FRIEDRICH-LOEFFLER-INSTITUT
FLI
Bundesforschungsinstitut für Tiergesundheit
Federal Research Institute for Animal Health

Crossprotection within Serotype A

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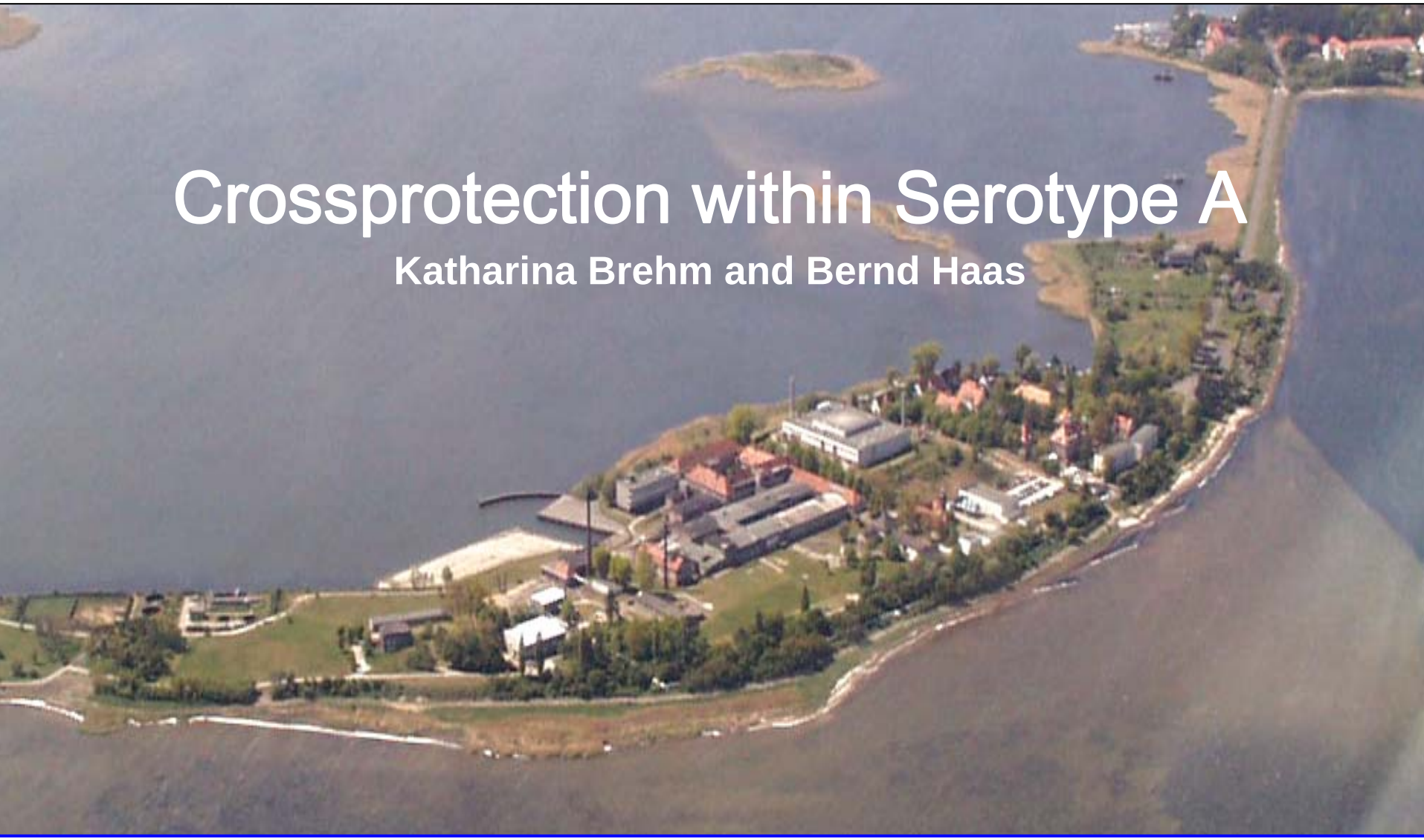
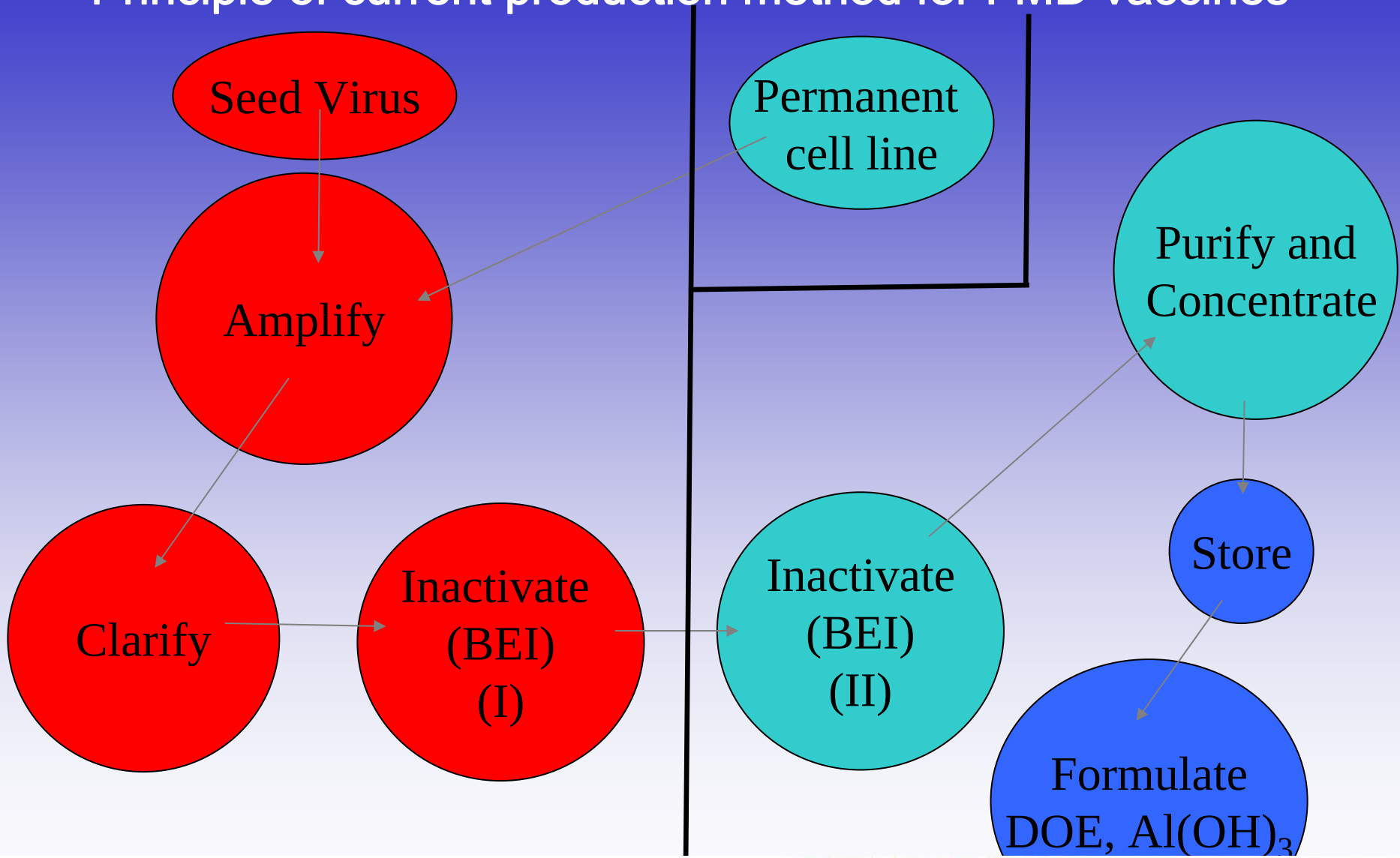


Principle of current production method for FMD vaccines



Problems of current FMD Vaccines:

Gap between vaccination and onset of protection

Duration of immunity

Limited crossprotection

Still low level of virus transmission/carriers likely

No perfect DIVA vaccine

Production under high security conditions

Stability at ambient temperature

RECOMMENDATIONS FROM THE WRL ON FMD VIRUS STRAINS TO BE INCLUDED IN FMDV ANTIGEN BANKS – JUNE 2006

High Priority

O Manisa (*covers PanAsia topotype)*
O BFS or Campos
A24 Cruzeiro
Asia 1 Shamir
A Iran '96
A22 Iraq – moved from medium to high
SAT 2 Saudi ~~Arabia *(or equivalent)*~~

(not in order of importance)

RECENT SEROTYPE A from the MIDDLE EAST

Medium Priority

A Eritrea –moved from low to medium
SAT 2 Zimbabwe
AIran 87 or A Saudi Arabia 23/86 *(or equivalent)*
SAT 1 South Africa
A Malaysia 97 *(or Thai equivalent such as A/NPT/TAI/86)*
A Argentina 2001
O Taiwan 97 *(pig-adapted strain or Philippine equivalent)*
A Iran '99

(not in order of importance)

EGYPTIAN SEROTYPE A

Low Priority

A15 Bangkok related strain
A87 Argentina related strain
C Noville
SAT 2 Kenya
SAT 1 Kenya
SAT 3 Zimbabwe
A Kenya

(not in order of importance)

Criteria for the decision to apply protective vaccination

Population density of susceptible animals

Clinically affected species

Movement of potentially infected animals or products out of the protection zone

Predicted airborne spread of virus from infected holdings

Suitable vaccine available?

Origin of outbreaks (traceability)

Incidence slope of outbreaks

Distribution of outbreaks

Public reaction to total stamping out policy

Acceptance of regionalisation after vaccination

Economic assessment of competing control strategies

It is foreseeable that the 24/48 hours rule cannot be implemented effectively for two consecutive days?

Significant social and psychological impact of total stamping out policy

Existence of large holdings of intensive livestock production in a non-densely populated livestock area

Improved vaccine strain selection

WP5 of FMD_ImproCon

Heterologous challenge experiments vs. in vitro tests

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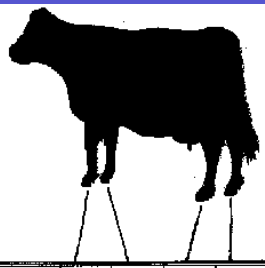
EP - Challenge test



Tier	Dosis	VL	VR	HL	HR		
1	1/ 1	+	+	+	+	P	5/5
2	1/ 1	+	+	+	+	P	
3	1/ 1	+	+	+	+	P	
4	1/ 1	+	+	+	+	P	
5	1/ 1	+	+	+	+	P	
6	1/ 4	+	+	+	+	P	4/5
7	1/ 4	+	+	+	+	P	
8	1/ 4	+	+	+	+	P	
9	1/ 4	+	+	+	+	P	
10	1/ 4	-	-	-	-	F	1/5
11	1/16	+	+	+	+	P	
12	1/16	-	-	-	-	F	
13	1/16	-	-	+	-	F	
14	1/16	-	-	-	-	F	
15	1/16	-	-	-	-	F	
16	Kontr.	-	-	-	-	F	
17	Kontr.	-	-	-	-	F	

3 groups of 5 cattle

1 Dose
¼ Dose
1/16 Dose

2 Control animals

intradermolingual infection 21 d.p.i

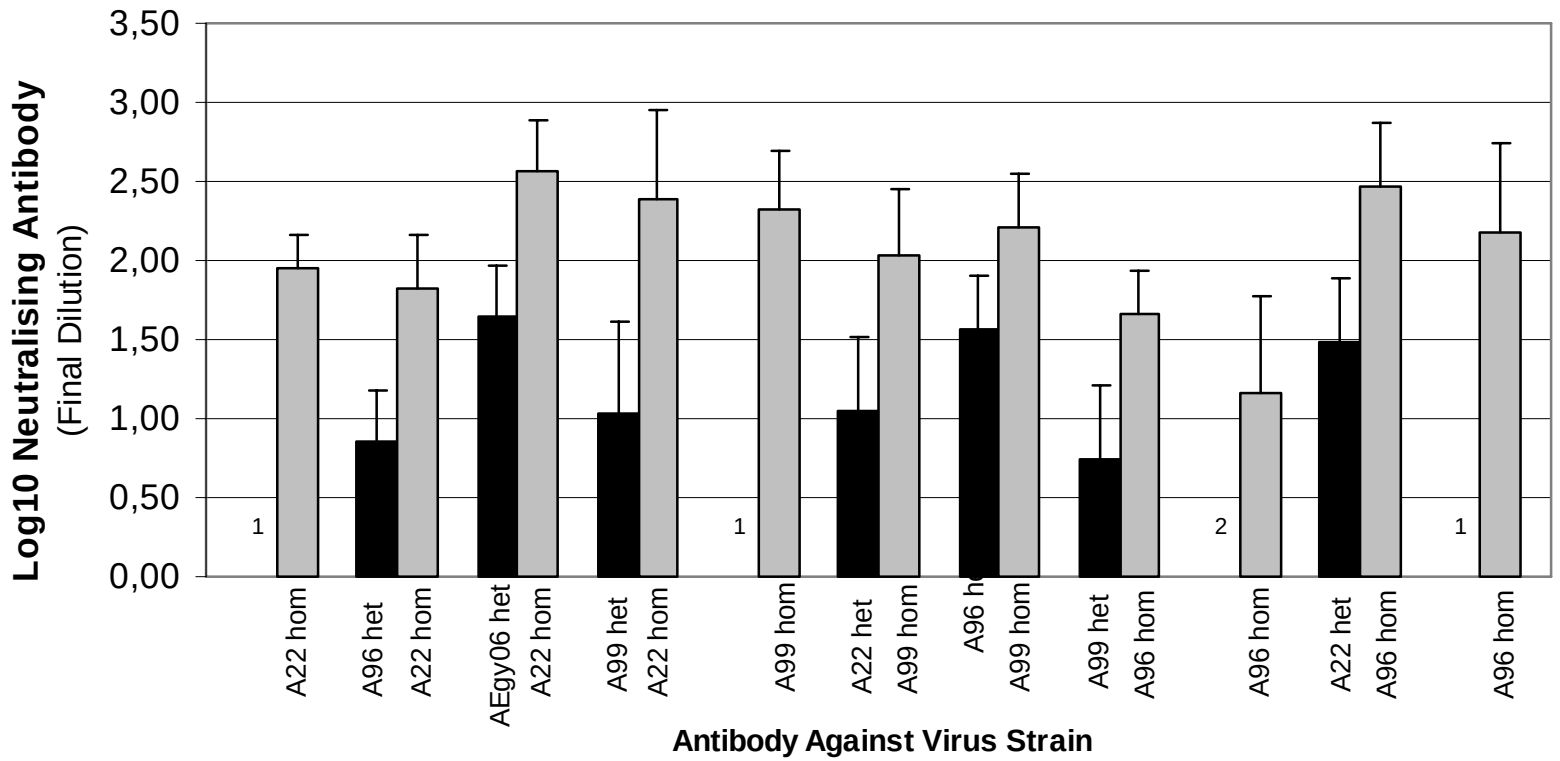
Virus / Vaccine	A 22 Irak	A 24 Cruzeiro	A Iran 96	A Iran 99
A 22 Irak	≥ 32 PD 50	2,64 PD 50	6,06 PD 50	3,84 PD 50
A 24 Cruzeiro	n.d.	13,93 PD 50	n.d.	n.d.
A Iran 96	2,00 PD 50 8,00 PD 50	n.d.	≥ 32 PD 50	10,56 PD 50
A Iran 99	13,93 PD 50	n.d.	18,38 PD 50	≥ 32 PD 50

A22 vaccine – A Egypt 06: 10,56 PD50

Challenge Results

Vaccine/ challenge	A22/ A22	A22/ Alr96	A22/ AEgypt 06	A22/ Alr99	Alr99/ Alr99	Alr99 / A22	Alr99/ Alr96	Alr96/ Alr99	Alr96 / A22	Alr96 / A22	Alr96/ Alr96
dose											
1/1	5/5	5/5	5/5	5/5	5/5	5/5	5/5	5/5	2/5	5/5	5/5
1/4	5/5	2/5	3/5	2/5	5/5	4/5	5/5	3/5	2/5	4/5	5/5
1/16	5/5	2/5	3/5	0/5	5/5	3/5	3/5	3/5	1/5	1/5	5/5
control	0/2	0/2	0/2	0/2	0/2	0/2	0/2	0/2	0/2	0/2	0/2
PD50	32	6.06	10.56	3.84	32	13.93	18.38	10.56	2	8	32
r-value		0.09	0.12	0.04		0.10	0.23	0.12	n.a.	0.10	

Homologous and Heterologous VNT-Titres, 21 d.p.v.



Definition r-value

$$r1 = \frac{\text{titre of bovine reference serum against field isolate}}{\text{titre of bovine reference serum against homologous reference strain}}$$

Ferris and Donaldson, 1992:

r1 = 0 to 0.19: highly significant serological variation from the reference vaccine strain

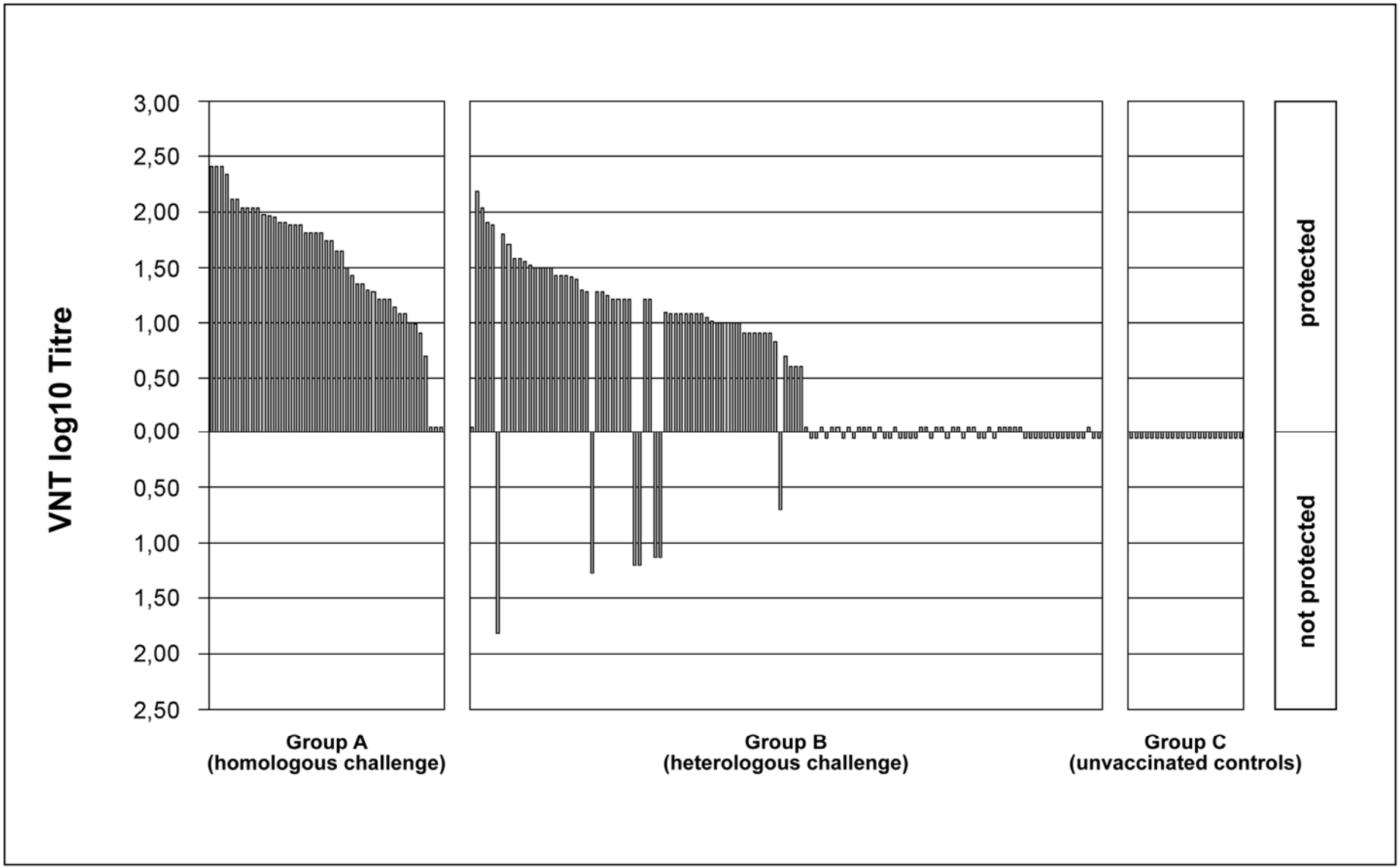
r1 = 0.2 to 0.39 represent an area of concern. They show significant differences from the reference strain, but protection may be satisfactory if a sufficiently potent vaccine is employed.

r1 = 0.4 to 1.00 are not significantly different from the reference vaccine

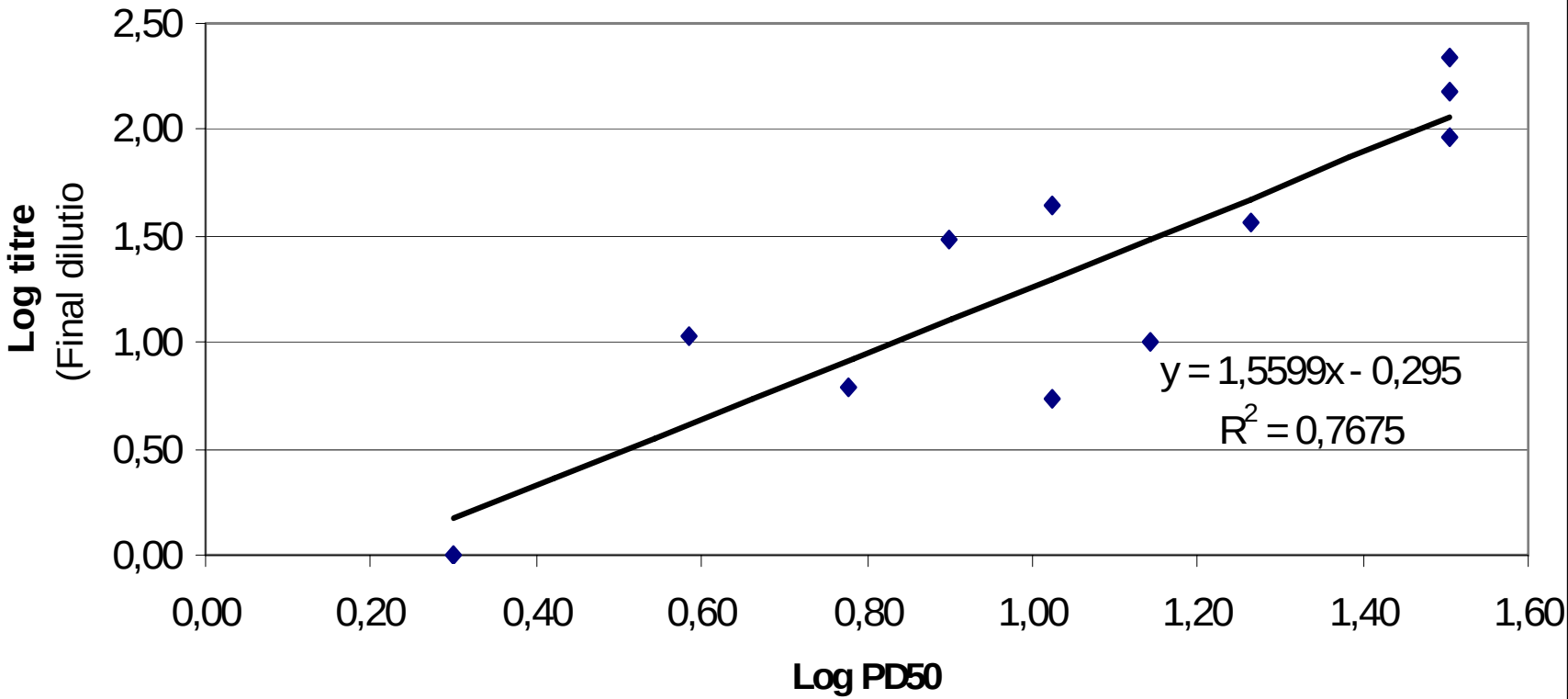
strain

Barnett et al, 2001 :

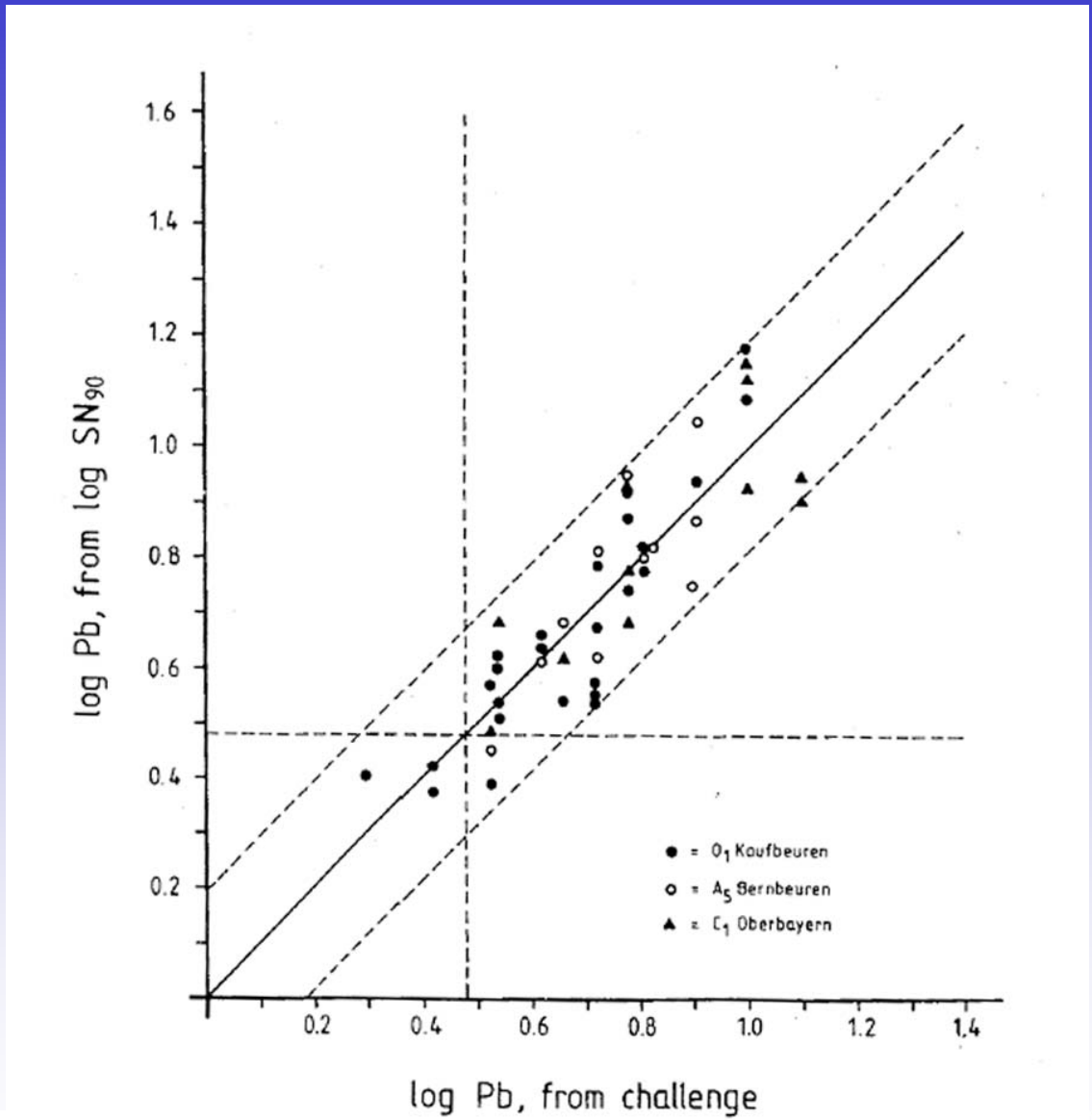
r-values of 0.3 to 1 = indicative of reasonable level of cross protection


VNT log10 Titre
3,00
2,50
2,00
1,50
1,00
0,50
0,00
0,50
1,00
1,50
2,00
2,50
protected
not protected
Group A
(homologous challenge)
Group B
(heterologous challenge)
Group C
(unvaccinated controls)

VNT and Protection

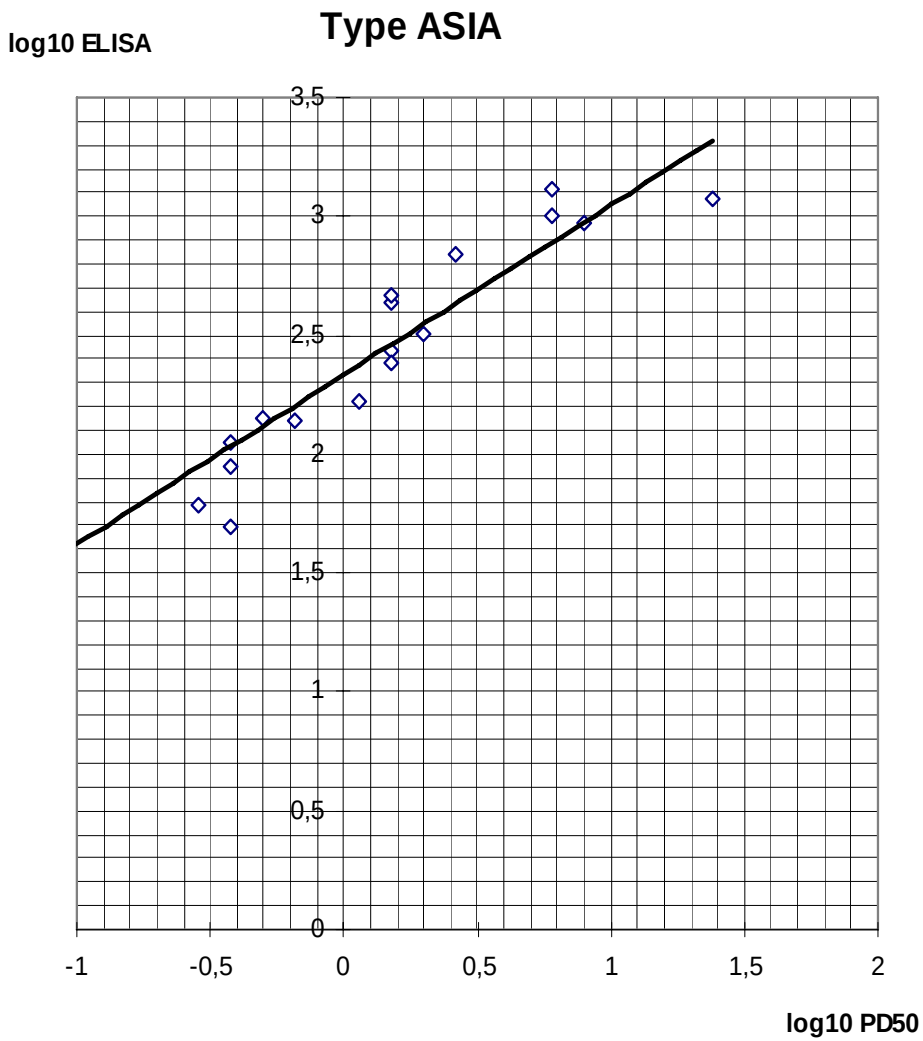


Historical Data: VNT and Protection (homologous)



Ahl et al. 1990

Historical Data: LPB-ELISA and Protection (homologous)



$y = 0{,}7135x + 2{,}3336$

$R^2 = 0{,}8988$

Conclusion:

High potent emergency vaccines offer cross protection within serotype A

But there are good reasons for caution:

Many vaccines won´t reach ≥32 PD50

What´s true for „A“
may not apply to other serotypes, e.g. „O“

There are still gaps in fundamental knowledge
on host immune responses
and viral determinants of protection!

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Thank you for your attention!