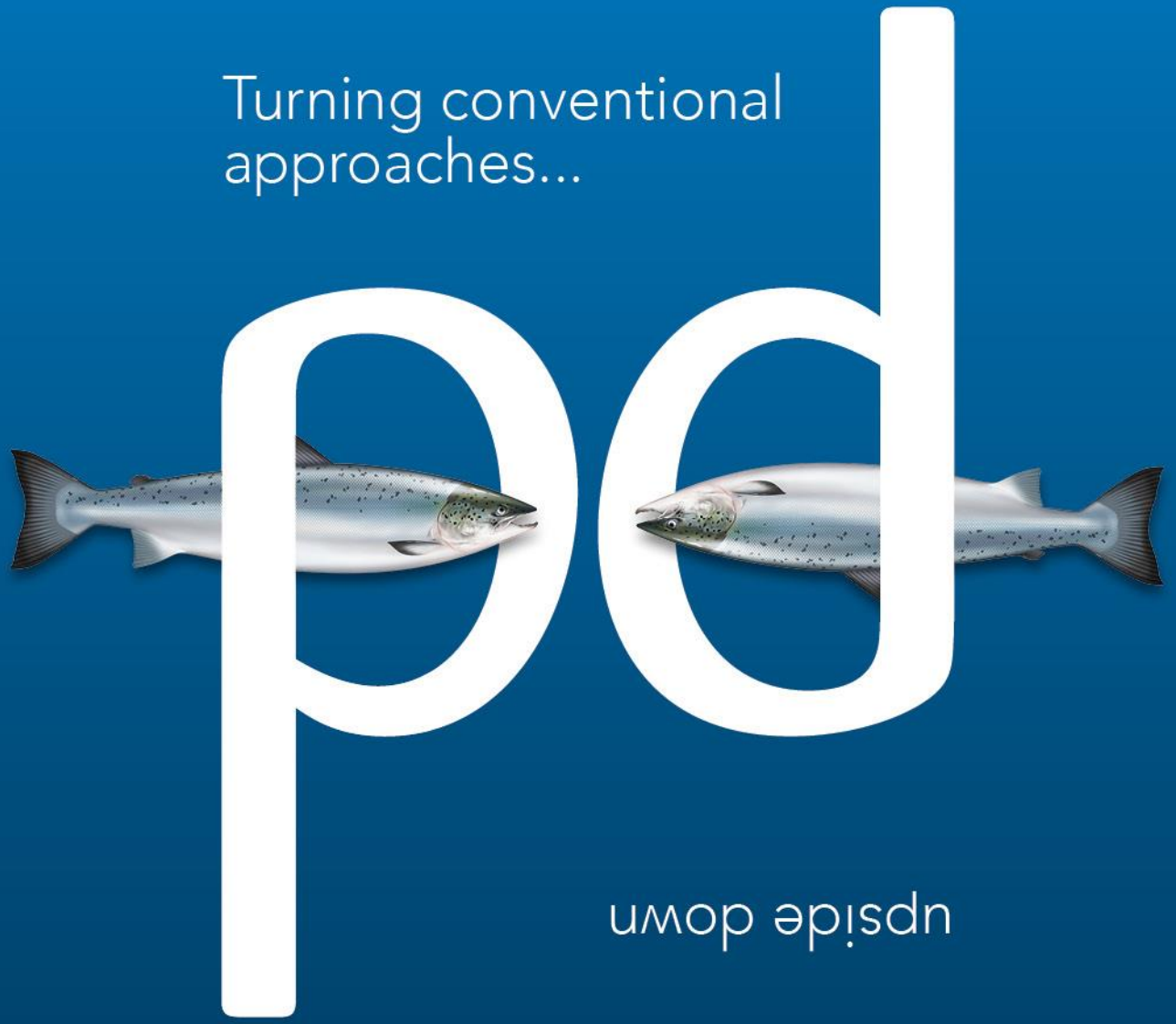
Elanco

Turning conventional approaches...



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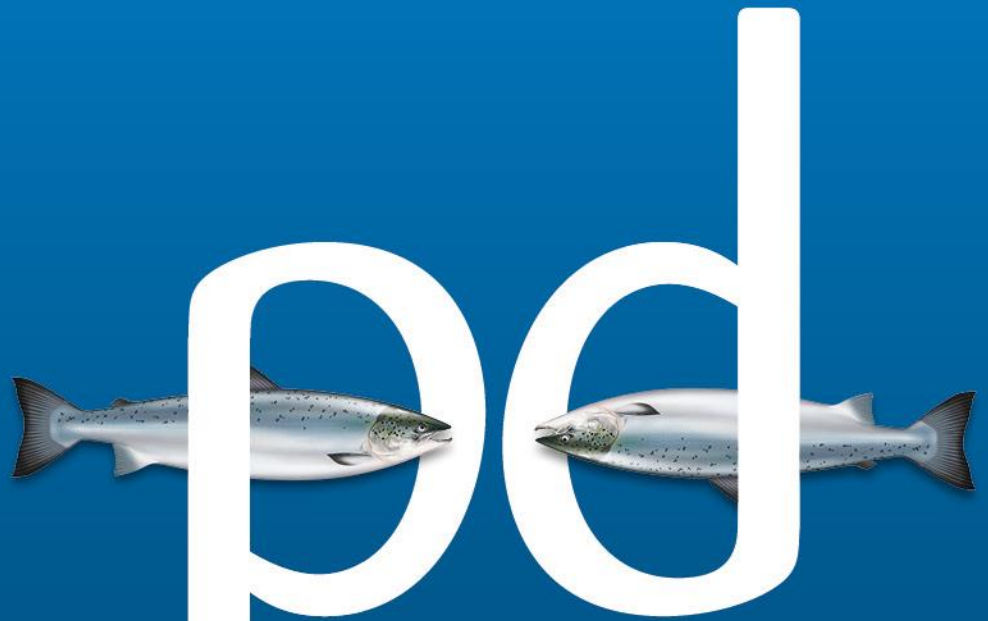


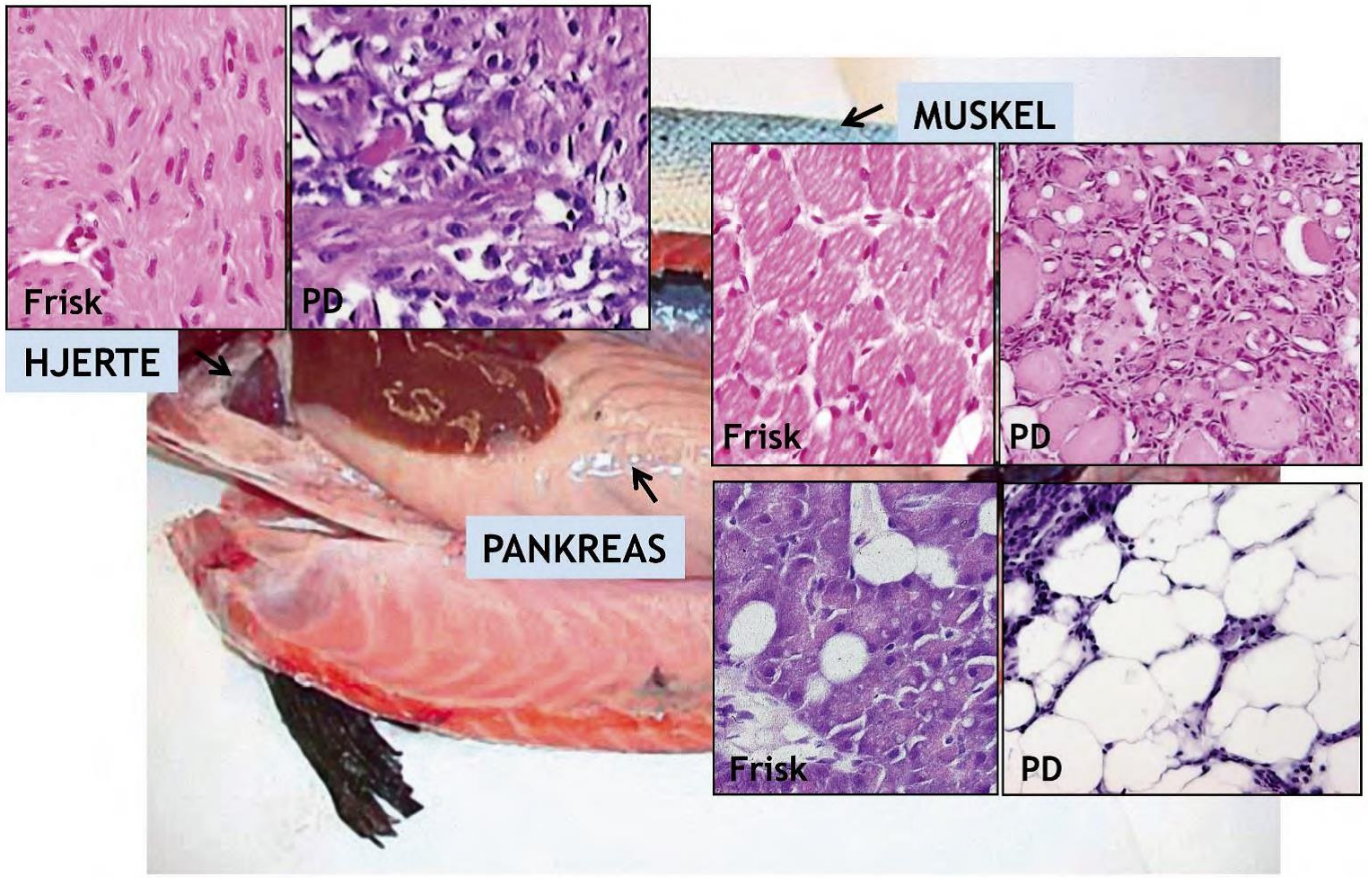
SAV3 challenge model optimization for testing DNA vaccine duration of immunity and safety, and efficacy results from comparative studies

Pancreas Disease (PD) cohabitation model optimization

- Elanco Animal Health has developed CLYNAV, a DNA vaccine for Pancreas Disease (PD) in Atlantic salmon
- Need to show relevant clinical end points in time frame that covers field exposure
- This means being able to hold fish and challenge them at 6-12 months post vaccination
- Challenge parameters ~35 kg/m^3, 14 ºC with 40% vaccinates, 40% controls, 20% Trojans worked for 1 and 3 month studies

Page 38 Norwegian Fish Health Report 2016

- Illustration by Anne Berit Olsen



Model – desired clinical observations

- Fecal cast production
- Reduced feed intake
- Pancreas destruction
- Heart damage and recovery
- Skeletal muscle damage
- Impaired weight gain
- Slinkiness – thin fish

- Mortality in small Saline control fish, but reduced as they grow large with time in salt water (SW)
- Mortality in Trojans

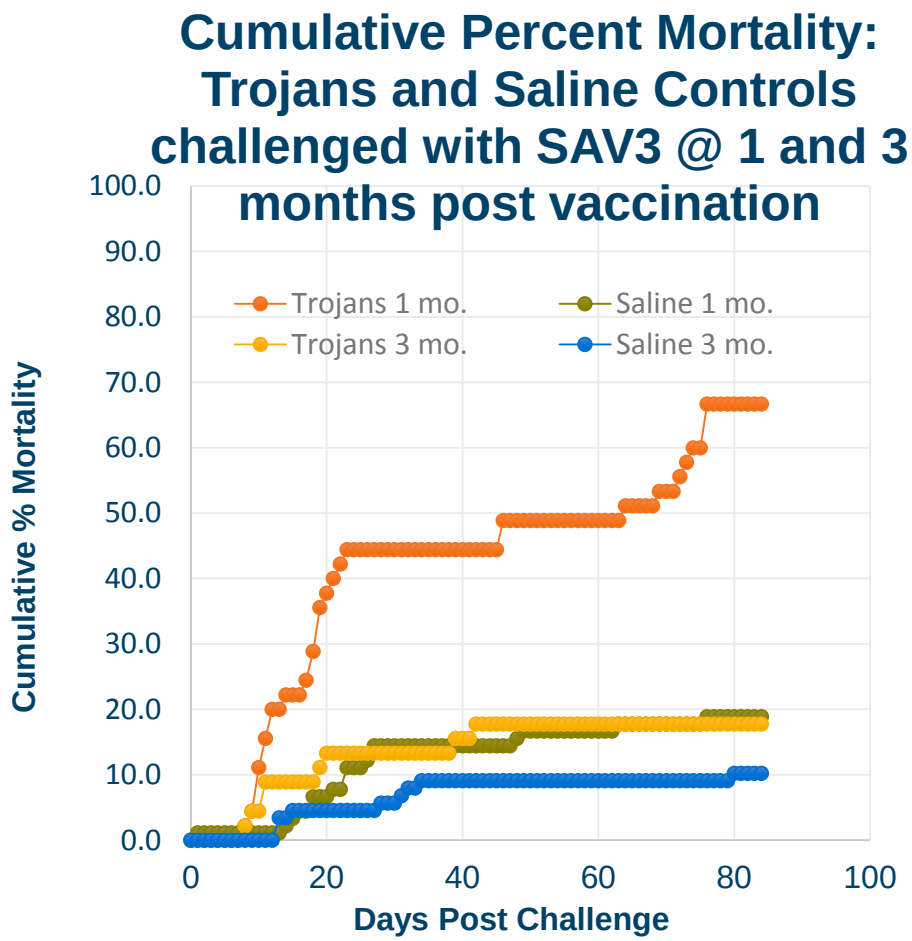
Trojan

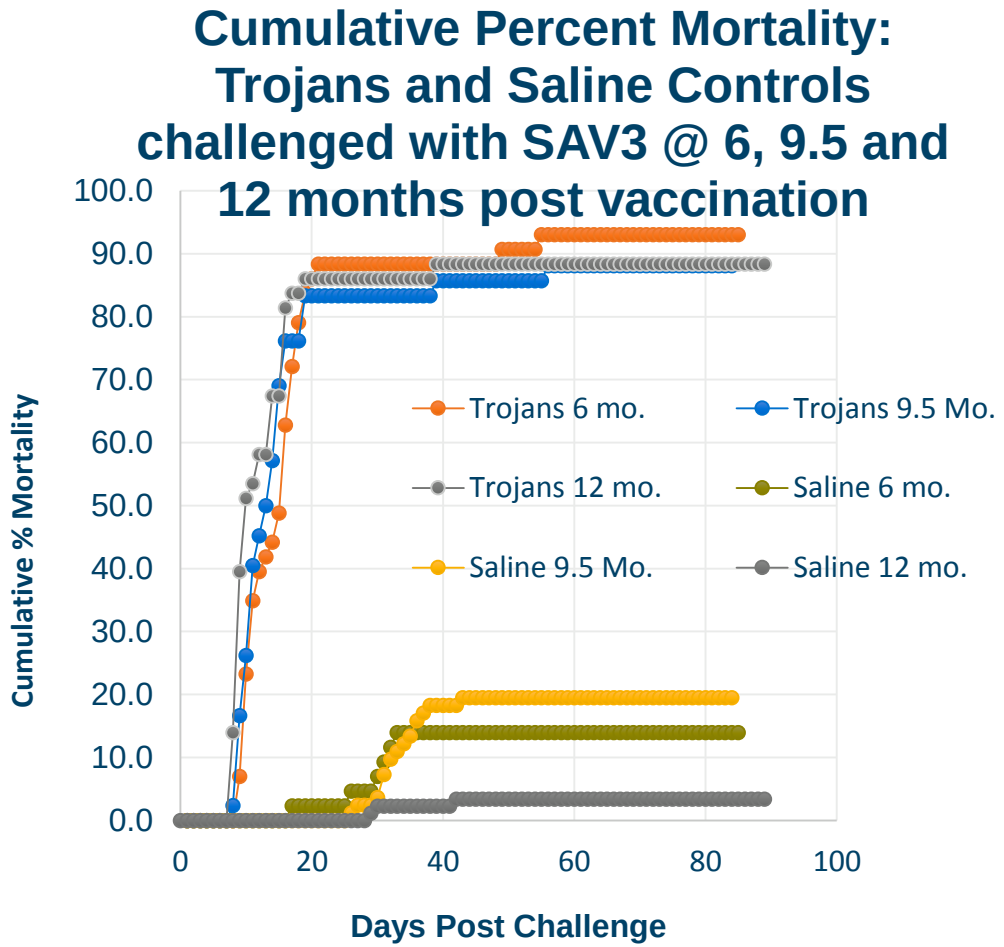
- Constrained by tank size – want good growing conditions without sacrificing challenge severity
- If fish at 4 weeks in SW shed more than 9 weeks
- What about at 0 weeks?
- Use freshly smolted, smallest size possible and SW worthy by chloride testing
- Used same percentage = 20%

Trojan

	6 month challenge	9.5 month challenge	12 month challenge
Trojan size at challenge	50 g	39 g	57 g
Size TX / Controls	246 g	488 g	904 g
% of pop	20%	20%	20%
% Biomass	4%	1.6%	1.3%
Temperature °C	13.5	14.1	14.4
Salinity ppt	32	31.2	32.1

Trojan and Saline mortality kinetics





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Clinical signs and gross pathology of PD

	6 Month DPC (1Tank)	9.5 Month DPC (3Tanks)	12 Month DPC (3Tanks)
• Loss of appetite	10-48	12-15 to 45-46	12-14 to 39-41
• Faecal casts	6-55	9-14 to end	3-6 to end
• Surface swimming	9-10	9-12 to 11-13	8 and 31
• Resting on bottom	27-58	9 to 35 / 72	9/ 21-37 to 37-51
• Loss of body condition	54, 85	22, 55, 84	54, 89
• Gross pathological signs	21, 54, 85	22, 55, 84	19, 54, 89


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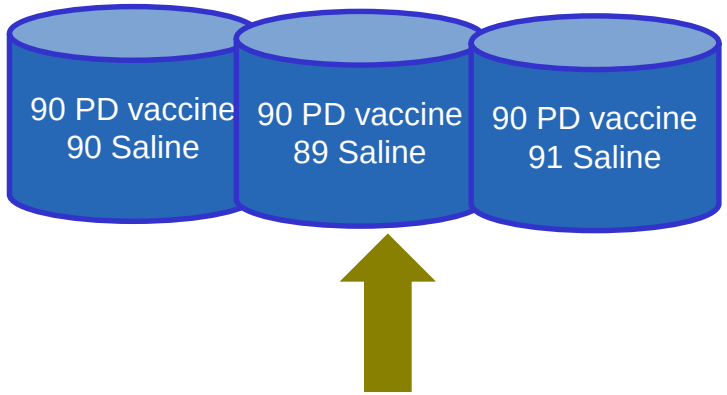
Vaccination & 6 month DOI



S1 21 ± 2 DPC	S2 52 ± 2 DPC	S3 84 ± 5d DPC
Weights	Weights	Weights
Heart, pancreas, R&W muscle	Heart, pancreas, R&W muscle	Heart, pancreas, R&W muscle
Mortality	Mortality	Mortality

* Newly smolted fish ~ 50 g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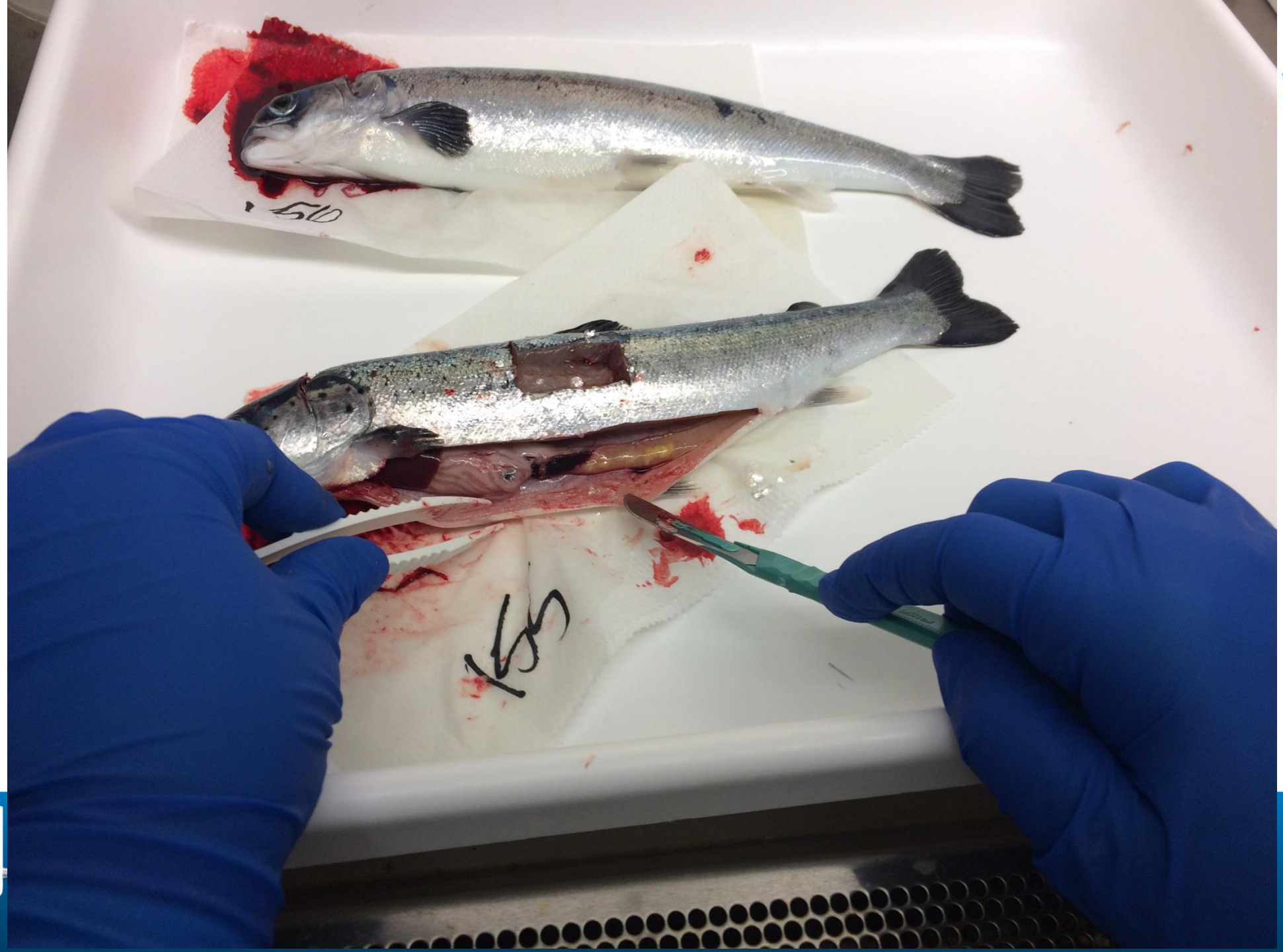
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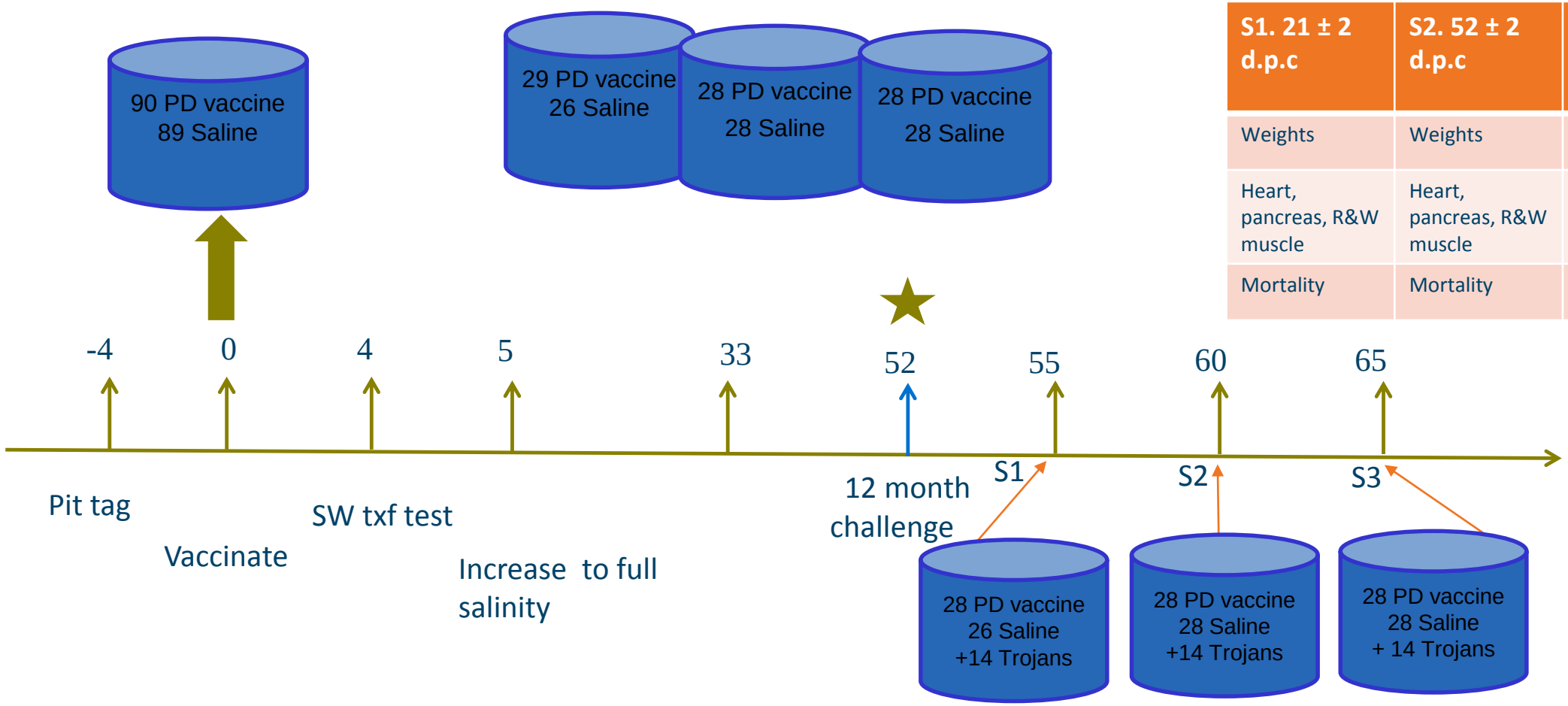
Vaccination & 12 month DOI



S1. 21 ± 2 d.p.c	S2. 52 ± 2 d.p.c	S3. 84 ± 5d d.p.c
Weights	Weights	Weights
Heart, pancreas, R&W muscle	Heart, pancreas, R&W muscle	Heart, pancreas, R&W muscle
Mortality	Mortality	Mortality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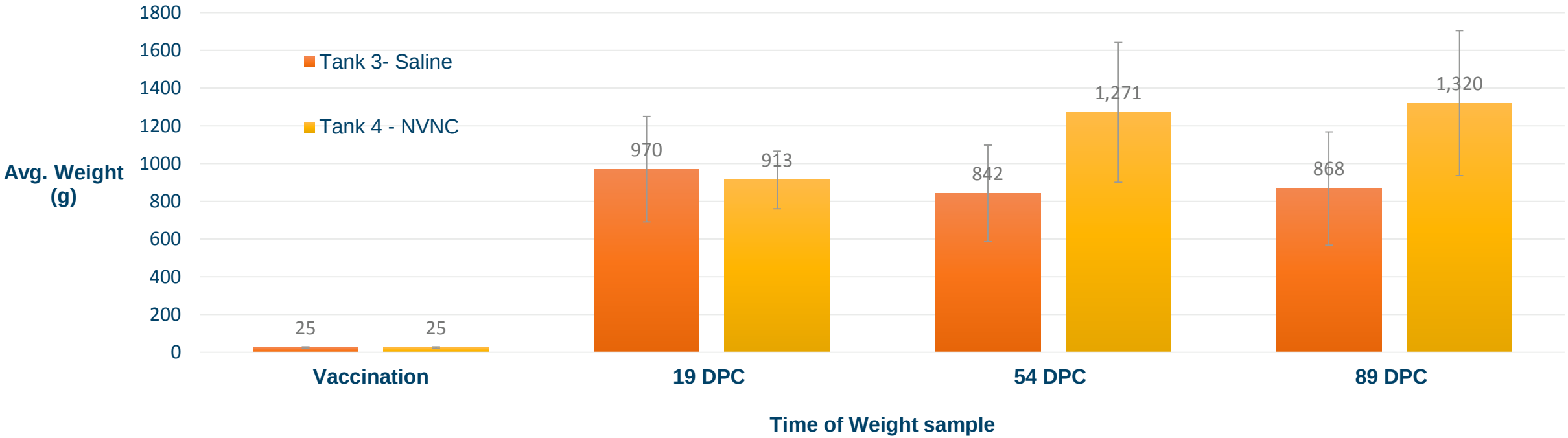
Weights – 12 Month Challenge

Average weight at Vaccination & 19,54 & 89 DPC with SAV3 Saline vs. Not Vaccinated Not Challenged group

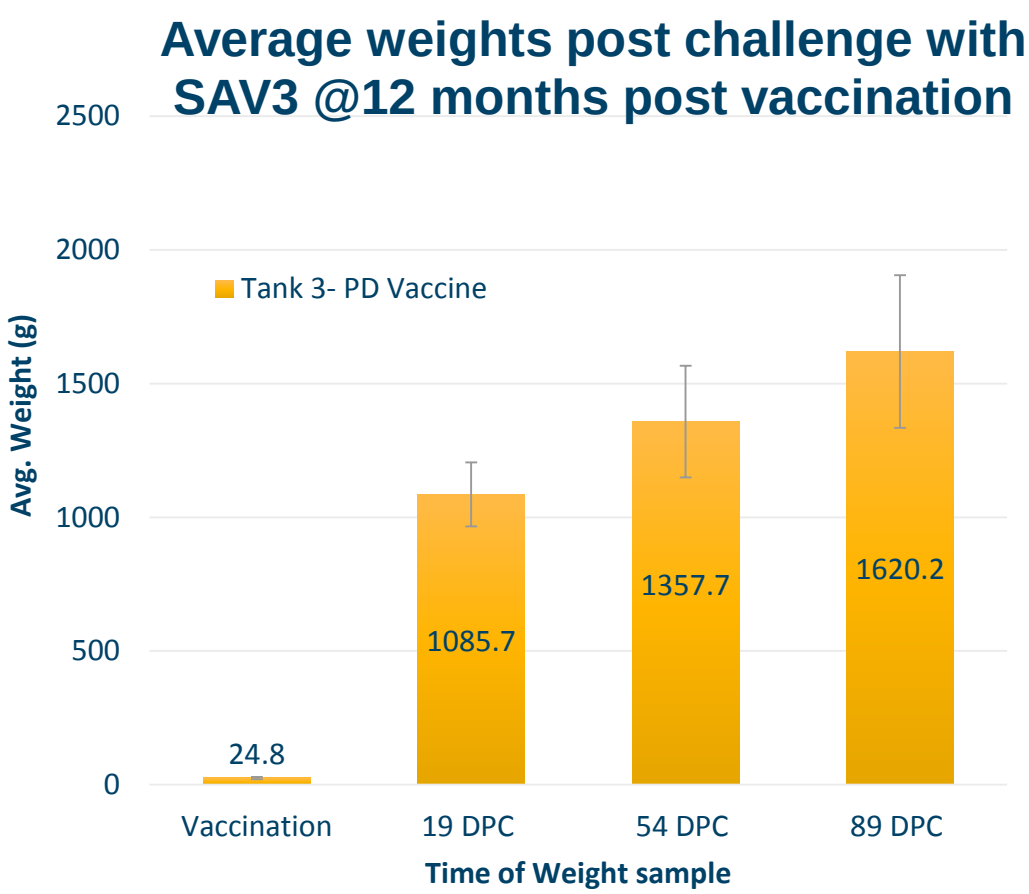


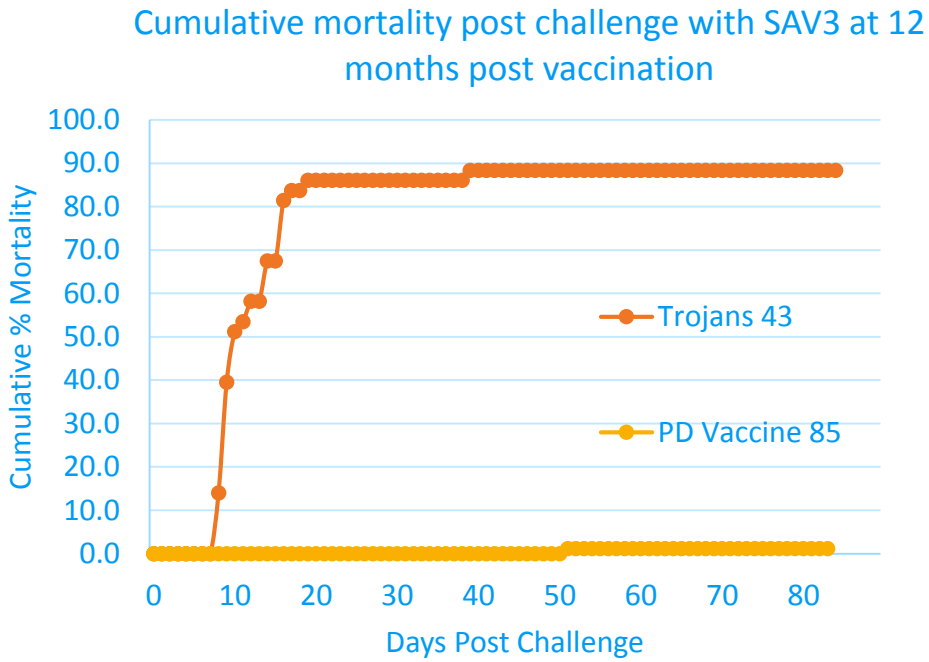
Analysis

- Histo raw scores
- Index
- Comparison to NVNC
- Comparability across challenges
- Weight change
- Survival analysis

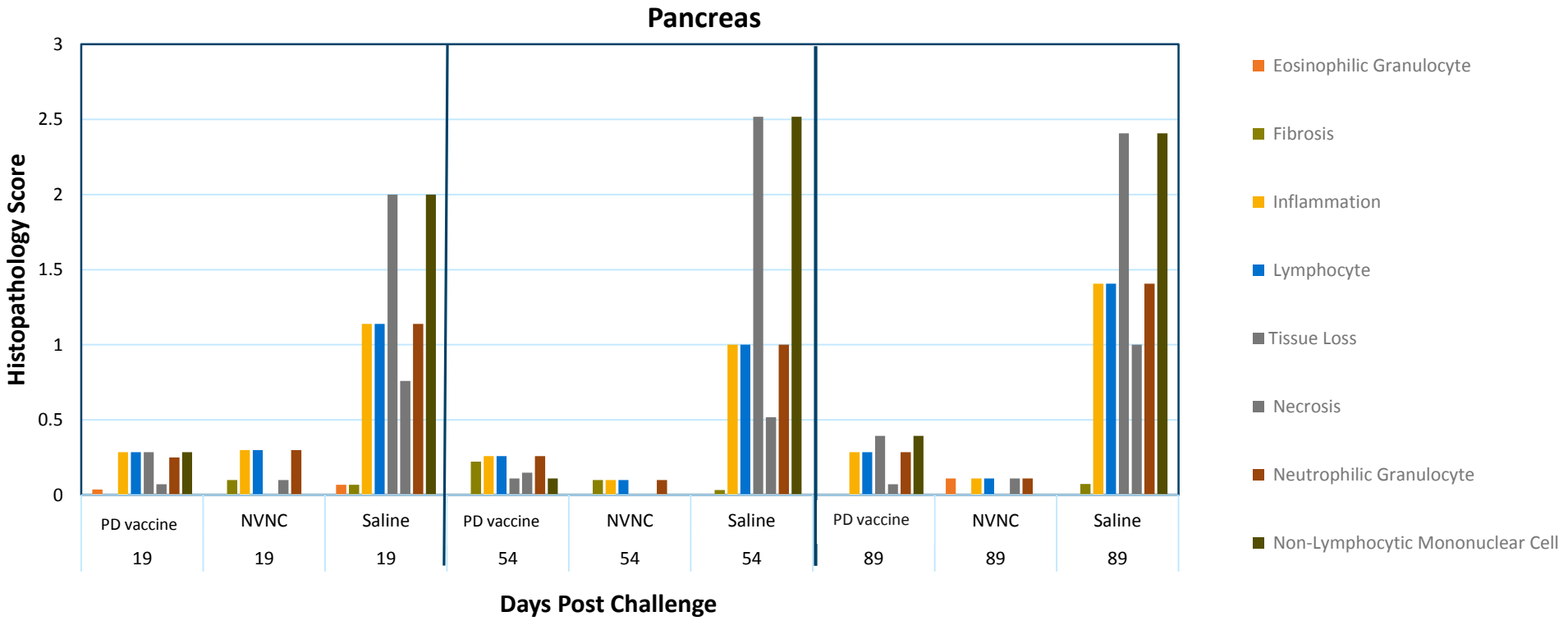
Testing of the Model

12 month DOI of a PD Vaccine: weights and mortality





Pancreas histopathology at 12 Month Challenge



Optimized Trojan cohabitation model

- Ensures consistency of challenge in fish ranging from 50 g to 1 Kg in Saltwater
- Provides predictable, consistent behavioural changes, gross lesions and pathology in target organs (heart, pancreas and skeletal muscle) – most notably the destruction of pancreatic tissue
- Demonstrates the clinical weight loss in non-protected fish in a relevant time frame