

Sustainable Performance

AQUAVAC[®]

Vaccine development & Monitoring of field performance of a new PD vaccine in Norway

PD TriNation 2016,
Aberdeen 12th Oct

Ingunn Sommerset



MSD Animal Health



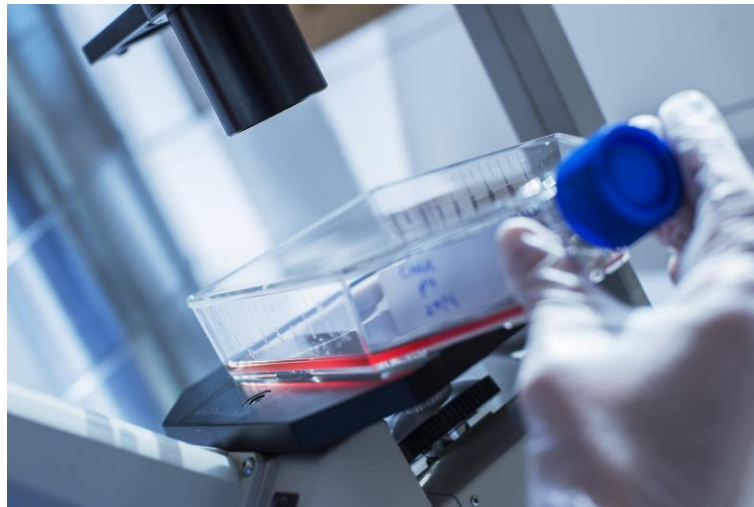
Human Health



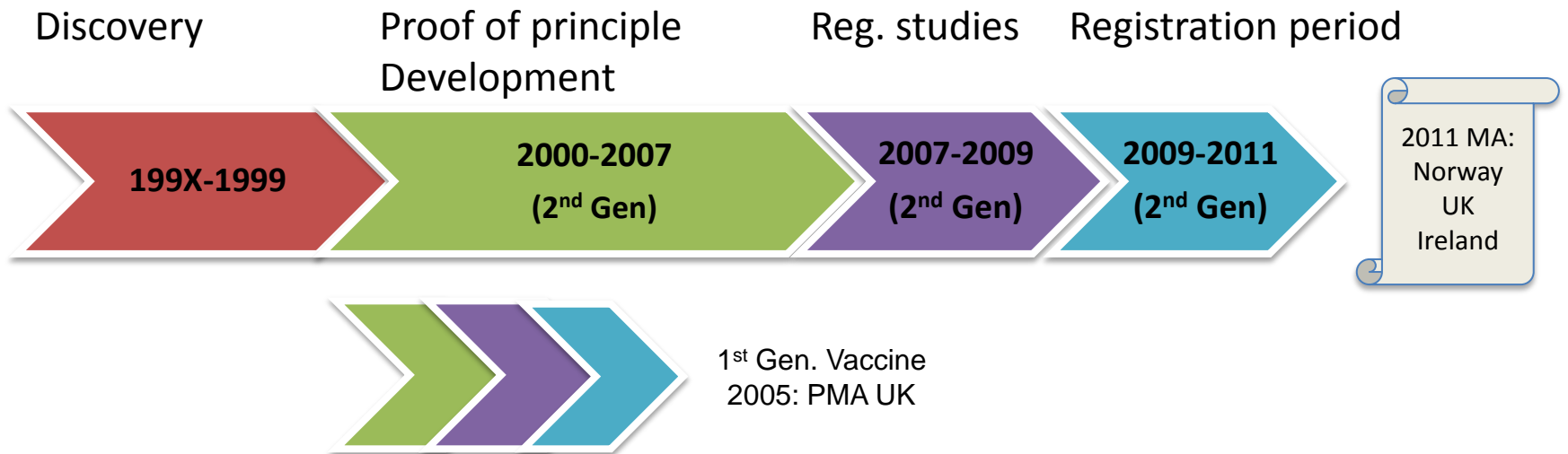
Animal Health



Development of industrial vaccines – different stages

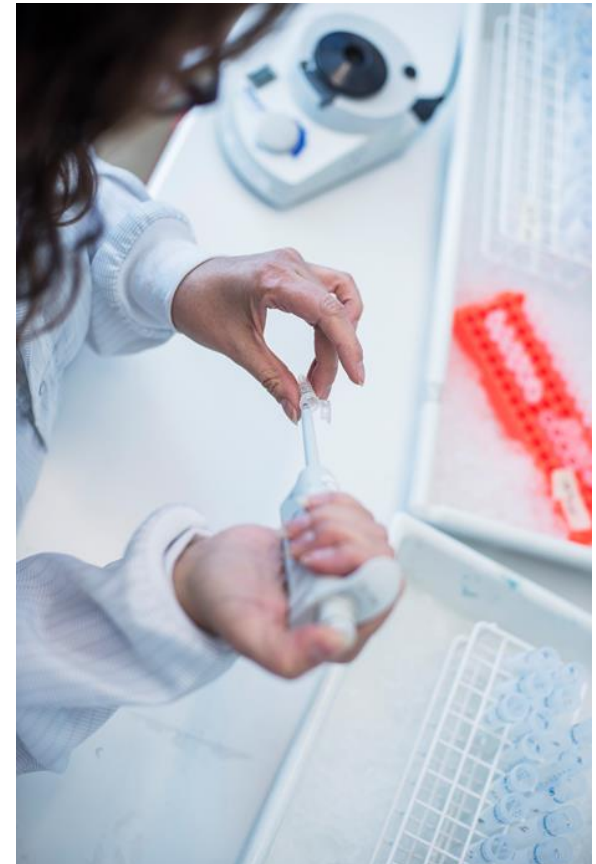


Development first commercial PD vaccine – actual time period



Documentation needed for vaccine market authorization

- **Quality of all components:**
- Active Substance (antigen)
 - Starting material (biological seed): identity, purity and proven free of any contaminants which can cause TSE
 - Production process and in process controls
 - Final antigen: sterility, potency, stability
- Adjuvant, excipients, buffer/solvent, containers, caps etc.
 - Starting material, production process, sterility, storage stability etc.

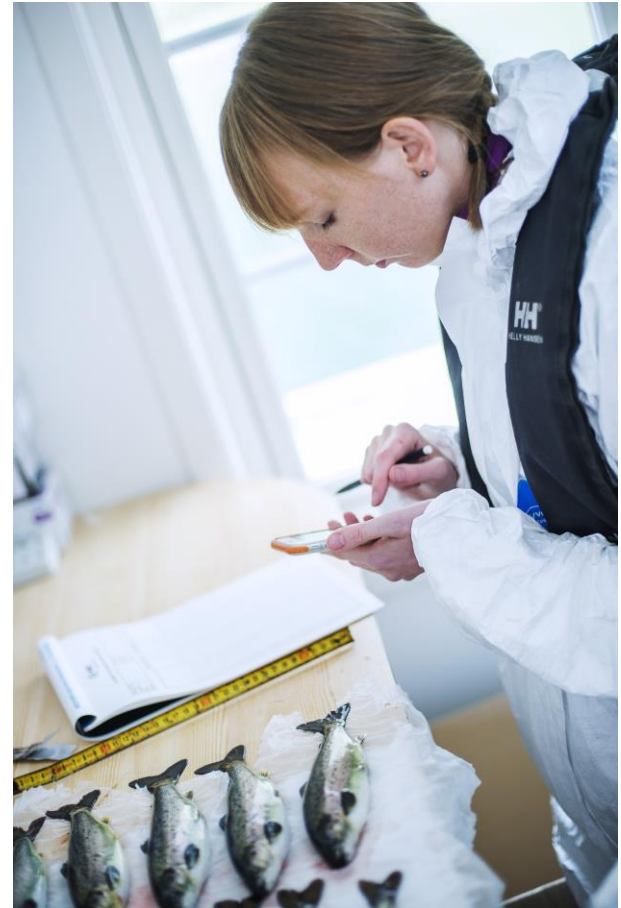


Documentation needed for vaccine market authorization

- **Quality of Final Product** = the vaccine filled in containers (GMP)
 - Production process - formulation and in process controls
 - Final product sterility and physical parameters
 - Final product potency – validated test linked to vaccine efficacy
 - Final product stability

Regulatory standard (GLP/GCP)

- **Safety:** laboratory and field trials
- **Efficacy:** laboratory and field trials
 - Onset of immunity
 - Duration of immunity



Documentation needed for vaccine market authorization

- Challenge with vaccines for salmonides vs. non-fish species:
 - The vaccine must be safe and efficacious under a variety of different field conditions: *temperatures, fish size, fish age, genetic background, smoltification regimes, water quality, management, challenge pressure, pathogen variability etc.*
- Not possible to have all the information ideally needed for a product launch from registration studies e.g. field monitoring study data.

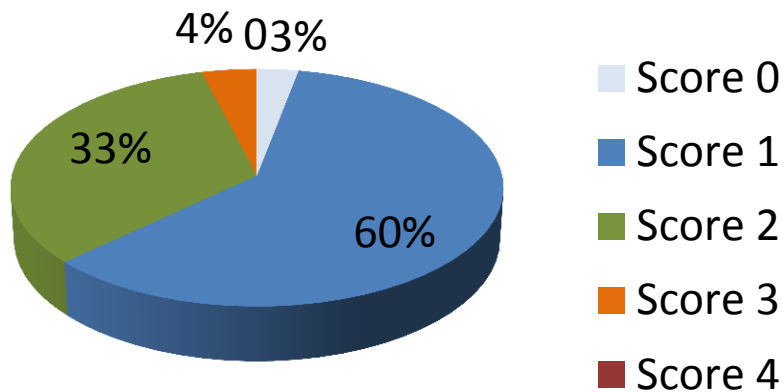
Important to follow up the vaccine AFTER market authorization is granted

Field monitoring of new multivalent PD vaccine

- Aquavac PD7 with Norwegian MA in Feb-2015
- Product launch June 2015 – mainly sold in SAV3 area
- First generation of PD7 vaccinated smolts in sea
 - Autumn smolt 2015 (H15)
 - Spring smolt 2016 (V16)
 - Autumn smolt 2016 (H16)
- Field monitoring through regular pharmacovigilance reporting
- Proactive field monitoring:
 - Vaccination process quality controls
 - Vaccine side effects: sea transfer, mid-production and slaughter visits
 - Vaccine (PD) efficacy: follow up official PD-flags (phone/e-mail) and when possible site visits

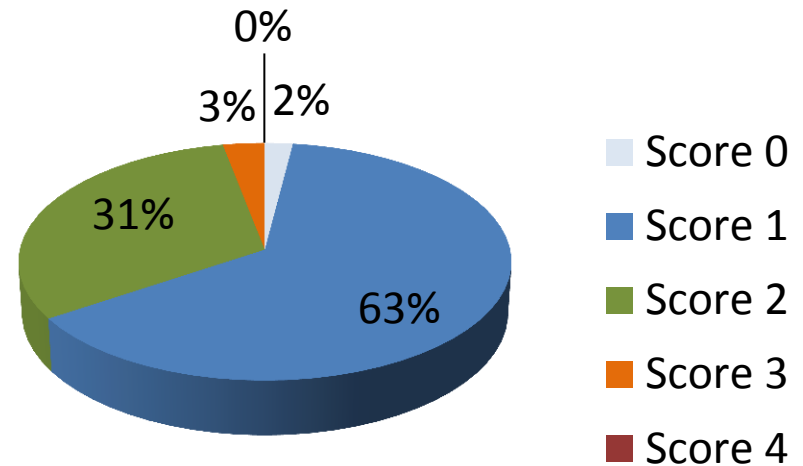
Field monitoring – vaccine side effects autumn 2015 and spring 2016 smolts

Speilberg Scores Sea Transfer Controls



No fish = 1623
No sites = 20
Mean score: **1.39**

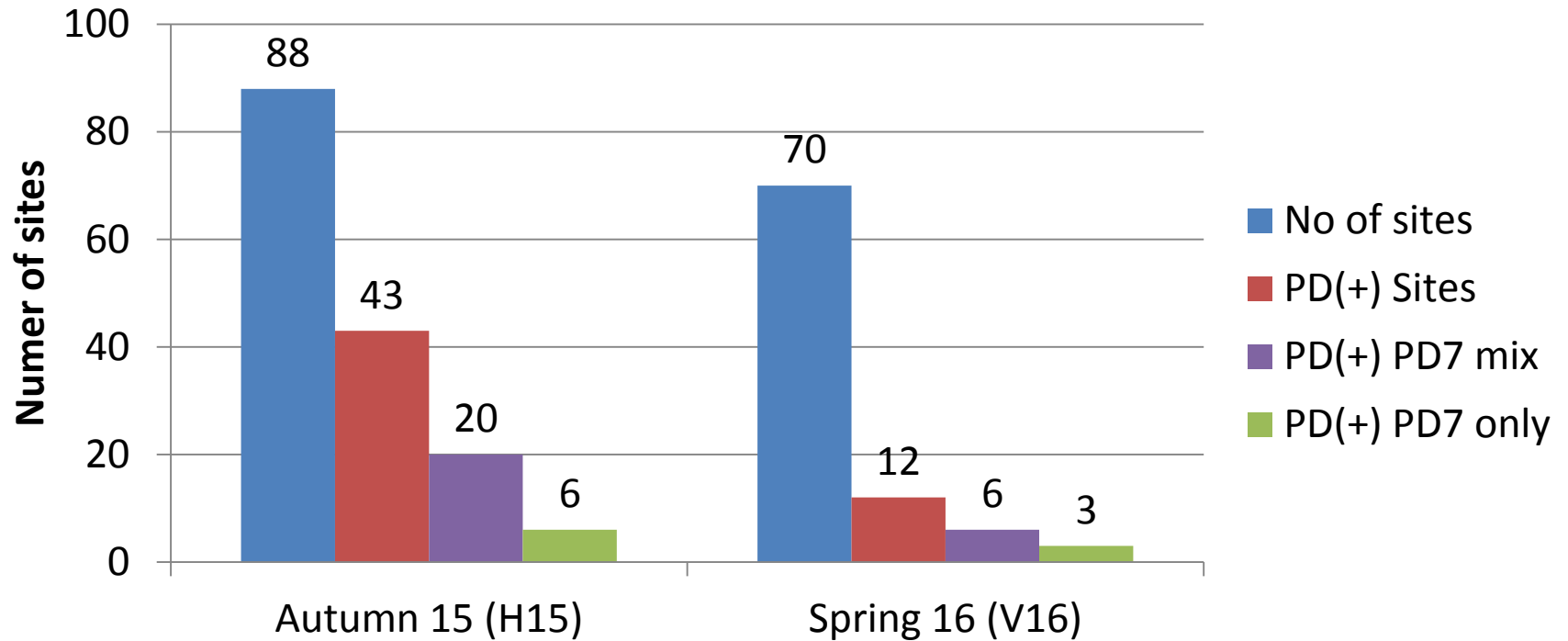
Speilberg Scores Mid. Prod. Controls



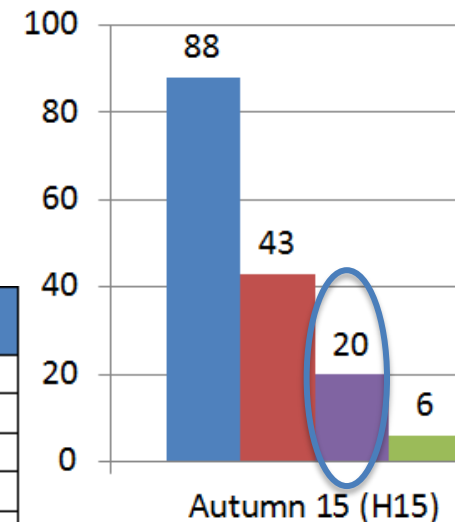
No fish = 1163
No sites = 25
Mean score: **1.35**

PD monitoring of autumn 2015 and spring 2016 smolts

Status 30-Sept 2016: SAV3 sone



PD positive sites with one or more cages containing PD7 vaccinated fish: autumn 2015 smolts



Date PD+	PD7 in all cages	PD7 cages/total cages	Av. PD mort % all cages	PD mort % PD7 cages	Comments	Details
des. 15	no	1/10	7,0	2,2		
apr. 16	no	1/6	6,0	9,4		
mai. 16	no	2/6	3,4	1,2		Case 1
jun. 16	no	10/11	11,0	7,5		
jun. 16	no	2/6	0,5	0,3		
jul. 16	no	1/5	7,6	1,6		
jul. 16	no	3/6	3,3	0,4		
jul. 16	no	2/9			Incomplete info	
jul. 16	no	2/4	7,2	3,5		
aug. 16	no	1/4			No info	
aug. 16	no	5/10	10,3	4,8		Case 2
aug. 16	no	?			One cage with PD7?	
aug. 16	no	5/6			Incomplete info (low mortality)	
mai. 16	yes	7/7	12,3	12,3		Case 3a
mai. 16	yes	5/5	5,6	5,6		
jun. 16	yes	6/6	1,5	1,5		
jul. 16	yes	6/6	3,1	3,1		
jul. 16	yes	6/6			No info	
jul. 16	yes	3/3	1,8	1,8		Case 3b
sep. 16	?	?			Probably PD7? Lack info	

Smolt from same supplier

Case study 1:

PD diagnosis May
2016

				Accumulated until 19.07.16		
Cage	Vaccine	Date Sea Tranf.	Weigth (g)	Total Mort. (%)	PD Mort (%)	SGR
1	CPD + 6way	03.11.2015	80	11,5	1,78	0,89
2	CPD + 6way	03.11.2015	72	8,0	4,25	0,87
3	CPD + 6way	28.10.2015	79	8,4	4,47	0,86
4	CPD + 6way	28.10.2015	77	11,1	7,33	0,89
5	Aquavac PD7	15.09.2015	88	3,0	1,25	0,99
6	Aquavac PD7	15.09.2015	98	3,1	1,13	0,99
			Average	7,5	3,4	

Case study 2:

PD diagnosis Aug-
2016

				Accumulated until 21.09.16		
Cage	Vaccine	Date Sea Tranf.	Weigth (g)	Total Mort. (%)	PD Mort (%)	SGR
1	CPD + 6way	15.09.2015	77	7,2	Mort (%). Pre PD-outbreak 1,6 - 3,5	0,87
2	Aquavac PD7	06.10.2015	93	3,8		0,90
3	Aquavac PD7	06.10.2015	93	3,7		0,89
4	CPD + 6way	11.09.2015	79	9,1		0,91
5	Aquavac PD7	06.10.2015	83	3,8		0,92
6	Aquavac PD7	06.10.2015	83	5,9		0,92
7	CPD + 6way	15.09.2015	78	21,0		0,86
8	Aquavac PD7	15.09.2015	74	6,6		0,95
9	CPD + 6way	15.09.2015	74	18,2		0,91
10	CPD + 6way	11.09.2015	77	21,8		0,83
				Average mort (%)		11,6
				Average PD7 cages (%)		4,8
				Average other cages (%)		15,8

Case Study 3a and 3b:

PD May-16. Two subsequent lice treatments shortly after PD diagnosis and gill problems

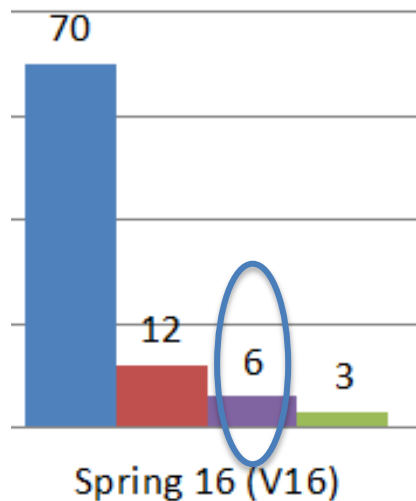
Cage	Vaccine	Date Sea Tranf.	Weigth (g)	Accumulated until 18.07.16		SGR
				Total Mort. (%)	PD Mort (%)	
1	Aquavac PD7	26.09.2015	92	10,1	8,3	1,08
2	Aquavac PD7	26.09.2015	94	16,8	15,1	1,04
3	Aquavac PD7	26.09.2015	90	12,9	10,9	1,01
4	Aquavac PD7	26.09.2015	97	14,5	12,8	1,01
5	Aquavac PD7	26.09.2015	90	15,0	13,0	1,00
6	Aquavac PD7	30.10.2015	138	16,3	14,8	0,85
7	Aquavac PD7	30.10.2015	150	13,5	11,5	0,81
			Average	14,2	12,3	0,97

PD diagnosis July-16.

Cage	Vaccine	Date Sea Tranf.	Weigth (g)	Accumulated until 11.09.16		SGR
				Total Mort. (%)	PD Mort (%)	
1	Aquavac PD7	31.10.2015	82	4,8	1,2	0,98
2	Aquavac PD7	31.10.2015	82	5,6	2,4	1,03
3	Aquavac PD7	30.10.2015	105	3,0	1,8	0,97
			Average	4,3	1,8	0,99

Same smolt supplier/transport

PD positive sites with one or more cages containing PD7 vaccinated fish: spring 2016 smolts



Date PD+	PD7 in all cages	PD7 cages/total cages	Av. PD mortality % Total	Comments
jul. 16	no	1/6	no info	Mild outbreak
jul. 16	no	9/10	no info	Mild outbreak
jul. 16	no	1/5	no info	Mild outbreak
aug. 16	yes	3/3	no info	One cage w. many runts
aug. 16	yes	8/8	no info	SAV2 Low mort.
sep. 16	yes	6/6	no info	SAV2 Low mort.

Summary

- Development and market authorization of new salmon vaccines takes 4 – 10 years, and for difficult pathogens even longer...
- High variability of environmental, biological and management practices in salmon farming -> Need to follow up new products after market authorization
- Status of 1st year of PD monitoring of Aquavac PD7 in SAV3 zone
 - Total 55 PD positive sites – 26 sites with PD7 in one or more cages
 - Autumn 2015 smolts: PD7 performs better than previous PD-vaccination regime at 8 out of 13 sites (4 of 13 unknown, 1 of 13 worse)
 - Approx. 50% of total mortality in PD positive sites is assigned to PD
- Problem with field monitoring under commercial settings: different level of time and/or willingness in sharing mortality data
- *Need of a new, independent, large scale cohort study to evaluate the effect of PD vaccination?*

Acknowledgements

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