

Fish Vaccination - A brief overview

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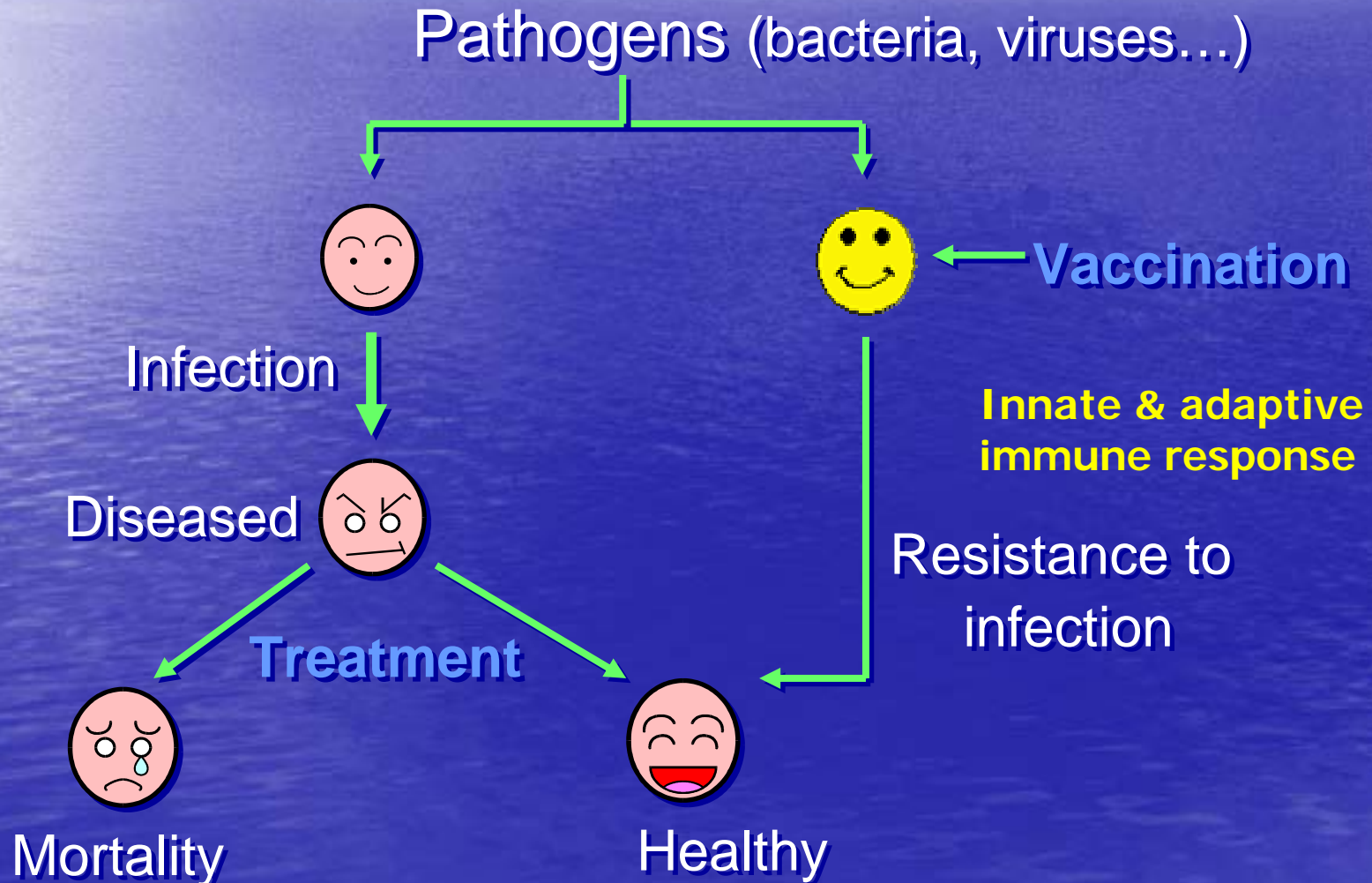
Presentation Plan

- Rationale for fish vaccination
- What diseases do we want to control?
- Ideal fish vaccines
- Types of vaccine available
- Route of vaccine administration
- Current vaccines and their efficacy and recommended vaccination programmes
- Adverse reactions

Basis of Fish vaccination

- Fish have a functional immune system similar to mammals (innate & adaptive)
- Major differences with other vertebrates is that their metabolism and immune response is temperature dependent.
- An ideal vaccine should be :
 - safe
 - immunogenic
 - produce similar protection to natural challenge
 - Should prevent or limit effects of disease

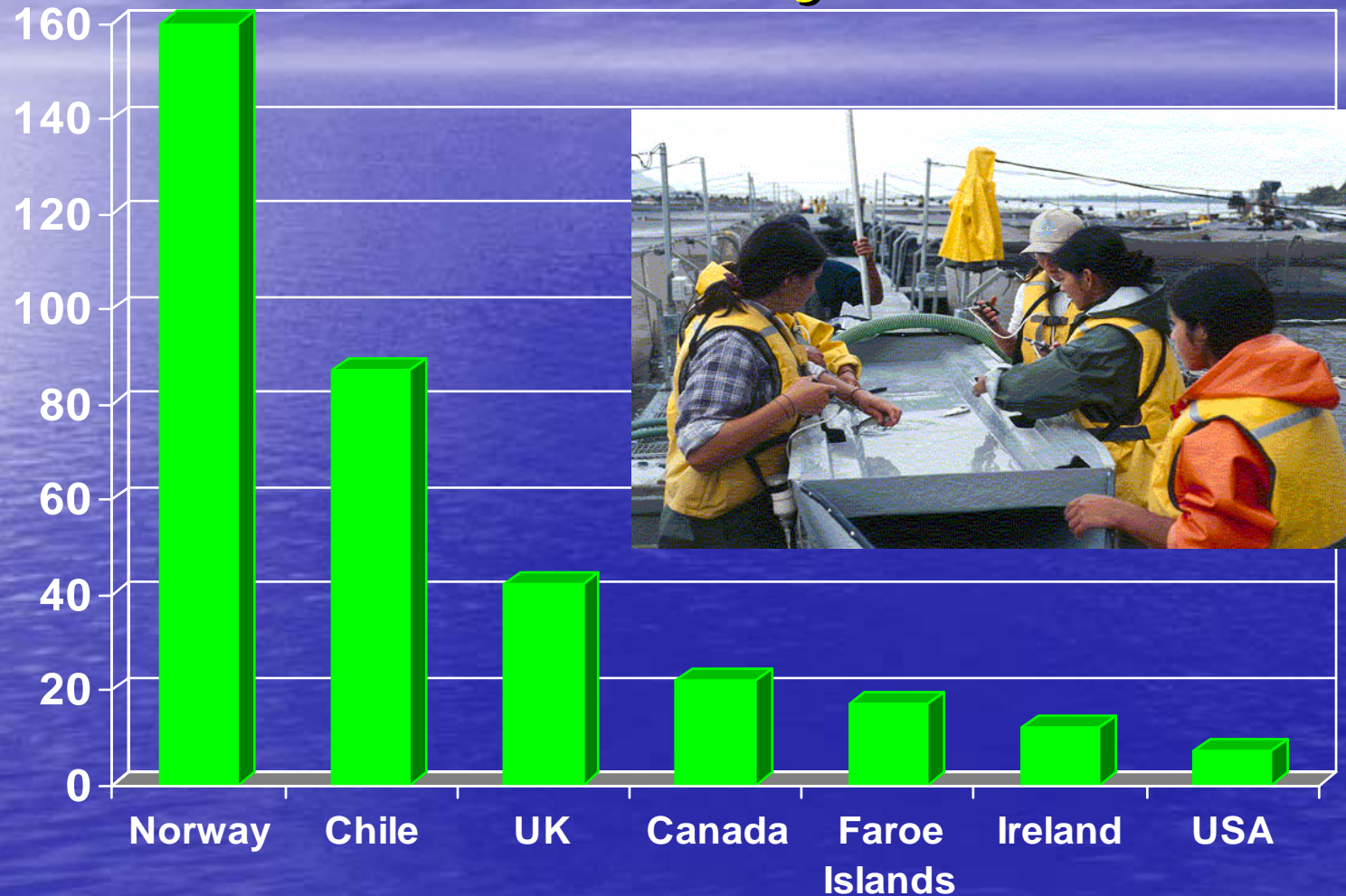
Basis of Fish vaccination



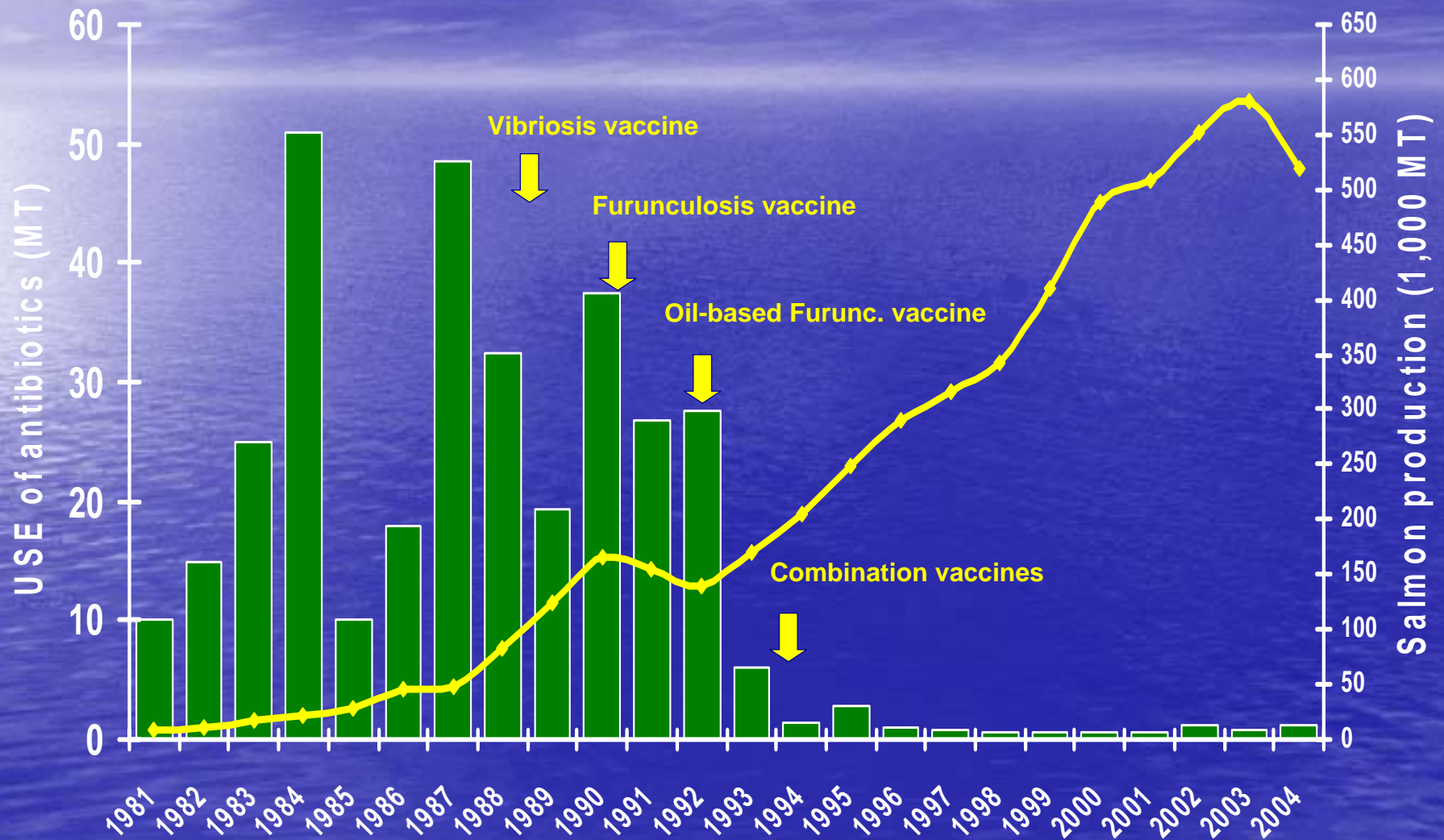
Atlantic salmon production (MT) by country in 2003



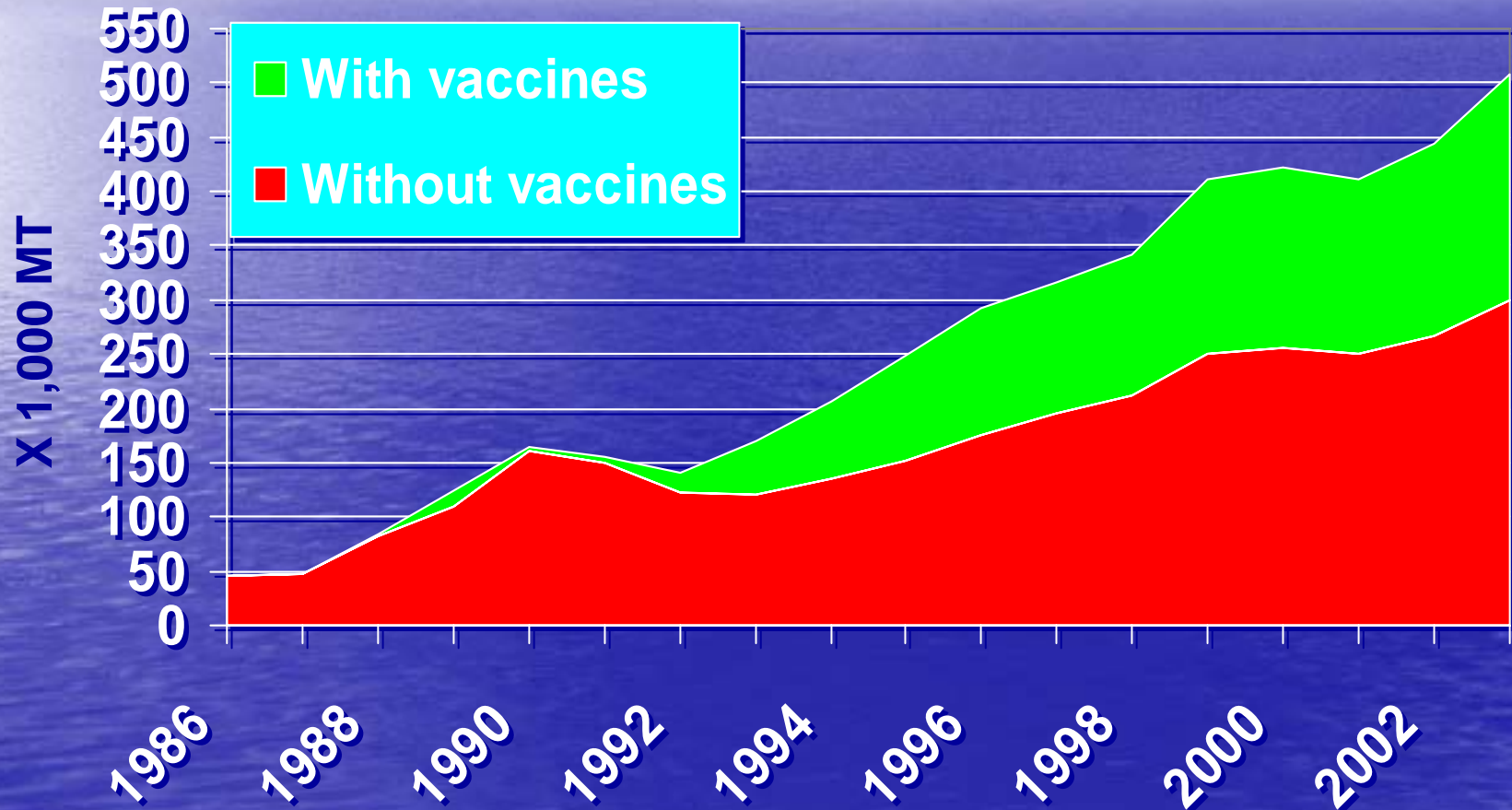
Vaccine doses (millions) used in the salmon industry in 2002



Norwegian Salmon Production, Use of Pure Antibiotics and the Effect of Vaccines



Production of Atlantic salmon in Norway – estimated effect of vaccination (1986 - 2003)



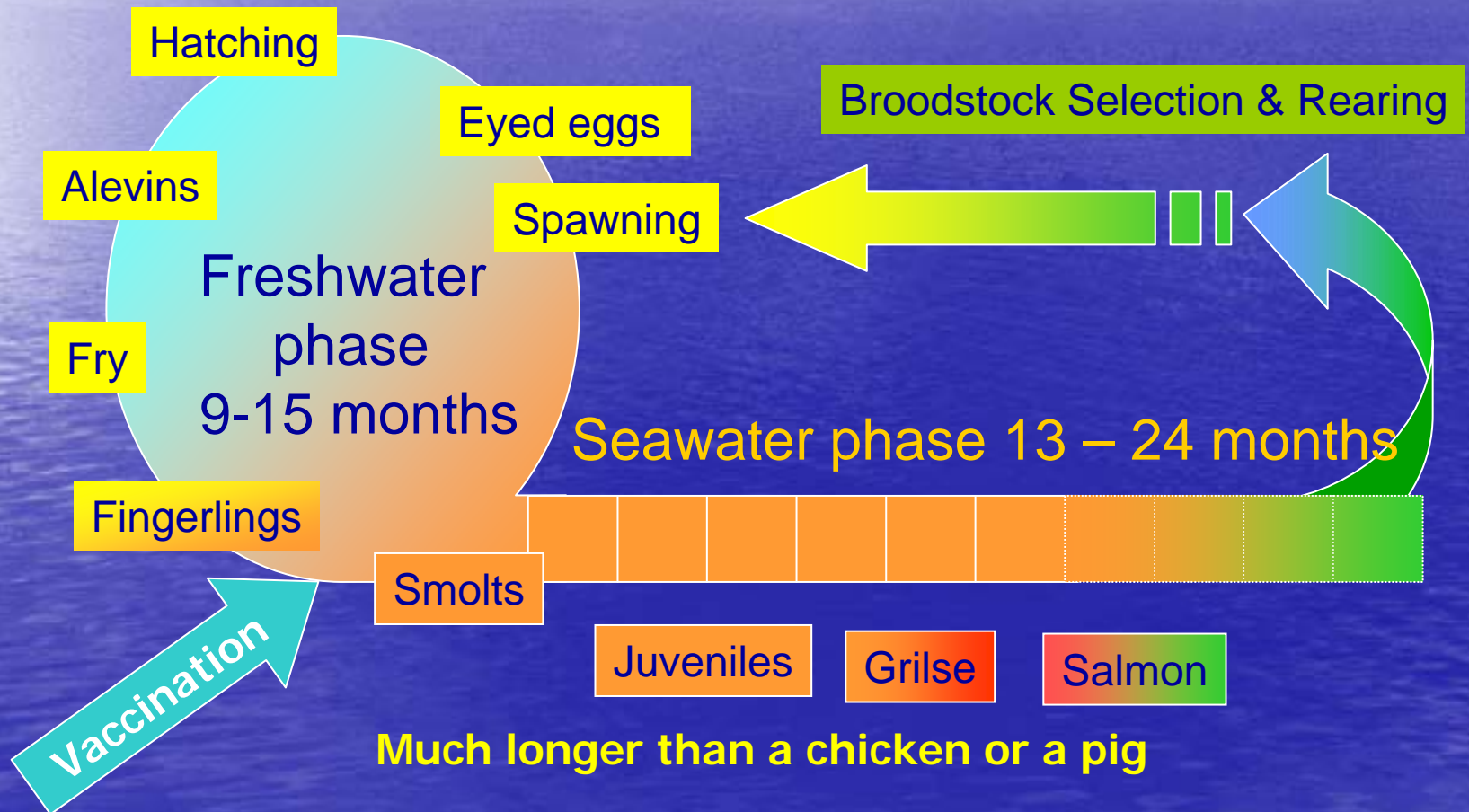
Rationale for fish vaccination

- **Vaccination** is the best method to increase survival rate and profitability in aquaculture when used in combination with several factors which are necessary to guarantee the highest possible survival rate
 - **Good nutrition**
 - **High-quality fingerlings**
 - **Good farming and husbandry practices**
 - **Health management**

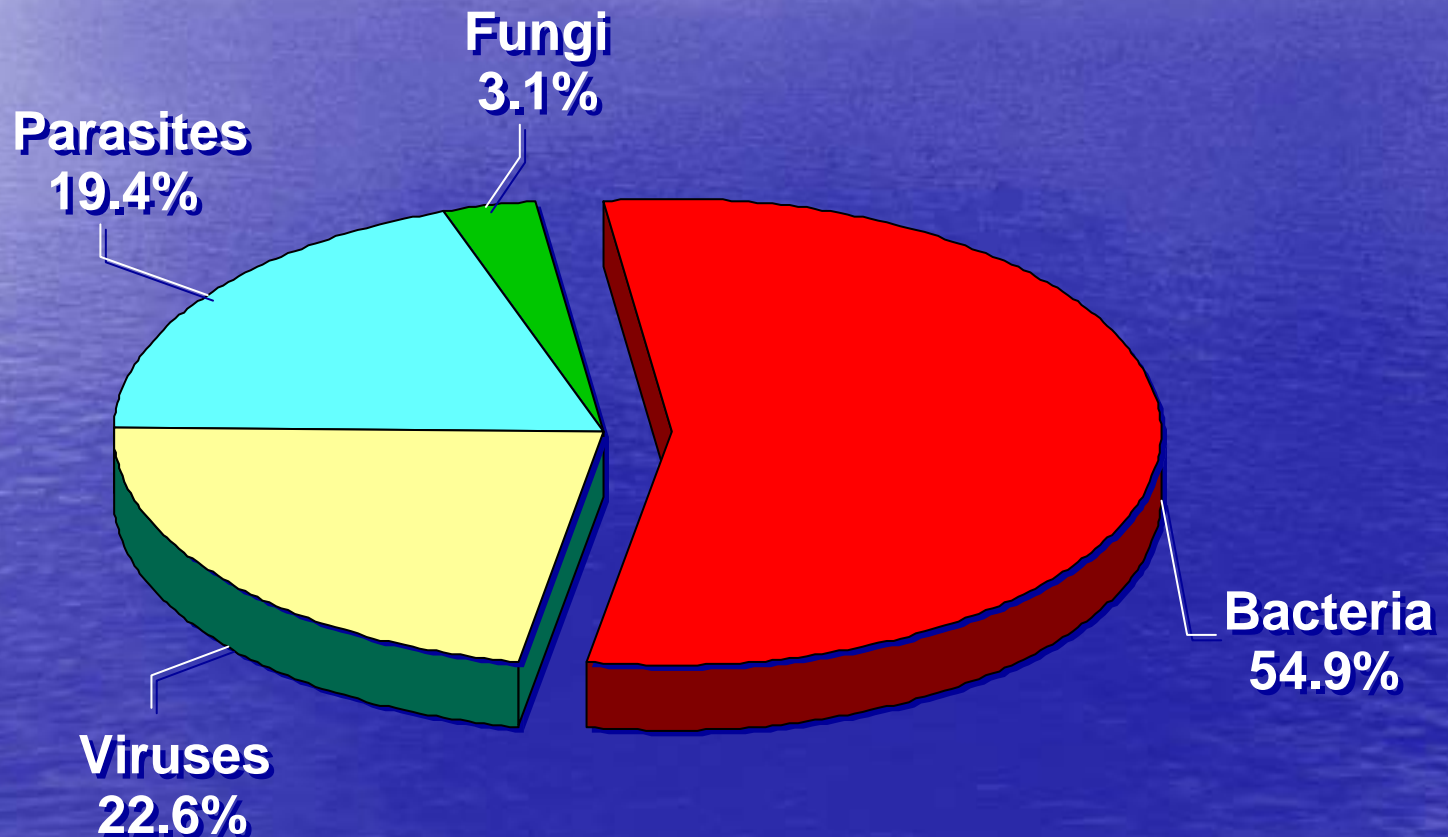
Important considerations for fish vaccination

- Species (Salmon, Cod, Sea bass)
- Status of the immune system
- Production cycle and life history
- What diseases do you want to control?
- When do these diseases occur?
- Farming technology (Handling, mechanisation)
- Environment (temperature, salinity)
- Stress factors, nutrition and cost benefit

Atlantic Salmon Production Cycle



Causes of Infectious Diseases in Aquaculture



Globally Important Bacterial Pathogens in Salmonid Aquaculture

- *Listonella (Vibrio) anguillarum*
- *Vibrio salmonicida*
- *Moritella viscosa*
- *Aeromonas salmonicida*
- *Aeromonas hydrophila*
- *Yersinia ruckeri*
- *Renibacterium salmonis*
- *Lactococcus/Streptococcus* sp.
- *Piscirickettsia salmonis*



Globally Important Viral Pathogens in Salmonid Aquaculture

- **Infectious Pancreatic Necrosis (IPN)**
- **Salmon Pancreas Disease (SPD)**
- **Sleeping Disease of Trout (SD)**
- **Infectious Salmon Anaemia (ISA)**
- **Viral Nervous Necrosis (VNN)**
- **Infectious Haematopoietic Necrosis (IHN)**



The Ideal Fish Vaccine?

- Sustained immunity and protection
- Early mass application
- Efficacious for a broad number of species
- Safe
- Cheap and cost effective
- Easily produced
- Stable
- Will not interfere with diagnosis
- Easily licensed

Fish Vaccine Types

Dead vaccines

- Inactivated virus or bacterial antigens
- Sub-unit vaccines
- Recombinant vaccines

Live vaccines

- Attenuated live
- Gene deleted live
- DNA

What Fish vaccines are Used?

- Most commonly used antigens in fish vaccines to date are inactivated or killed bacterial and viral
- Most successful use has been against furunculosis (*Aeromonas salmonicida*) in salmon
- Several inactivated antigens now present in most commonly used salmon vaccines, i.e. multivalent
- Recombinant sub unit vaccine used for IPN
- DNA vaccines for IHN and VHS in development

Commercially available registered inactivated antigens world-wide

- *A. salmonicida*
- *V. salmonicida*
- *V. viscosus*
- *V. ordalii*
- *V. anguillarum*
- *Y. ruckerii*
- *R. salmoninarum*
- *F. psychrophilum*
- *F. columnarae*
- *P. salmonis*
- *L. garvieae*
- *S. iniae*
- *P. piscicida*
- *E. ictaluri*
- IPN
- PD
- IHN
- VHS
- ISA*
- Iridovirus -Japan



Number of licensed fish vaccines

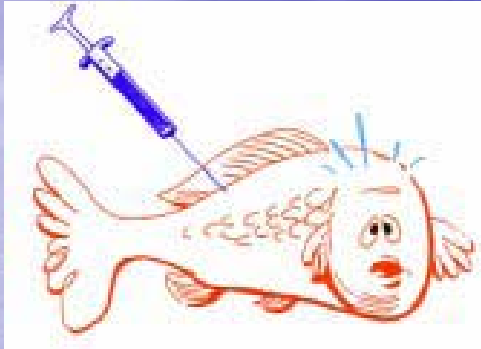
| Country | No Vaccines |
|---------|-------------|
| Norway | 1 |
| Chile | 9 |
| USA | ~30 |
| JAPAN | 13 |
| UK | 6 |
| Canada | 19 |

| Country | No Vaccines |
|---------|-------------|
| Greece | 6 |
| Italy | 6 |
| France | 1 |
| Spain | 4 |
| Faroese | 16 |
| Ireland | 2 |

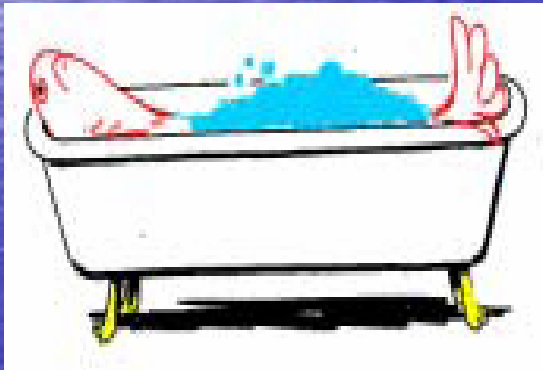
Summary of international survey on vaccine efficacy

| Disease | Very Good | Good | OK | Poor |
|---------------------|-----------|------|----|------|
| Classical vibriosis | 12 | 4 | 1 | 1 |
| Coldwater Vibrio | 4 | | | |
| Winter ulcers | | 2 | | |
| Warm water Vibrio | | 2 | | |
| Furunculosis | 5 | 7 | 2 | |
| Yersiniosis | 13 | 1 | 2 | |
| Pasteurellosis | 3 | 2 | | |

Vaccination Methods



- **Injection vaccination**
 - Intraperitoneal (adjuvanted or not)
 - Intramuscular (DNA)



- **Immersion vaccination**
 - Bath method
 - Dip method
 - Spray vaccination

Vaccination Methods



- **Spray vaccination**

A variant of immersion

Could be used in larger fish where injection not possible



- **Oral (active) vaccination**
Micro-encapsulation method
Bio-encapsulation method

Fish vaccination process



- Fish are transported in pipes from the rearing tanks to an anaesthetic bath.
- The anaesthetized fish are injected by the vaccination team.





Injection vaccination – by hand





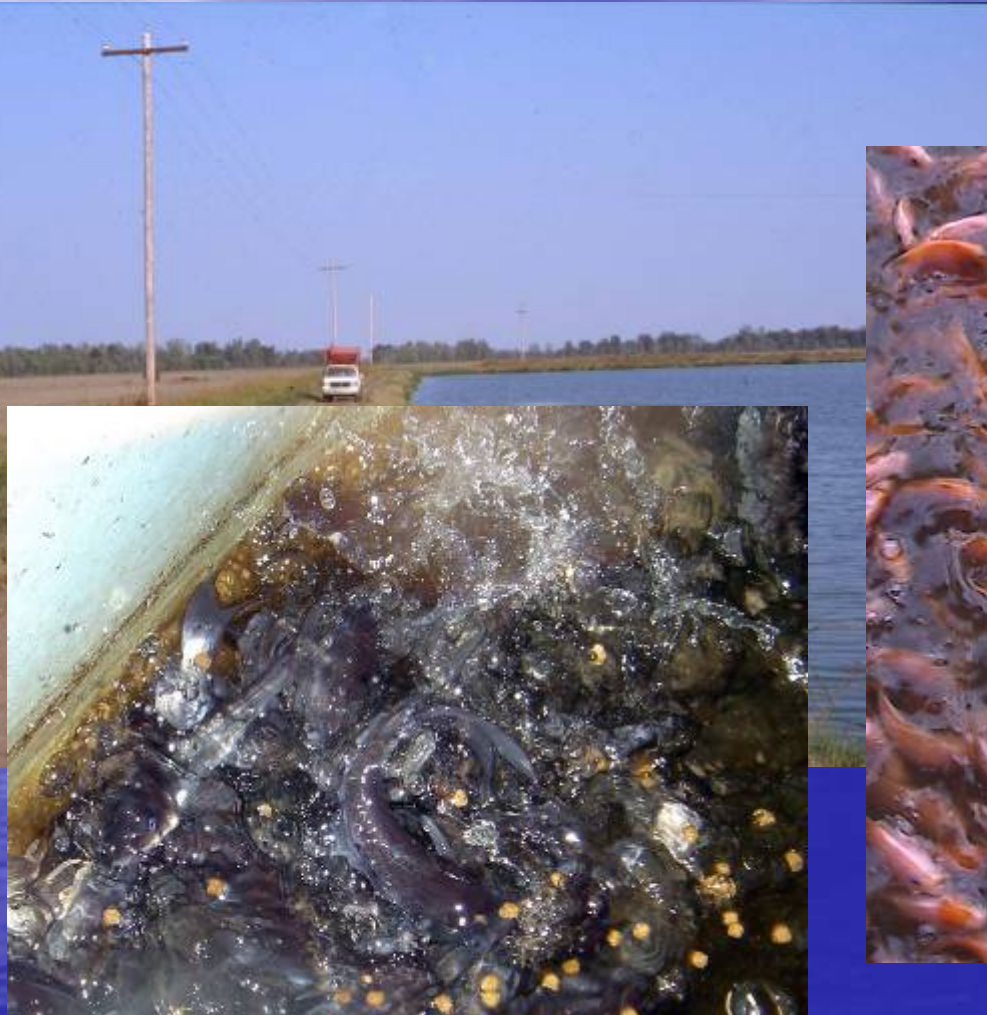
Injection vaccination - by machine



Fish immersion vaccination



Oral vaccination



Advantages & disadvantages of immersion vaccination

- Suitable for mass vaccination of all sizes of fish
- Reduced stress for fish
- Lower labour costs
- Less risk to vaccination team
- Major disadvantages are the large amount of vaccine required and lower level of protection and duration of immunity

Advantages & disadvantages of Injection vaccination

- Most common method of vaccine delivery in fish
- Highly efficient in generating both humoral (antibody) and cellular cytotoxic response
- Unsuitable for small fish
- Needs sophisticated machinery or large skilled workforce
- Significant handling stress and risk of post vaccination fungal infections
- Local reactions

Advantages & disadvantages of Oral vaccination

- Vaccine mixed with feed
- Easiest method for mass vaccination of all sizes of fish
- Saves labour and avoids stress
- Large quantities of antigen required
- Requires all fish to be feeding
- Protection generally weak and of short duration

Choice of Application method

- Determined by
 - Vaccination window
 - Size of fish
 - Duration of protection required
 - Type of pathogen
 - Type of immune reaction required
 - Single versus multivalent product
 - Cost of vaccine and smolts

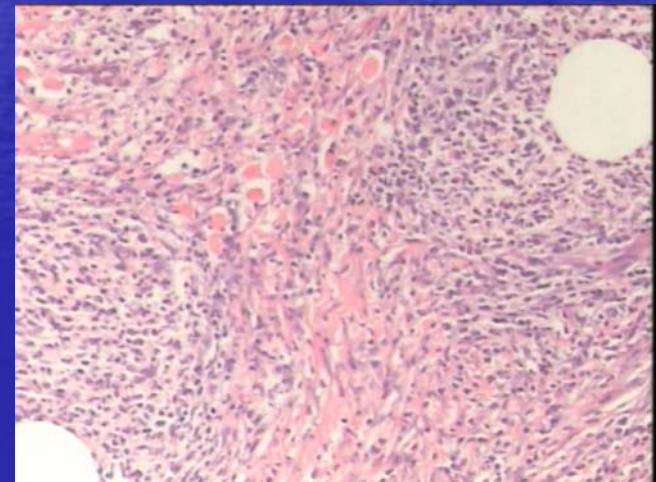


Comparison of fish vaccination methods

| | Immersion | Injection | Oral |
|-------------|-----------|-----------|------|
| Application | ++ | + | +++ |
| Stress | ± | - | +++ |
| Costs | ++ | - | ++ |
| Efficacy | ++ | +++ | ± |
| Duration | + | +++ | ± |

What is a local reaction in a Fish?

- Adhesions and melanisation
- Inflammatory response producing local and/or diffuse peritonitis with adhesions in internal organs and abdominal wall.
- Invasion of fibroblasts, macrophages and lymphocytes
- Large number of melanomacrophages.
- Can result in multiple granulomata



What factors influence development of local reactions?

- Adjuvants
- Antigens
- Formation of vaccine
- Dose volume
- Photo period
- Temperature @ vaccination
- Size of fish @ vaccination
- Hygiene @ vaccination
- Interaction of all or any of above

Consequences of severe local reactions

- Reduced growth
- Increased feed conversion ratio
- Condemnation at processing
- Slows up manual & automatic gutting process
- Welfare issue

Measurement of Local Reactions

- Speilberg or Midtlyng score (Midtlyng et al 1996..)
- Subjective measurement
- Requires training and standardization and checking
- Score range: 0 = no reaction 6 = very severe
- < 2 – satisfactory
- 3 – gives cause for concern
- >4 – if 10% are > or = 4 could be considered an adverse reaction. 20-25% growth reduction
- Distribution of scores more important than mean.
- Examine a minimum of 30 fish per group at least 3 times during field production cycle

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Spielberg Scale for adhesions (0-6)

- **0** = no visible lesions
- **1** = very slight adhesions most frequently around the injection site
- **2** = minor adhesions which may connect the colon spleen and/or caudal pyloric caecae to the abdominal wall. Broken down easily
- **3** = Adhesions extending to anterior or cranial abdomen including the liver and/ or gonads

Speilberg Scale for adhesions (0-6)

- 4 = more extensive lesions involving all organs and abdominal wall & may be damage to the peritoneum
- 5 = Organs more or less fused together and with numerous adhesions to the body wall which are difficult to remove. Usually visible melanisation of the peritoneum
- 6 = Similar to 5 but more pronounced with extensive melanin deposition on various organs and in the muscle. Evisceration results in damage & downgrading

Safety: Melanisation Scale 0- 3

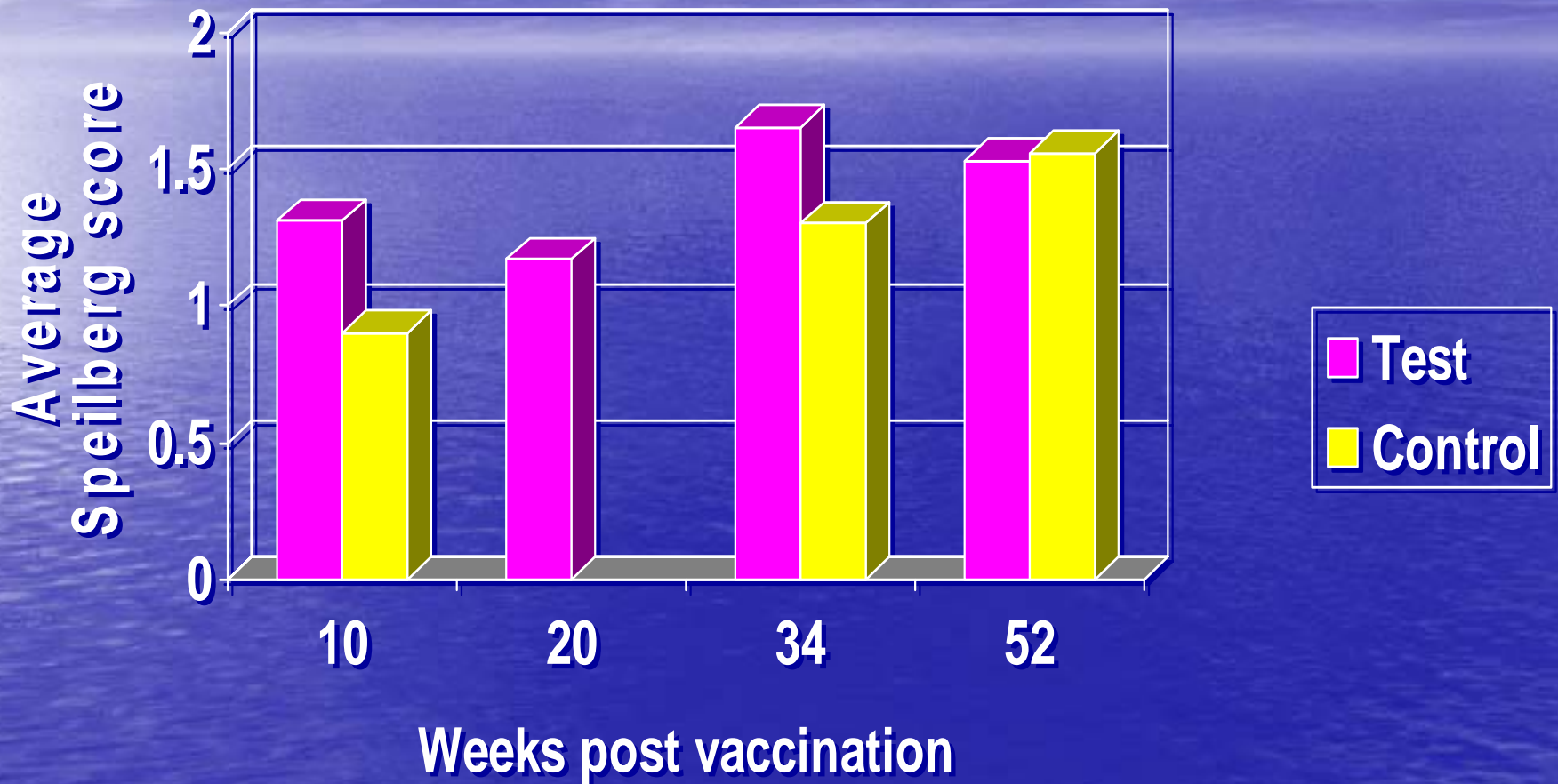
- **0** = No melanin
- **1** = Small amount on viscera
- **2** = Highly visible melanin and/ or slight pigmentation of abdominal wall which is easily removed
- **3** = Melanisation of abdominal wall and fillet - removal results in damage and downgrading.

Local reaction evaluation

- Subjective
- Granulomata will increase score even if not widespread
- Melanisation of fillet unacceptable
- Severe lesions in anterior/cranial region may be serious for potential broodstock
- Position and nature of adhesions and melanin deposits is important to note

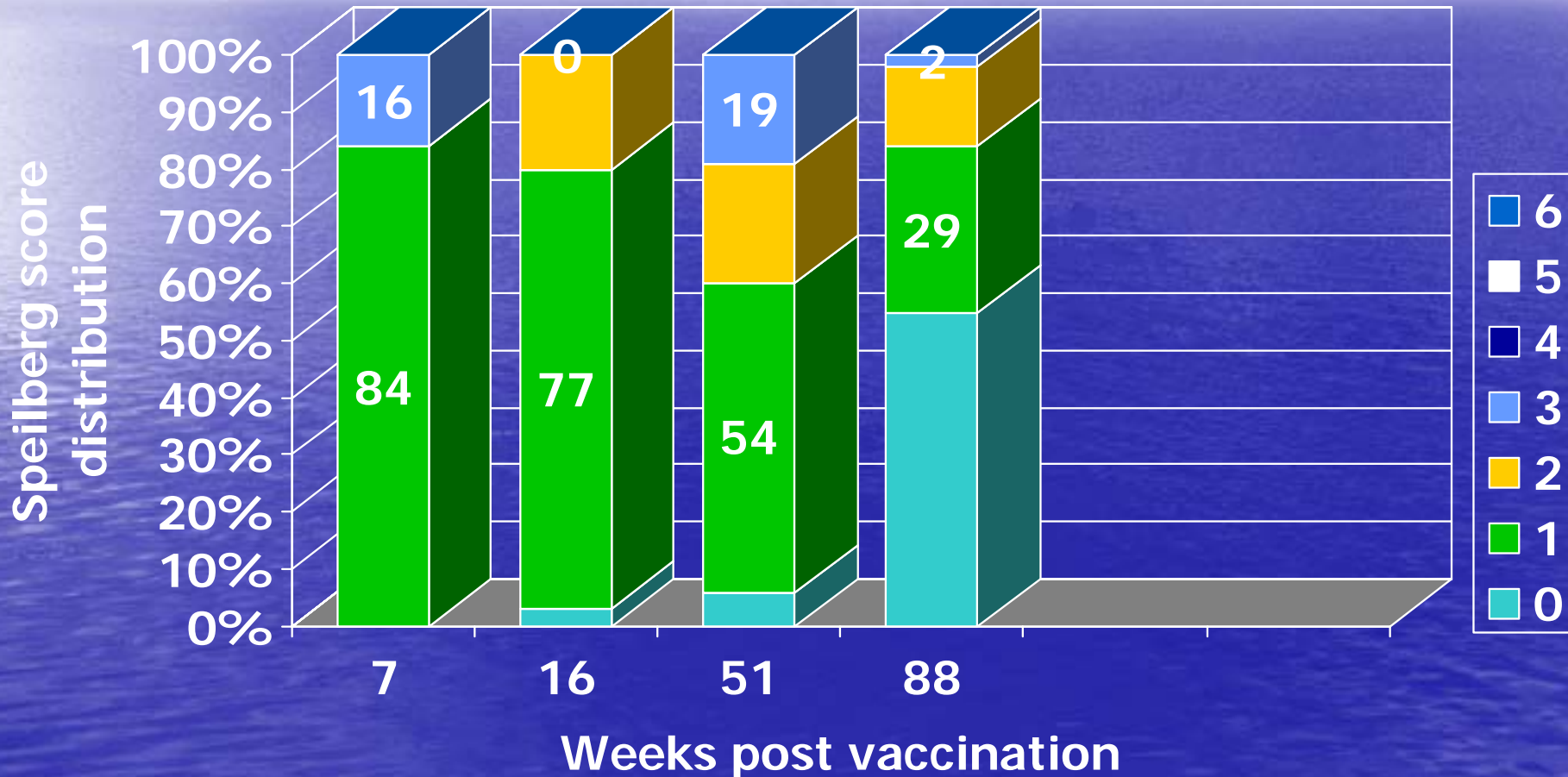
Ref FVS Monograph on Local reactions

Histogram of Local Reactions



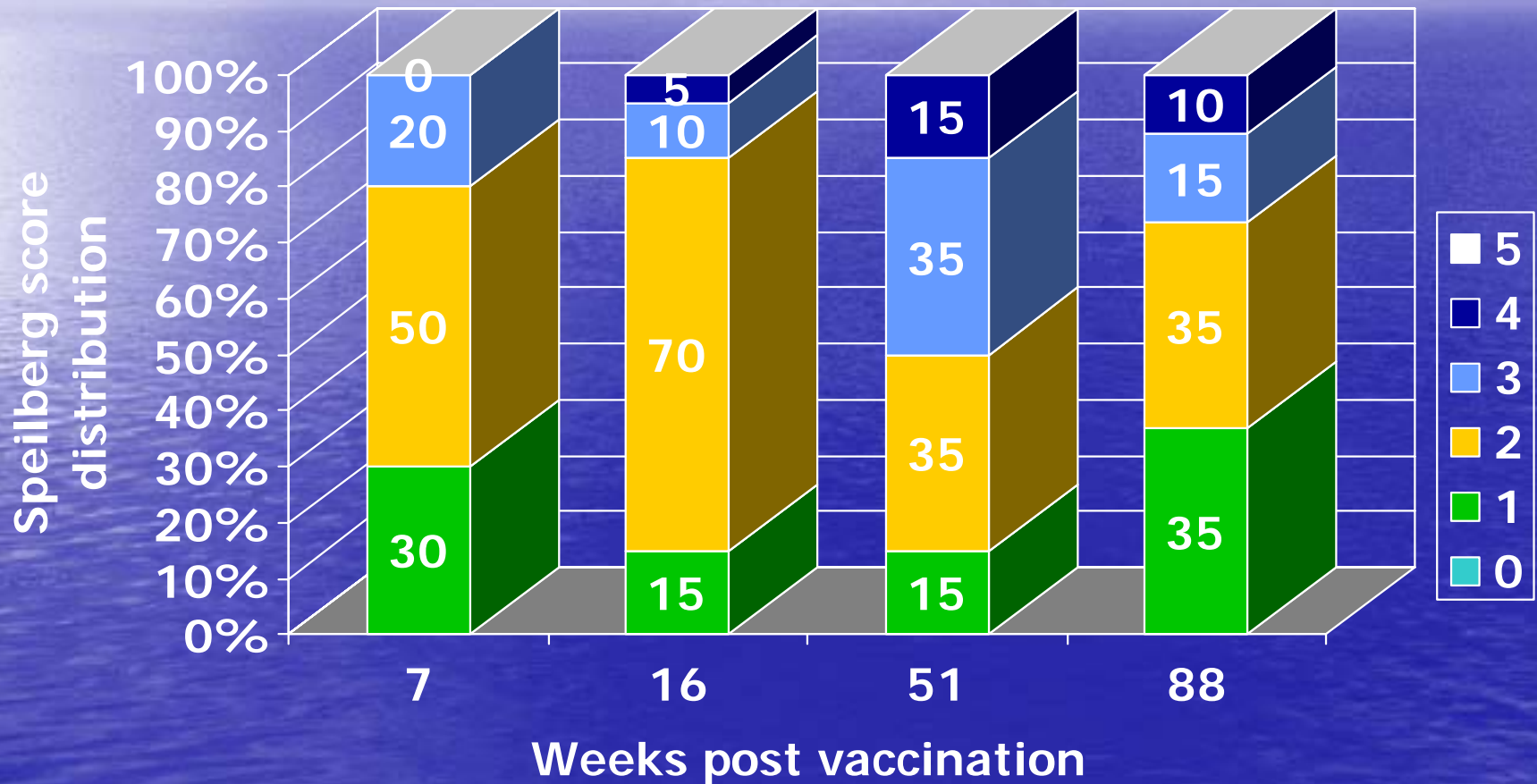
Local Reaction Distribution Chart

Satisfactory profile



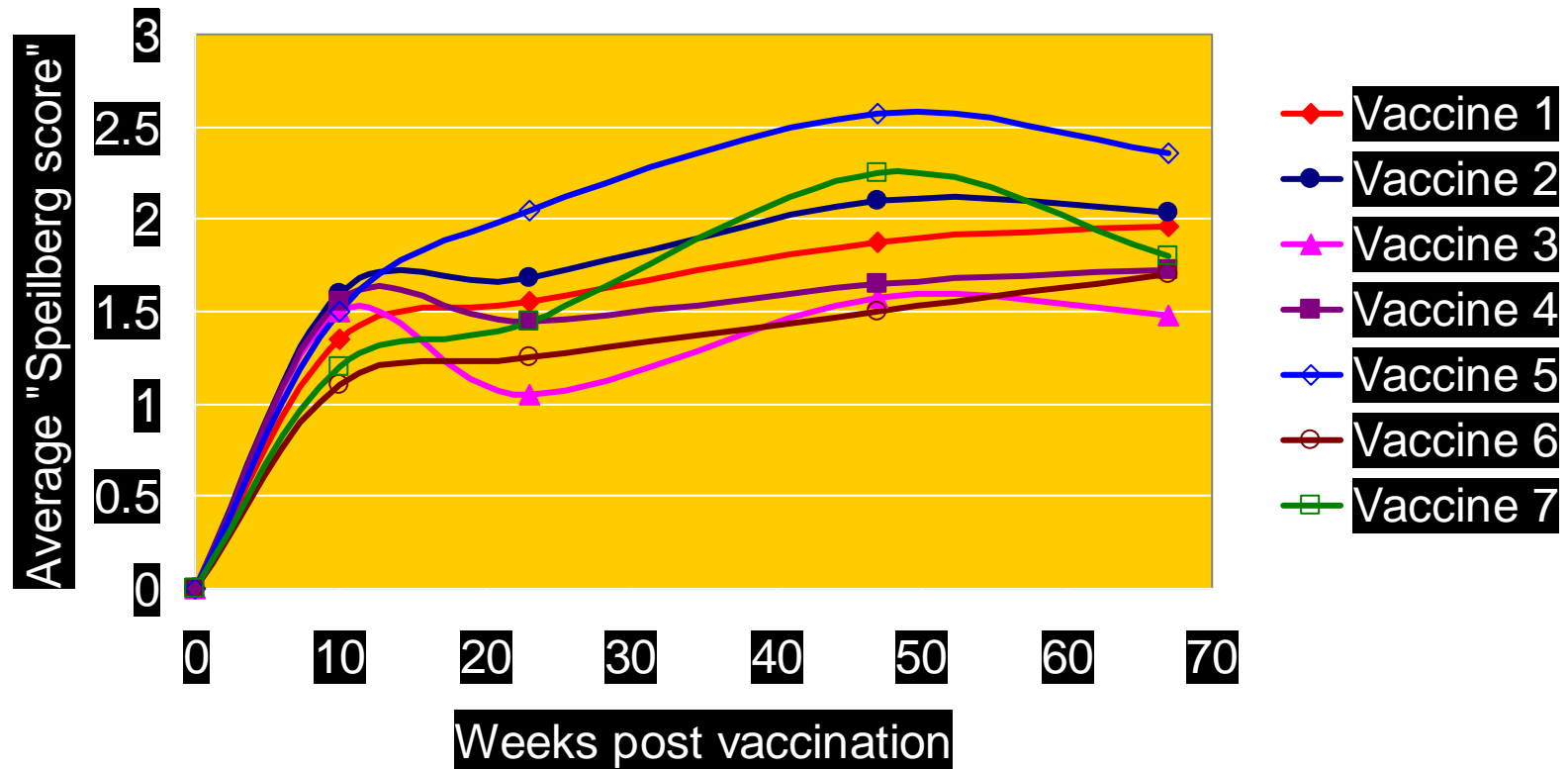
Local Reaction Distribution Chart

Unsatisfactory profile





Local reaction profiles of different vaccines

Mean "Speilberg scores" from vaccination until harvest



The ideal vaccination strategy

- Oral vaccines of high efficacy which could be given in or on the food as required
- Immersion vaccine  injection 
oral boosters as required.
- Currently salmonid industry relies on a single injection of a multivalent vaccine (6-7 antigens)
- Danger of antigen overload & antigenic competition
- New vaccines and vaccine strategy required

Other important aspects of a vaccination strategy

- **Size of fish at vaccination**
 - Smaller the fish ↑ risk of higher local reactions
- **Temperature @ vaccination**
 - Higher the temperature ↑ risk of higher local reactions
- **Onset of immunity** is temperature dependent
- **Adjuvants**
 - Various have been tried but oil based give best protection
- **Type and number of antigens**
 - Monovalent vs multivalent

Future vaccine developments may benefit from:

- Increased knowledge of the fish immune system
- Increased knowledge of pathogen and virulence mechanisms
- Novel expression systems
- Marker (live) vaccines
- Improved DNA vaccines
- Passive immunisation
- Improved adjuvants
- Oral delivery systems
- Immunostimulants

Fish vaccination Le FIN

- Aquaculture needs effective and safe vaccines to be sustainable
- Fish vaccinology is still a young and maturing science but amazing advances can be made
- These need to be translated into licensed products
- Hopefully this will mean lots of work for vaccine assessors!

Thank you for your Attention



Acknowledgement:
William Enright
Intervet International Ltd
for use of many of the
figures and photographs