IBV

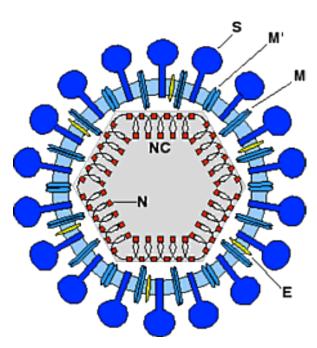
HOW TO DEAL WITH TODAY'S MOST RELEVANT FIELD STRAINS WITHIN THE EUAFME REGION?

· zoetis. ·



IB VARIANTS HISTORY EUAFME PERSPECTIVE

- 1930's: Massachussetts (mortality 40-90%)
- 1951: first variant in US: Connecticut
- 1980's: Dutch variants D274, D1466, Belgian variant B1648
- 1990's: 793B variants
- 2000: Italy-02
- 2004: QX IBV
- Xindadi, Variant 2, Q1
- 2010: over 65 variants described worldwide

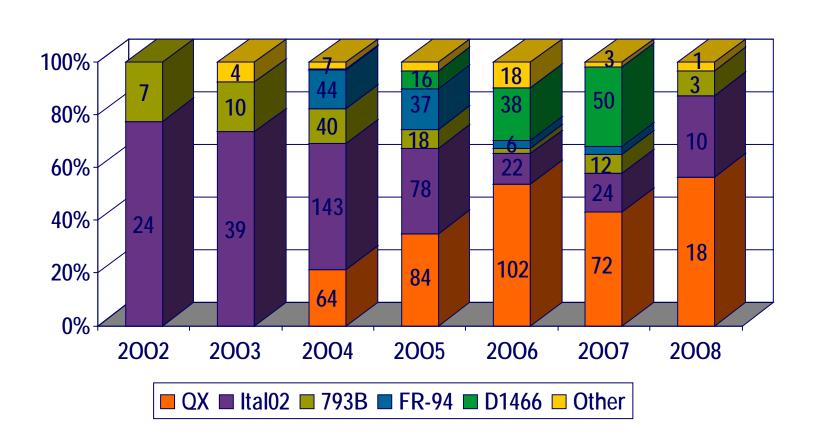


ZOETIS DIAGNOSTICS



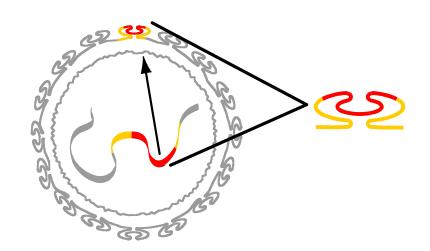
- Started in 2002 at Liverpool University in collaboration with Professor R.C. Jones, initially Western Europe
- Over 8000 flocks tested in Liverpool until 2008 (nested RT-PCR)
- In 2010, continued in Weesp, the Netherlands (RTq-PCR), EUAfME
- Mid 2012 April 2014 Anicon, Germany
- Since April 2014, newly built Centre of Excellence in Torce, France

IB FIELD STRAINS WESTERN EUROPE LIVERPOOL DATA



TEST METHOD RT-qPCR

- Tracheal and/or cloacal samples (mostly diseased flocks) pooled per flock
- Cell lysis
- Filtering RNA by centrifugation
- 2 RT-qPCR tests
 - First PCR (N protein)
 - On/off
 - Second PCR (S protein)
 - Every strain has different primers and probes
- Sequenced if "unknown"



INTERPRETATION

- Some things to consider
 - Poultry density of the area
 - Vaccination schedule
 - Routine monitoring or clinical signs
 - History of the farm



- No differentiation vaccine or field strain with RT-qPCR
- After sequencing, vaccine or field strain?

IB	NL	Belgium	Germany	UK	France	Spain	Portugal	Turkey
	n=212	n=72	n=64	n=174	n=9	n=62	n=32	n=40
IBQX	81%	58%	80%	31%	22%	42%	53%	0%
Mass	25%	31%	39%	39%	44%	31%	41%	53%
IB793b	17%	42%	17%	15%	67%	10%	19%	8%
D274	5%	10%	9%	13%	0%	18%	0%	0%
ARK	0%	3%	0%	51%	0%	2%	0%	0%
Italy 02	0%	0%	0%	1%	0%	45%	6%	0%
Variant 2	0%	0%	0%	0%	0%	0%	0%	60%
D1466	0%	1%	0%	0%	0%	0%	0%	0%

n=1322 (17 countries)

IB	NL	Belgium	Germany	UK	France	Spain	Portugal	Turkey	Poland	Baltics
	n=280	n=86	n=50	n=234	n=46	n=126	n=26	n=9	n=32	n=19
IBQX	80%	58%	84%	22%	24%	54%	46%	11%	31%	11%
Mass	21%	47%	36%	46%	63%	19%	15%	22%	63%	32%
IB793b	18%	30%	6%	50%	37%	23%	8%	0%	56%	37%
D274	9%	14%	14%	12%	4%	4%	4%	0%	6%	21%
ARK	1%	2%	0%	35%	0%	0%	0%	0%	0%	0%
Italy 02	0%	0%	0%	0%	2%	19%	27%	0%	0%	0%
Variant 2	0%	0%	0%	0%	0%	0%	0%	56%	0%	0%
D1466	1%	3%	0%	0%	0%	1%	0%	0%	0%	0%

n= 1385 (16 countries)

QX also isolated in Greece, Hungary, Czech Republic, South Africa and ME

IB	NL	Ве	Ger	UK	Fr	Spain	Port	Turkey	Poland	Baltics	Roman	RSA	Zimbab
	n=592	n=133	n=79	n=197	n=92	n=71	n=55	n=9	n=55	n=47	n=14	n=23	n=14
IBQX	64%	54%	71%	6%	24%	17%	31%	11%	53%	11%	50%	74%	50%
Mass	35%	34%	44%	62%	62%	49%	38%	67%	49%	62%	43%	65%	71%
IB793b	36%	42%	35%	69%	38%	62%	25%	0%	40%	74%	29%	22%	14%
D274	16%	24%	22%	29%	0%	4%	5%	0%	20%	19%	7%	4%	0%
ARK	0%	1%	0%	31%	1%	0%	0%	0%	0%	0%	0%	0%	0%
Italy 02	0%	0%	0%	0%	0%	24%	0%	0%	0%	0%	0%	0%	0%
Variant 2	0%	0%	0%	0%	0%	0%	0%	33%	0%	0%	0%	0%	0%
D1466	1%	5%	3%	1%	0%	0%	0%	0%	2%	0%	0%	0%	0%

2013 n= 1879 (21 countries)

QX also isolated in Cyprus, Belarus and Denmark

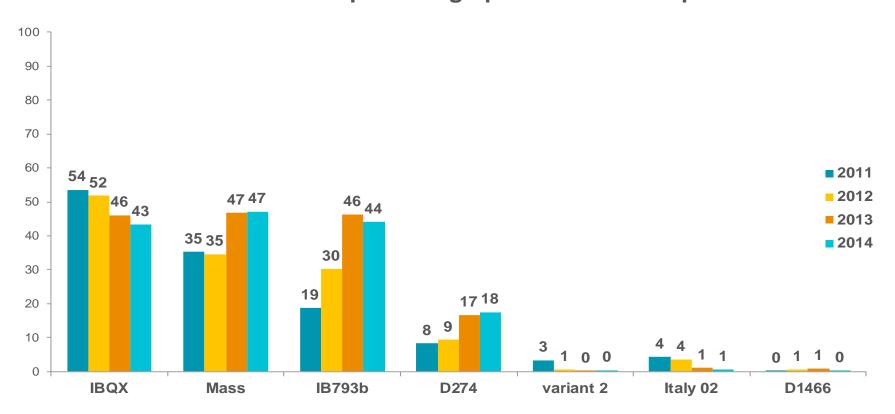
IB	NL	Be	Ger	UK	Fr	Spain	Port	Ukr	Lith	Pol	Den	Rom	Zimb
	n=562	n=56	n=91	n=250	n=178	n=26	n=47	n=47	n=35	n=95	n=19	n=74	n=4
IBQX	74%	68%	53%	16%	20%	23%	30%	43%	23%	38%	32%	34%	50%
Mass	41%	27%	43%	43%	78%	15%	49%	49%	57%	42%	100%	45%	75%
IB793b	36%	41%	42%	60%	46%	54%	49%	62%	69%	45%	0%	39%	0%
D274	18%	20%	20%	33%	0%	4%	21%	13%	20%	27%	0%	16%	0%
ARK	0%	0%	0%	16%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Italy 02	0%	0%	0%	0%	0%	31%	4%	0%	0%	0%	0%	0%	0%
Variant 2	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
D1466	1%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%

2014 n= 1931 (23 countries)

QX also isolated in Bulgaria

2011-2014 IB PCR POSITIVE SAMPLES

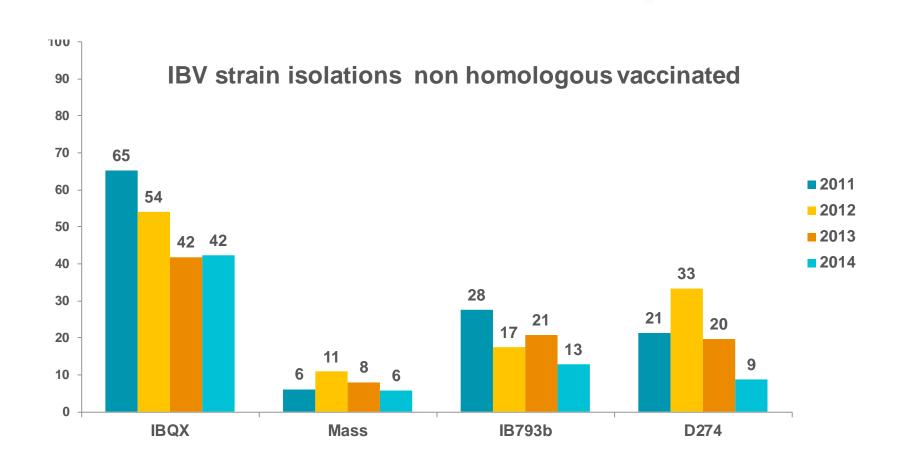
IBV strain isolations percentage positives of total positives



SELECTION CRITERIA

- Selection filters made based on non homologous vaccinations.
 Following results were taken out of the total amount:
 - Homologous vaccinated birds
 - Unknown vaccination schedules
 - Breeders and layers (vaccination scheme often not entirely known)
 - Field strains with no existing homologous vaccines
 - Vaccines without presence homologous field strains
- Not taken into account:
 - Poultry density
 - Vaccination schedules neighboring farms
 - Vaccination history
- Recalculated as percentage of total isolations of that specific strain

2011-2014 FIELD STRAINS EUAFME

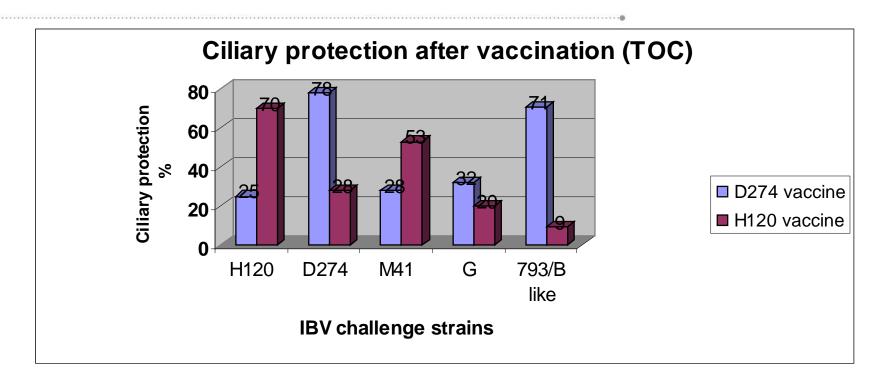


CROSS PROTECTION TRIALS

BACKGROUND CROSS PROTECTION TRIALS

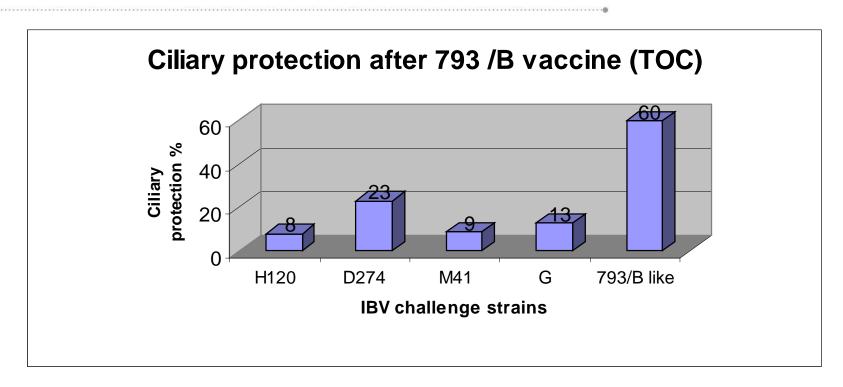
- IBV is a moving target
- Not for every pathogenic strain a vaccine is available or needed
- Knowledge on possible cross protection offered by available vaccines and combination of vaccines is valuable
- IB793b field virus sometimes still pops up in different countries
- Italy O2 field virus still very present in Spain for the least
- Pathogenic IBV variant 2 strain circulating in Turkey and the Middle
 East region

D274: CROSS PROTECTION



G. Dhinakar Raj, R.C. Jones 1996

793B: CROSS PROTECTION



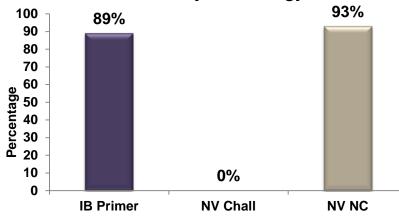
G. Dhinakar Raj, R.C. Jones 1996

¹CROSS PROTECTION TRIAL AGAINST ITALY 02

Group	Treatment	Vaccination	Challenge D21 4.2log ₁₀
1	IB Primer	Day 0	Italy O2
2	None	-	Italy O2
3	None	-	None

Study conducted at the University of Liverpool, Department of Veterinary Pathology

Results:
Ciliary activity in tracheal explants five days after challenge with Italy 02



¹RC Jones, KJ Worthington, I Capua, CJ Naylor Efficacy of live infectious bronchitis vaccines against a novel European genotype, Italy 02 Vet. Rec. 2005 Vol. 156 No. 20 pp. 646-647

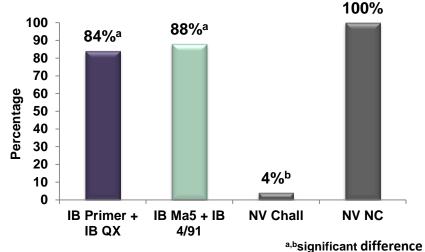
²CROSS PROTECTION TRIAL 1 AGAINST IB793B

Group	Treatment	Vaccination	Challenge D21 10 ^{5.0} EID ₅₀
1	IB Primer + IB QX	Day 0	IB 793b
2	IB Ma5 + IB 4/91	Day 0	IB 793b
3	None	-	IB 793b
4	None	-	None

Study conducted at Zoetis VMRD, Olot

Results:

Ciliary activity in tracheal explants five days after challenge with IB 793b



²Data on file, Study Report No. 3H16C-08-10-362 (Olot code 120-A2-E-02-10)

a,bsignificant difference between groups (P<0,0001)

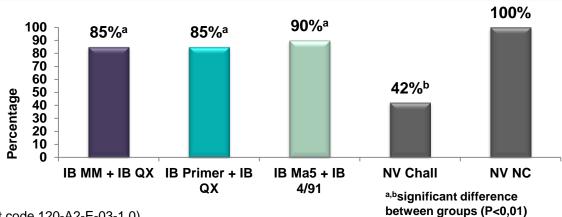
³CROSS PROTECTION TRIAL 2 AGAINST IB793B

Group	Treatment	Vaccination	Challenge D35 10 ^{5.0} EID ₅₀
1	IB MM + IB QX	Day 0 Day 14	IB 793b
2	IB Primer + IB QX	Day 0 Day 14	IB 793b
3	IB Ma5 + IB 4/91	Day 0 Day 14	IB 793b
4	None	-	IB 793b
5	None	-	None

Study conducted at Zoetis VMRD, Olot

Results:

Ciliary activity in tracheal explants five days after challenge with IB 793b



³Data on file, Study Report No. 3911 C-08-1 0-392 (Olot code 120-A2-E-03-1 0)

⁴CROSS PROTECTION TRIAL 2 AGAINST VARIANT 2

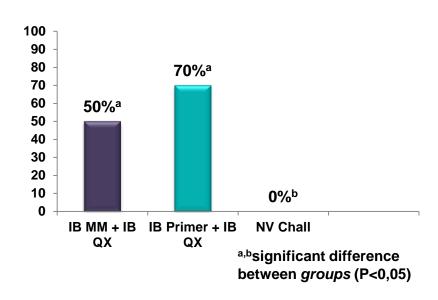
Group	Treatment	Vaccination	Challenge D35 10 ^{4.0} EID ₅₀
1	IB MM + IB QX	Day 0 Day 14	Variant 2
2	IB Primer + IB QX	Day 0 Day 14	Variant 2
3	None	-	Variant 2

Study conducted at the GD Animal Health Centre, Deventer

Results:

Ciliary activity in tracheal explants five days after challenge with variant 2





⁴Data on file, Study Report No Zoetis B815R-NL-13-216

CONCLUSION

- Based on deeper analysis of the IB PCR results from 2011-2014, QX seems to be still by far the predominant field stain isolated, thus focus should be on protection against this strain
 - QX prevalence varies among countries and among years, which is expected for a new strain "invading" the Region, reaching over 80% of isolations in some countries in recent years
 - IBQX is now spreading in new countries where situation is expected to be similar to NL and Germany 5 years ago
- The variant 2 strain is not spreading to Europe yet, but constant monitoring to check for possible further spread of this pathogenic strain is important
- Vaccination programs should be assessed based on risk, meaning not waiting for outbreaks and identification of strains but considering the strains that are circulating around
- Next to full homologous protection against Mass, D274 and IB QX, the combination of IB Primer with IB QX gives strong to very strong cross protection against ItalyO2, IB 793b and Variant 2

zoetis