INTERREGIONALE BLUTSPENDE SRK
TRANSFUSION INTERREGIONALE CRS

The use of International Standards for quality control of NAT

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Topics

- Organisation of NAT testing in Switzerland
- Test methods and equipment
- Encountered problems with international reference material
- Summary
- Open questions

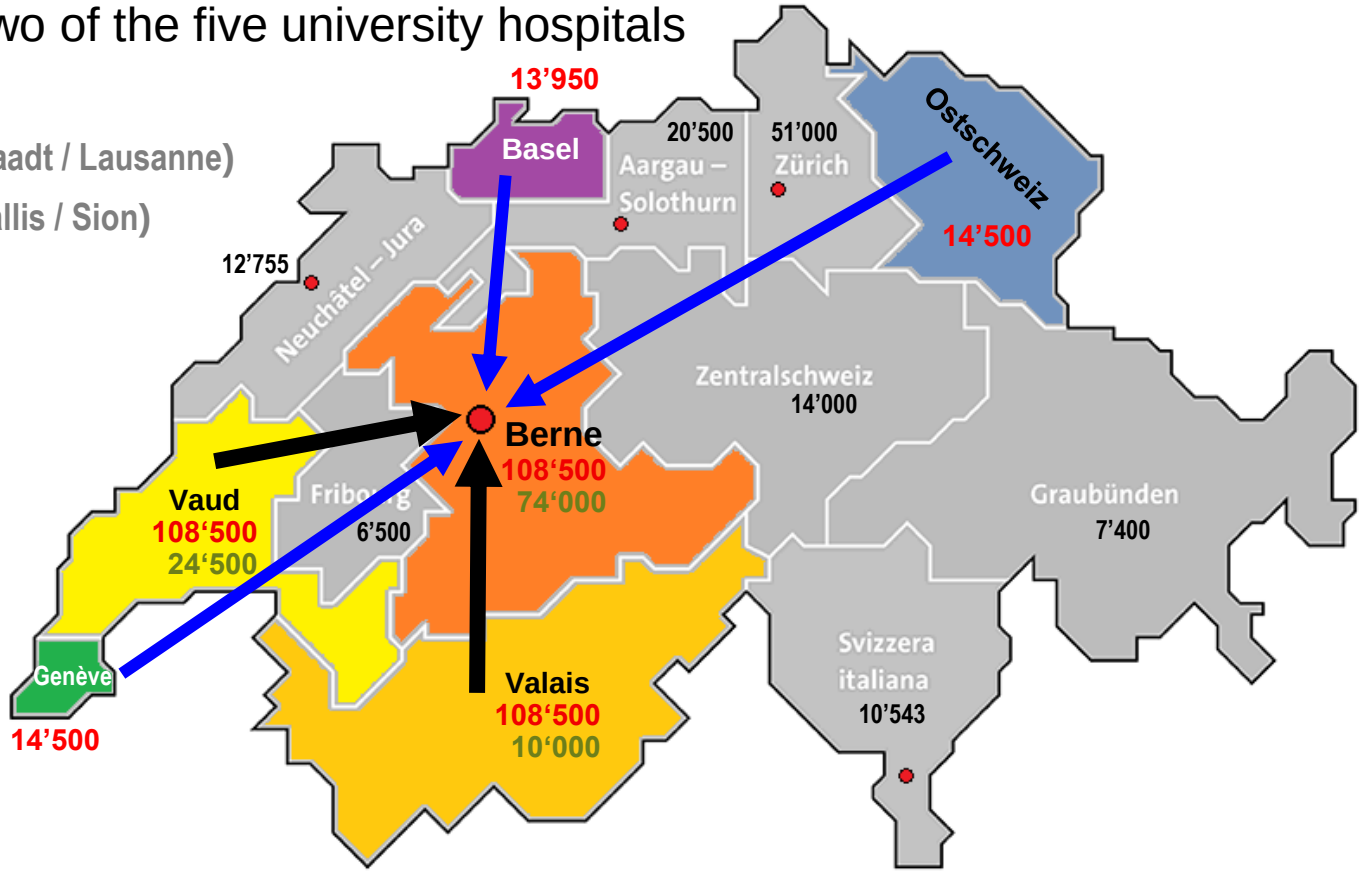
Organisation of Swiss Blood Transfusion Services

- The Blood Transfusion Service (BTS) is an institution under the Swiss Red Cross (SRC).
- The Swiss government commissioned the SRC since 1951 to supply Switzerland with sufficient blood and blood components.
- The blood supply relies on donations from non-remunerated volunteer donors
- 11 regional BTS collecting ca. 300’000 donations / year

Interregionale Blood Transfusion / Catchment area

- 5 NAT testing facilities in Switzerland
- Interregional Blood Transfusion (IRB) collects nearly 40% of all donations and supplies two of the five university hospitals

Region Berne
Region Vaud (Waadt / Lausanne)
Region Valais (Wallis / Sion)



- NAT testing facility in Berne tests for 3 other regional BTS (approximately 55% of the Swiss blood donations)

Legal base / Guidelines

- Therapeutic products act (CH)
- Ordinance concerning authorisations for medical products (CH), articles 17 to 19
- National guidelines of the blood transfusion service SRC
- Sensitivity limits for mandatory NAT assays set by Swissmedic*)
  - 25 IU/ml for HBV
  - 50 IU/ml for HCV
  - 500 IU/ml for HIV-1

*) Swiss regulatory and supervisory authority for pharmaceuticals and medical devices

Test Methods and Equipment

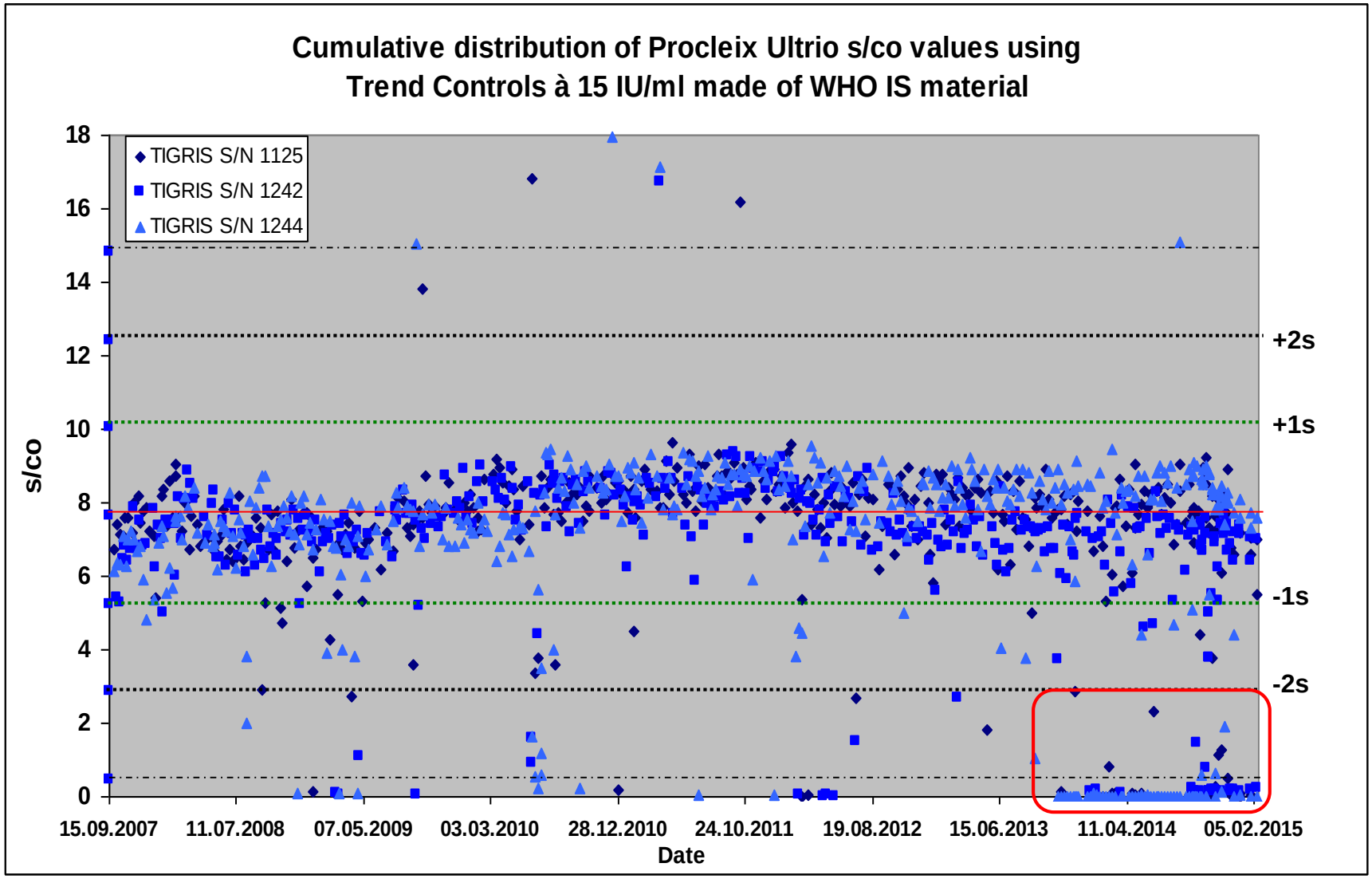
- **NAT testing (2007 – 2014):**
  - **1 site** with Procleix Ultrio Assay (ID-NAT) / Procleix Tigris System (Grifols)

  - **5 sites** with cobas TaqScreen (MP of 6) / cobas s201 System (Roche)

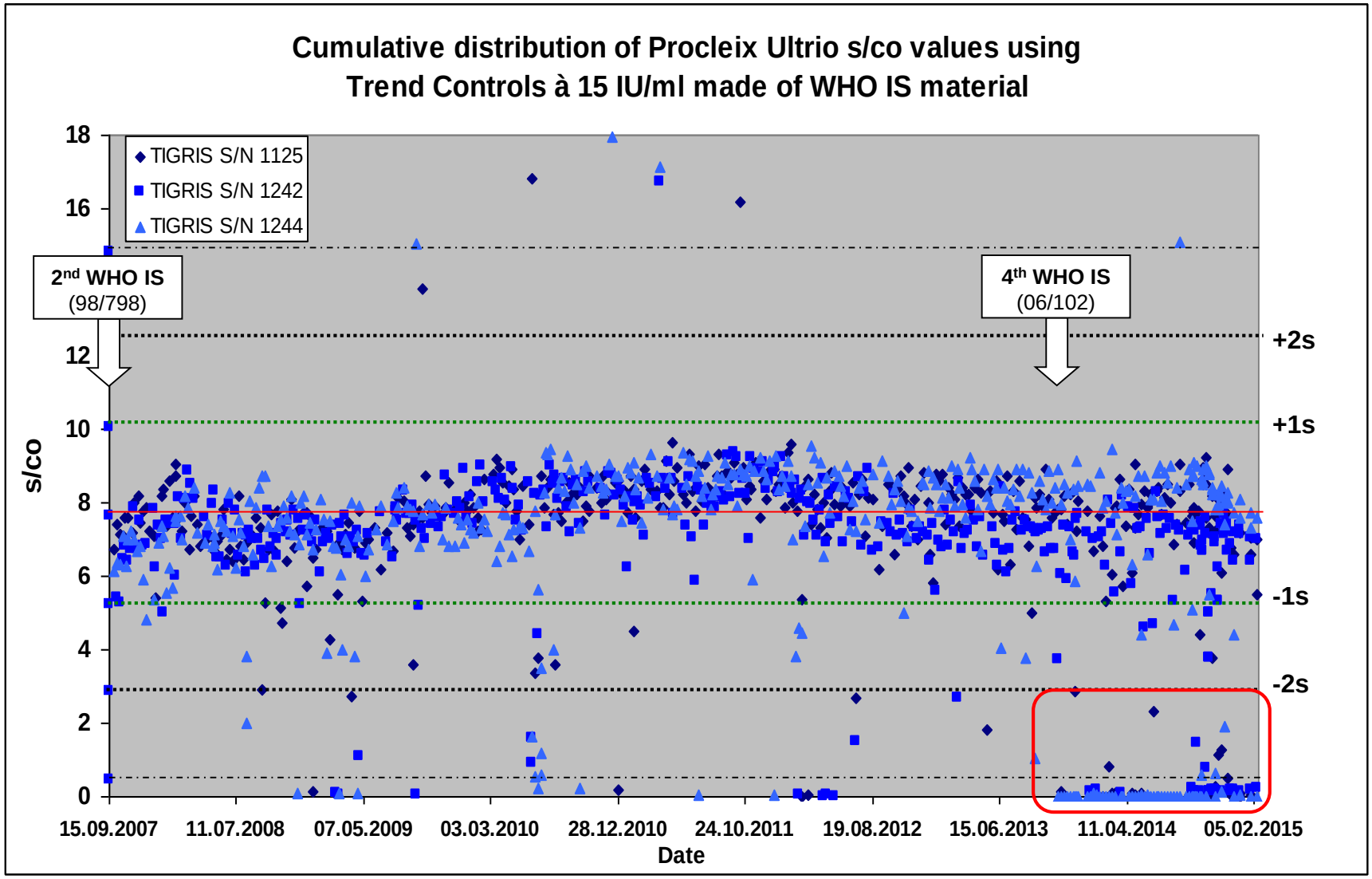
- **NAT testing (since 2015):**
  - **3 sites** with cobas MPX test (ID-NAT) / cobas 6800/8800 System (Roche)

  - **2 sites** with Procleix Ultrio Elite Assay (ID-NAT) / Procleix Panther System (Grifols)

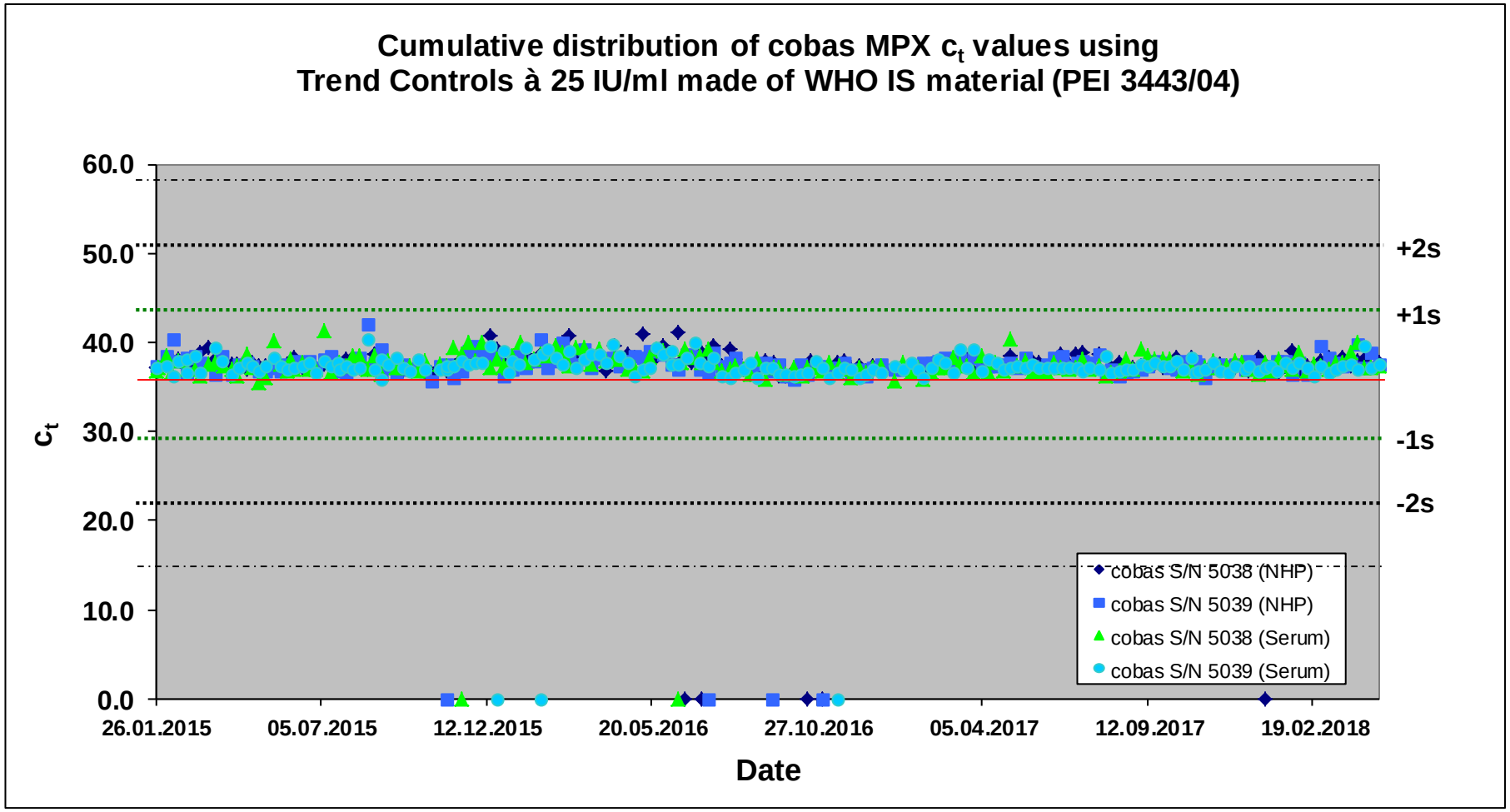
Trend Control to Monitor HCV NAT



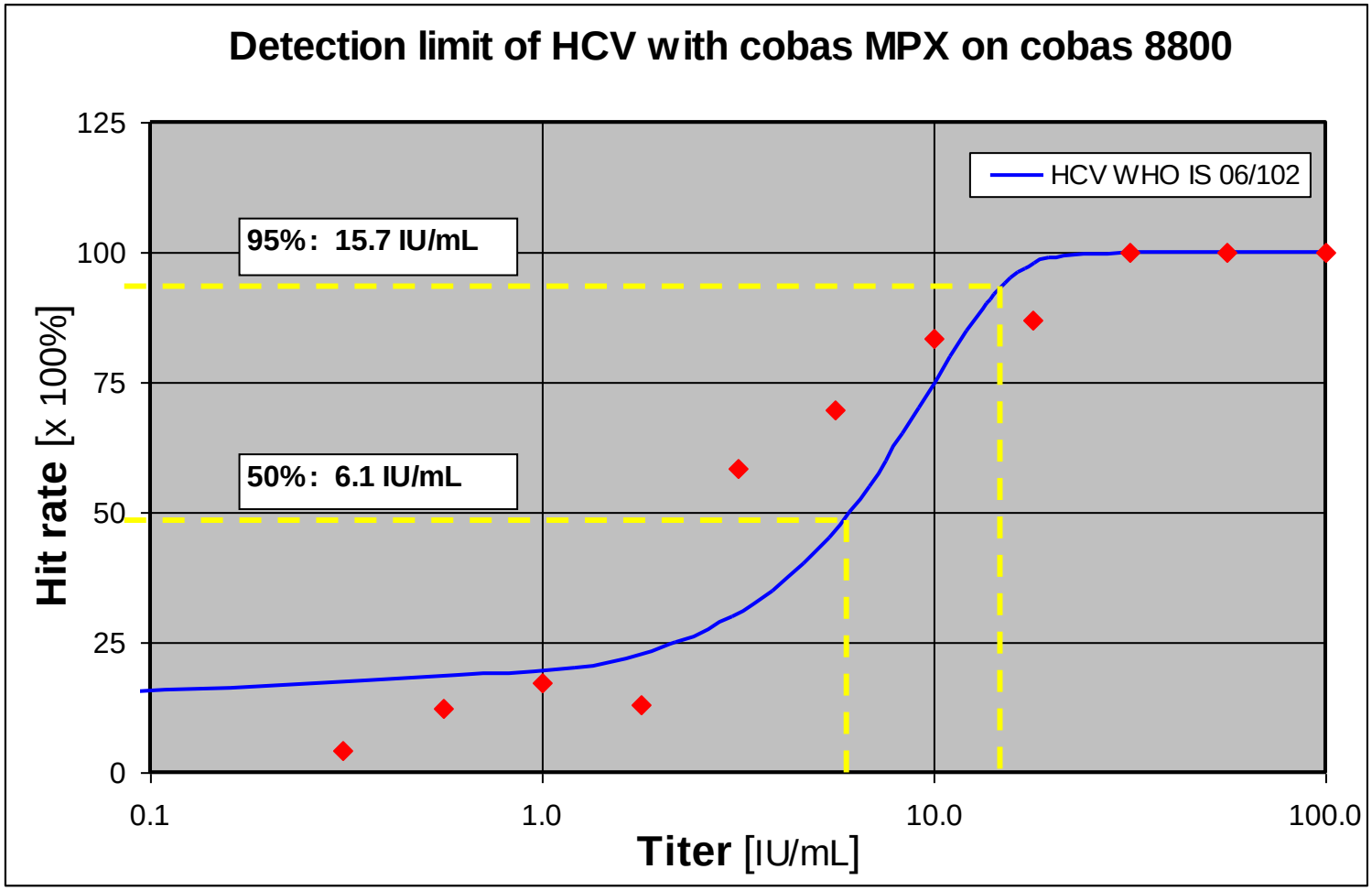
Trend Control to Monitor HCV NAT



Trend Control for HCV (current situation)



Assay Validation - Probit Analysis



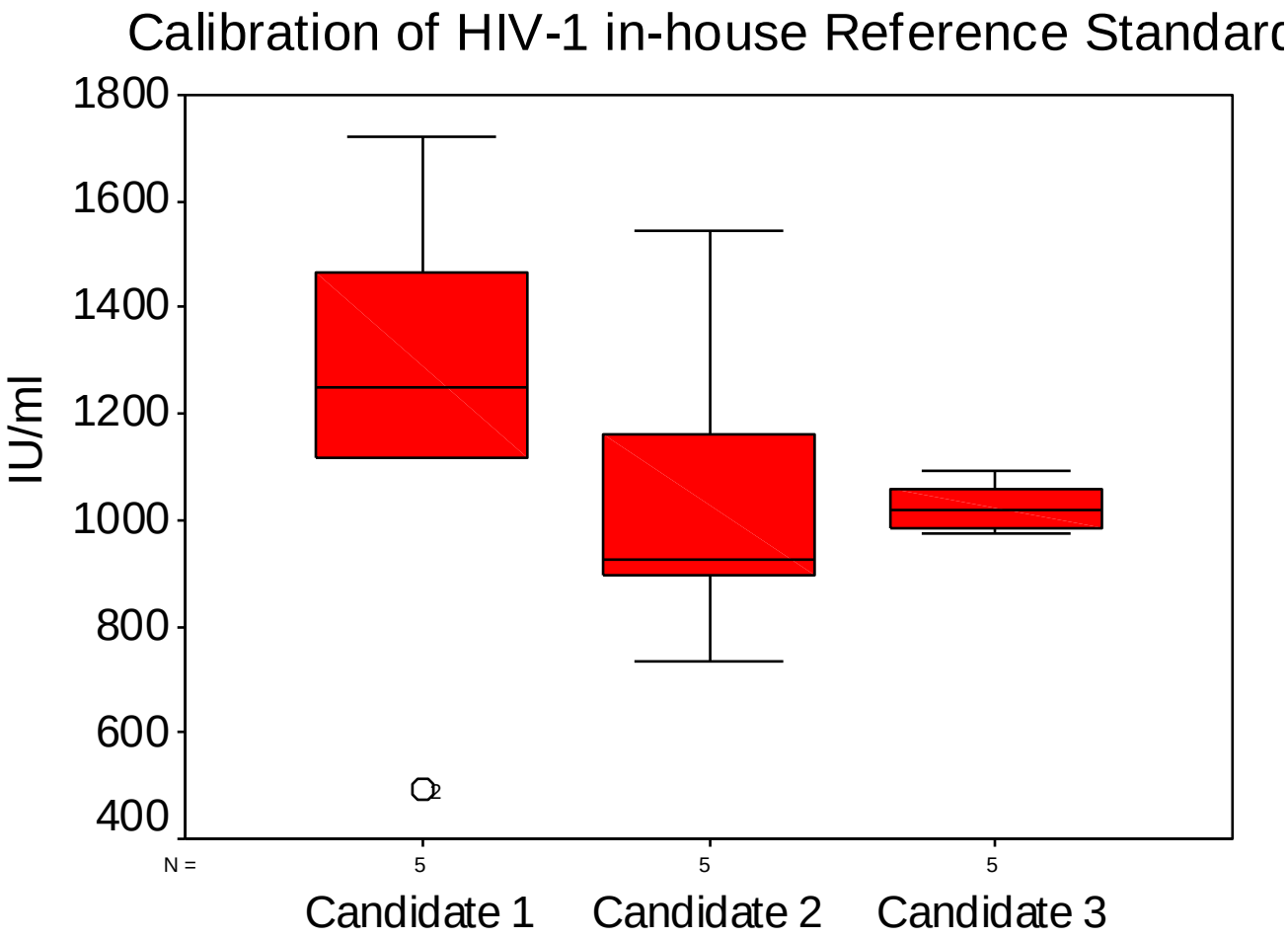
Limit of detection (LOD) for HCV

	cobas MPX test (cobas 8800 / IRB)			LOD MPX test (Roche)
	95 %	99 %	50 %	**95 %**
2nd WHO IS (98/798 NIBSC)	---	---	---	**7.0 IU/ml** (5.9 – 8.6)
4th WHO IS (06/102 NIBSC)	**15.7 IU/ml** (11.1 – 30.2)	19.7 IU/ml (13.8 – 38.8)	6.1 IU/ml (3.7 – 10.4)	**n/a**

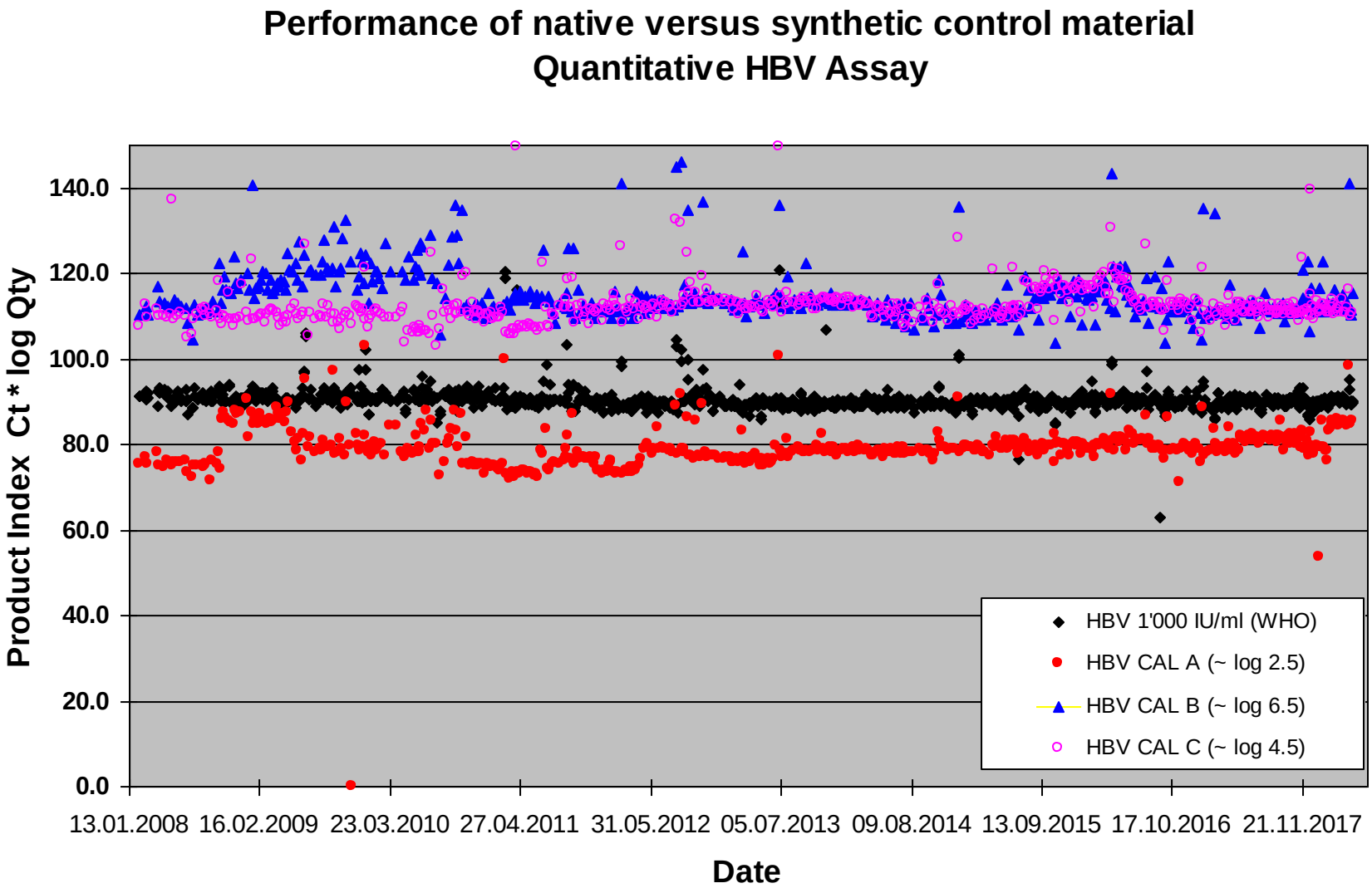
Limit of detection (LOD) for HCV

	cobas MPX test (cobas 8800 / IRB)			LOD MPX test (Roche)
	95 %	99 %	50 %	**95 %**
2nd WHO IS (98/798 NIBSC)	**8.3 IU/ml** (5.6 – 20.3)	10.7 IU/ml (7.1 – 27.0)	2.6 IU/ml (0.8 – 5.1)	**7.0 IU/ml** (5.9 – 8.6)
4th WHO IS (06/102 NIBSC)	**15.7 IU/ml** (11.1 – 30.2)	19.7 IU/ml (13.8 – 38.8)	6.1 IU/ml (3.7 – 10.4)	**n/a**

Secondary Reference Material



Native vs. Synthetic Control Material



Summary

- 12-fold increase in HCV trend control failure with 4th HCV WHO IS
- Discrepancy in LOD for HCV when using 2nd versus 4th HCV WHO IS
- Observed potency is lower then assigned units for 4th HCV WHO IS
- Loss of potency occurred even under appropriate storage conditions
- International Standards for HIV and HBV were ok
- Good and stable international reference material is valuable for **…**
  - establish secondary standards
  - defining sensitivity limit of new assays
  - validate instruments and NAT assays
  - monitor instrument and kit performance
  - calibrate quantitative assays
  - monitor the inter-assay and cross platform reproducibility

Open questions and pitfalls

- Availability of international reference material is limited:
  - primary vs. secondary reference material
  - native vs. synthetic reference material
  - accuracy of replacement standards
  - transport and storage issues
  - infectiosity vs. stability
  - acceptance issue of secondary standards
- Balance between quality controls and economic pressure
  - Number of quality control samples is increasing
  - Number of test samples is decreasing
  - Human influence on test outcome has become insignificant in highly automated test systems
- Guidance needed for material vigilance issues with reference materials
  - how many drop-out cases are acceptable
  - what if controls are to close to the detection limit (supply of patients could be at-risk)
  - what if kit reagents show poor performance
  - economic pressure

Thank you for your attention !