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My memory of the very beginning of blood safety NAT

Micha Nübling, PEI

IPFA/PEI 28th Workshop
Porto

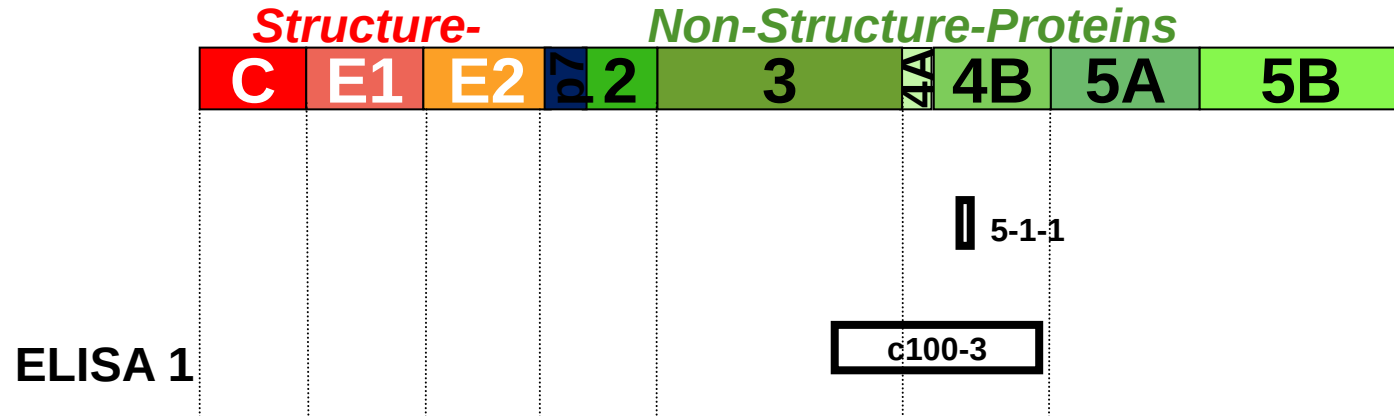


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des Bundesministeriums für Gesundheit.*

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1989: HCV (previously: NANBH) identified



- 1983 Invention of PCR
- 1993 Noble Prize to KB Mullis
-PCR confirmation of antiHCV EIA reactivities



Virus transmissions by plasma derivatives

Product	Inactivation procedure	Transmission of	Number of transmissions	Year
PPSB	β -Propiono-lacton, UV	HIV1	>10	1989/90
Factor VIII	Solvent-Detergent	HAV	>80	1991/92
ivIG	Cohn Fractionation	HCV	>250	1993/94
PPSB	Pasteurization	HBV	>30	1994
Factor VIII	Solvent-Detergent	HAV	>3	1995/96
Factor VIII	Solvent-Detergent	HAV	7	1997

Lot number (US)	Date of manufacture	Plasma screening (%)		HCV RNA		Hepatitis cases reporting use of lot*
		EIA 1	EIA 2	Lab A	Lab B	
2807M007	1988	0	0	—	NT	0
2317R102	1989	0	0	—	+	0
2317R121	1989	0	0	—	NT	0
2317R125	1989	0	0	—	—	0
2317R129	1989	0	0	—	NT	0
2317R134	1989	0	0	—	+	0
2317T114	1990	0	0	—	—	0
2317T121	1990	0	0	—	—	0
2317T124	1990	0	0	—	+	0
2317V149	1991	0	0	—	NT	0
2317V188	1991	0	0	—	—	0
2317V190	1991	0	0	—	—	0
2317X162	June 24, 1992	0.5	0	—	—	0
2317X204	Nov 13, 1992	99.7	0.3	—	—	2
2317A103	Jan 11, 1993	100	0	—	—	1
2317A106	Jan 18, 1993	3.7	96.3	—	—	6
2317A123	March 5, 1993	0.1	99.9	—	+	0
2317A124	March 8, 1993	69.1	30.9	—	—	3
2317A131	March 25, 1993	26.6	73.4	—	—	6
2317A142	April 15, 1993	0.2	99.8	+	+	3
2317A144†	April 19, 1993		100	+	—	18
2317A145	April 20, 1993	0.4	99.6	—	+	5
2317A147	April 23, 1993		100	—	—	2
2317A148	April 26, 1993		100	+	—	8
2317A149	April 27, 1993	0.3	99.7	+	+	2
2317A155	May 11, 1993		100	+	—	7
2317A158	May 14, 1993		100	+	+	7
2317A159	May 17, 1993	92.3	7.7	—	—	10
2317A164†	May 26, 1993		100	+	+	12
2317A166	May 28, 1993		100	+	+	8
2317A179†	June 21, 1993		100	+	+	28
2317A183	June 29, 1993		100	+	—	8
2317A186	July 4, 1993	0.1	99.9	+	+	2
2317A187	Aug 2, 1993		100	+	—	12
2317A197	Aug 19, 1993		100	+	+	0
2317A204	Sept 3, 1993		100	+	—	15
2807A111	Sept 12, 1993		100	—	—	7
2317A228	Oct 19, 1993		100	—	+	2
2317A236	Nov 3, 1993		100	+	+	3
2317A241	Nov 13, 1993		100	—	NT	3
2317A242	Nov 17, 1993		100	+	+	0
2317A248	Nov 30, 1993		100	—	+	0

NT=not tested, no additional sample available.

*From case reports received by Baxter; patients often received multiple lots.

†Lots distributed only in Europe with different lot numbers. The European lot numbers corresponding to 2317A144, 2317A164, and 2317A179 are 93D19AB11, 93E26AB11, and 93F21AB11, respectively.

Table: **Detection of HCV RNA in Gamagard lots in relation to type of anti-HCV screening and case reports**

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*M W Yu, B L Mason, Z P Guo, D L Tankersley, S Nedjar, F D Mitchell, R M Biswas

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US FDA

- HVC Ab testing increases PCR positivity of the **final product**
- EIA2 screened ivlg batch had highest amount of virus and most transmission cases
- Partitioning of HCV into final products because of HCV Ab depletion ?

Initial anti-HCV screening test	Anti-HCV reactivity of pools (anti-HCV 2nd)	Number (origin) of plasma pools	HCV PCR positive
None	+++	8 (USA, Europe)	8 (100%)
Anti-HCV 1st	+/-	85 (USA, Europe)	65 (76%)
Anti-HCV 2nd	—	123 (USA, Europe)*	49 (39%)†

*88 USA, 35 Europe. †46 (52%) USA, 3 (8%) Europe.

Table: **Test results obtained with commercial plasma pools**

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PEI

- PCR positivity of **plasma pools** (frequency, viral loads) decreases with antiHCV testing
- Still virus loads in plasma pools due to undetected window-phase infections

HCV-NAT and plasma derivatives

ivIG batch	HCV-PCR qual	HCV-PCR quant (geq/ml)	HCV-Trans- missions
A	neg / neg	--	2
B	neg / neg	--	7
C	neg / pos	< 600	8
D	pos / pos	< 600	28

Plasma- pools	HCV-PCR qual	HCV-PCR quant (geq/ml)
A1	pos	3.000
A2	pos	700
A3	pos	< 600
A4	neg	--
B1	pos	9.000
B2	pos	4.000
B3	pos	n.d.
B4	neg	--
C1	pos	< 600
C2	pos	< 600
C3	pos	2.000
C4	pos	< 600
C5	pos	20.000
D1	pos	20.000
D2	pos	40.000
D3	pos	10.000



MEETING REPORT

EPFA - NIBSC Workshop on

'Nucleic Acid Amplification Assays and Plasma Products'
23 November, 1994, Helsinki, Finland

Conclusions

- * “Nucleic acid testing will play an increasingly important role in safety testing of blood products”
- * “NAT not yet suitable for testing of pools and batch release - no validated assays available”
- * “High inter- and intra-laboratory variance”
- * “Urgent need for standardisation of NAT”





Regulatory measures

- 1994

HCV NAT plasma pools for iv Immunglobulins



EMA Guideline on virus inactivation steps



Standardization

- 1997 WHO 1st International Standard HCV RNA

Validation requirements

Sensitivity requirements

Regulatory measures

- 1999 HCV NAT for plasma pools in EU





Regulatory measures



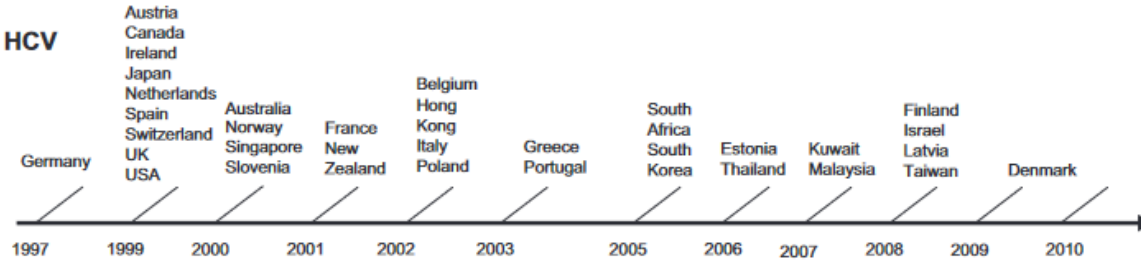
- 1999 HCV NAT blood donations 5.000 IU/ml

- 2002 HIV-1 NAT blood donations 10.000 IU/ml
- 2012 Dual target design

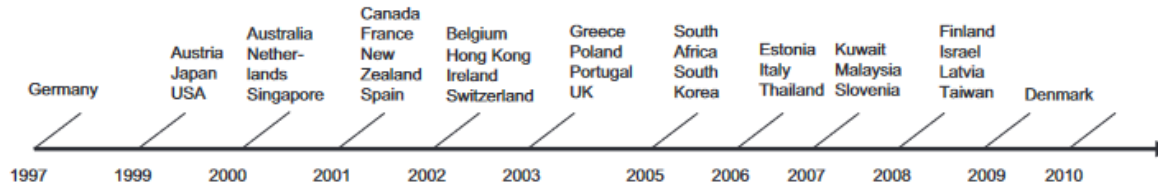


Introduction of NAT testing

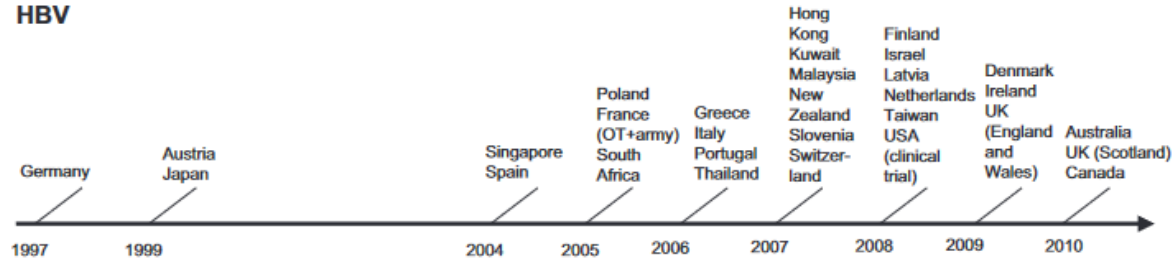
HCV



HIV-1



HBV



IPFA/PEI 28th International Workshop on Surveillance and Screening of Blood-borne Pathogens



- IPFA/PEI Workshops as unique platform for scientific exchange