



KEMENTERIAN KESEHATAN RI

# **RAISING THE STANDARD OF BLOOD DONOR SCREENING TO MEET BLOOD AND PLASMA NEEDS OF INDONESIA**

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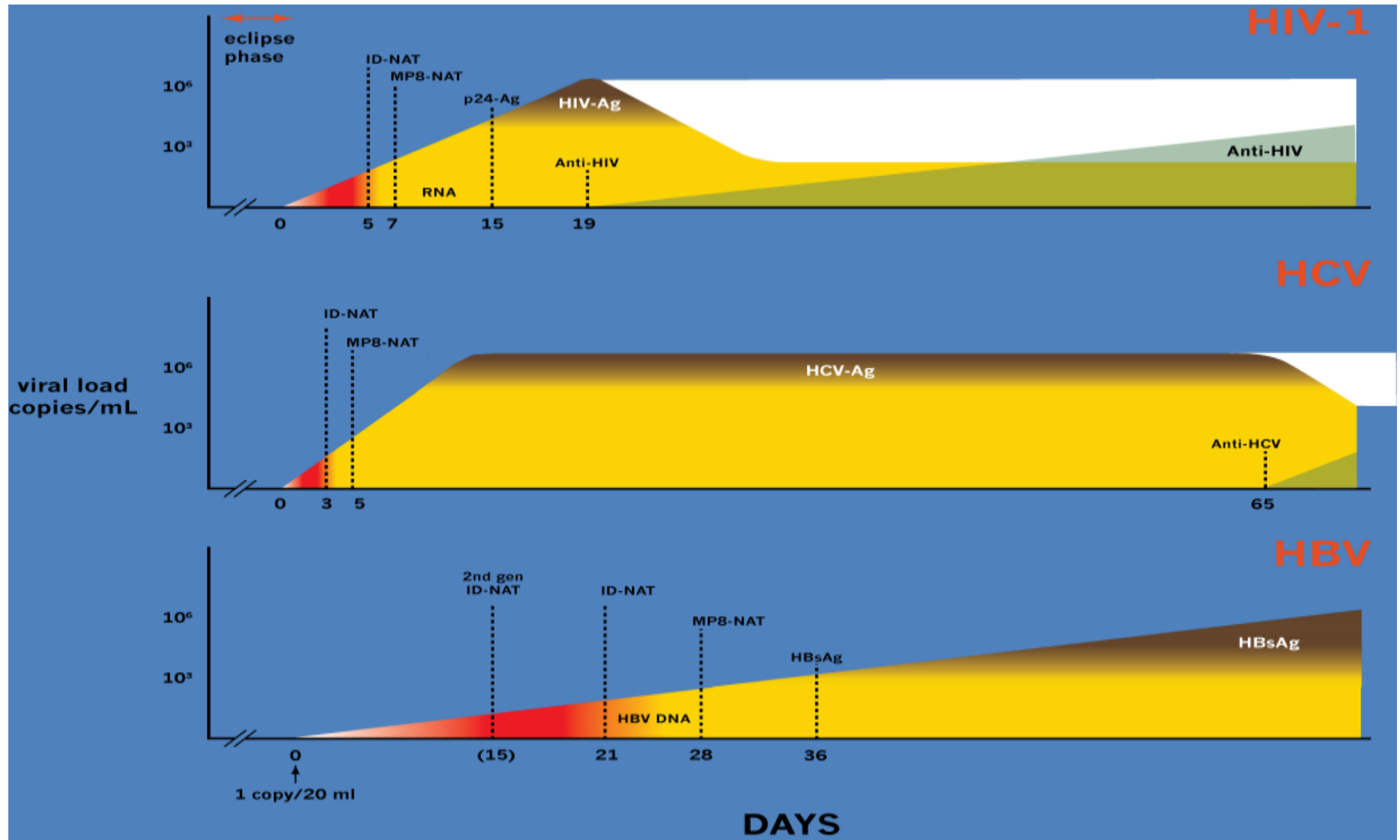
# OUTLINE

- Background
- Windows periode of transfusion transmitted infections
- Research on blood safety in Indonesia
- Indonesia's experience in using NAT
- National standard on blood safety
- Closing

# BACKGROUND

- Transfusion Transmitted Infections (TTIs) is one of transfusion reaction that can be prevented
- TTIs mostly caused by viral or bacterial infection with asymptomatic chronic condition
- The person with asymptomatic chronic infection, could accidentally donate their blood
- Carefull blood donors selection and effective TTIs blood screening should be done to have safest blood for transfusion
- TTIs will impact to community health

# WINDOWS PERIODE OF TRANSFUSION TRANSMITTED INFECTIONS



Busch MP et al. Transfusion 2005;45:254-264, Assal A et al. Transfusion 2009;49:289-300, Weusten J et al, Transfusion 2011;51:203-15

# **RESEARCH ON BLOOD SAFETY IN INDONESIA**

# PREVALENCE OF HIV INFECTION & HEPATITIS IN INDONESIA

- HIV, HBV and HCV can be transmitted through transfusion
- Prevalence data of TTIs

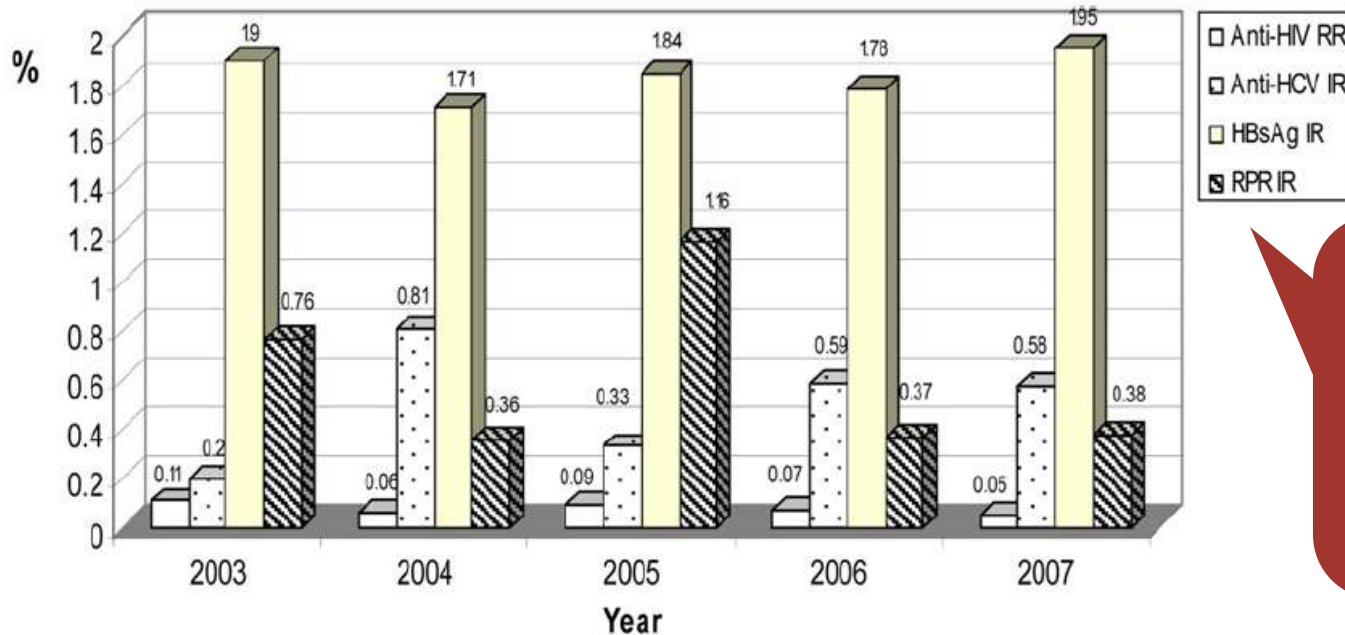
Marker	In population	In blood donors <sup>4</sup>	In children with blood disorders
HBsAg	9,4% <sup>1</sup>	1,9%	
Anti-HCV	0,44% <sup>1</sup>	0,6%	39% <sup>2</sup>
Anti-HIV	0,2% <sup>3</sup> in adult	0,02%	

- Indonesia has been classified into medium to high endemic of hepatitis B.

1. Ministry of Health of Indonesia. Research & Development Body. Report of Riskesdas Biomedis, 2007  
 2. Fraser Chanpong, et al. Hepatitis C Among Child Transfusion and Adult Renal Dialysis Patients In Indonesia. Am. J. Trop. Med. Hyg., 66(3), 2002, pp. 317-320.  
 3. Epidemiological Fact Sheets on HIV/AIDS & Sexual Transmitted Infections.UNAIDS, UNICEF, WHO. 2004  
 4. Yearly Report of 2010 on Blood services, Central Blood Center - Indonesian Red Cross

# Blood screening with ELISA & NAT shows the percentage of TTIs reactive blood in Indonesia is still high

## Percentage of TTIs reactive from 211 Blood Centers in Indonesia<sup>1</sup>



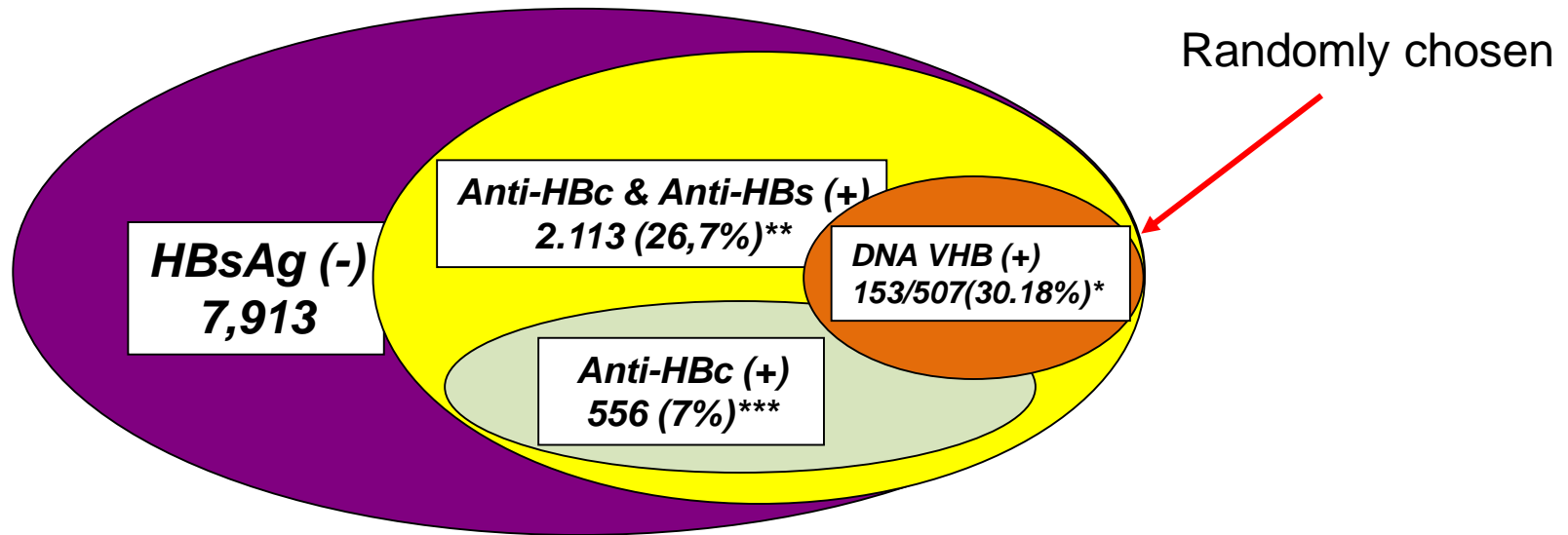
Approximately 3 % of donated blood in Indonesia was discarded due to TTIs reactive (using ELISA)

- Research in 2005 on 931 sero-negative blood donor's sampel in Indonesia showed that 0,64% was NAT reactive<sup>2</sup>. Confirmation testinmg showed 0.5% was HBV positive and 0.1% was HCV positive.

1. Y.S.M. Soedarmono, Donor issues in Indonesia: A developing country in South East Asia. *Biologicals* 38 (2010) 43-46

2. Soedarmono, et al. Nucleic Acid Testing of First Time Indonesian Blood Donors. *Vox Sanguinis* (2005) 89 (suppl.2) : 24

# MOLECULAR STUDY ON BLOOD SAFETY IN INDONESIA (2010)\*



- **Infectious blood donor (= Hepatitis B *Occult*):**
  - = 30,18% from HBsAg (-) and anti-HBc (+) blood
  - = **10%** from all HBsAg (-) blood
  - HBV DNA titer is  $< 3,2 \times 10^3$  copy/ml



Detection of DNA is **more effective** for blood safety

\* Soedarmono, Dissertation of PhD Program in Biomedics, University of Indonesia, 2010

\*\* Previous infection and immune to hepatitis B

\*\*\* Previous infection, low level HBV carrier, *Window period*, isolated anti-HBc, mutation



# Factors caused failure of HBsAg detection

## 1. Low viral load → low expression of HBsAg in blood

### – Evidence\*:

- the DNA titer of 153/507 HBsAg negative with HBV DNA positive was  $<3,2 \times 10^3$  copy/ml
- Need more analytical sensitive serological assay

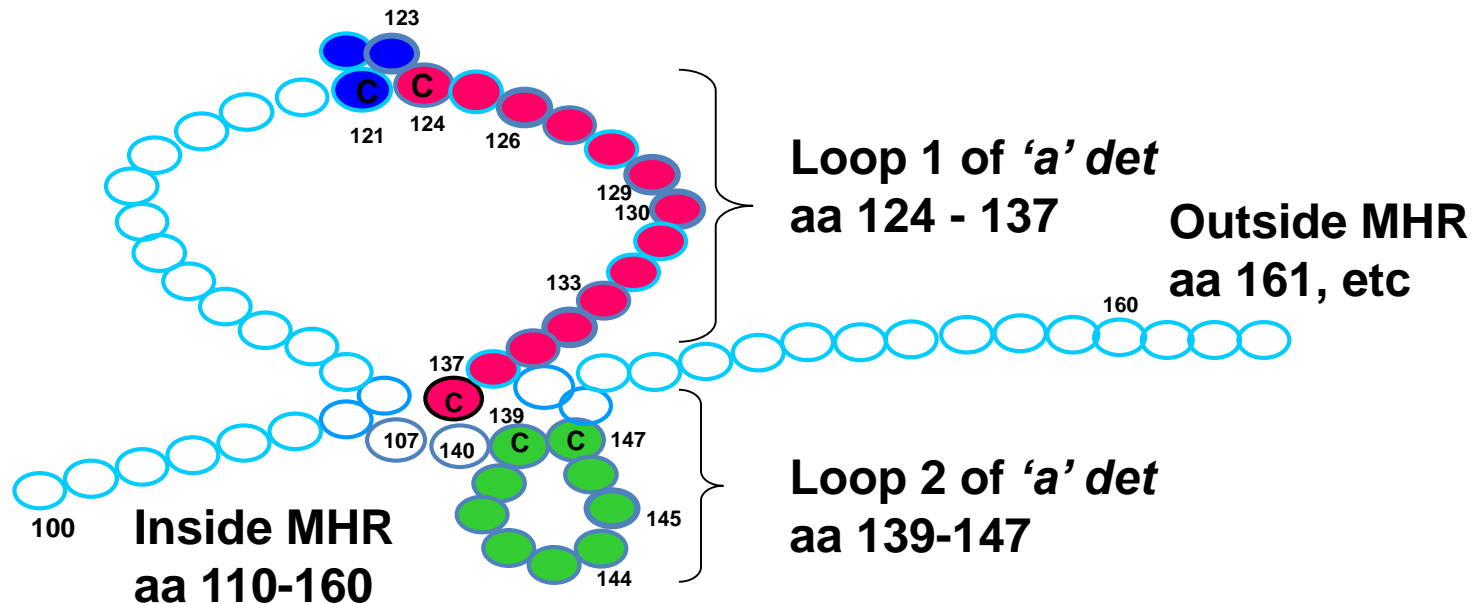
## 2. Molecular factor

### – Evidence\*:

- 100/153 of the DNA positive samples had HBsAg Mutation
- Mutation on S gen, especially in the 'a' determinant → caused changes in HBsAg antigenicity:
  - anti-HBs can not recognize the HBsAg → **False Negative of blood screening**
  - anti-HBs as a result of vaccination can not neutralized the HBsAg → **vaccination failure**
  - HBIG can not neutralized HBsAg → **treatment failure**

\* Soedarmono, Dissertation of PhD Program in Biomedics, University of Indonesia, 2010, .

# MUTATION IN “a” DETERMINANT



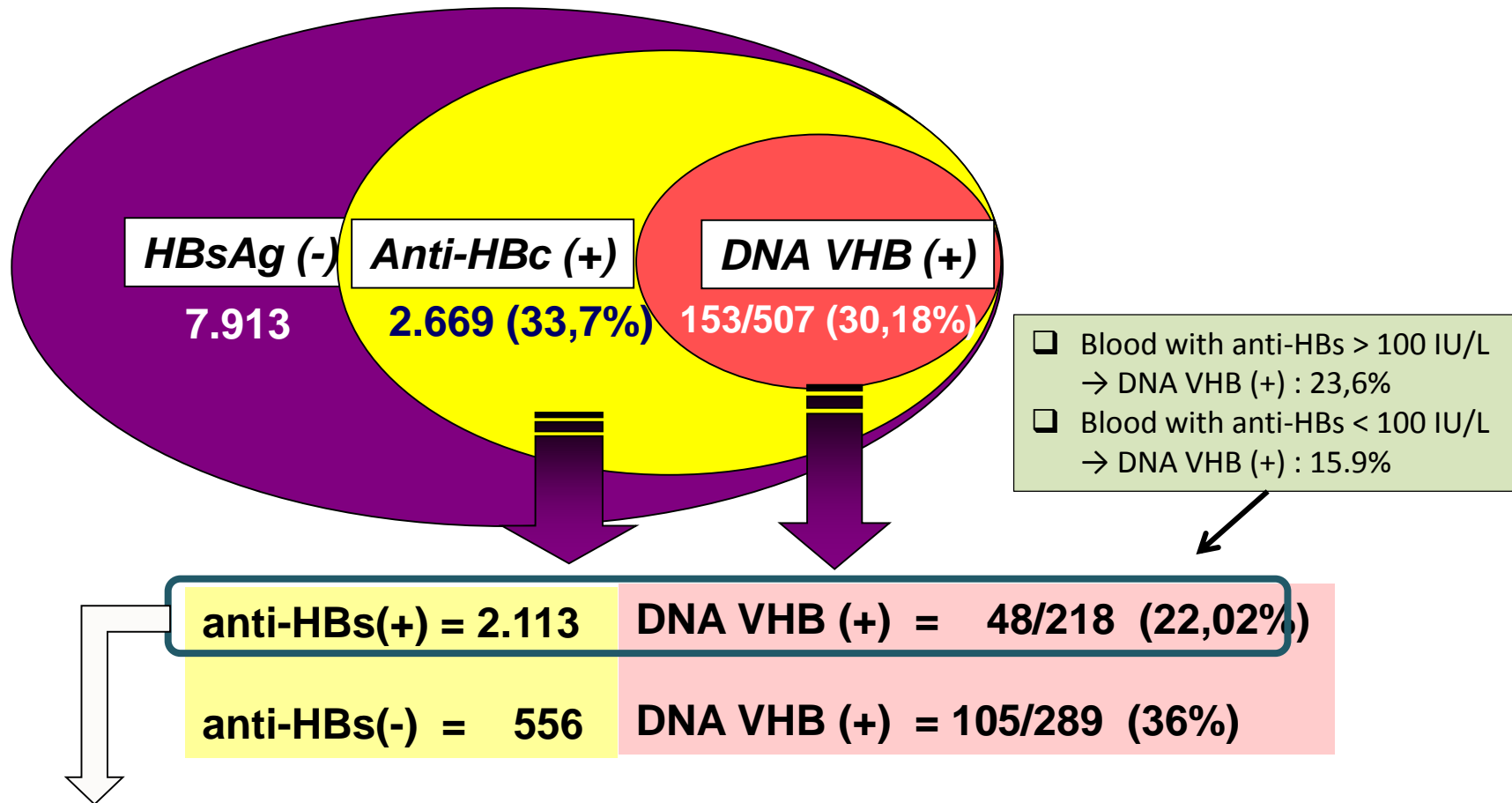
From 100 specimens with mutation in which the titer of HBV is very low (DNA :  $<3,2 \times 10^3$  copy/ml)\*

- 73 specimens: show mutation in 'a' determinant
- 27 specimens: show mutation outside 'a' determinant (*outside/inside MHR*)

\* Soedarmono, Dissertation of PhD Program in Biomedics, University of Indonesia, 2010, .

# Does anti-HBs need to be tested on blood donor?

[anti-HBc(+) blood with anti-HBs titer of > 100 IU/L can be transfused\*]



**anti-HBs does not guarantee that blood free of HBV**

\* In America, Germany and Japan

# NAT STUDY ON 3,038 SAMPLES (2013)

Samples origin	Total samples analyzed	Sample with concordant negative	Sample with serology yield (Serology RR, Ultrio NR)	Sample with concordant positive (Serology RR, Ultrio IR)	Sample with NAT yield Seronegative, (Ultrio RR, dHXV positive)	Sample with NAT yield but NAT discr negative (Seronegative, Ultrio RR, dHXV negative)
Kota Depok	114	109	0	4	0	1
Kab. Bekasi	475	467	2	4	1	1
Kota Jakarta	761	756	1	3	0	1
Kota Tangerang	1,688	1,618	25	37	4	4
<b>Total</b>	<b>3,038</b>	<b>2,950</b>	<b>28</b>	<b>48</b>	<b>5</b>	<b>7</b>
<b>%</b>	<b>99.7%</b>	<b>96.81%</b>	<b>0.92%</b>	<b>1.57%</b>	<b>0.16%</b>	<b>0.22%</b>

**0.38% were total NAT yield**

RR= Repeat Reactive

NR= Non Reactive

# Plasma Bag Results: NAT Discriminated and Non-discriminated Yields

Samples origin	Sample with NAT yield And NAT discriminatory positive	Sample with NAT yield but NAT discr negative
Kota Depok	0	1
Kab. Bekasi	1	1
Kota Jakarta	0	1
Kota Tangerang	4	4
<b>Total</b>	<b>5</b>	<b>7</b>
<b>%</b>	<b>0.16%</b>	<b>0.22%</b>

All five NAT IR yields discriminated as HBV

Seven NAT IR could not be discriminated though confirmed to be repeat NAT reactive

1 sample was occult anti-HBc positive

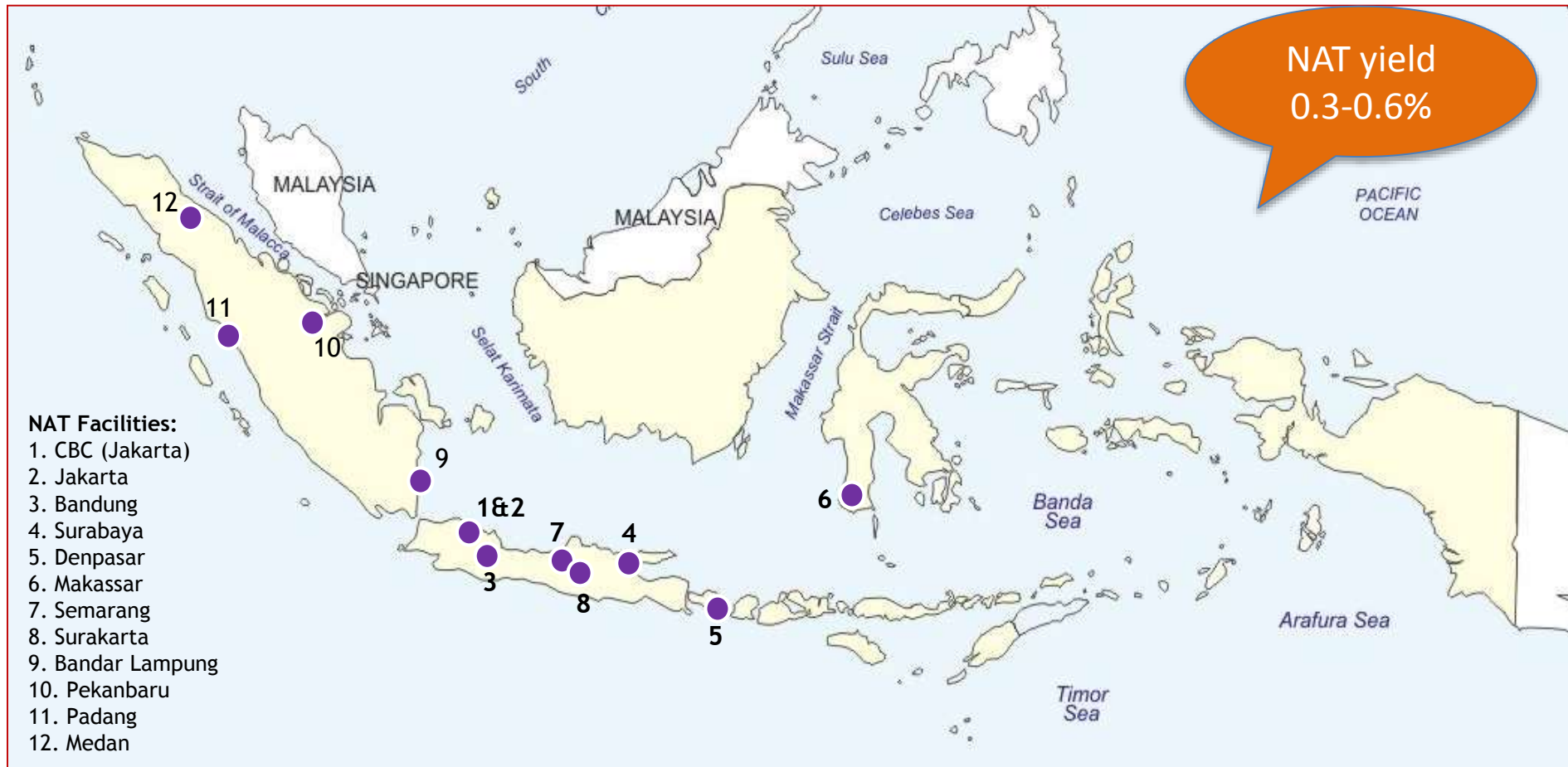
1 sample was anti-HBc & anti-HBs positive

For the 3038 donations tested, this translates to 1/607 prevalence for HBV

These samples likely have very low viral load to be reproducibly detected by NAT screening and discriminatory assays

# INDONESIA'S EXPERIENCE IN USING NAT

- NAT was introduced in 2008
- Since 2009, the MOH subsidized NAT reagent for 30% of donated blood in some BCs
- Starting in 2015 the government of Jakarta subsidized 100% of NAT reagents for Jakarta BC.



# PROBLEMS IN NAT TESTING

- Results of NAT Multiplex Repeated Reactive but NAT Discriminatory Negative (replicate testing on plasma bag need more budget)
  - Results of NAT Discriminatory Positive and Diagnostic Test at the hospital (that mostly were still used EIA method) Negative
- Difficult for donor counseling

# RAISING THE STANDARD OF BLOOD DONOR SCREENING

- Basis:
  - Unsafe blood transfusion and plasma derivatives products usage will impact on community health
  - Indonesia has moderate to high prevalence of HBsAg
- Blood and plasma as raw material should be as safe as possible, keys are:
  - Careful donor recruitment and selection
  - Effective TTIs blood screening and testing algorithm
  - Correct processing, storage and distribution



# MOH DECREE ON NATIONAL STANDARD OF BLOOD SERVICES (ISSUED in 2015)

Emphasized:

- Standardized input (building, equipment and material, competent staff)
- Standardized process and output of blood for transfusion and plasma for fractionation
- The standard on TTIs screening method:
  - EIA plus NAT (however, currently centralized NAT could only be run in limited area due to geographic and transportation difficulties)
  - The rapid test is only used by BCs that located in areas where EIA centralization is not possible due to poor infrastructures

# CLOSING

- Research shows serology testing can not detect window period infection
- TTIs impacts on community health
- New technology was created to increase safety of blood for transfusion and plasma for fractionation
- Regardless of geography and infrastructure burden, serology plus NAT testing is recommended for Indonesia that has high prevalence of HBsAg
- Despite its weakness, the NAT is a technology offered to improve blood safety