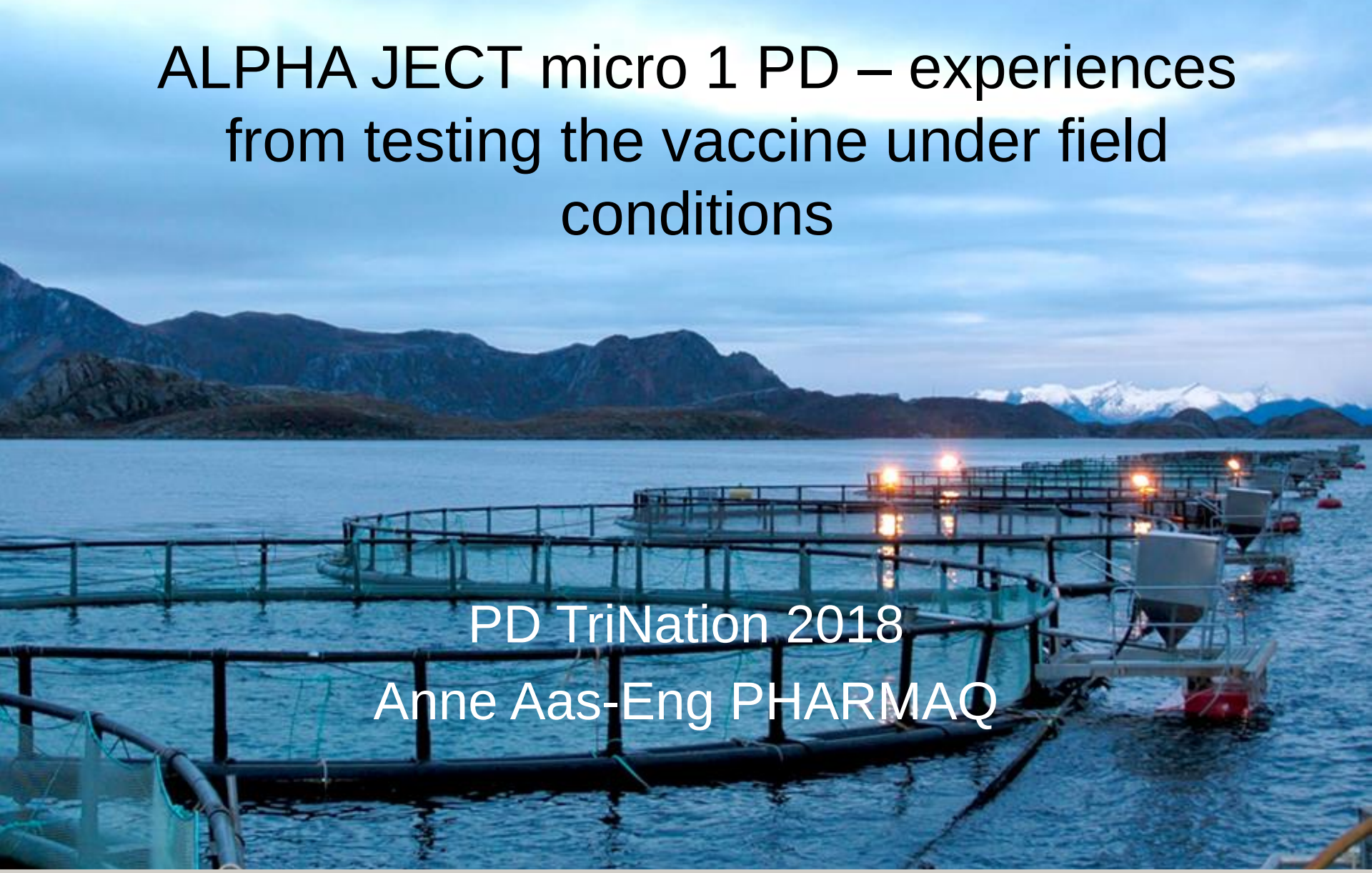
ALPHA JECT micro 1 PD – experiences from testing the vaccine under field conditions



PD TriNation 2018

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ALPHA JECT micro 1 PD

- Monovalent PD vaccine based on inactivated strain of SAV 3
- Dose-volume: 0.05 ml
- Documented for simultaneous administration with ALPHA JECT micro 6
- Marketing authorisation obtained in Norway, UK and Ireland in 2015
- Launched for sale spring 2017

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Commercial scale field trials

- Purpose: Document safety and efficacy after vaccination under commercial scale conditions
- Mandatory as part of documentation to obtain marketing authorisation for the vaccine
- The fish are followed from vaccination to slaughter and trials are conducted according to Good Clinical Practice (GCP)
- Parameters investigated:
  - Safety: Acute toxicity, local reactions (adherences, melanin), growth
  - Efficacy: Differences in survival between test- and control group during outbreaks of PD
- Two trials were conducted:
  - FT-1 (August 2008 - autumn 2010)
  - FT-2 (November 2010 – spring 2013)

Critera for field trial locations

Fish

- Same strain and origin
- Average weight at vaccination >35g and comparative groups should be as equal in weight as possible
- Not previously vaccinated
- Known and documented disease history
- Disease free the last month before vaccination

Location

- Within endemic zone for PD
- Minimum 4 seawater cages (cage-to cage design) or 2-3 cages (mixed-cage design) should be available for the trial
- Equal size of tanks and cages
- Approximately equal number of fish per tank and cage
- Investigator (fish health biologist/veterinarian)

FT-2: November 2010 – spring 2013

Test group:

ALPHA JECT micro 1 PD + ALPHA JECT micro 6 (or Norvax Minova 6)

Simultaneous injection - 0.05 ml + 0.05 ml (0.1 ml)

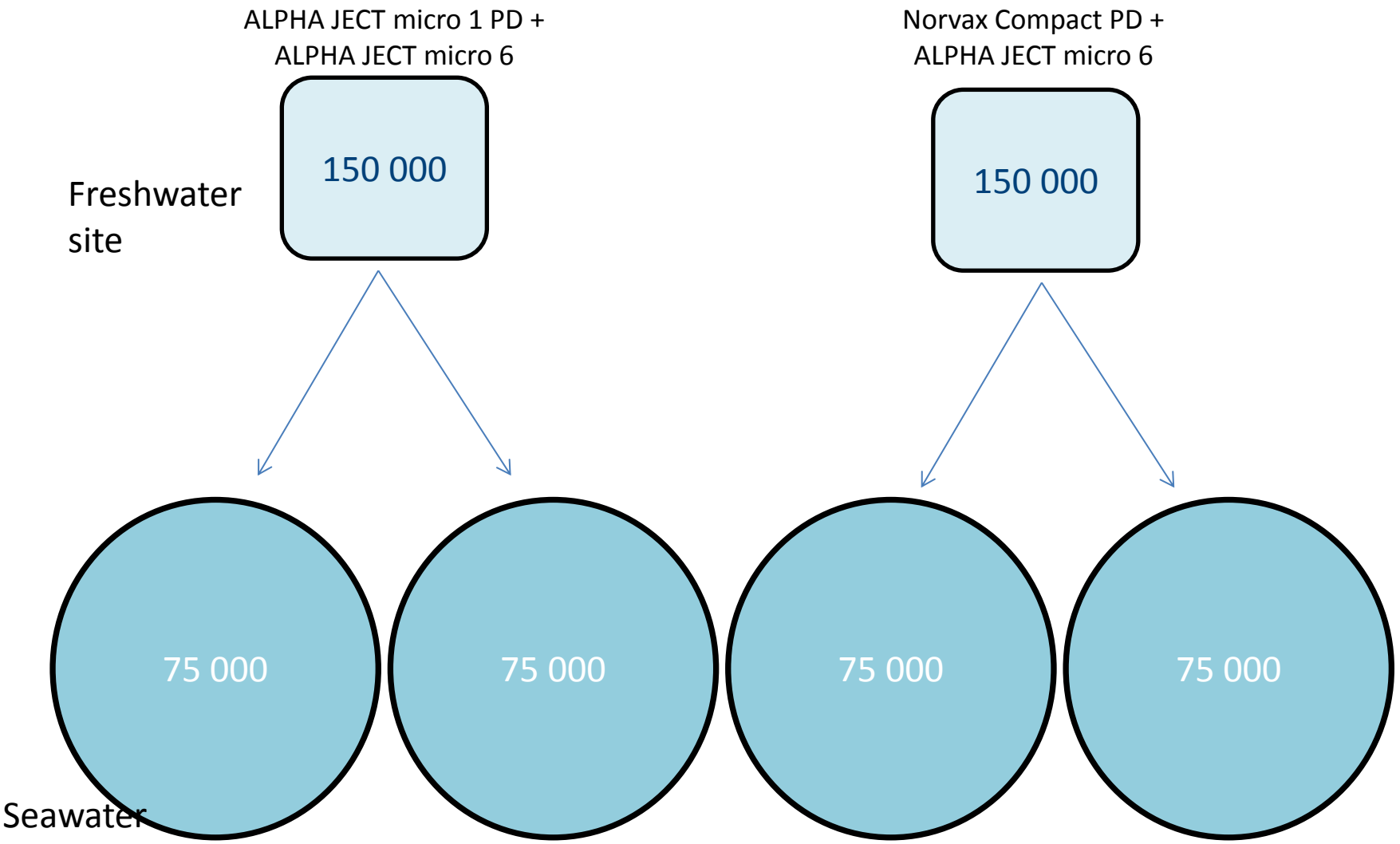
Control group:

Norvax Compact PD + ALPHA JECT micro 6 (or Norvax Minova 6)

≥230 degree-days between injections - 0.1ml + 0.05 (0.1 ml)

- 17 locations in SAV3 area
- Number of locations optimised based on estimations from the Norwegian Veterinary Institute in order to secure valid efficacy data
  - Locations with cage-to-cage design (≥ 4 cages)
  - Locations with mixed groups in each cage (2-3 cages)

Cage-to-cage design



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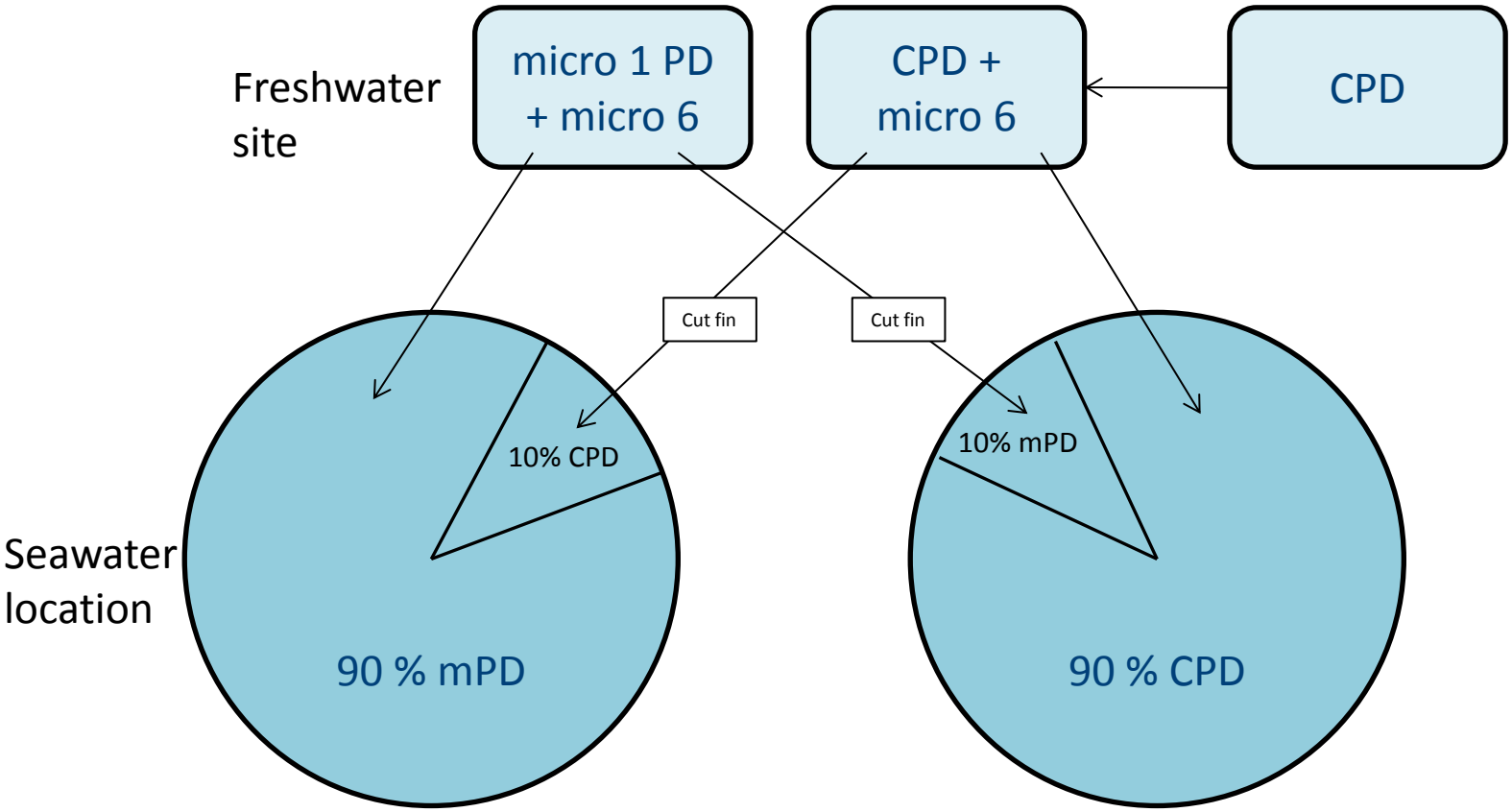
Mixed cage design

- Minimum 10% of the fish marked by removal of adipose fin
- ”Reverse” distribution fordeling i merdene



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Detections and clinical outbreaks

- SAV was detected at 11 of the 17 locations during the trial
  - One SAV2 detection, the remaining were SAV3
- Clinical outbreaks of PD were confirmed at six locations
  - Only data from three of these were valid
- Three of the outbreaks did not generate valid data
  - Protocol deviations caused by under- or over dosing of vaccines, prior vaccination, prior disease history, different origin of fish.
  - Violation of group integrity by splitting, sorting and/or mixing of fish groups
  - Mortality data from outbreaks in these groups had to be excluded form the analysis.

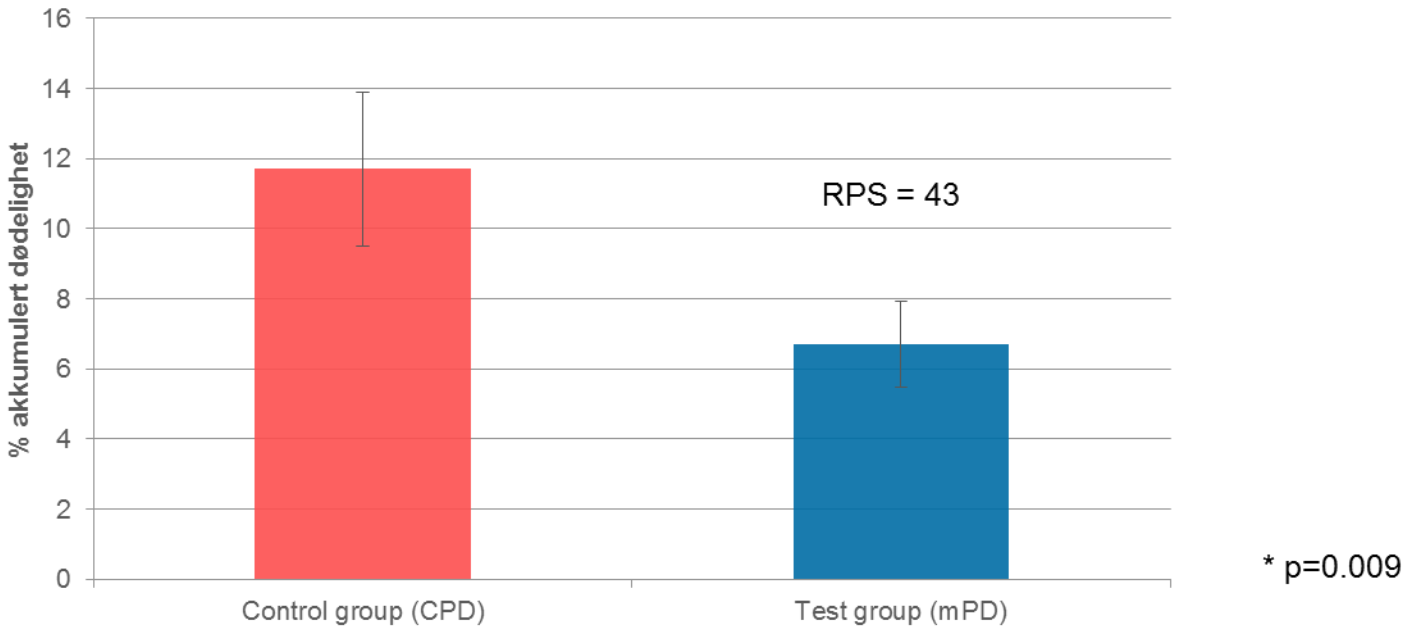
Statistical analysis of mortality data

- An overall statistical analysis of the mortality data collected during the outbreaks was conducted by Dr. Anja Kristoffersen and Dr. Peder Jansen at The Norwegian Veterinary Institute.

- The analysis included number of mortalities from PD outbreaks in 7 cages with mixed groups from the three approved locations shown.

- «Mixed effect model» was used in combination with varians analysis (Anova).

Statistical analysis of field efficacy



Mean accumulated mortality during outbreaks of PD were reduced to almost the half in the test groups (6.7%) compared to the control groups (11.7%) The difference between the vaccines were significant (p=0.009) with a 95% confidence interval from 1.9 to 8.1.

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Summary

- To obtain valid data from GCP field trials in commercial scale is demanding.
  - Operational considerations made by owners i.e. moving, sorting, mixing of groups and slaughter may compromise the results
  - Interfering infections often occur and hampers interpretation of results
- Mixed cage designs are preferable
  - Secures that test and control groups are exposed to the same conditions
  - Only data from mixed cage locations generated valid data in our field trial
- Fish co-vaccinated with ALPHA JECT micro 1 PD and ALPHA JECT micro 6 had a significantly higher survival rate compared to the control group during natural outbreaks of PD.
- Duration of protection under field conditions was documented up to 15 months after the fish are transferred to seawater based on results from UIK 15.2.

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