Medicines & Healthcare products Regulatory Agency

NIBSC
Confidence in Biological Medicines

SoGAT – current progress and future challenges for standardisation of NAT assays for Infectious Disease

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SoGAT – 20 years in a nutshell

Established - to deal with NAT detection of blood borne viruses

- sensitivity
- specificity

Developed - into international forum for sharing data and information that improves the quality of NAT based diagnostics

- calibration

Focus - on infectious diseases BUT aware of related issues in other fields

Approach – pragmatic principles of Biological Standardisation

SoGAT

The aims of SOGAT are:

to develop, evaluate and provide international standards and secondary reference reagents for qualitative and quantitative nucleic acid assays for infectious diseases

to exchange information on the technical and scientific aspects of nucleic acid assays, assist in the development of regulatory approaches and exchange views on the technology and its application between professionals in:

- control authorities
- academic laboratories
- manufacturers of blood products
- kit manufacturers
- diagnostic laboratories
- blood banks

to organise collaborative studies to evaluate candidate materials, validate methods and establish reproducibility between laboratories

to develop standards in support of new technologies

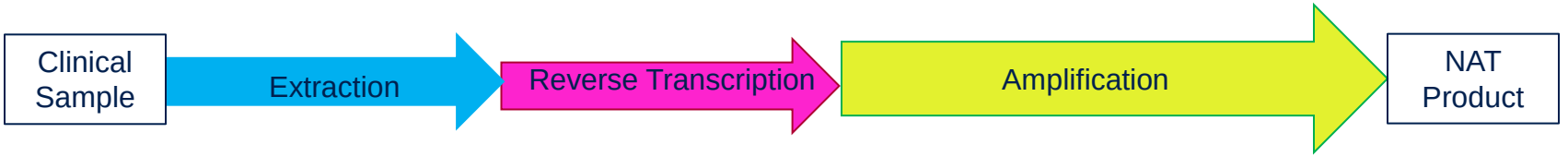
Challenge for NAT based diagnostics

Perception

Challenge for NAT based diagnostics

Perception

Reality



Outcomes

Better NAT based assays

More robust and reproducible diagnostic assays

Improved health – prevention and clinical management

Outputs from SoGAT

WHO ECBS endorsed International Standards:

- HCV (1998 – now 5th IS),
- HIV-1 (1999 – now 4th IS)
- HBV (2000 – now 3rd IS)
- Parvovirus B19 (2000 – now 3rd IS)
- HAV (2001 – now 2nd IS),, HIV-2 (2009)
- CMV (2010)
- EBV (2011)
- HEV (2012 - PEI)
- HDV (2014 - PEI
- JC (2015), BK (2015)

Genetic Variation- HIV panels x2 (WHO) and HCV panel (NIBSC)

Prioritisation for future reference needs- HHV-6a+b, HAdV, VZV

Outputs from SoGAT II

Documents:

Guidance for Preparation and Calibration of Secondary References (aim 2016)

Scientific activities to address key questions:

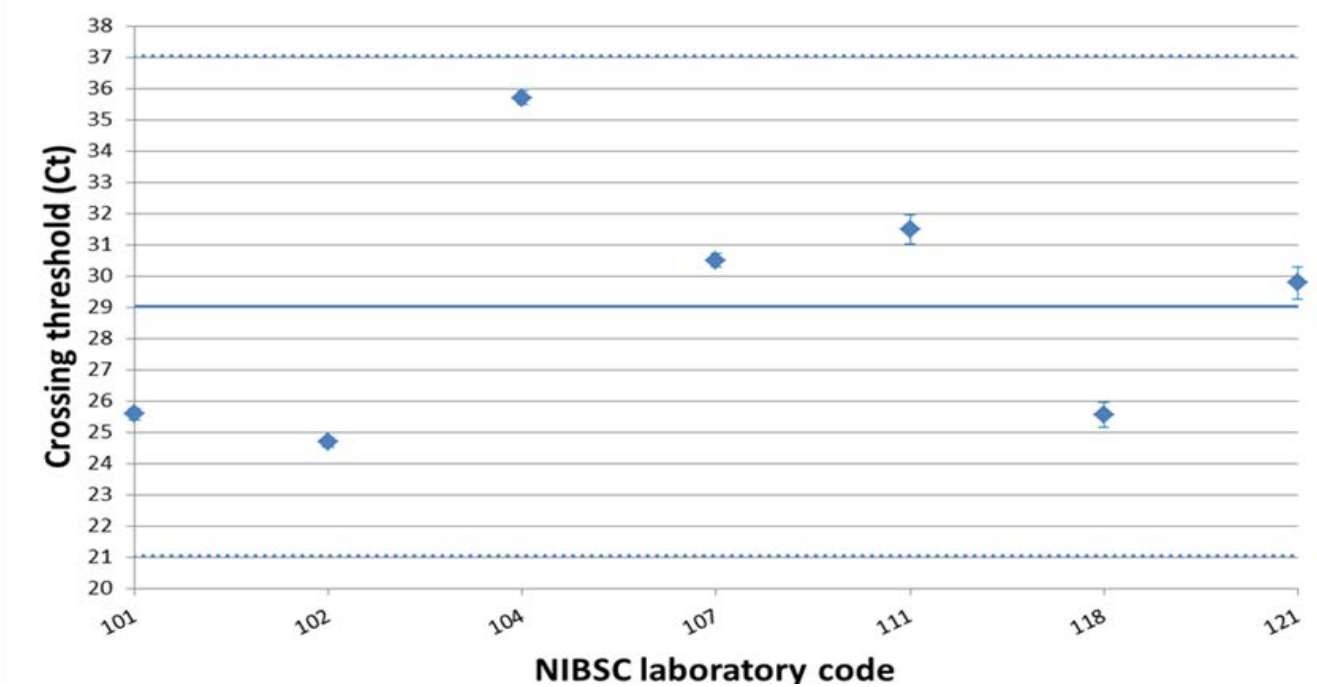
Commutability –

- contributions to WHO document
- Participate in studies

New technologies eg Digital PCR

The need for a primary calibrant -2015

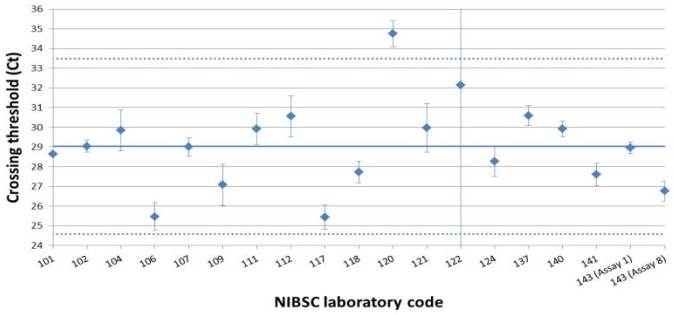
Measuring JC load (no IS)



The value of relative potency -2015

Measuring CMV load

Ct



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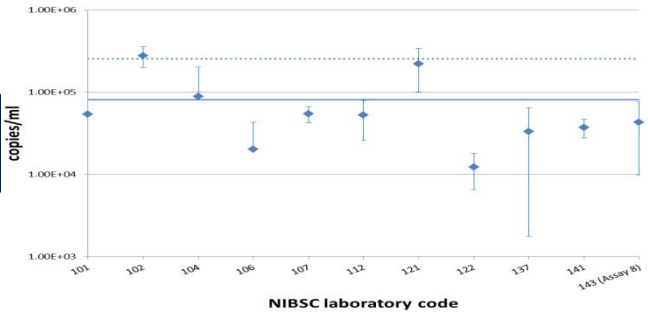

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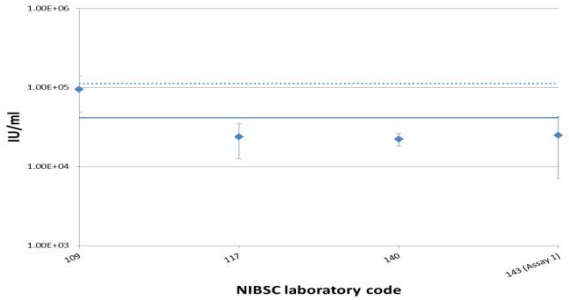
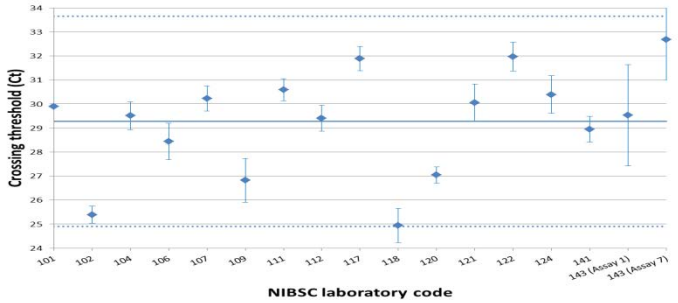
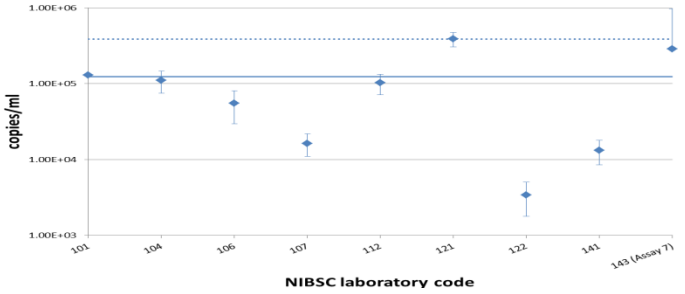
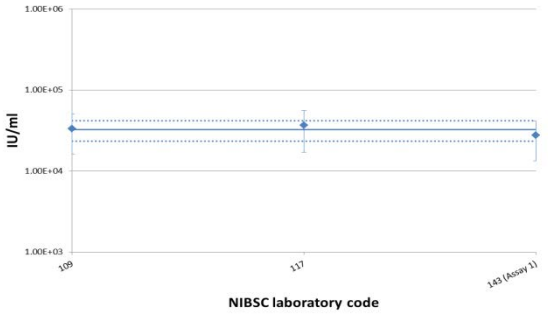


Measuring EBV load







Production and Evaluation of IS

Spring meeting - allows review before WHO ECBS

IS project >2years – reviewed 3 times by SoGAT

Sourcing and Selection of candidate materials

Sourcing of (quasi)-clinical samples

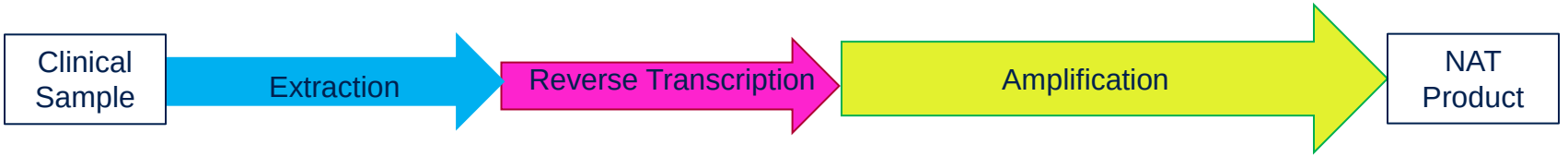
Contacts for participation of collaborative studies

Early review of data – identification and trouble shooting of nascent problems

Selection of Candidate Materials

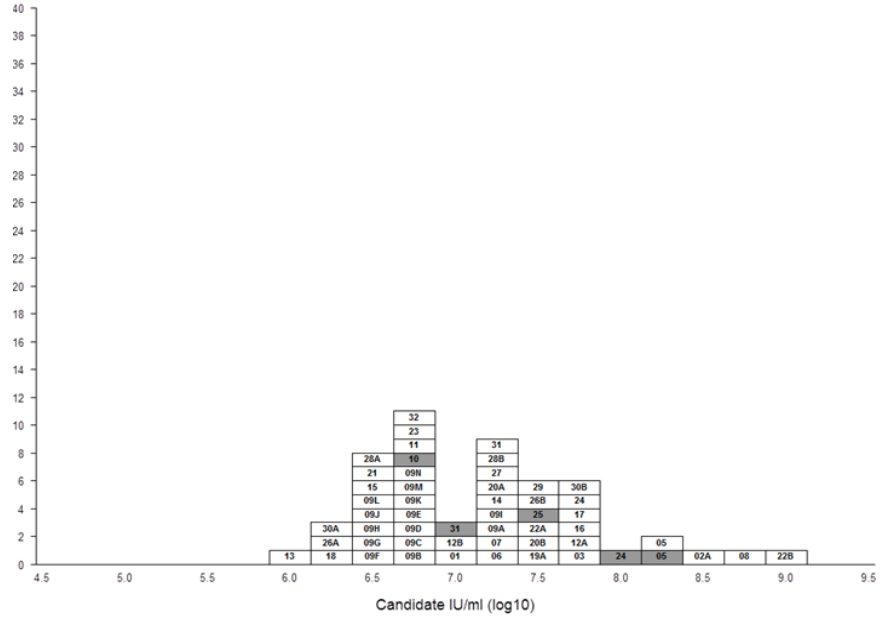
Perception

Reality

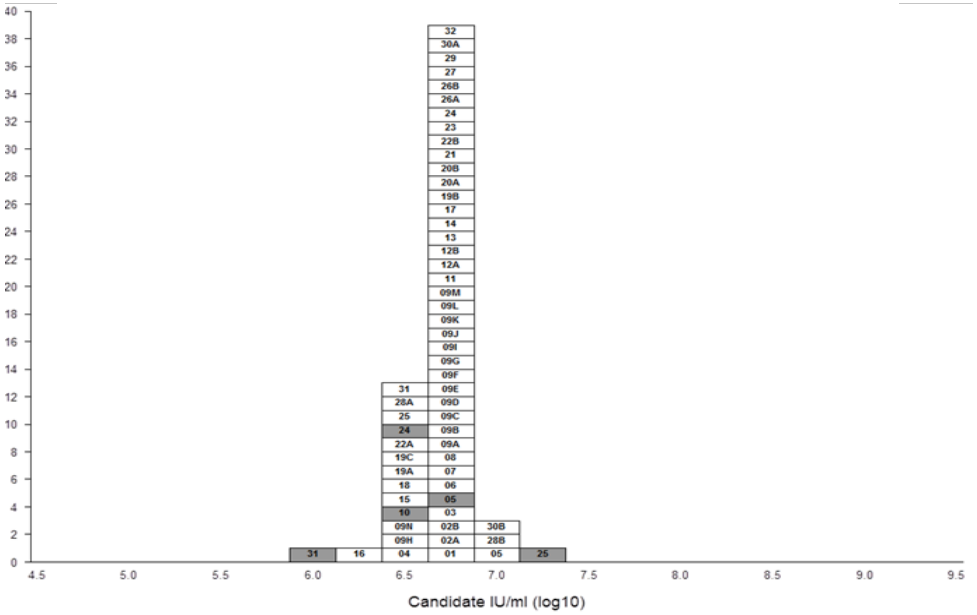


Data from CMV Collaborative Study -2010

Candidate 1- plasmid construct



Candidate 2- Whole virus



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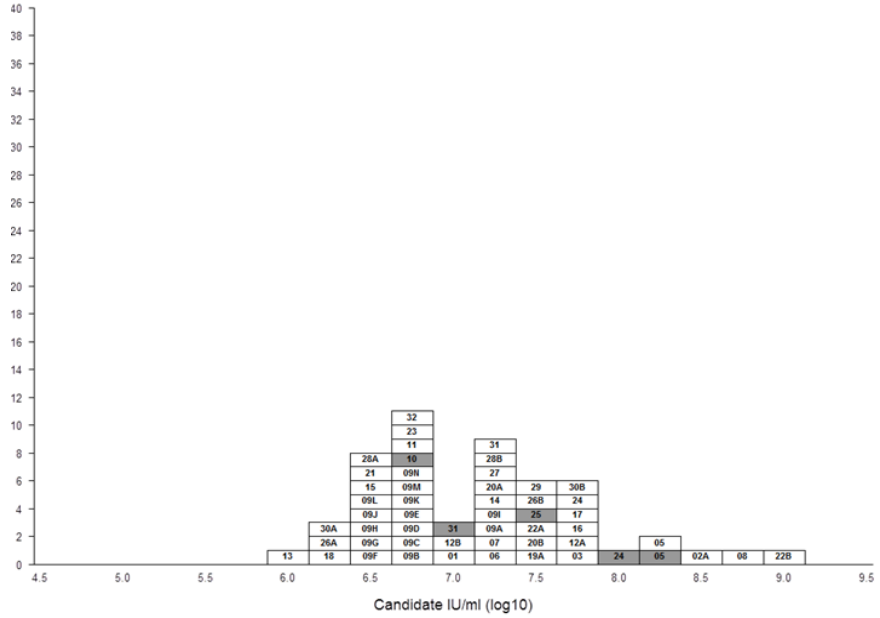
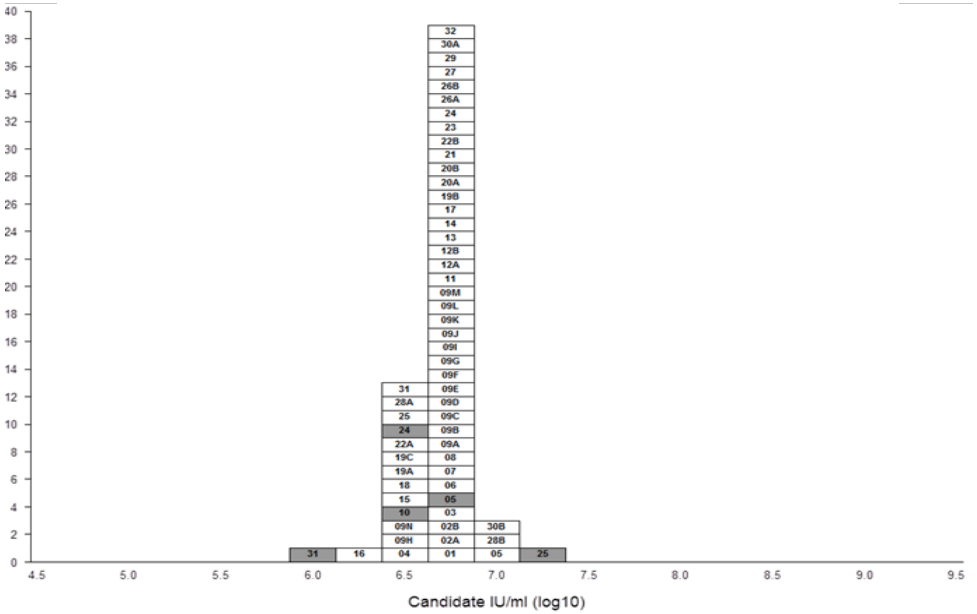


Candidate 2- Whole virus



Similar data from Interim Ebolavirus IS established 2015

Commutability

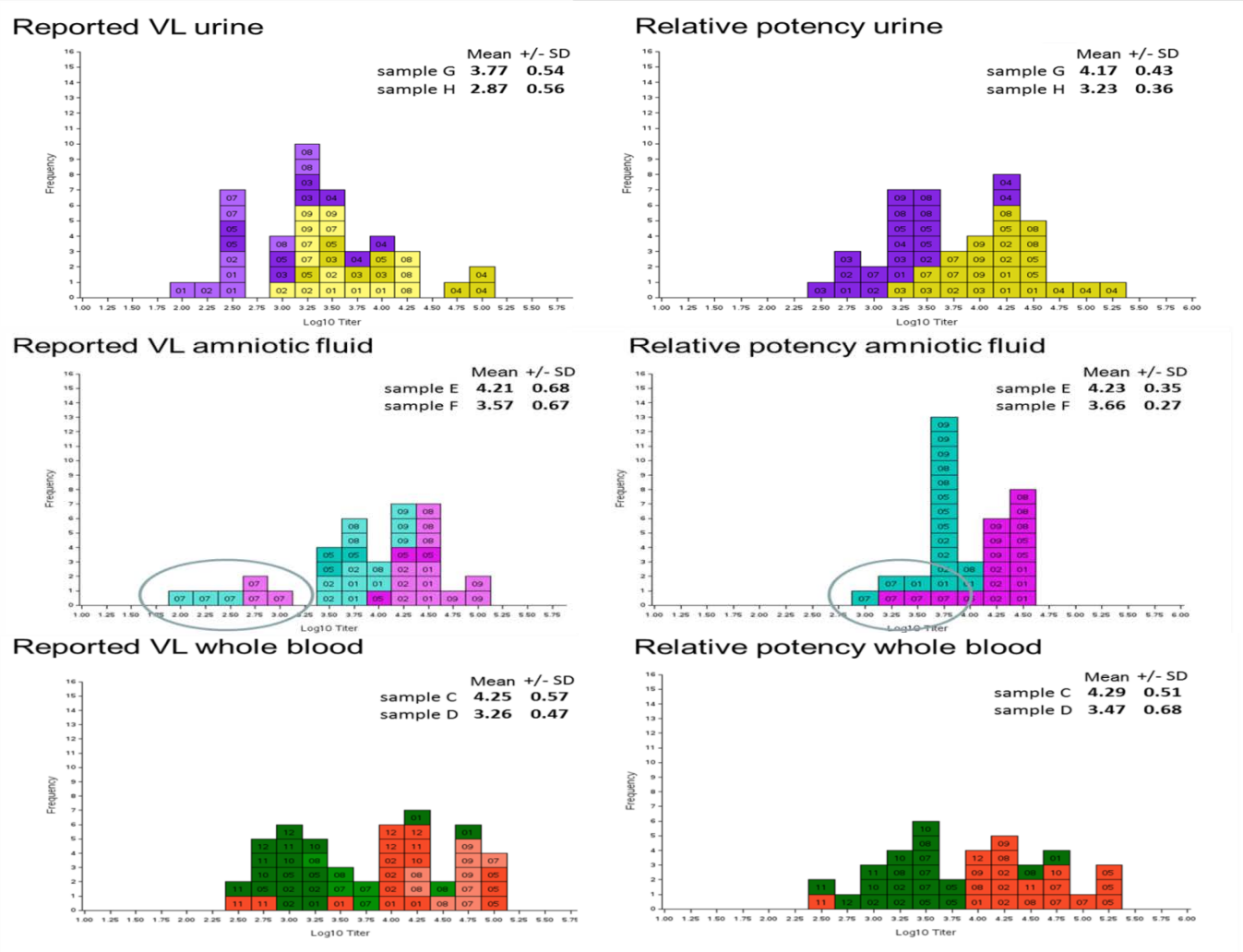
Early IS's

- blood borne viruses limited problem
- Plasma almost universal matrix of blood industry
- IS and other references diluted in plasma or equivalent

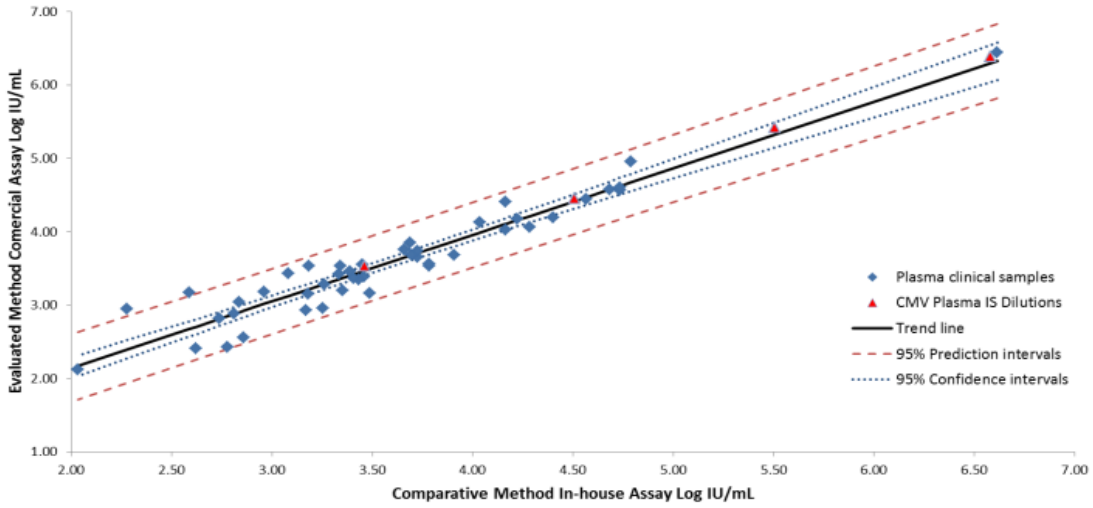
Clinical Virology markers

- a greater challenge much discussion at SoGAT
- Broader range of matrices tested in labs plasma/WB/CSF
- Too complex to include in initial collaborative study
- Efficiency of extraction of nucleic acid variable
- Evidence of non-commutability- assay or standard?

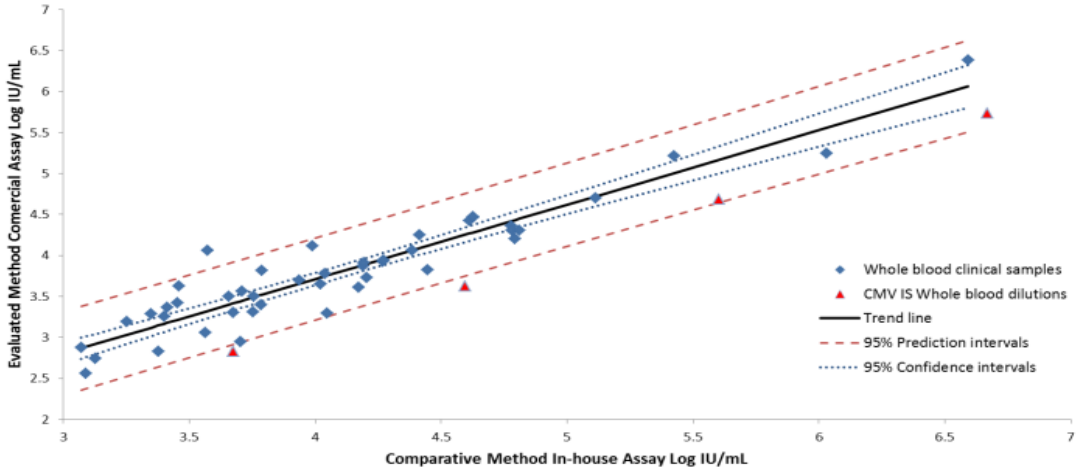
Commutability – hCMV IS Studies 1



Commutability – hCMV IS Studies 2



Plasma Samples



Whole Blood Samples

Current Activities of SoGAT

Encouraging the use of International Standards

- Increasing availability; batch sizes and stability data
- Publishing more data on IS via website and journals

Encouraging use of Relative Potency (IU)

- Share data eg Toxo data multi-copy gene
- Work with EQA scheme organisers, clinical guideline producers

Supporting further commutability studies

- Prioritise according to clinical need
- Publish data on commutability incl SoGAT website
- Review IFCC commutability guidelines when published

Current Activities of SoGAT

Secondary Reference Materials

- Work with WHO ECBS to produce Guidance document on the production of secondary reference materials by Oct 2016

Unstandardised Assays

- Work to prioritise list of new standards
- Can suitable interim standards be developed as stop-gap?

New Areas

- Genetic testing
- Serological Reference materials

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