 12.1		
Factor VIII Deficient Plasma	11	6.9	24.8	3.8 - 10.0		
Heat-activated normal plasma	2	6.0		5.4 - 6.6		
Other	5	5.8		3.2 - 13.0		
Unknown	1	7.4				
Commercial (buffered)	108	6.9	28.4	1.4 - 17.2		
Buffer	53	6.8	25.7	1.4 - 12.8		
Buffer + Albumin	6	6.6		4.2 - 9.0		
Factor VIII Deficient Plasma	24	6.5	31.1	1.9 - 17.2		
Heat-activated normal plasma	5	8.6		6.0 - 12.0		
Other	20	7.4	32.2	3.8 - 14.0		
Unknown	5	6.7		5.0 - 13.8		
Other	5	6.7		5.0 - 13.8		

Conclusions 2012

- The here proposed “Quality Improvement Cycle” appears to be a powerful way to analyze factors influencing the inter-laboratory variation.
- The persistent high coefficient of variation of the FVIII inhibitor assay results in external quality control surveys has a multifarious cause and is therefore difficult to improve.
- Nevertheless, yet it is possible to reduce the inter-laboratory variation by further standardization all aspects of the assay.
- The standardization has to be implemented in the right way by the participants.

What are the obstructions to implement new or improved methods?

Dr. Albert Huisman

Head of Hemostasis lab UMC Utrecht

Procedures and barriers for the introduction of a new or improved method: the example of inhibitor testing.

Dr. Matthijs van Leeuwen

Department of Social & Cultural Psychology

Department of Communication Science

Behavioural Science Institute

Radboud University Nijmegen

Resistance to change: How to facilitate the implementation of new methods in the lab.