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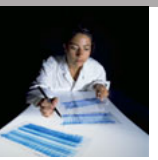
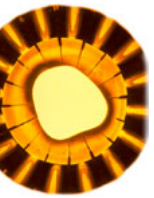




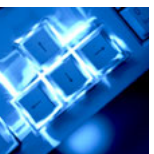

The Concept of Commutability

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Definition of commutability

Degree to which a material yields the same numerical relationships between results of measurements by a given set of measurement procedures, purporting to measure the same quantity, as those between the expectations of the relationships for the same procedures applied to those types of material for which the procedures are intended

New definition under discussion

Closeness of the agreement between the mathematical relationship of the measurement results obtained by two measurement procedures for a stated quantity in a given material and the mathematical relationship obtained for the quantity in routine samples

Definition of commutability

- In other words:
  The ratio between the results of two procedures must be the same for the calibrator as for the routine samples
- A commutable calibrator is showing a similar behaviour to routine samples when different measurement procedures are applied
- Commutability is related to the corresponding measurement procedures and calibrator combinations but is not automatically valid for other combinations

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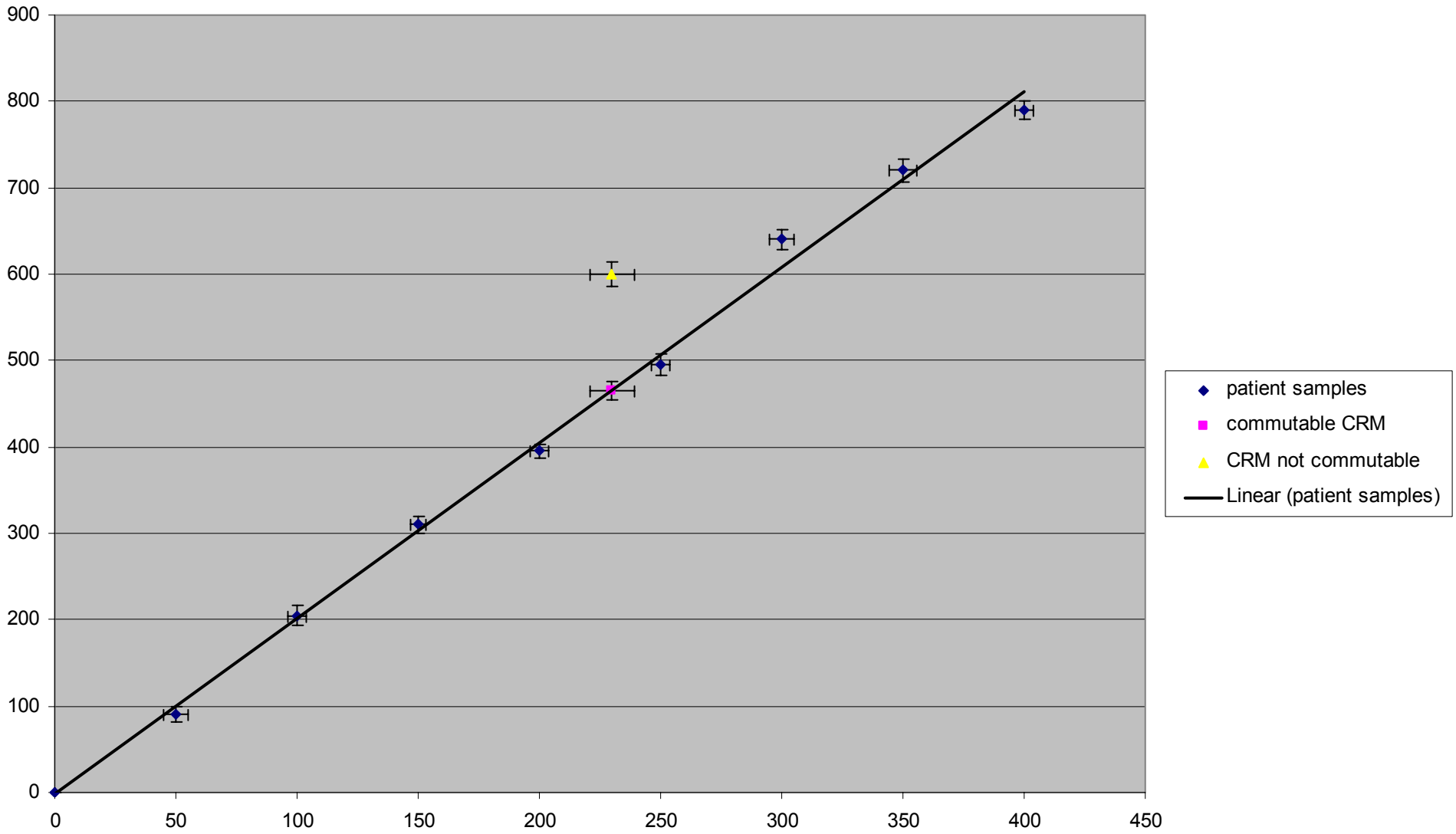
Commutability



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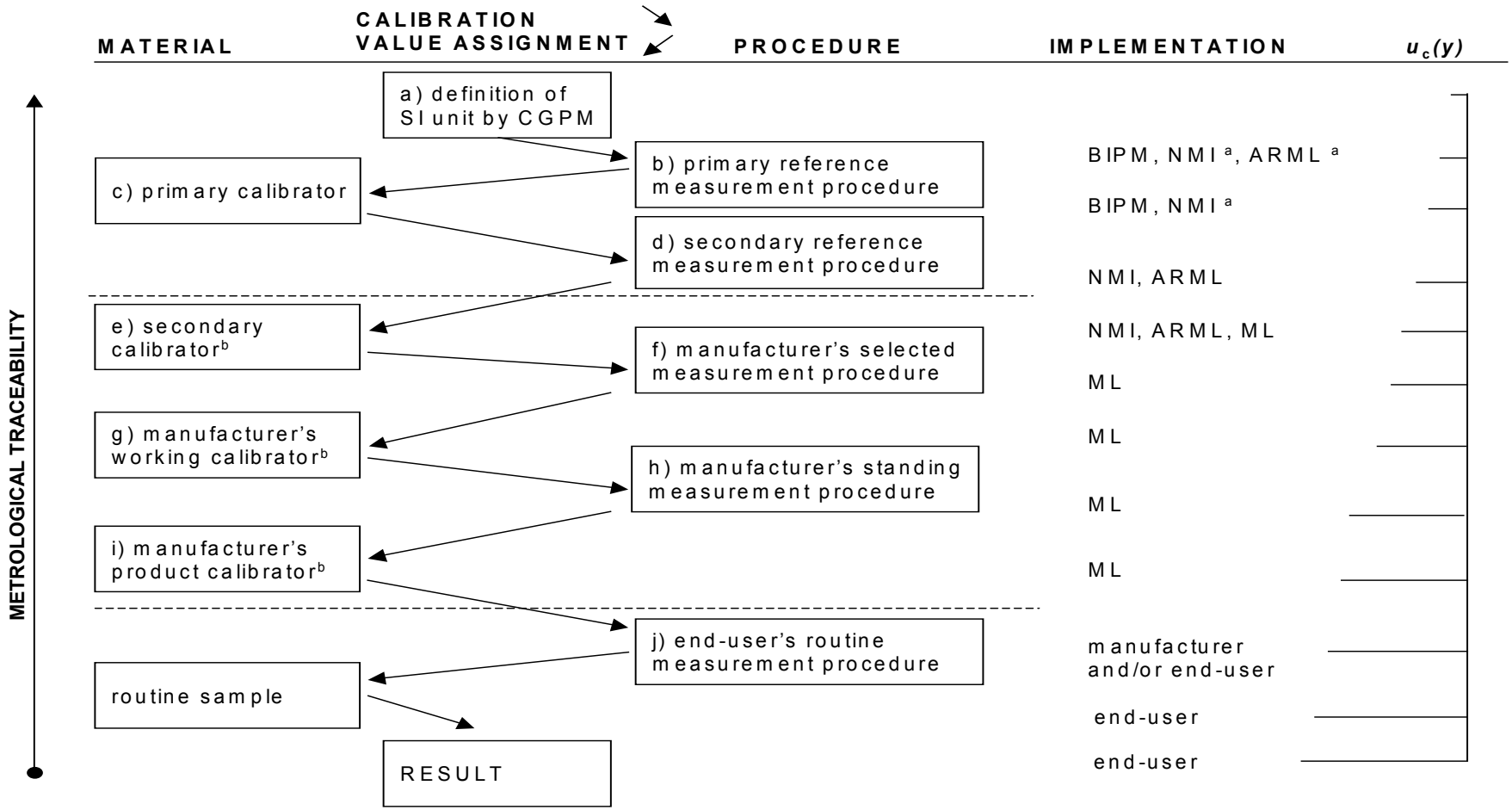
prEN ISO 17511



Uncertainty according to GUM

- Accumulation through the traceability chain
- Uncertainty of calibrator or CRM and uncertainty of value assignment go into the uncertainty of the calibrator on the next lower level
- Also arbitrary calibrators based on consensus should bear an uncertainty (type B based on commutability assessment)
- Combined uncertainties (k=2) of measurements at the routine level should overlap if routine procedures claim to determine the same measurand

Commutability rel. to traceability

- Calibrators must be commutable for the corresponding measurement procedures used in the traceability chain for valua transfer to ensure unbroken chain of comparisons
- Commutable calibrators over as many as possible levels of the traceability chain could reduce the overall combined uncertainties
- If commutable throughout the whole traceability chain could be used for overall trueness control
- High importance for designing reference systems

Implementation of traceability

- Measurement procedures must measure the same type of measurand and must have the same type of specificity or selectivity (check by applying routine procedure and reference procedure on the same samples)
- Commutability should not be a specificity or selectivity issue

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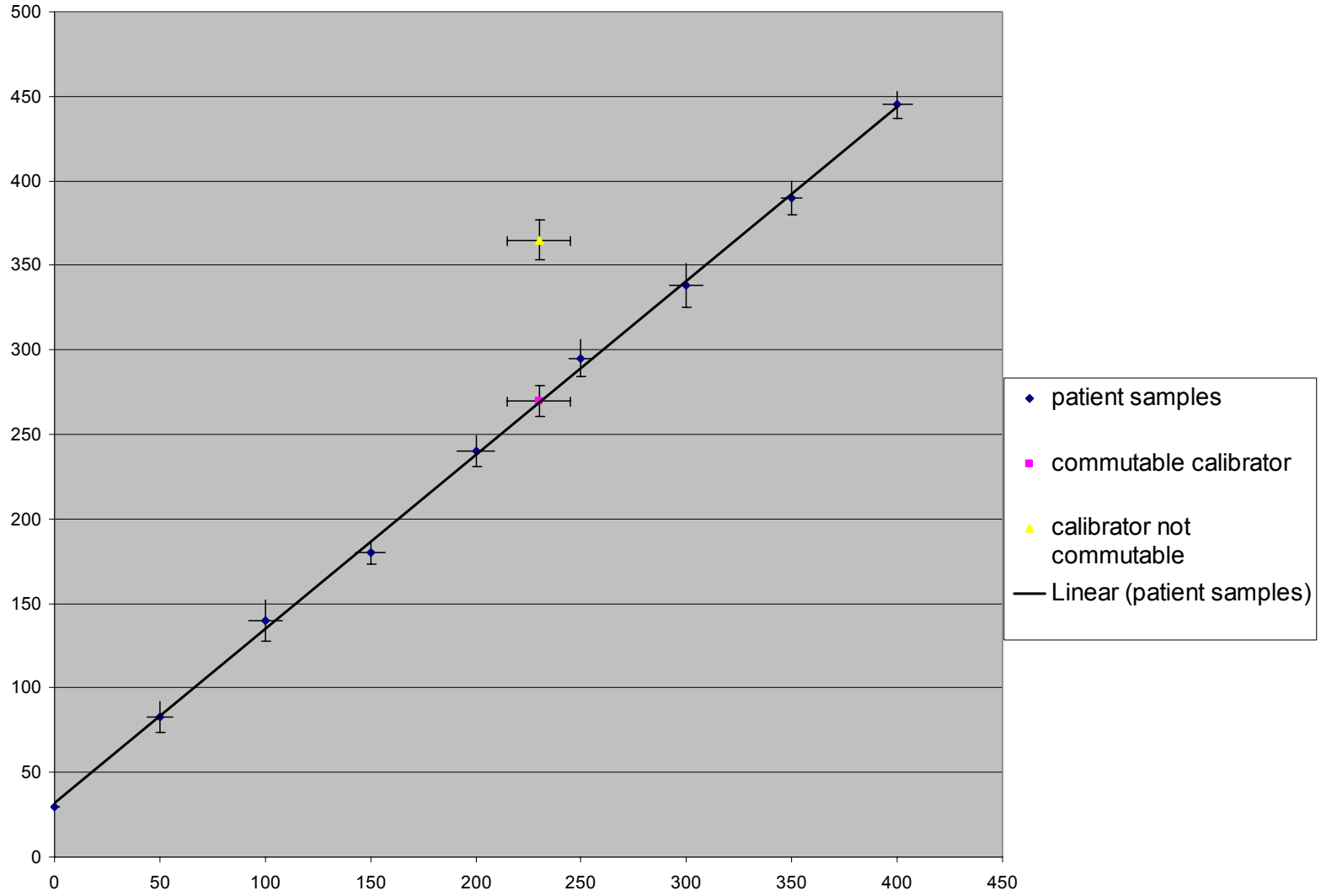
Commutability



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Assessment of commutability

- Evaluation of paralellism, linearity/precision etc. by dilution of calibrators to be assessed and routine samples
- Comparison with a reference method

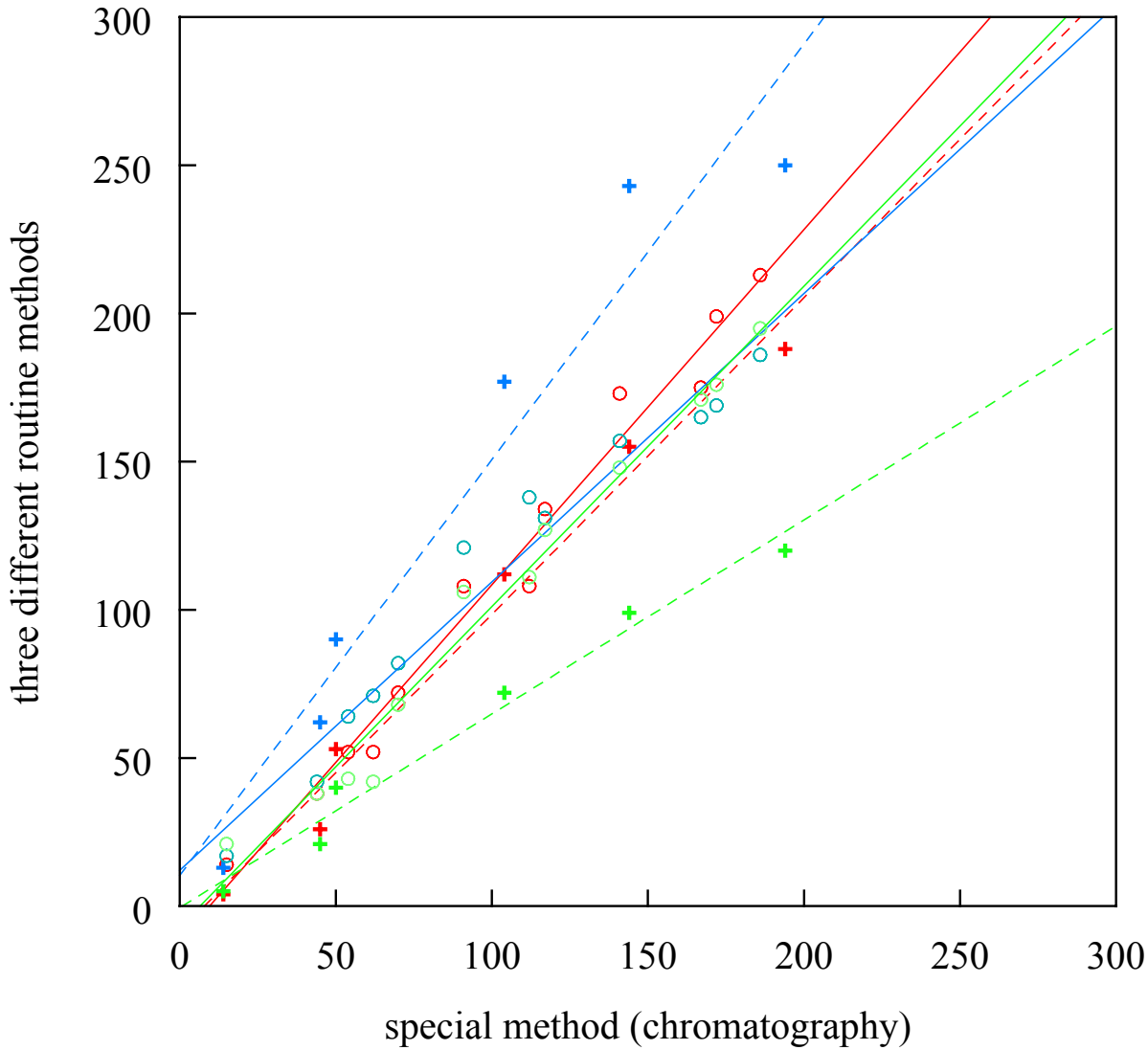
Awareness for commutability issues helps to interpret data correctly and to uncover possible problems

Limitations

- A commutability study reflects only the situation at the moment and need to be updated as soon as new technical developments e.g. new assays are available
- Commutability assessment is assay / material combination specific, is not generally valid and has to be open for new combinations to include technical progress
- Difficult for CRM producers to ensure commutability of their materials with existing and upcoming tests (such information could be obtained from IVD producers during development of new assays)

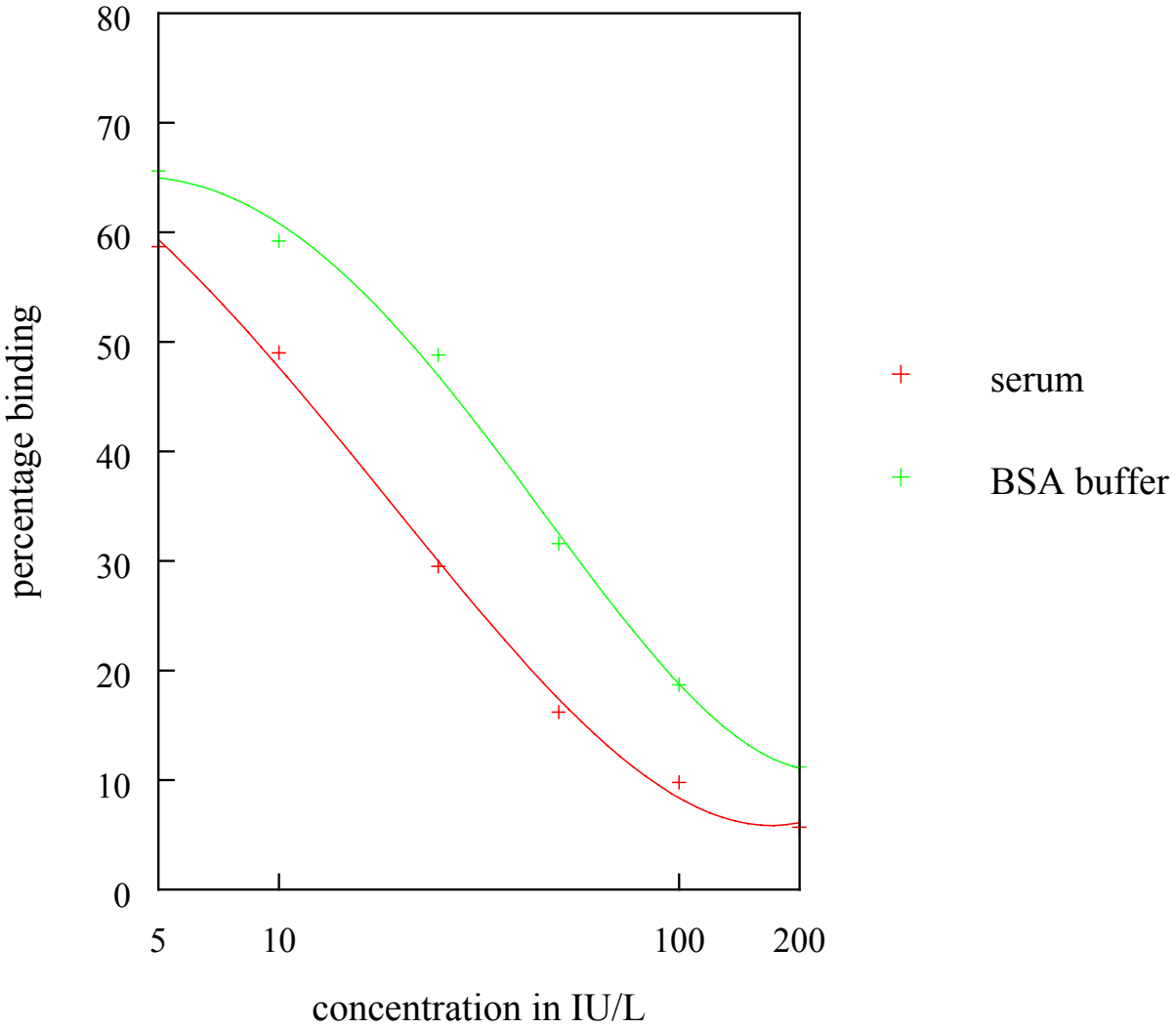
Thyroxine (nmol/L)

serum (o) and T4-free serum (+)



Insuline Standard WHO 66/304

effect of medium

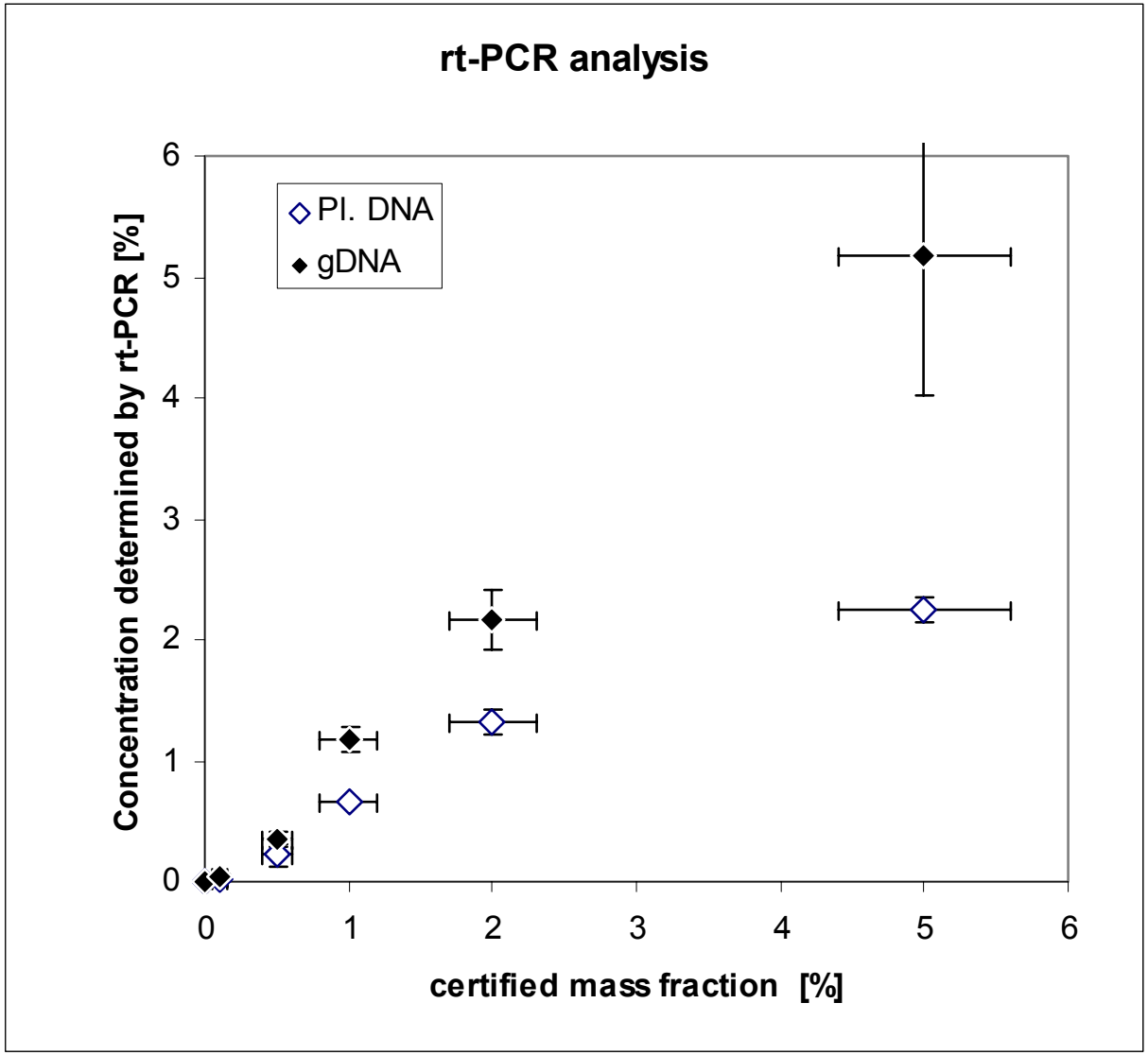


Glycated haemoglobin Hb1Ac

IFCC WG on glycated haemoglobin:

- Feasibility study on candidate matrix CRMs
  - Several candidate materials investigated
  - Assays available where either commutable with frozen or freeze dried materials but none of the two was commutable with all methods
  - One assay working with fresh patient samples was not commutable with any of the candidate materials

Genetic Testing



TSE tests

- Frozen tissue slices
- Prion distribution highly heterogeneous
  - homogenisation to produce uniform samples
- Diluted homogenates for assessment of detection limit and possibly as reference materials (QC, batch release)

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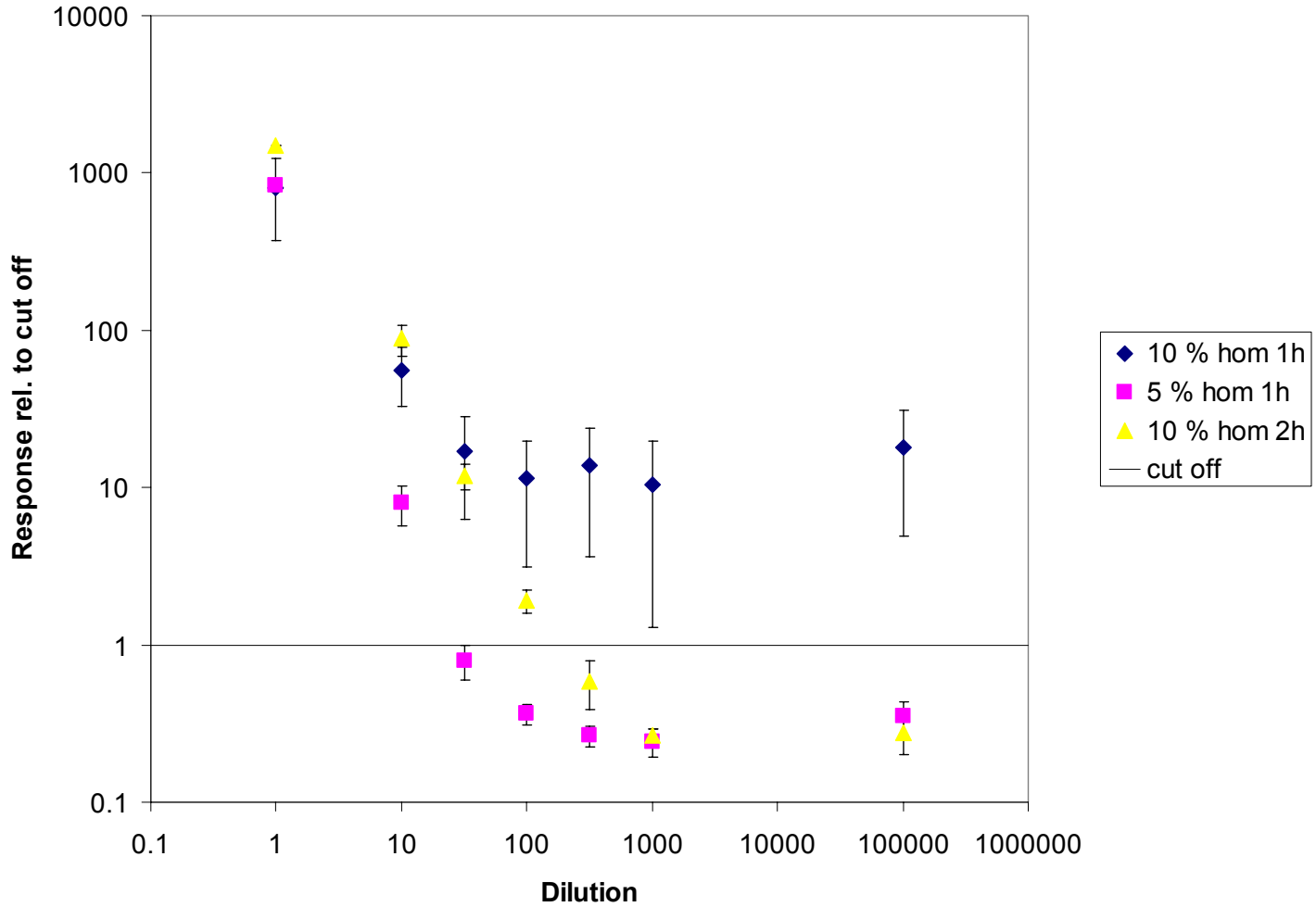
TSE tests



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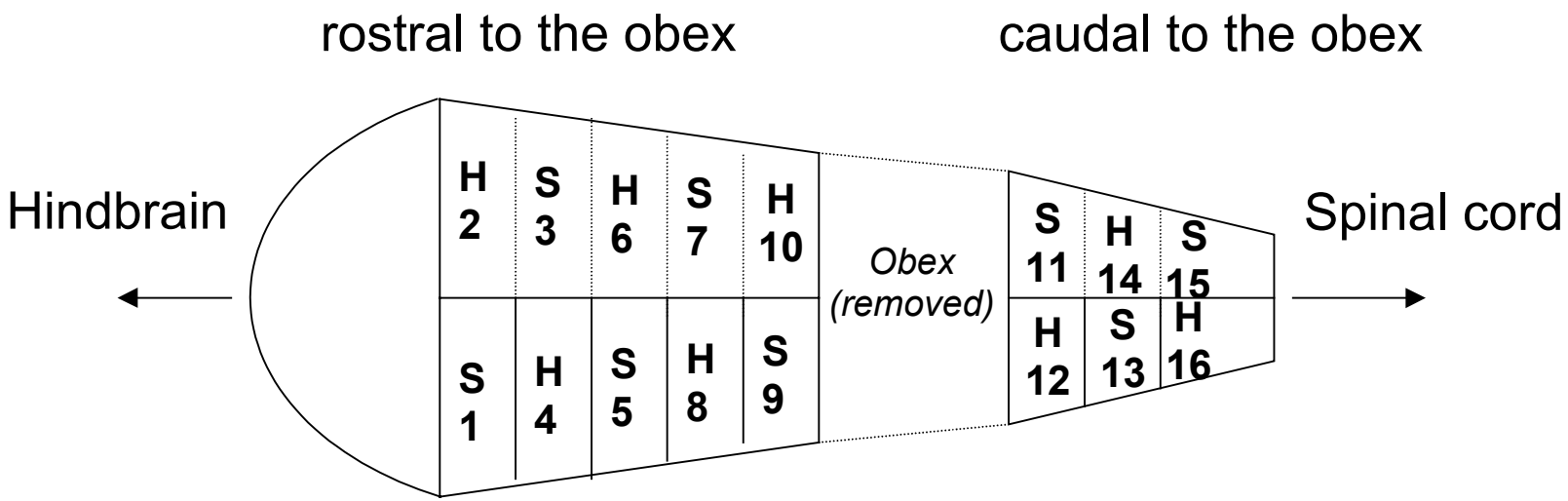
TSE tests

- Serial dilution of homogenates, 3 minutes turraxing, 50 % tissue / 50 % water
  - All dilutions (1:10, 1:30, 1:100, 1:1000) gave negative results for test B
  - Also another test, being able to detect 1:100 dilutions starting with the same raw materials but applying another protocol for sample preparation, gave negative results

TSE tests


rostral to the obex
caudal to the obex
Hindbrain
Spinal cord
H 2
S 3
H 6
S 7
H 10
S 1
H 4
S 5
H 8
S 9
Obex (removed)
S 11
H 14
S 15
H 12
S 13
H 16

TSE tests

Prionics (BioRad, UCSF equiv)			
	Mean 6 repl.	Mean 6 repl.	
Brain 1			
S13	798702	649436	H14
H16	378307	260169	S15
Brain 2			
S1	982583	1427382	H2
H4	1859564	1488782	S3
S5	1623361	2123930	H6
Brain 3			
S1	394656	364340	H2
H4	648820	699870	S3
S5	787848	874879	H6
Brain 4			
S13	235878	343811	H14
H16	177351	124649	S15

Test Enfer			
	Mean 4 repl.	Mean 4 repl.	
Brain 1			
S1	1331	218	H2
H4	321	1128	S3
Brain 2			
S1	2439	183	H2
H4	12	238	S3
S5	331	99	H6
Brain 3			
S1	1563	1081	H2
H4	223	1618	S3
S5	2294	424	H6
S13	399	134	H14
H16	120	171	S15

Reference system for TSE tests

- Based transgenic bovine PrP expressing mice
  - monoclonal
  - homozygous
- Samples after various incubation times for assessment of detection limit (TSE detection at preclinical stage)
- Check of stability of expression system by
  - genetic characterisation
  - prion expression levels

Reference systems

- Identification of generic components and application of metrological principles
- Case to case design of reference systems (involvement of relevant expertise)
- Traceability to SI or stated reference may not improve comparability or even be counterproductive if not the whole biological and measurement system is taken into consideration
- Systems e.g. based on commutable stated references may be more appropriate