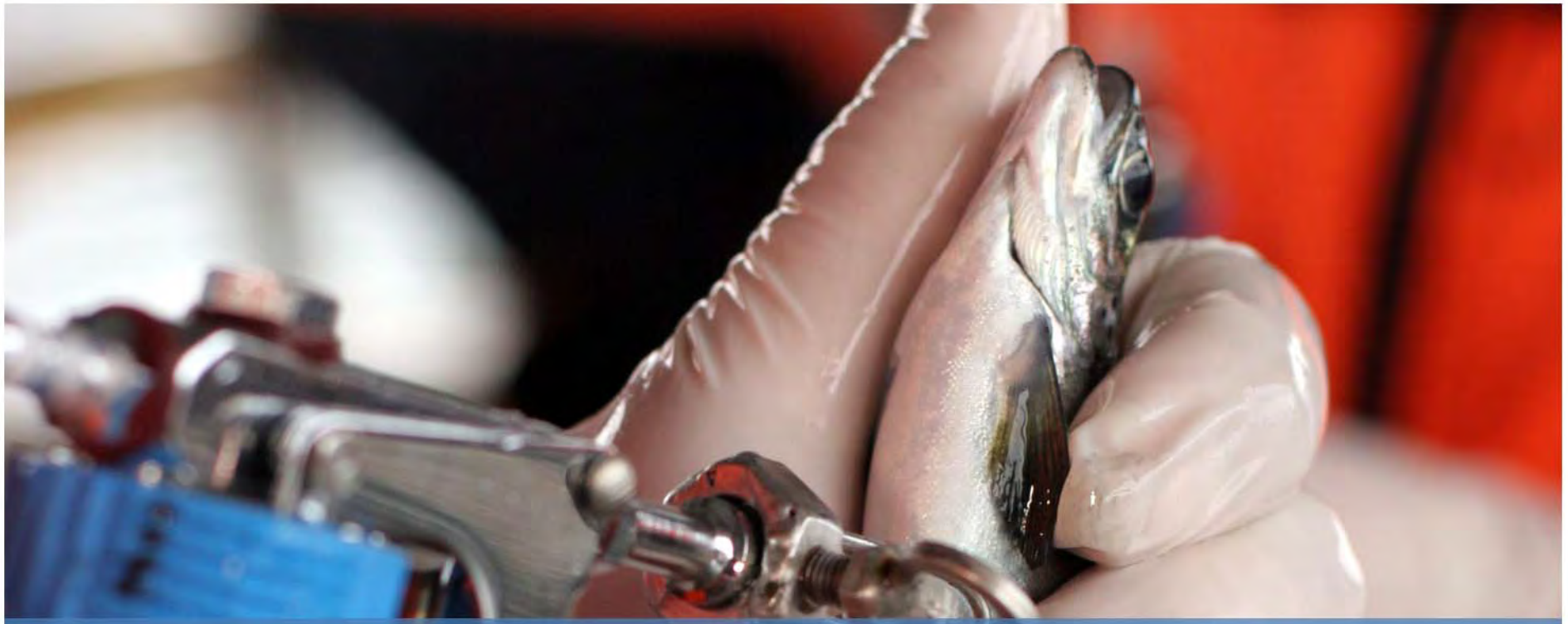

Vaccination with efficacious vaccines, a health tool in Tilapia

Conference Rio de Janeiro 18.09.2013

Edel Anne Norderhus, Director Product Development, R&D PHARMAQ

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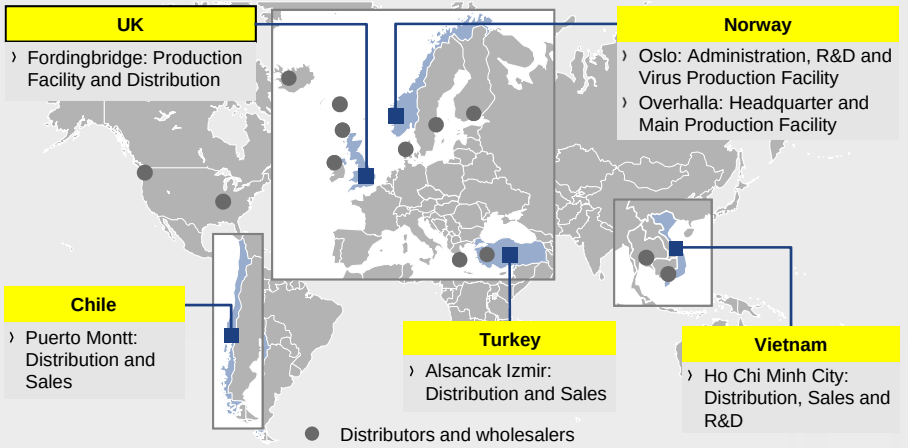
PHARMAQ: Company Overview

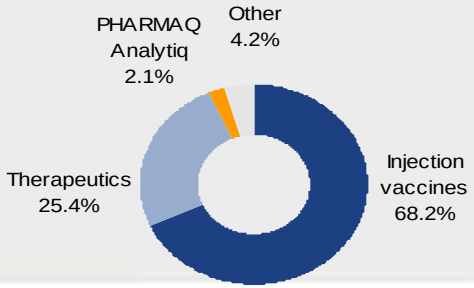
Business Description

- A leading global Aquatic Animal Health company, specialising in vaccines and therapeutics.
- The only global pharmaceutical company with core focus on aquaculture, fish health
- Established in 2004 as an independent company based on more than 25 years of R&D into aquatic health by Alpharma
- Based in Norway, with manufacturing and R&D facilities , and international subsidiaries in Chile, the UK, Vietnam and Turkey
- Strong market share in high growth market
- April 2013 Permira, a global European private equity fund acquired Pharmaq

Principal Locations



Sales split Product Type

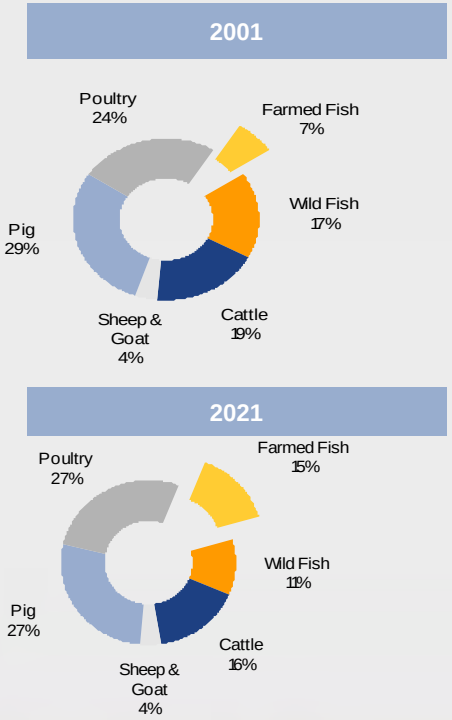


Source: PHARMAQ

Aquaculture is the Fastest Growing Source of Edible Protein Globally

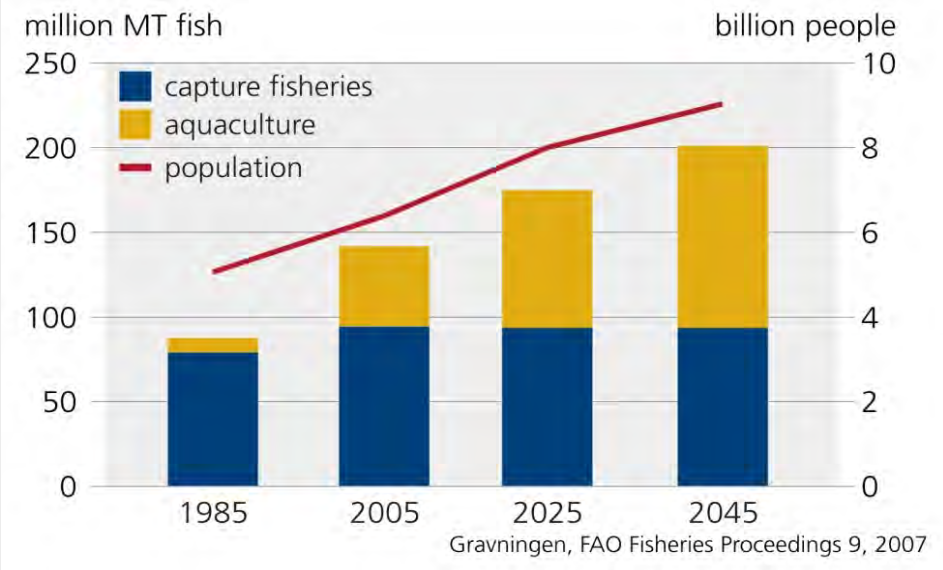
Farmed Fish as Percentage of Total Global Meat Consumption[2]

- ✓ Farmed fish predicted to represent 15% of global meat consumption by 2021 (compared to 7% in 2001)[(2)]



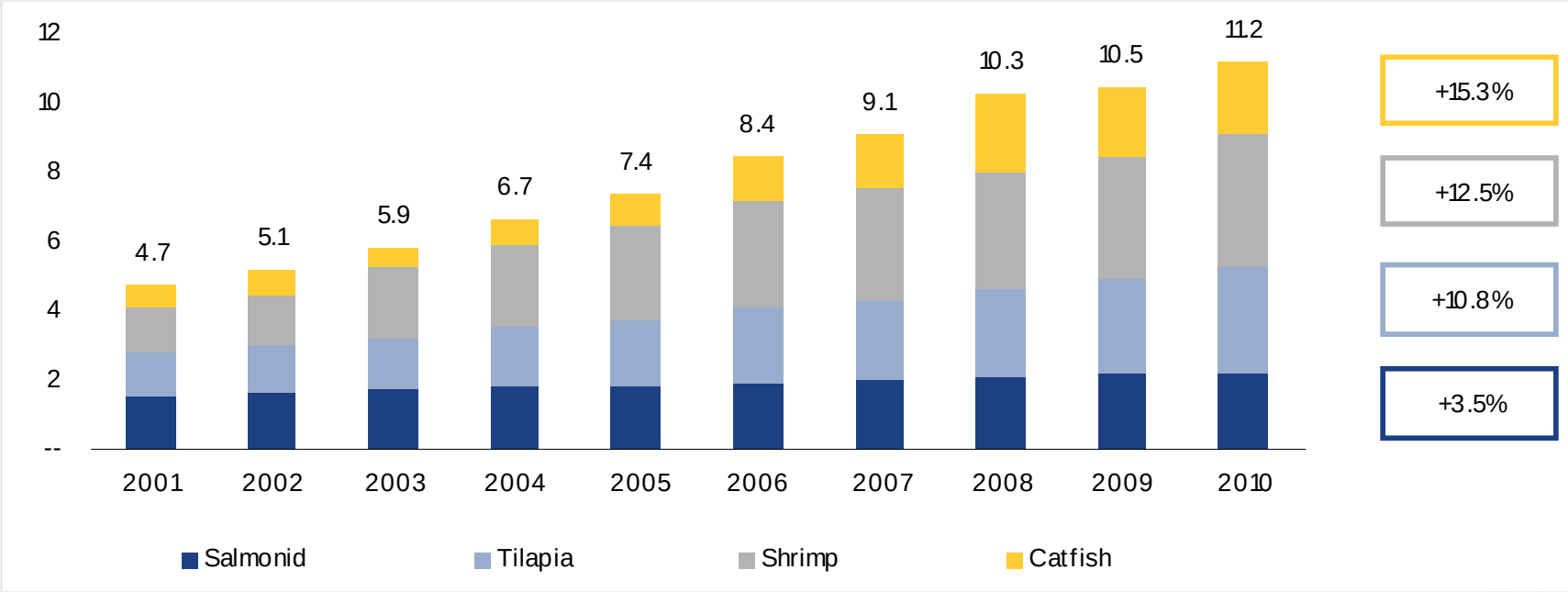
Source: Vetnosis;

Future growth in seafood supply depends on Aquaculture



Aquaculture production of selected species 2001-2010(mT)

Aquaculture Production of Selected Industrialised Species 2001 – 2010 (mT)



CAGR

2001 – 2010

+15.3%

+12.5%

+10.8%

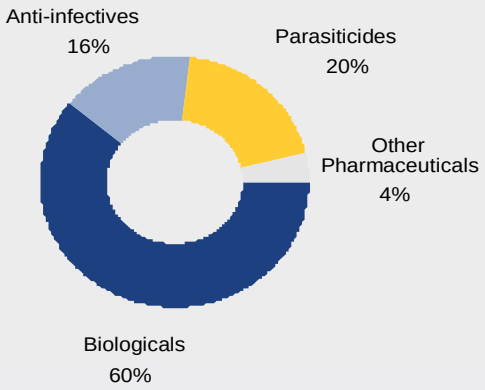
+3.5%

Sources: Vetnosis, FAO; Notes: Salmonid include Atlantic salmon and rainbow trout; tilapia includes Nile tilapia + other tilapia; shrimp includes shrimps and prawns; catfish includes other pangas catfish + channel catfish + other torpedo-shaped catfish

Fish Health Management

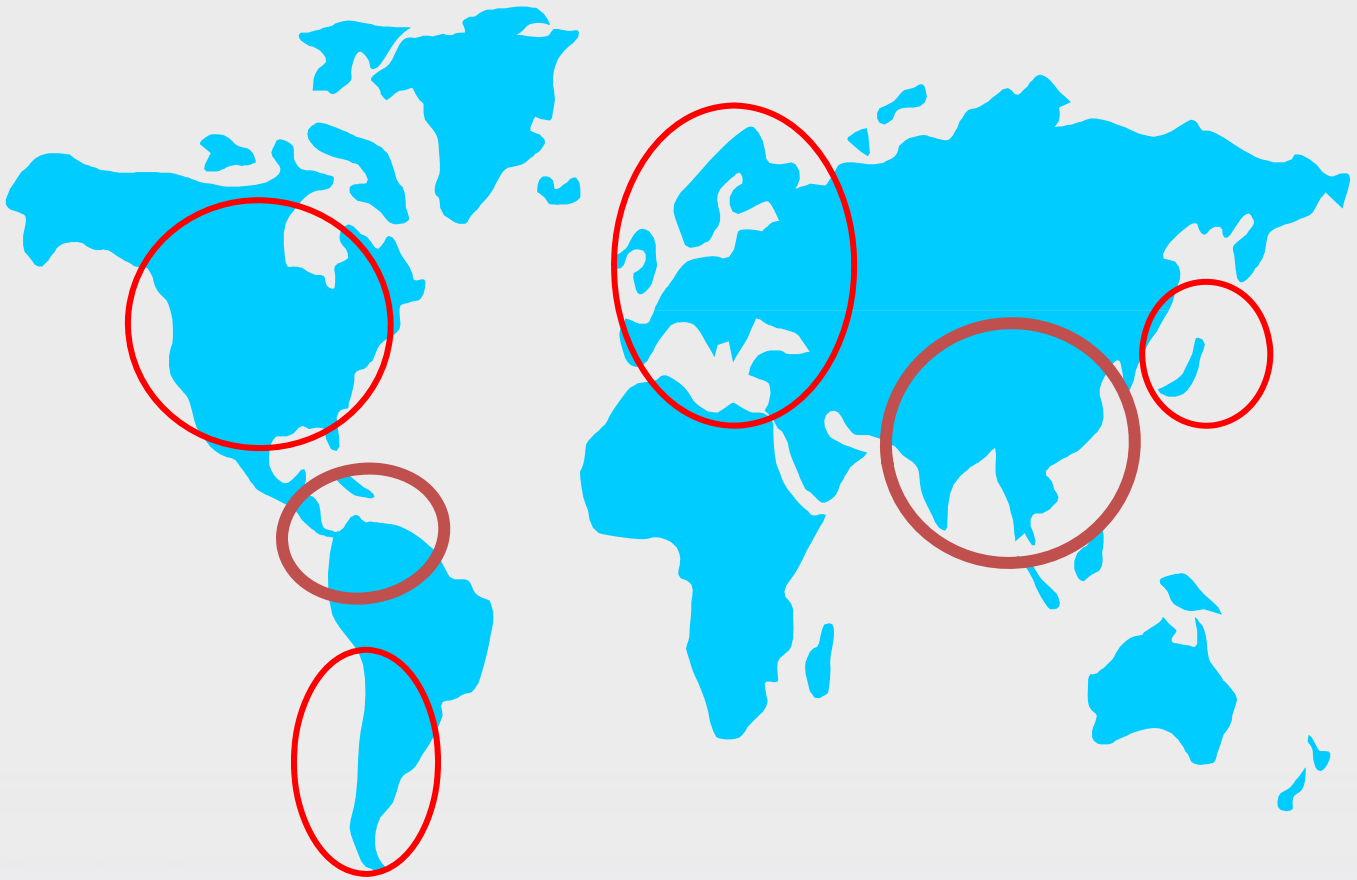
- Good fish health with low incident of disease is overall objective in the farming of fish
- Diseases are still one of the most important challenges
- Disease and health management are closely linked Poor rearing conditions, over-stocking, handling and inadequate nutrition can act as stressors that make infection and losses by disease more likely..
- Preventing disease is therefore a priority in any aquaculture production.
- Vaccination is one of the most important preventive measures in aquaculture
- In many countries, authorities and fish farmers have improved their policies, regulations, diagnostic expertise, rearing equipment and routines as well as preventive and therapeutic strategies. This improves their ability to handle diseases.

Industrialised Fish Healthcare Market Sales split by product in 2011



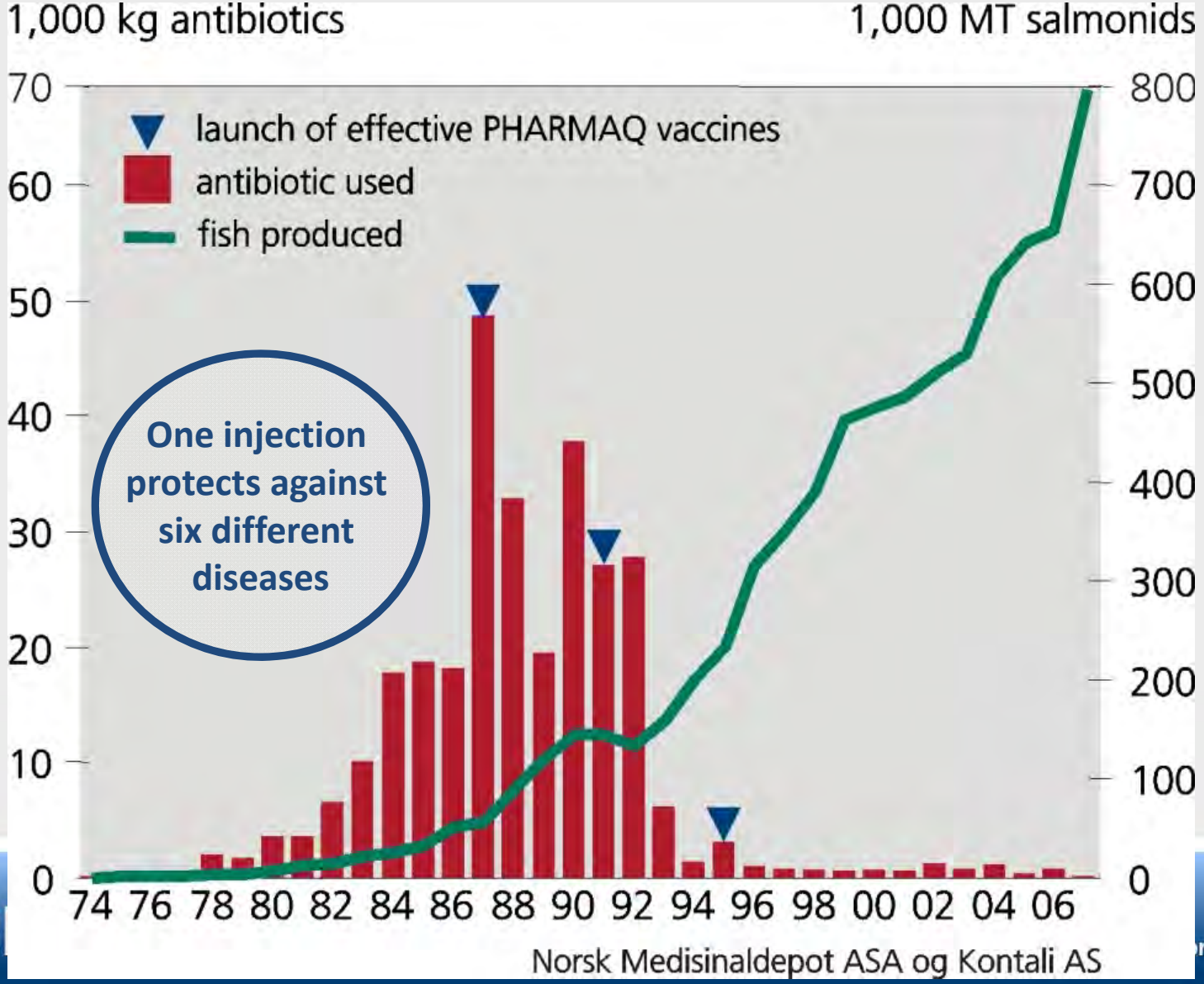
Source: Vetnosis

Geographical areas where vaccination are common practice



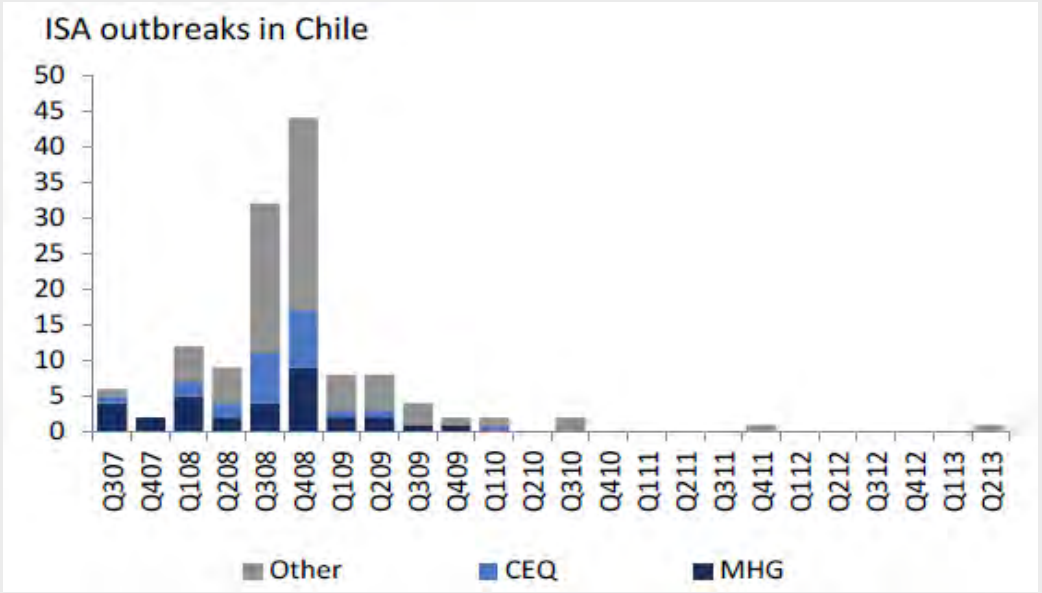
Vaccines are available mainly where aquaculture is commerzialised

From treatment to prevention in Norwegian aquaculture

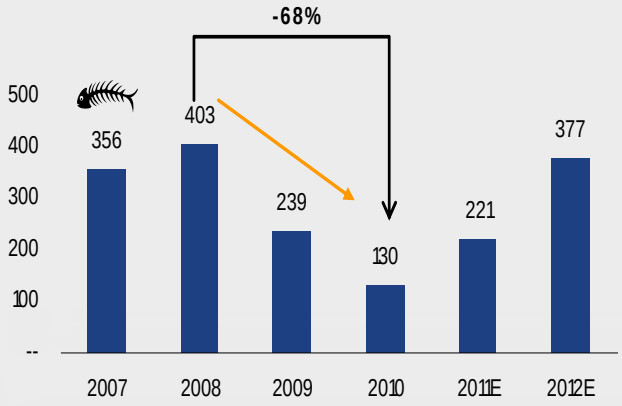


ISA situation in Chile

The ISA situation has been under control since the introduction of ISA vaccines in 2009



Chilean Atlantic Salmon Production (kT)



Major Changes in the Law of Aquaculture

- Creation of 35 neighborhoods with coordinated health management
- New density limit during the on growing period (sea water): 17 kg / m^3
- 3 month fallowing period for each neighborhood
- Mortality silage
- No more Atlantic smolt production in lakes
- Maximum Nº per fish on sea sites: < 1.2 million

Vaccine development

PHARMAQ strategy is to develop and launch vaccines for tilapia to improve fish health. Since 2008 we have visited countries in Latin America and Asia in order to have a broad vision of the disease problem in farmed tilapia

Streptococcus agalactiae is causing significant mortality and mobility in cultured tilapia.

Other bacteria that cause problem, but to a lesser extent;

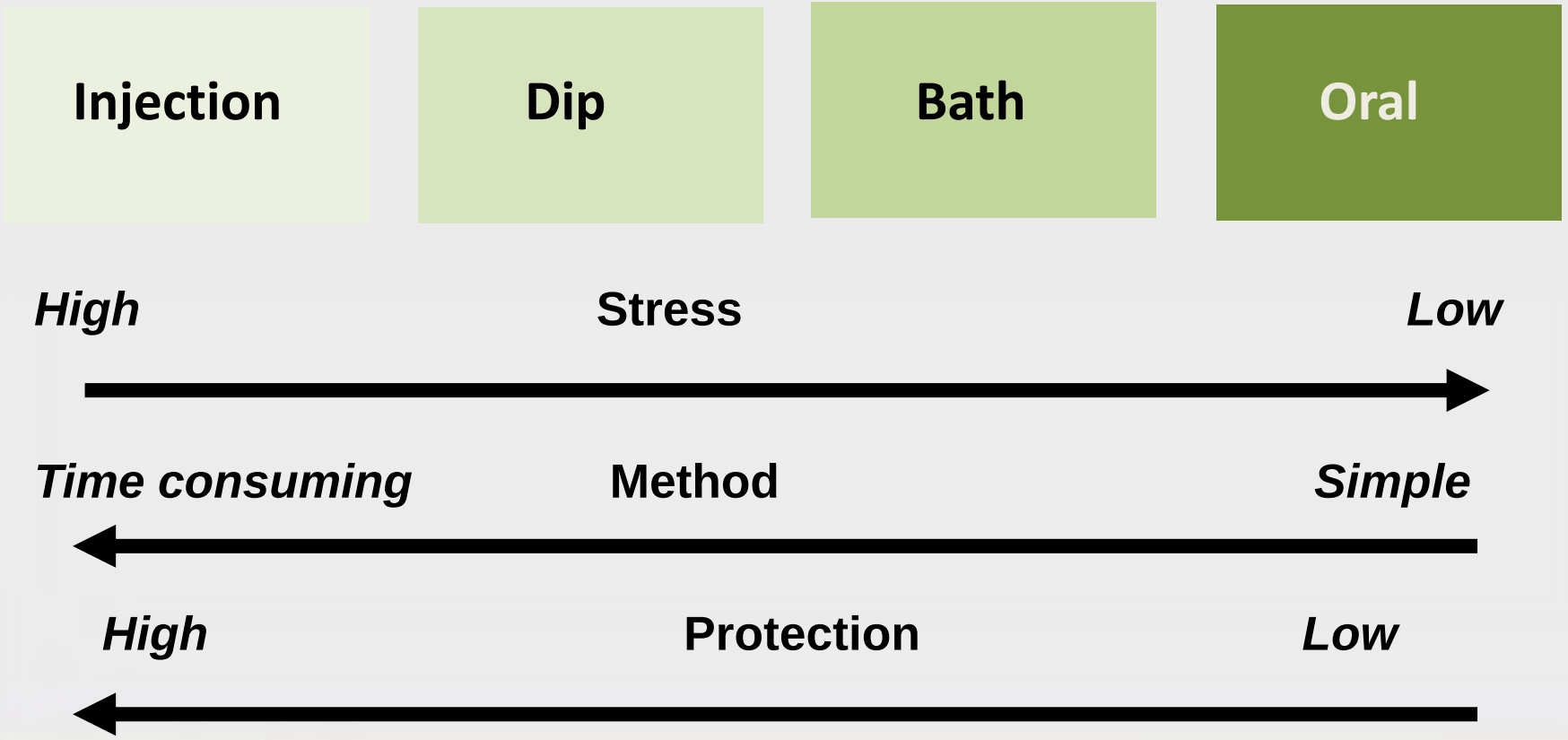
- *Streptococcus inea,*
- *Flavobacterium columnare,*
- *Aeromonas hydrophila*
- *Francisella spp*

Vaccine development.

The last year PHARMAQ has been working on a *Streptococcus agalactiae v*accine

To test the efficacy we have develop
 a challenge model.
Several lab trials have been perform to test different vaccine candidates in order to decide the most optimal compostion of the vaccine
.
Last year we also performed a field trial.

There are different way of vaccinated the fish:



Type of controlled lab studies related to product development

- Development of challenge model
- Virulence studies
- Dose-response studies
- Efficacy – product documentation
- Cross protection
- Safety studies (acute toxicity and local side effects)

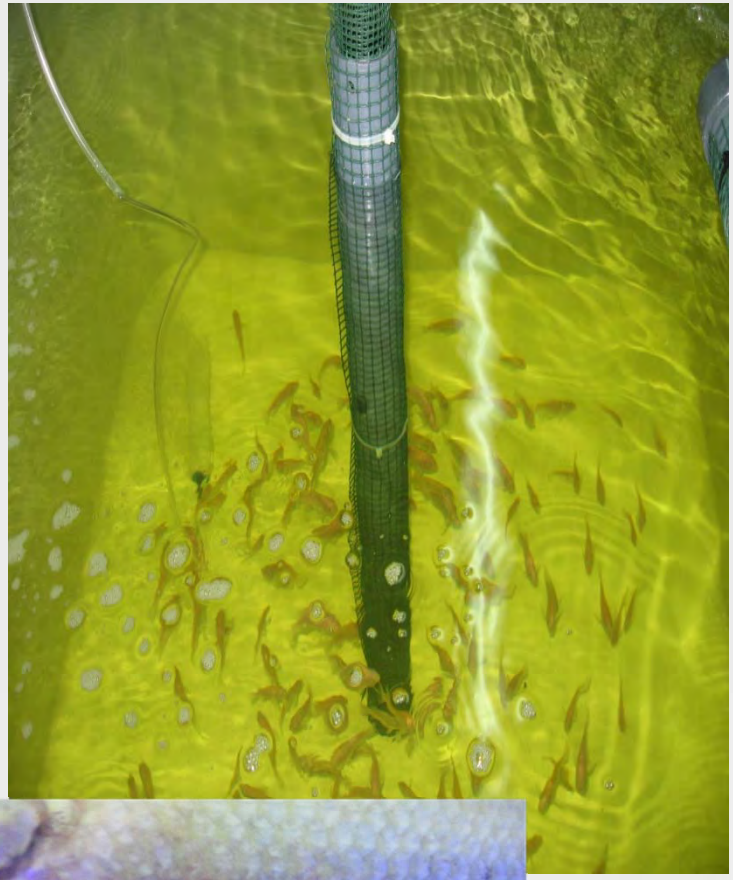
A fish vaccine must be developed for each species and region

Efficacy study in tilapia

- Testing different vaccine candidates (TiLa) against *S.agalactiae*
- Minimum 50 fish (vaccinated and control)

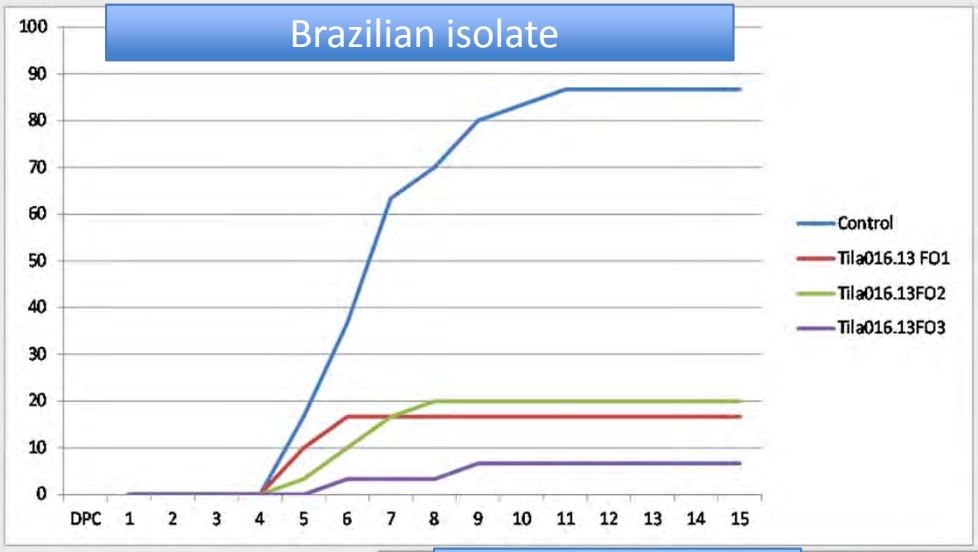
  Challenge ip, some weeks post vaccination

  Vaccinated and control groups in common tank (parallel tanks),

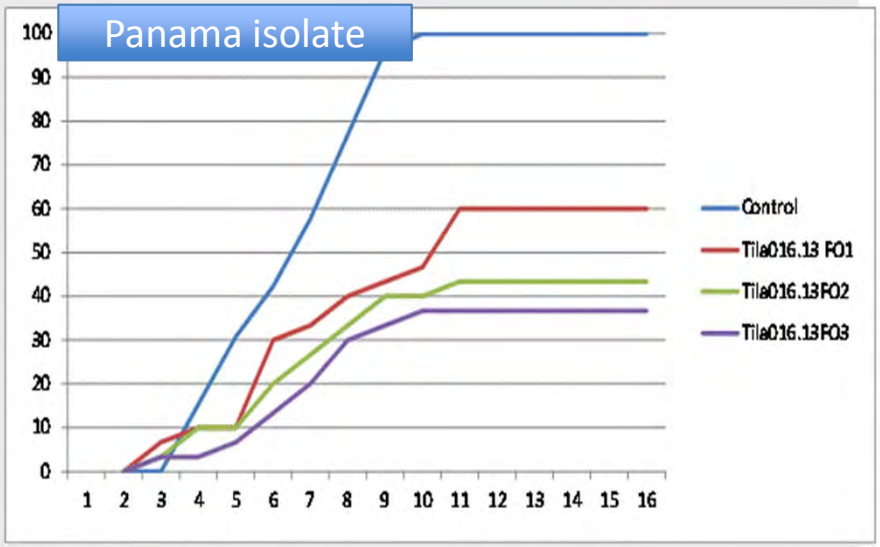


Dose/response trial -Challenge with different *S,agalactiae* isolate from Costa Rica, Brazil and Panama

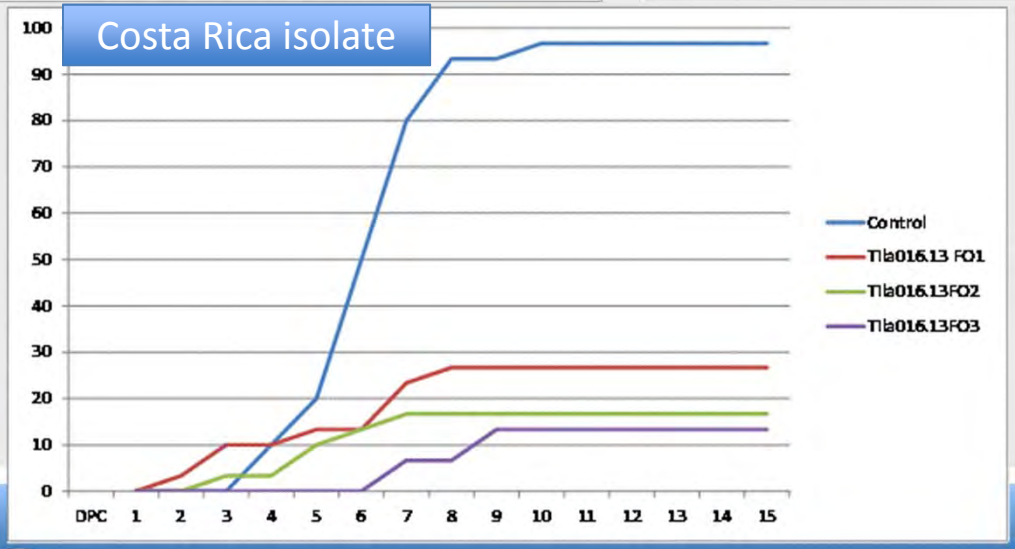
Brazilian isolate



Panama isolate



Costa Rica isolate



Field study 2012
Inactivated monovalent *Streptococcus agalactiae* vaccine

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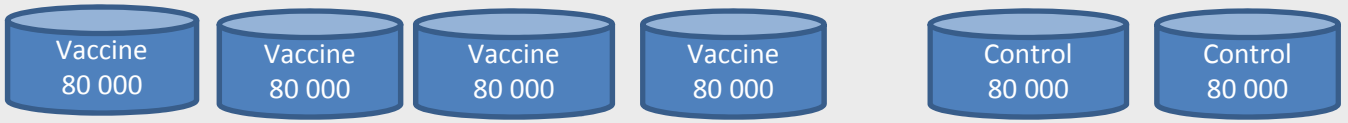
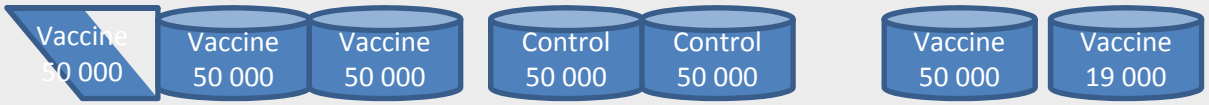
Field trial with TiLa 1 vaccine

- Vaccination May - June 2012
- Vaccination 320 000 fish
- 160 000 control unvaccinated fish (2 ponds)
- Allocation 4 ponds – 700 m3 (phase 1)



- **Transfer 3 months later to last ongrowing (phase 2) 400 g:**



Water line – high challenge pressure

Water line – lower challenge pressure

Side effect evaluation 4 mpv and at harvest (January 2013)

Evaluation post vaccination – TiLa 1 vaccine

SAFETY	EFFICACY
• Mortality – 21 days acute toxicity period post vaccination	• Differences in accumulated mortality between vaccinated and control following clinical outbreaks of streptococcosis from vaccination to slaughtering – 8 months
• Induction of local reactions (Adhesions and pigmentation – Speilberg scala)	
• Growth performance after vaccination	

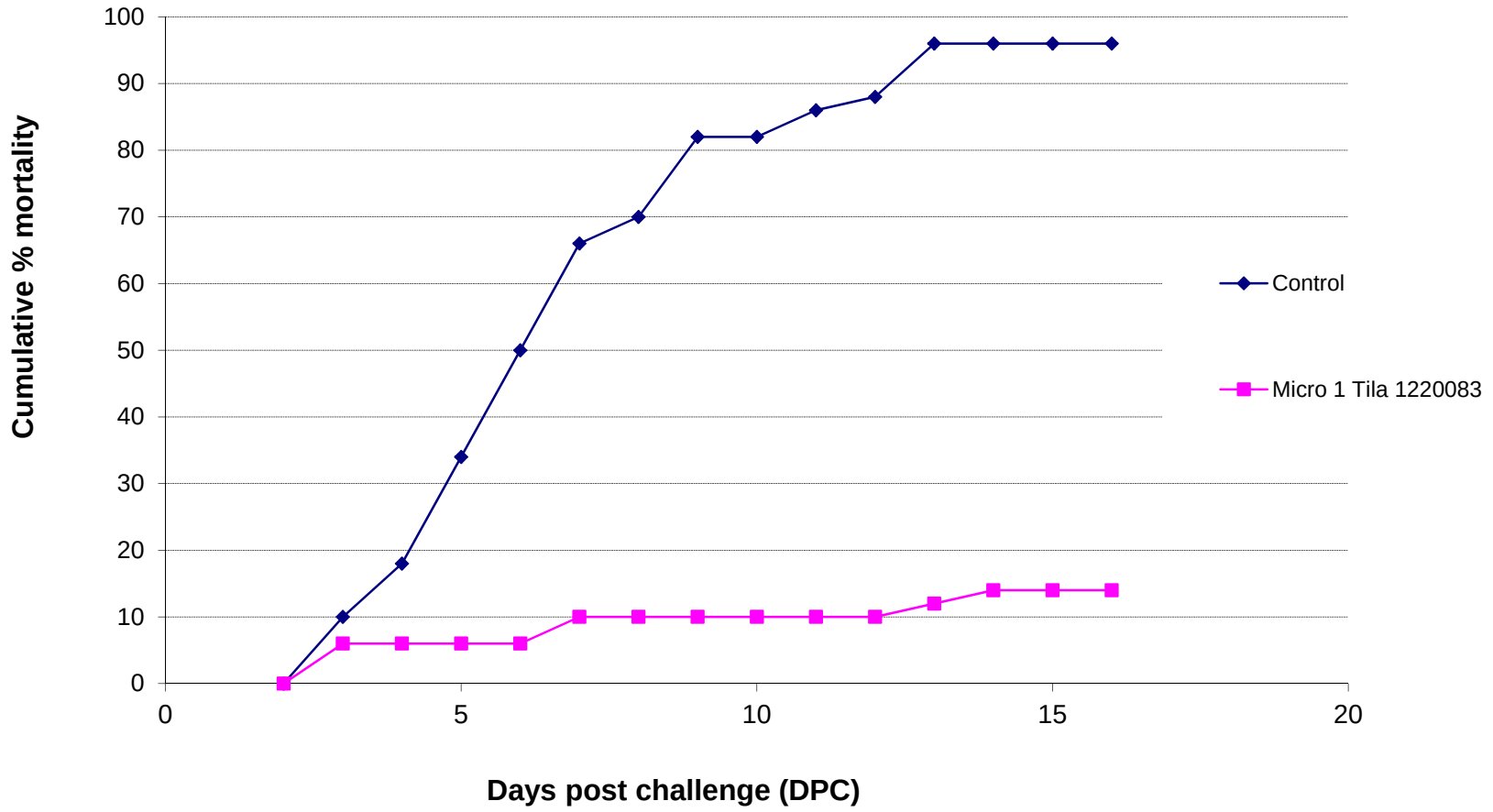
Safety Results Field Study

TiLa 1 vaccine	Control
• Not any abnormal behaviour or mortality related to the vaccine	-
• Some mortality due to mechanical external lesions and fungus infection	• Some mortality due to mechanical external lesions and fungus infection
• Low adhesions scores • 0.4 at 4 and 8 months post vaccination. • Melanization was not observed at any time point	No adhesions or melanization

Efficacy Results Field Study

TiLa vaccine	Control
• **First ongrowing phase-** no outbreak of disease recorded. Similar survival rate between vaccinated and control groups.	
Second ongrowing phase	
• No outbreak of disease in vaccinated groups	Streptococcosis recorded and verified in control groups
• 7 % mortality due to other causes than streptococcosis	18 % mortality including streptococcosis
• No antibiotic treatment	Antibiotic treatment performed

Lab trail TiLa 1 vaccine used in field trial



Important factors to continue further growth

Spread of diseases will continue to be a considerable challenge and a limiting factor for growth.

- Emphasis on preventive measures and knowledge on basic causes of loss-making diseases needed.
- High level of research and new innovations in fish health are key to future sustainable growth, vaccines, treatments breeding and operations.
- Understanding the underlaying factors for the losses are key, the aquaculture industry could benefit from closer cooperation with suppliers and academic institutes to increase the knowledge
- Preventing disease should be a priority in any aquaculture production.
- Vaccination will be the most important preventive measures in farmed tilapia as it is for salmonids .
- Willingness of customers to invest in high quality fish health products. Understanding that it will repay at end of fish production

Obrigada pela atenção

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