

# Blood safety in the Blood Bank of Catalonia (Spain): Lessons learned during two decades of NAT screening

*Střešovický transfuzní den  
KRVÍ PŘENOSNÉ INFEKCE –  
STARÉ A NOVÉ HROZBY  
Prague, 15 November 2023*

**Silvia Sauleda, PhD  
Transfusion Safety Laboratory  
Banc de Sang i Teixits (Catalonia, Spain)**

Disclosures:

My Institution, Blood and Tissue Bank of Catalonia, has received financial support from Grifols for my participation in this session

My Institution has received financial support from Grifols for research projects



# Blood Banks and Transfusion Centers in Spain

## Public Health System

17 autonomous regions and 20 Blood Banks

1.7 M blood donations/year

100% volunteer non-remunerated blood donors



<https://www.sanidad.gob.es/profesionales/saludPublica/medicinaTransfusional/redTransfuEspana/RedTransEspana.htm>

# Impact of NAT implementation in Spain: Blood safety & Sufficiency

- Safety: Implement optimal strategies according to risk
- Sufficiency: Defer only when necessary
- Sustainability: Preserve the Public Health System

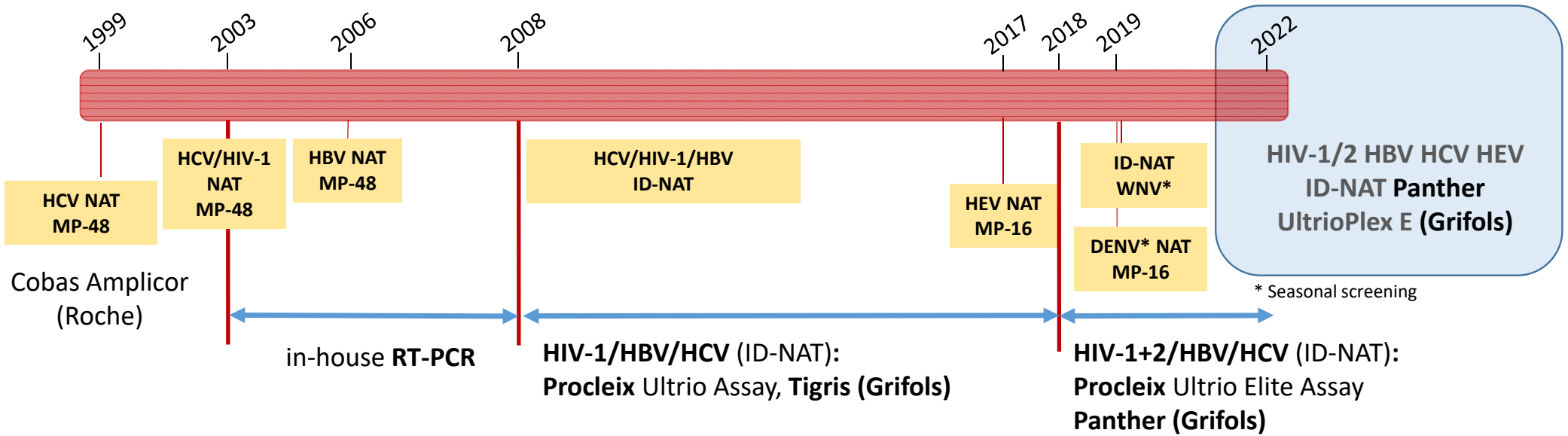


# Impact of NAT implementation in Spain: Blood safety & Sufficiency

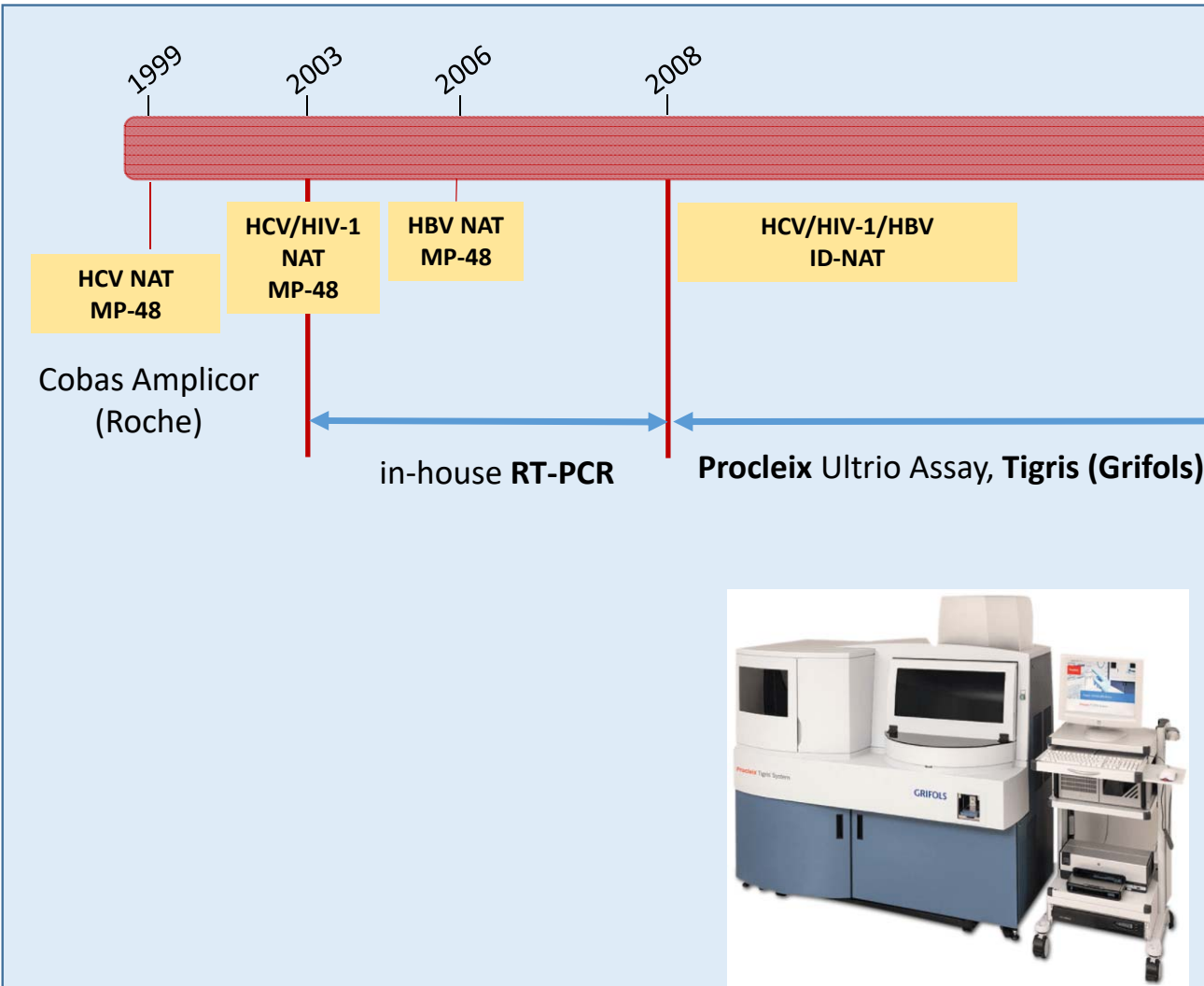
- Safety:
  - HIV-1 and HBV NAT: From minipool screening to ID-NAT
  - Hepatitis E NAT: Clinical evidence beyond regulations
- Sufficiency:
  - Arboviruses in summer 2023: To defer or to screen?
- Sustainability: Preserve the Public Health System



# NAT testing chronology in Barcelona Blood Bank



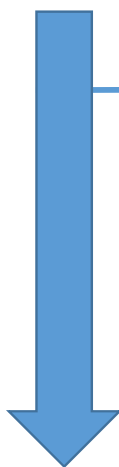
## NAT testing chronology in Barcelona Blood Bank



Why did we move from minipool to ID-NAT?

## Profile of blood donors in HIV-1 window period BST-Catalonia (January 2005-December 2009)

Semi-manual  
MP-48  
In-house PCR



Case	Sex	Age	Risk factor	HIV-1 viral load	donor type
WP-1	male	30 y.	MSM	11,000 IU/mL	repeat
WP-2	male	31 y.	MSM	830 IU/mL	repeat
WP-3	female	41 y.	-	>7 logs	1st time
WP-4	male	36 y.	MSM	>7 logs	repeat
WP-5	male	39 y.	MSM	<50 IU/mL	repeat
WP-6	male	23 y.	MSM	210 IU/mL	repeat

Fully-automated  
ID-NAT  
**Procleix Ultrio Assay, Tigris (Grifols)**

PEI recommended sensitivity  
HIV-1 NAT: 10,000 IU/mL





## Value of high sensitivity HIV/HCV/HBV NAT screening in Spain

- Donors in serological window period (HIV, HCV, HBV)
- Donors with acute resolving infection (late HBV WP)
- Donors infected with escape mutants to HBsAg

- Donors with occult hepatitis B infection (OBI)

Occult hepatitis B (OBI) definition:

HBV DNA < 200 IU/mL, HBsAg negative, anti-HBc positive (IgM negative)

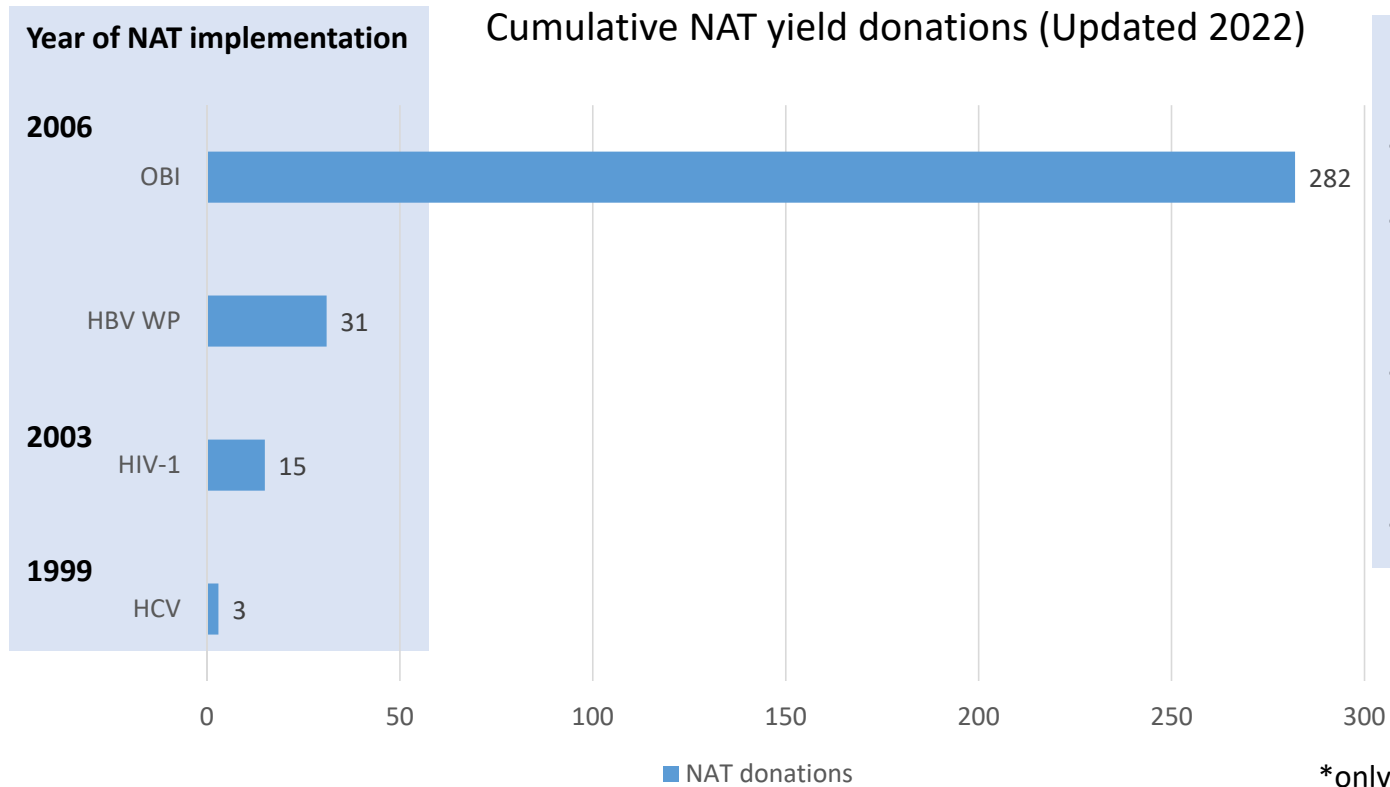


Semi-manual  
MP-48  
In-house PCR



Fully-automated  
ID-NAT  
**Procleix Ultrio Assay, Tigris (Grifols)**

# NAT yield for HCV, HIV-1, HBV and HEV Blood and Tissue Bank (Catalonia, Spain)

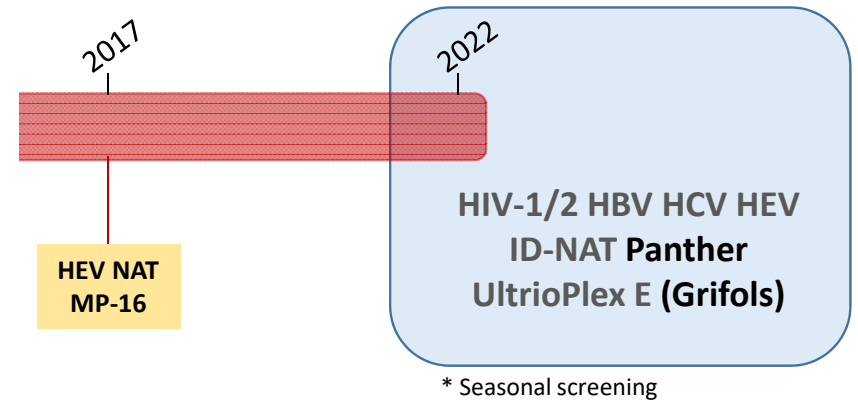


## Incidence of NAT yield cases:

- OBI: 1/15,600 (4.4M donations)
- HBV WP: 1/142,000 (4.4M donations)
- HIV-1 WP: 1/352,000 (5.3M donations)
- HCV WP: 1/1,976,000\* (5.9M donations)

\*only HCV NAT is mandatory according to Spanish regulations

## NAT testing chronology in Barcelona Blood Bank



Why did we implement hepatitis E NAT?



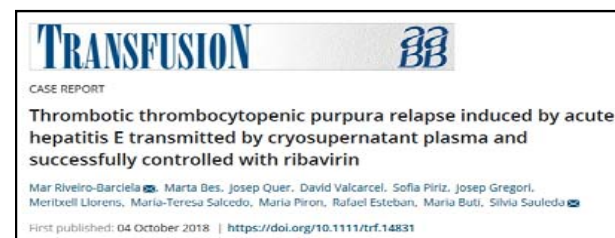
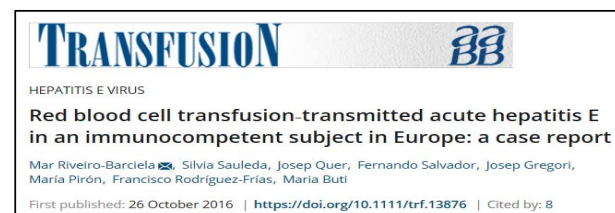
# HEPATITIS E VIRUS: A transfusion-transmitted infectious disease

- HEV genotype 3 is widely distributed in Europe and infection is usually asymptomatic and self-limited
- In at-risk patients (pre-existing liver disease, immunosuppressed), HEV infection may cause:
  - acute liver failure
  - chronic hepatitis E may require antiviral treatment with Ribavirin, shown to be effective in 70% of cases
  - extra-hepatic manifestations, namely neurological complications
- If HEV RNA testing is not available, hepatitis E infection might not be diagnosed
- **If HEV NAT screening is not implemented, hepatitis E virus might be transmitted to blood recipients**

# Transfusion-transmitted Hepatitis E virus infections in Catalonia

## 3 Reported cases in Catalonia (2015-2017)

- **Case 1, 2015 – Red cell concentrate:**  
Immunocompetent patient, Viral load 75000 UI/mL, 3f  
Severe acute hepatitis E
- **Case 2, 2017 – Cryosupernatant plasma:**  
Immunocompetent patient, Viral load 10000 UI/mL, 3f  
Acute, and persistent, hepatitis E
- **Case 3, 2017 – Pooled platelets:** oncology patient  
Acute hepatitis E



# Effect of Hepatitis E Virus RNA Universal Blood Donor Screening, Catalonia, Spain, 2017–2020

Marta Bes, Maria I. Costafreda, Mar Riveiro-Barciela, Maria Piron,  
Angie Rico, Josep Quer, Lluís Puig, Silvia Sauleda

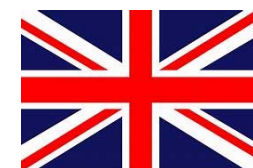
Emerging Infectious Diseases • [www.cdc.gov/eid](http://www.cdc.gov/eid) • Vol. 28, No. 1, January 2022

- **November 2017: Implementation of HEV NAT in minipools of 16 donations (Procleix HEV, Panther, Grifols)**
  - MP-16: logistical reasons and reduced costs
  - Sensitivity: 176 IU/mL in individual donation
- No more transfusion-transmitted HEV infections have been reported in Catalonia since HEV NAT implementation
- BST in Catalonia was the first blood bank in Spain to implement HEV NAT, followed by Asturias (2020), Aragon (2023) and Cantabria (2023)

# Fulminant Transfusion-Associated Hepatitis E Virus Infection Despite Screening, England, 2016–2020

Heli Harvala, Claire Reynolds, Su Brailsford, Katy Davison


Emerging Infectious Diseases • [www.cdc.gov/eid](http://www.cdc.gov/eid) • Vol. 28, No. 9, September 2022






**Hepatitis E post-transfusional transmission through apheresis platelets despite HEV NAT screening in minipools of 24 donations**





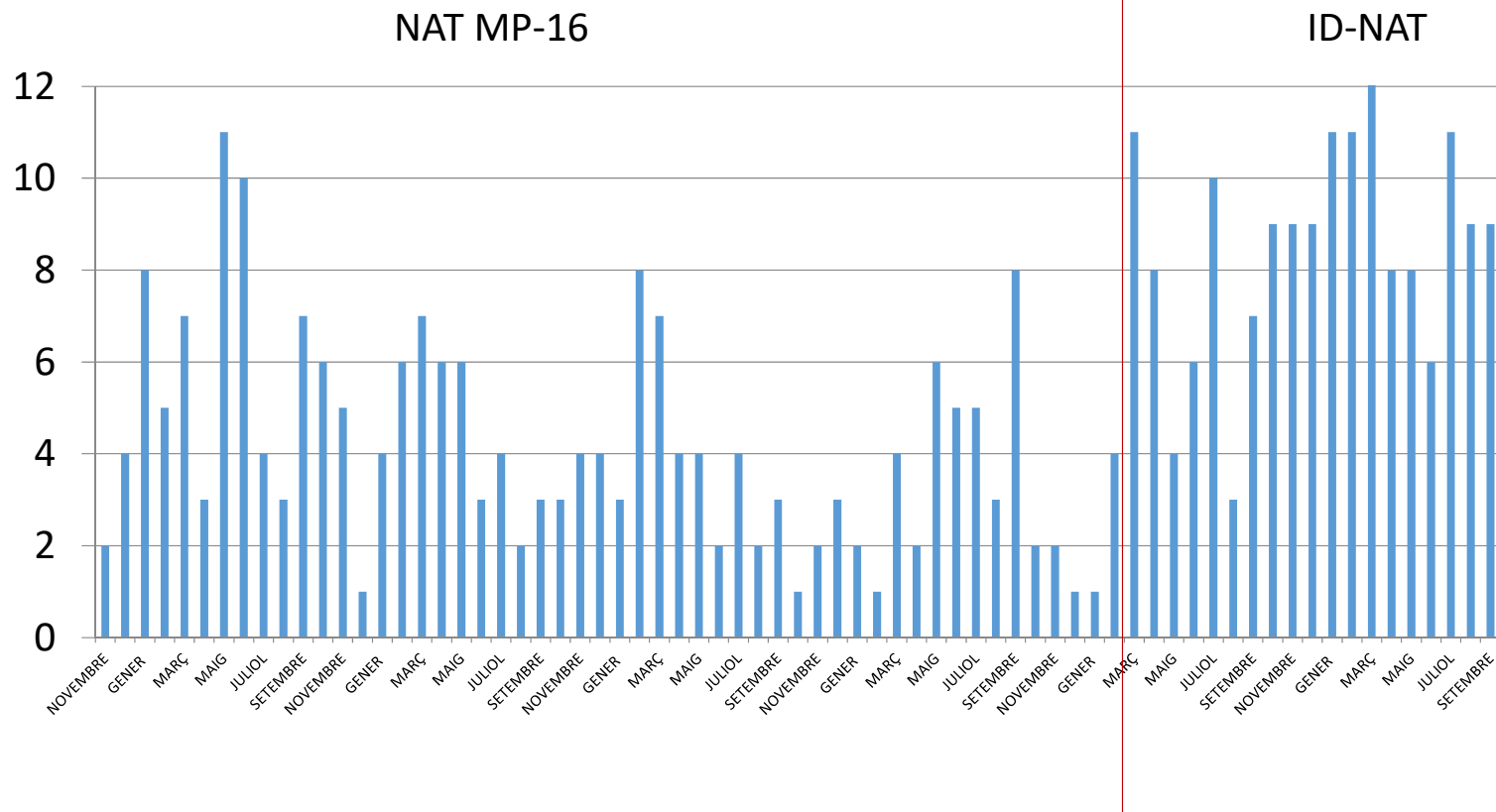


## Clinical performance of a new multiplex assay for the detection of HIV-1, HIV-2, HCV, HBV, and HEV in blood donations in Catalonia (Spain)

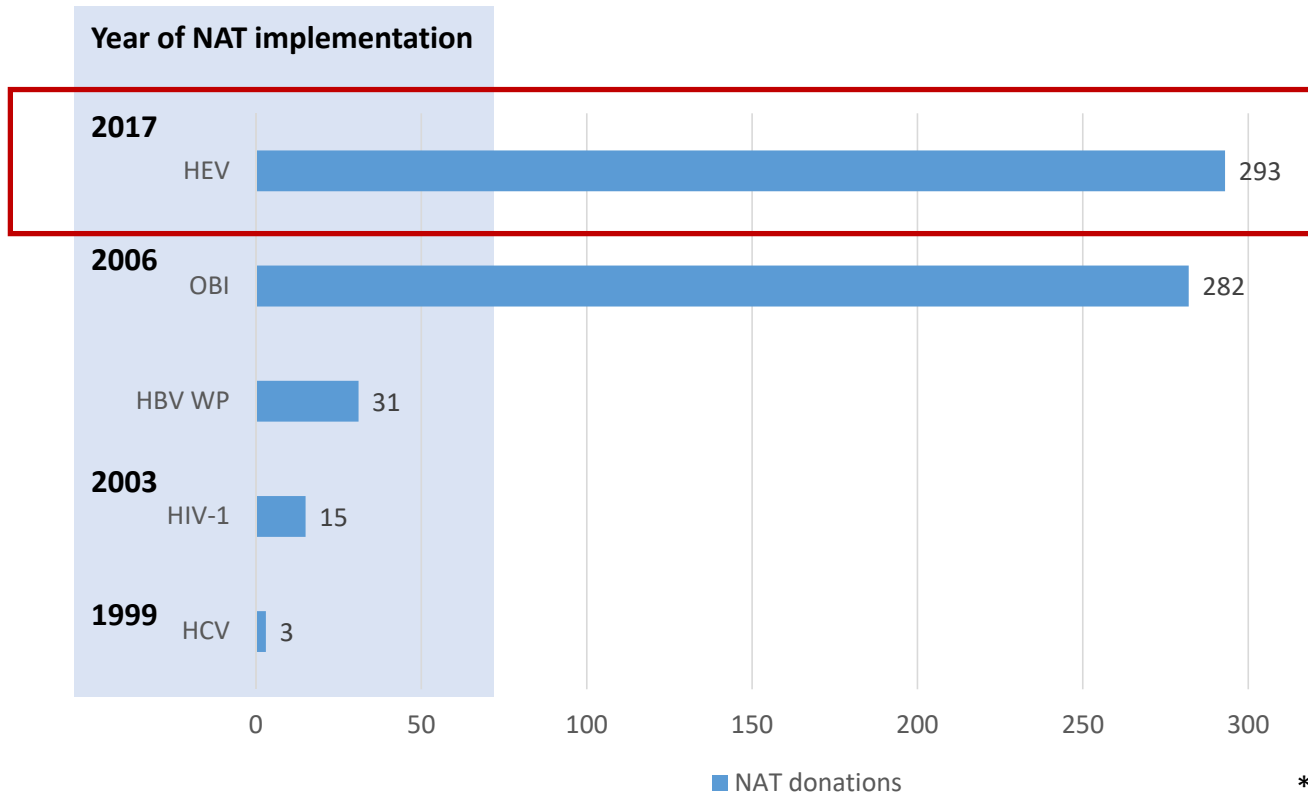
Silvia Sauleda<sup>1,2,3</sup>  | Marta Bes<sup>1,2,3</sup> | Maria Piron<sup>1,2,3</sup> | Edgar Ong<sup>4</sup> |  
Sonia Bakkour Coco<sup>5</sup>  | Jaume Carrió<sup>6</sup> | Jeffrey M. Linnen<sup>4</sup> 

- March 2022: **Implementation of HEV ID-NAT** (Procleix UltrioPlex E<sup>®</sup>, Panther, Grifols):
  - Simultaneous detection of HIV-1/HIV-2/HCV/HBV and HEV
  - HEV sensitivity: 3,6 IU/mL

## Clinical performance of a new multiplex assay for the detection of HIV-1, HIV-2, HCV, HBV, and HEV in blood donations in Catalonia (Spain)



# NAT yield for HCV, HIV-1, HBV and HEV Blood and Tissue Bank (Catalonia, Spain)



## Incidence of NAT yield cases:

**HEV NAT: 1/4,600 (1.4M donations)**

**OBI NAT: 1/15,600 (4.4M donations)**

**HBV WP: 1/142,000 (4.4M donations)**

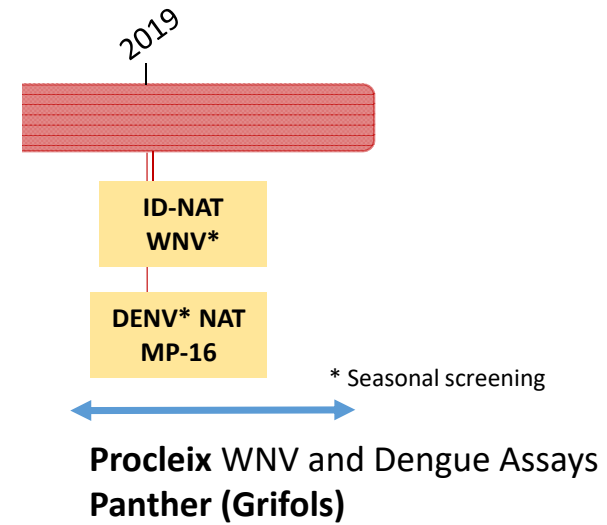
**HIV-1 WP: 1/352,000 (5.3M donations)**

**HCV WP: 1/1,976,000\* (5.9M donations)**

\*only HCV NAT is mandatory according to Spanish regulations

Cumulative NAT yield donations (2022)

## NAT testing chronology in Barcelona Blood Bank

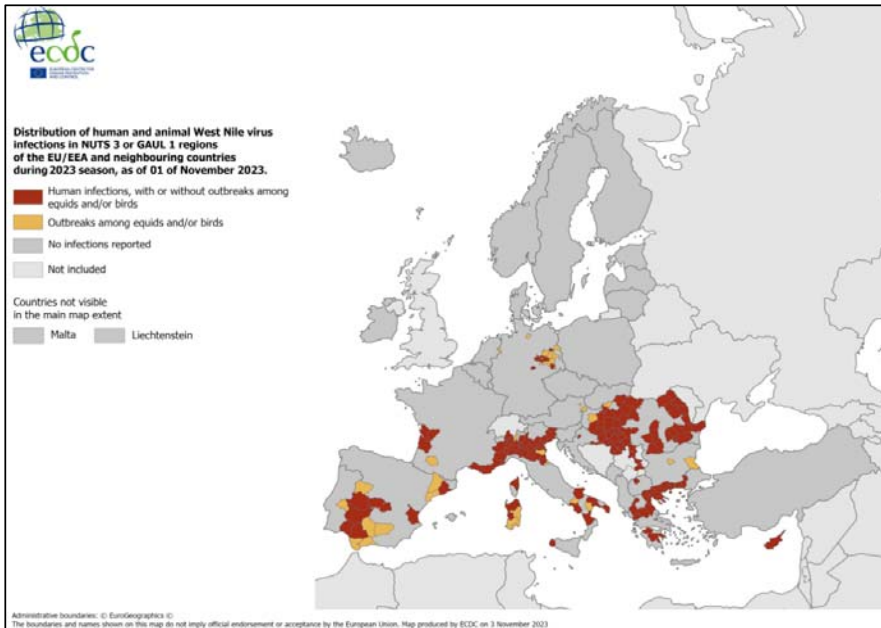


Why did we implement WNV and dengue NAT?



# Mosquito season and arboviruses in Europe 2023

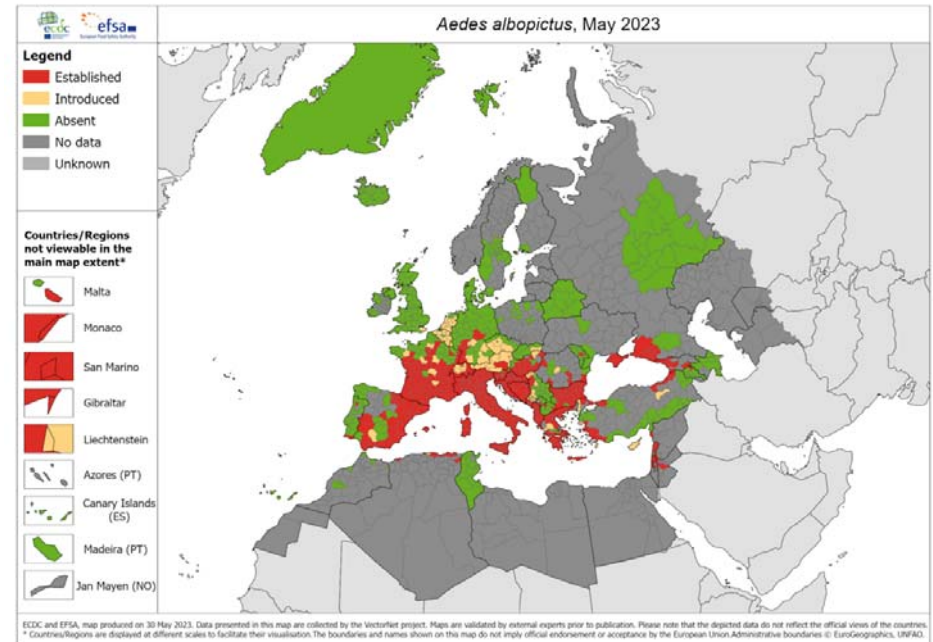
WNV circulation in humans and birds/horses



Europe: 784 WNV human cases (65 deaths)  
Spain: 16 WNV human cases (3 deaths) and 52 birds/horses outbreaks

Catalonia: 1 WNV human case and 15 birds/horses outbreaks

*Aedes albopictus* map and autochthonous Dengue cases



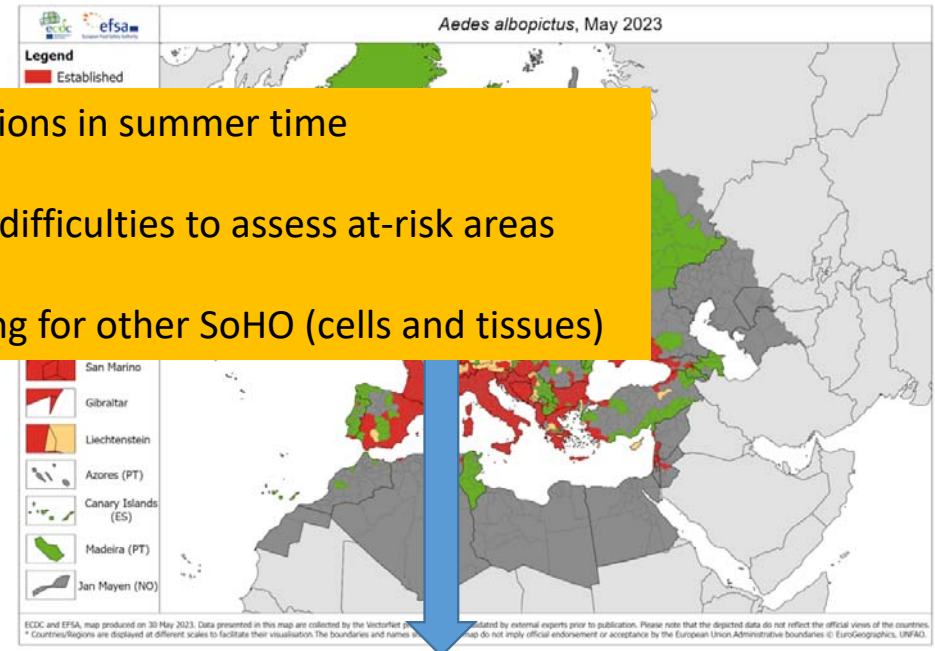
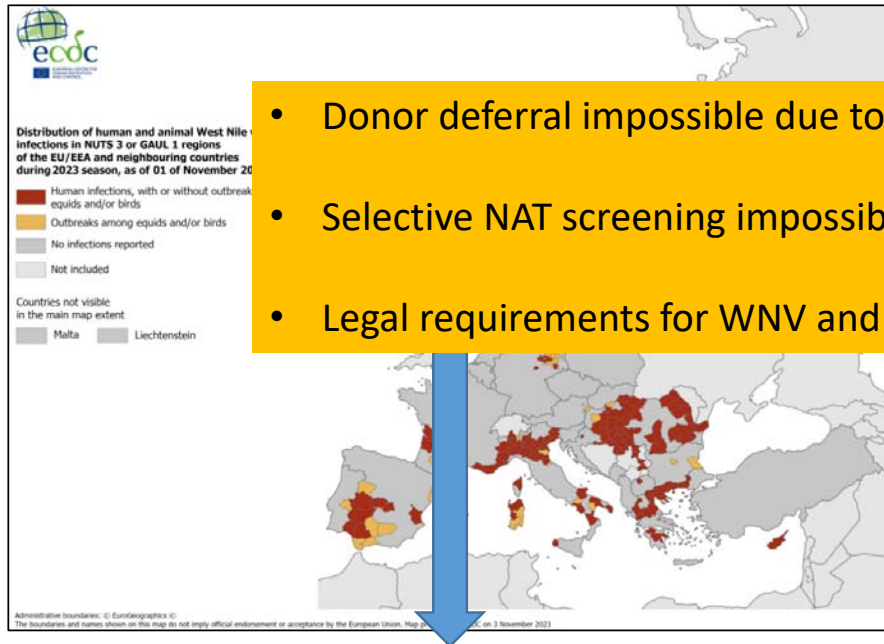
France: 41 autochthonous cases in 8 different outbreaks  
Italy: 72 autochthonous cases in 3 different outbreaks

Catalonia: 3 autochthonous cases in 2 different outbreaks

# Mosquito season and arboviruses in Europe 2023

WNV circulation in humans and birds/horses

*Aedes albopictus* map and autochthonous Dengue cases



- Donor deferral impossible due to loss of donations in summer time
- Selective NAT screening impossible due to the difficulties to assess at-risk areas
- Legal requirements for WNV and dengue testing for other SoHO (cells and tissues)

**BST Catalonia: Universal WNV ID-NAT ( EU Directive 2004/33/CE )**

**BST Catalonia: Universal DENGUE NAT MP-16**

# Validation of the pre-commercial assay Procleix<sup>®</sup> ArboPlex (Panther, Grifols)

## Preliminary Performance Characteristics of a New Multiplex Blood Screening Assay on a Fully Automated System that Detects 5 Mosquito-Borne Viruses

Bes M.,<sup>2</sup> Piron M.,<sup>2</sup> Groves J.,<sup>1</sup> Knight J., Livezey K., Cooper J., Rubies, C., Stramer S.L.,<sup>1</sup> Sauleda S.<sup>2</sup> and Linnen J.M.

Grifols Diagnostic Solutions, Inc., San Diego, CA, USA; <sup>1</sup>American Red Cross, Gaithersburg, MD, USA; <sup>2</sup>Banc de Sang i Teixits (BST), Barcelona, Spain

Poster, AABB Congress, Nashville 2023

- Simultaneous detection of WNV/Usutu, and dengue, Zika and Chikungunya
- Validated for ID-NAT and minipools of 16 donations
- Excellent sensitivity and specificity
- Assay pending IVDR-CE approval

Panel	Units	95% Limit of Detection Probabilities (95% Fiducial Limits)		
		ArboPlex Assay	Procleix DENV, WNV or ZIKV Assays Direct Testing	Procleix DENV, WNV or ZIKV Assays IFU*
CHIKV WHO (11785/16)	IU/mL	7.7 (6.0 – 11.3)	85.1 (40.6 – 707.4) <sup>^</sup>	N/A
DENV Type 1 IVT	Copies/mL	17.5 (13.3 – 25.9)	25.1 (17.0 – 46.5)	21.04 (16.75 – 28.35)
DENV Type 2 IVT		11.7 (8.9 – 17.4)	21.4 (14.9 – 38.6)	25.95 (20.19 – 36.16)
DENV Type 3 IVT		13.2 (9.9 – 19.9)	14.5 (10.1 – 26.9)	18.81 (14.49 – 26.80)
DENV Type 4 IVT		13.2 (9.9 – 20.2)	22.0 (15.7 – 38.1)	28.95 (22.14 – 41.14)
USUV (1477)		33.4 (25.1 – 53.6)	N/A <sup>^^</sup>	N/A
WNV L1 WHO (18/206)	IU/mL	3.8 (2.8 – 5.8)	6.2 (4.2 – 12.1)	7.1 (5.5 – 9.8)
WNV L2 WHO (18/208)		2.2 (1.7 – 3.3)	6.0 (4.1 – 11.3)	N/A
ZIKV WHO (11468/16)		2.5 (1.9 – 3.9)	1.4 (1.0 – 3.1)	2.90 (2.22 – 4.18)

## Summary

- After more than 20 years of NAT screening in Catalonia (Spain), we have witnessed great improvements on sensitivity and automation of NAT systems
- In BST-Catalonia, NAT screening has interdicted hundreds of infectious blood donations
- Simultaneous detection of HIV-1/2, HCV, HBV and HEV is a coherent solution to increase blood safety with minimal technical complexity
- In the near future, arboviruses will challenge our logistic and testing capacities to ensure blood safety and blood sufficiency
- Again, simultaneous detection of relevant arboviruses will provide a coherent solution to increase blood safety with minimal technical complexity



Muchas gracias!



Moltes gràcies!

Thank you!

