# *Summary of:*
# Pathogen reduction
## limitations and opportunities

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Zagreb, May 17th 2017

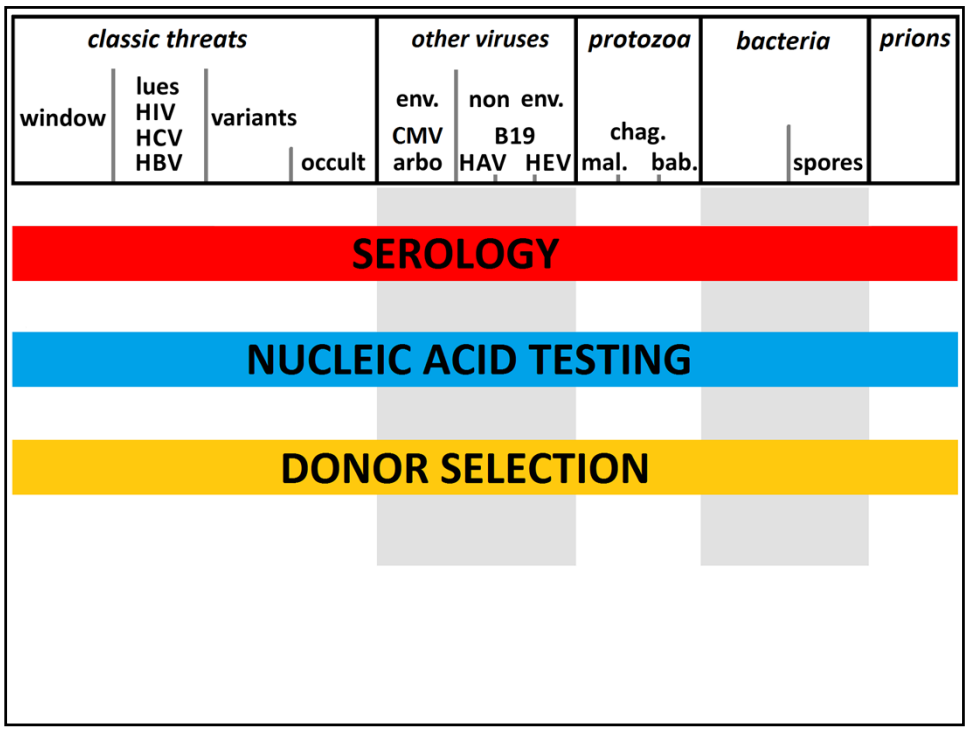
prof.dr. Hans L. Zaaijer, medical microbiologist
Sanquin - Blood-borne Infections
& Academic Medical Centre - Clinical Virology
Amsterdam NL

## Disclosure of interests of Hans Zaaijer

No conflicts of interests:

Hans Zaaijer is or was paid for
*unrestricted* lectures and teaching by:
ACTA, Abbott, Gilead, Griffols, ISBT,
Janssen-Cilag, Roche, and Virology Education.

No consultancy, no advisory boards, no shares,
or other interests in companies.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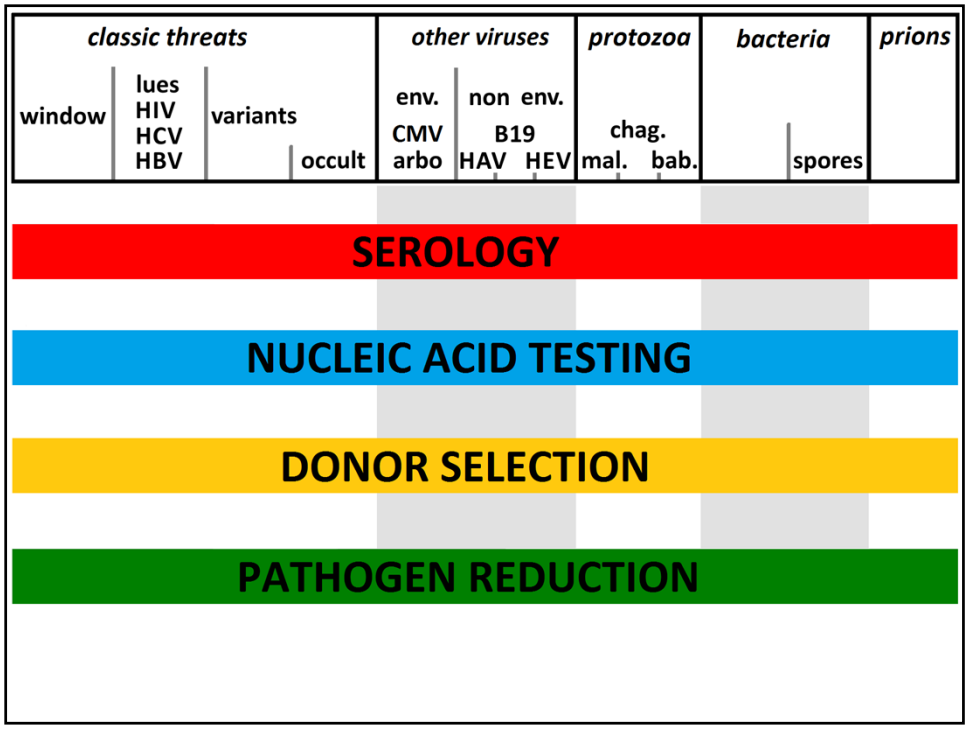
SEROLOGY
NUCLEIC ACID TESTING
DONOR SELECTION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PATHOGEN REDUCTION

## considerations (1)

So far our layers of microbiological safety include:

- donor selection, definite or temporary deferral.
- leukodepletion.
- serological screening.
- NAT based screening of donations and pools (HAV,B19,HEV).
- bacteriological culturing of platelets.
- plasma derivatives: inactivation (eg SD, heat) and removal (eg filter).
- ≥ 35 countries employ Intercept and/or Mirasol and/or Theraflex pathogen reduction for platelets and/or plasma. **No uniformity:** in Italy all 3 methods are applied, in Holland none.

How to fit in **pathogen reduction** (PR) ?

For this talk I aim at a near future,
in which PR is available for RBCs, platelets, plasma, WB.

## considerations (2)

Our blood supply is extremely safe, residual risks are small.
Hence:
an *additional* broad-spectrum safety step is cost ineffective.

We struggle with the window risk and emerging infections.

Window risk necessitates range of deferrals (MSM, tattoo, etc).
Emerging infections necessitate serial, ad hoc safety repairs:

- donor exclusions (temp: arboviruses. def: vCJD)
- additional donor screening (WNV, Q, babesia, zika, HEV)

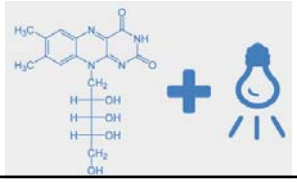
A new broad-spectrum safety measure should
replace classical safety measures,
and cover emerging agents and window donations:

**pathogen reduction ?**

## mechanism of action: damage DNA/RNA of pathogen

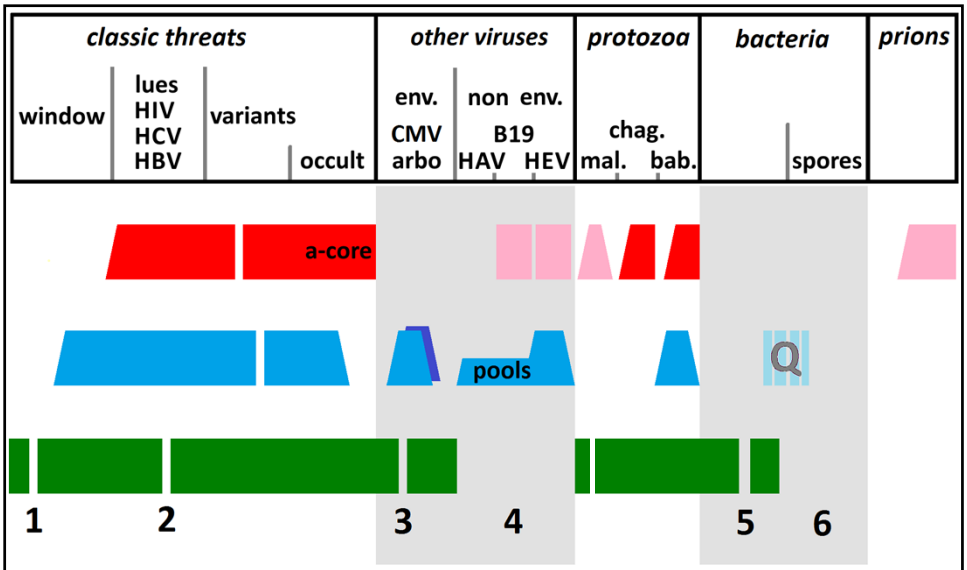

Theraflex (Macopharma)
plasma: methylene blue + light
(platelets: UVC only)

Intercept (Cerus)
plasma, platelets: amotosalen + UV
(RBCs: S-303 + glutathione)



Mirasol (Terumo BCT)
platelets, plasma, whole blood:
riboflavin + UV

www, April 27th 2017




2,3,4 [BVDV~HCV,PRV~CMV], HAV, PPV~B19; Kwon ea, Vox 2014.
4 HEV; Hauser ea, Blood 2014.
5,6 K.pneumoniae, B.cereus; Schmidt ea, Transfusion 2015.
1 HIV; Alvarez ea, Transfusion 2016 :

# Pathogen Reduction and validation (of principle + of individual runs)

How to interpret Alvarez ea, Transfusion 2016:
transmission of PR-treated HIV-window FFP ? (135 cps/mL)
- Human-, product-, technical- or iT-error?
- Weird subset of HIVs escaping PR?

**Serological and NAT based screening for HIV, HBV, HCV:**
Extensive and ongoing real life validation of test performance.
Positive controls in each test run. (NAT: in each sample).

**Pathogen Reduction and HIV, HBV, HCV:**
PR applied to material already neg. in serology and NAT.
Validation based on historical PCR and culture experiments.
In vivo validations? Macaques experiments? Proof is in the eating of the pudding.
No run controls.

# Pathogen Reduction is not a panacea

USA:
- babesia √
- zika √

Limited effectivity against non-enveloped viruses and 'spores' (Bacillus, Coxiella).

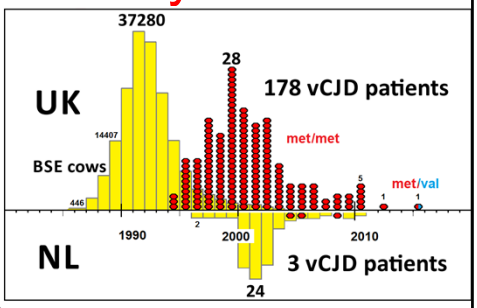
Bad luck for Holland:

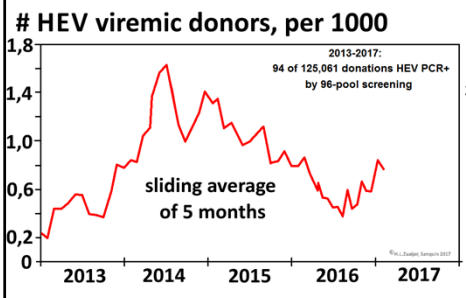
# Pathogen Reduction and zoonoses from the Dutch bio-industry

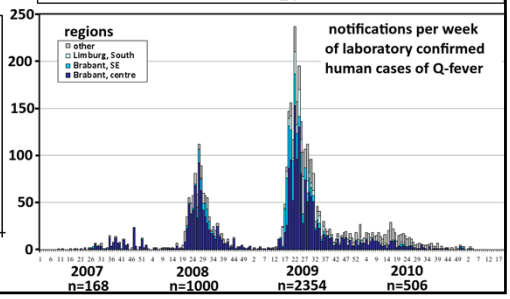
vCJD x

Q-fever x

HEV x




# Pathogen Reduction and Arbophobia

PR is probably highly effective against WNV, DenV, zikaV and ChikV,

- WNV is covered by NAT (USA, Italy), or by temporary donor exclusion (N-EU).

- No disease reported for DenV, ZikaV or ChikV via tranfusion even in immuno-suppressed recipients.
  No post-transfusion mikrocephaly reported (yet).
  So far only WNV is relevant.

# Integration of Pathogen Reduction

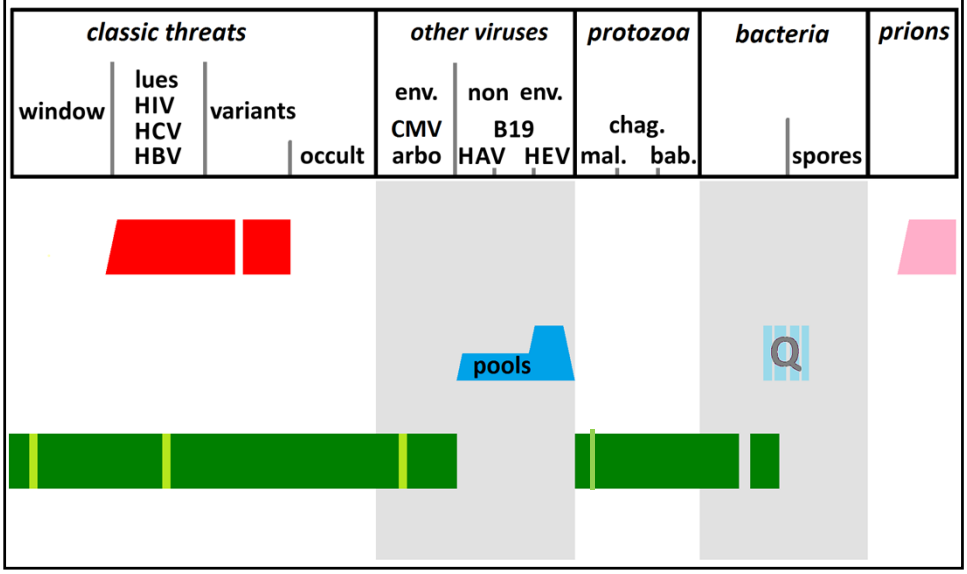
- assuming PR is available for WB and/or all components.
- assuming that efficacy for HIV, HBV, HCV, WNV, CMV is beyond doubt; including inactivation of high levels of viremia preceding seroconversion.

- PR not on top of serology and NAT, residual risks are too small to warrant an extra layer of safety.

Instead: consider to

1) introduce universal Pathogen Reduction. UPR
2) abolish NAT screening for HIV, HBV, HCV, WNV, zika.
3) abolish babesia screening, deferrals for malaria, arbo, MSM, etc.
4) continue serology for HIV, HBV, HCV (id. of infected donors; cheap fail-safe).
5) continue NATs for selected non-enveloped viruses.

# Universal Pathogen Reduction replacing other safety measures?



# Thank you

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