



# **Side-effects of vaccination: an example of the conflict between guidelines and real life.**

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## **Aims of this meeting:**

**Define what is best practice and to pinpoint where our present knowledge is inadequate**

**We want to focus on an area that is not directly associated to fish as research animals, but still highly relevant to discuss in this forum.**



**Modern fish farming is highly industrialized and relies heavily upon effective vaccines to minimize losses caused by infectious diseases.**



**A consequence of this is that every salmonid transferred to sea-water in Norway (approximately 150 million individuals per year) are intraperitoneally vaccinated with multivalent, oil-adjuvanted vaccines prior to sea-transfer.**





# Modern multivalent fish vaccines used in Norway usually contain the following antigens:

- *Vibrio anguillarum* (2 serotypes)                      **Vibriosis**
- *Vibrio salmonicida*                                      **Cold water vibriosis**
- *Moritella viscosa*                                      **Winter ulcers**
- *Aeromonas salmonicida*                              **Furunculosis**
- IPNV                      **Infectious pancreatic necrosis – IPN**



**Modern vaccines are effective and have reduced losses caused by bacterial infections to a minimum, while certain viral diseases (IPN and ISA) still may cause considerable losses, even in vaccinated fish (IPN).**

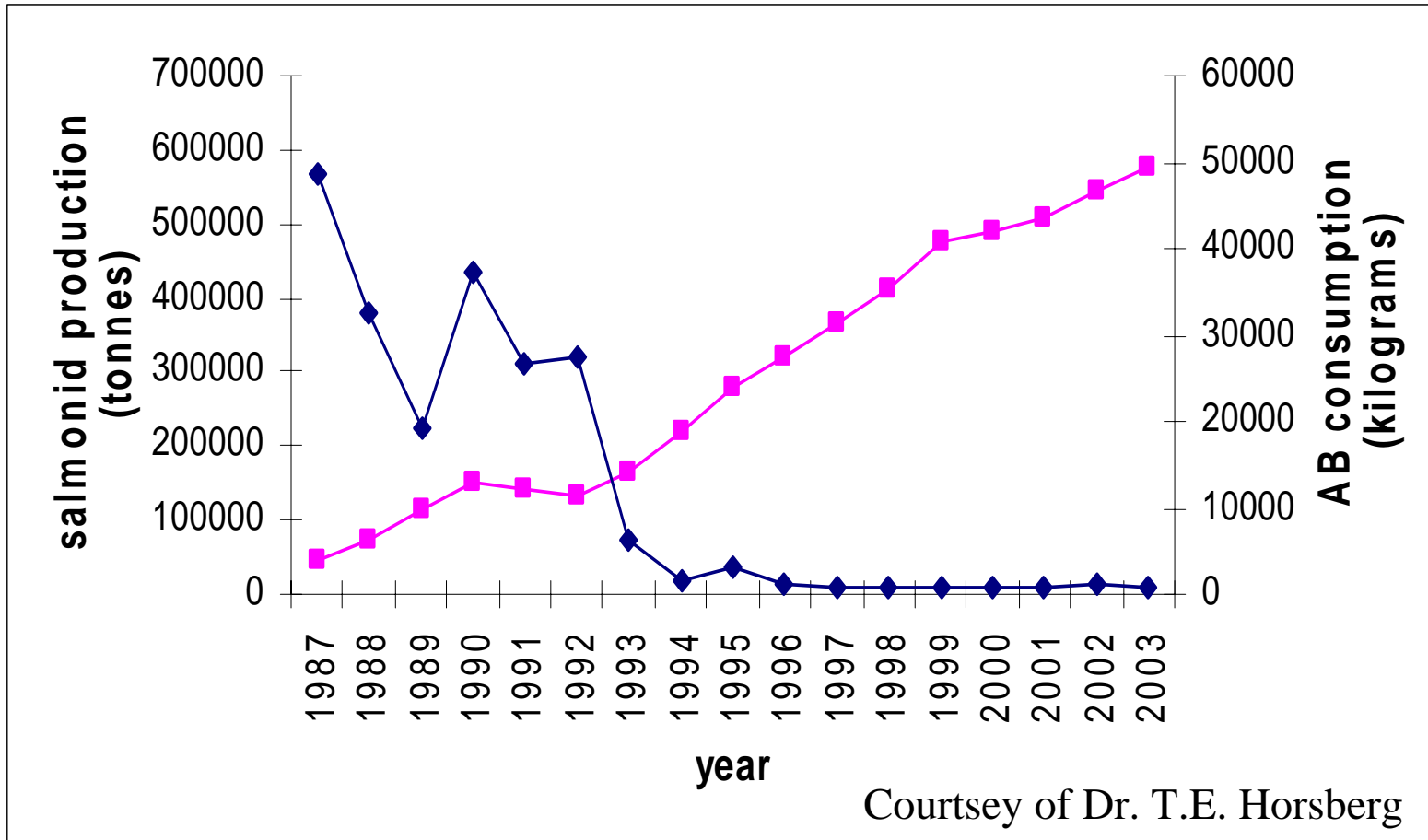
**Furunculosis in  
Atlantic salmon smolt**







**Modern fish farming is hardly possible without extensive use of effective vaccines. One very positive consequence is that the use of antibacterial drugs in Norwegian fish farming has been reduced to a minimum.**





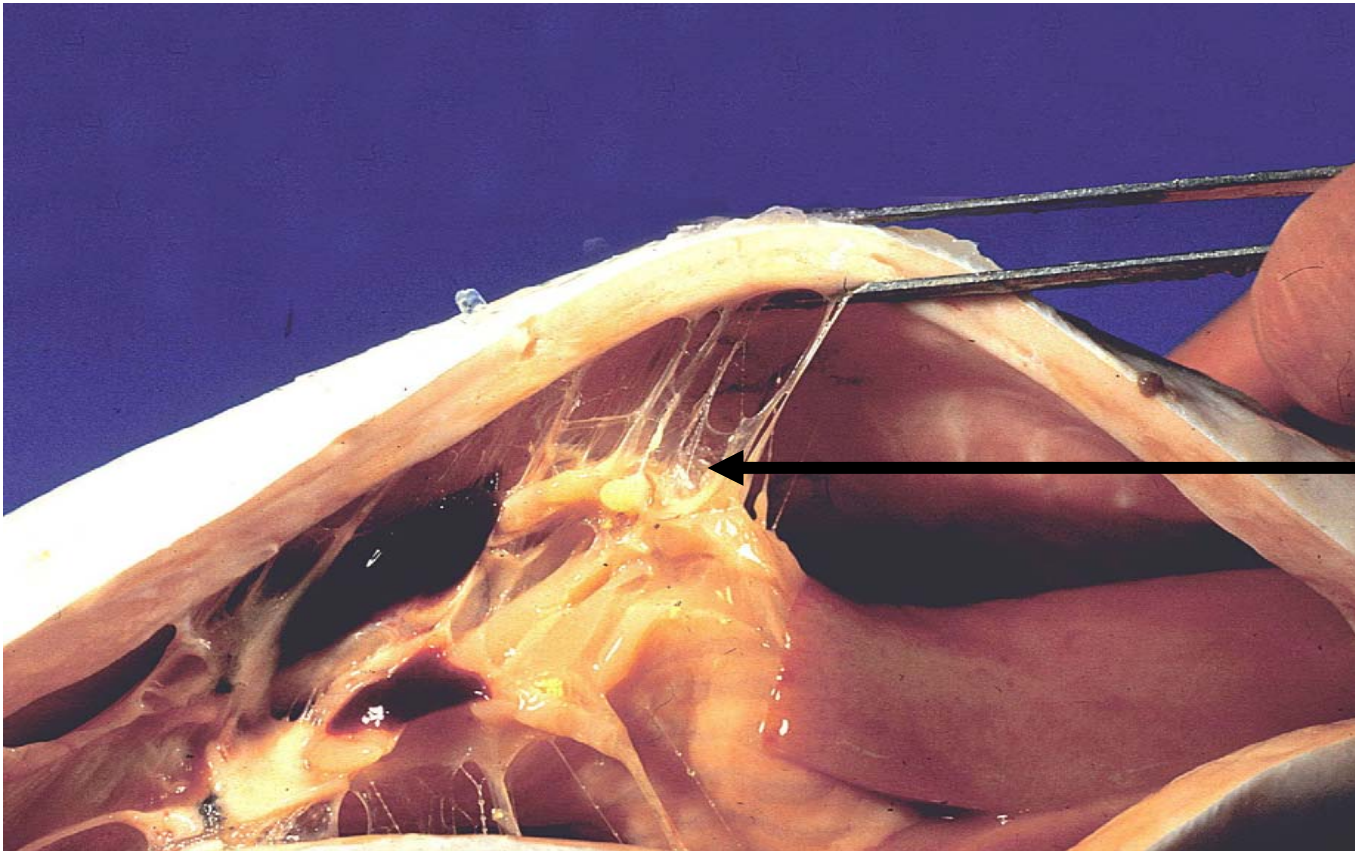
**Unfortunately, there is a strong correlation between effect and side-effects when using oil-adjuvanted vaccines in Atlantic salmon.**



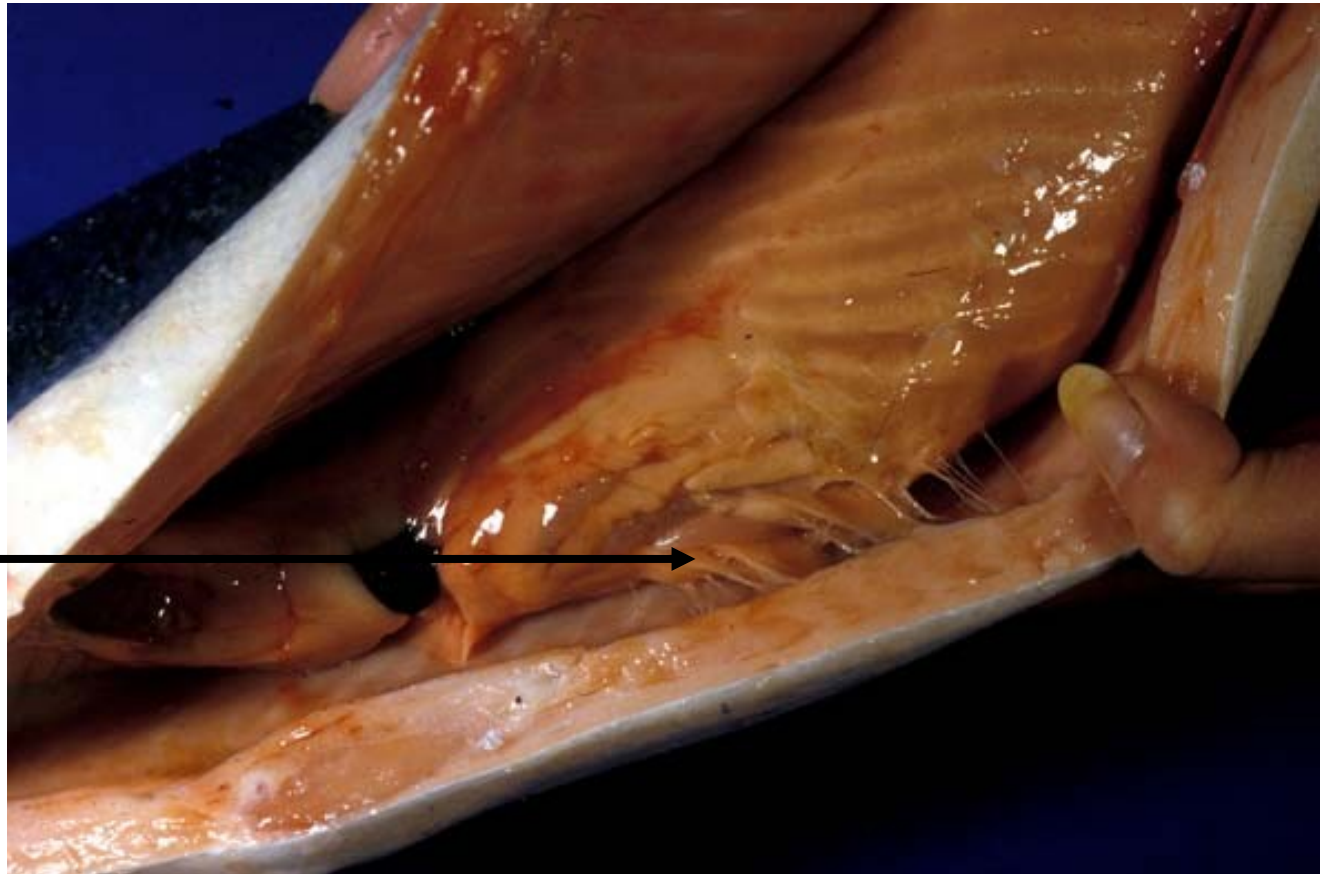




**Intraperitoneally administered oil-adjuvanted vaccines will always cause some degree of visible side-effects, first of all a granulomatous peritonitis with resultant adhesions between body wall and internal organs near the injection site.**



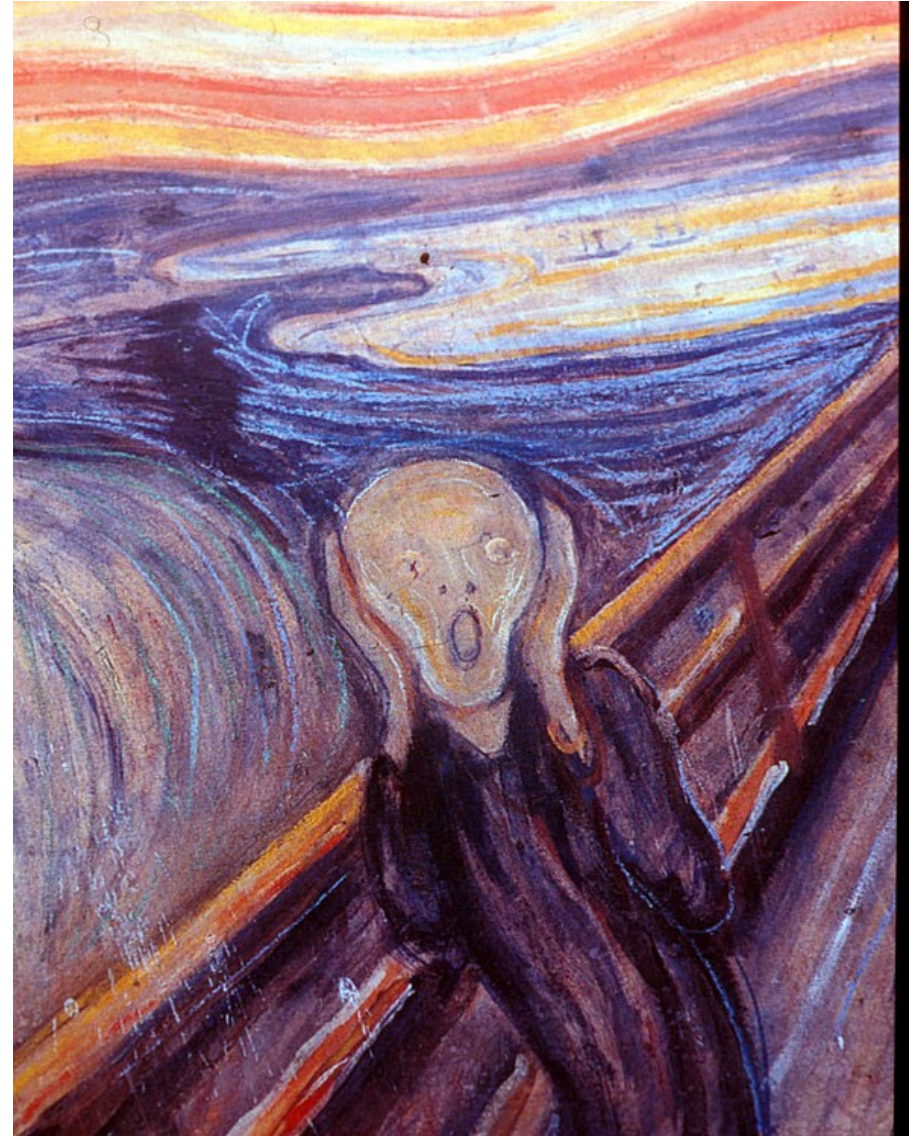
**In most cases, these lesions are within acceptable limits and cause no problems to the fish, to the farmer or to the consumers.**







**So why bother?**

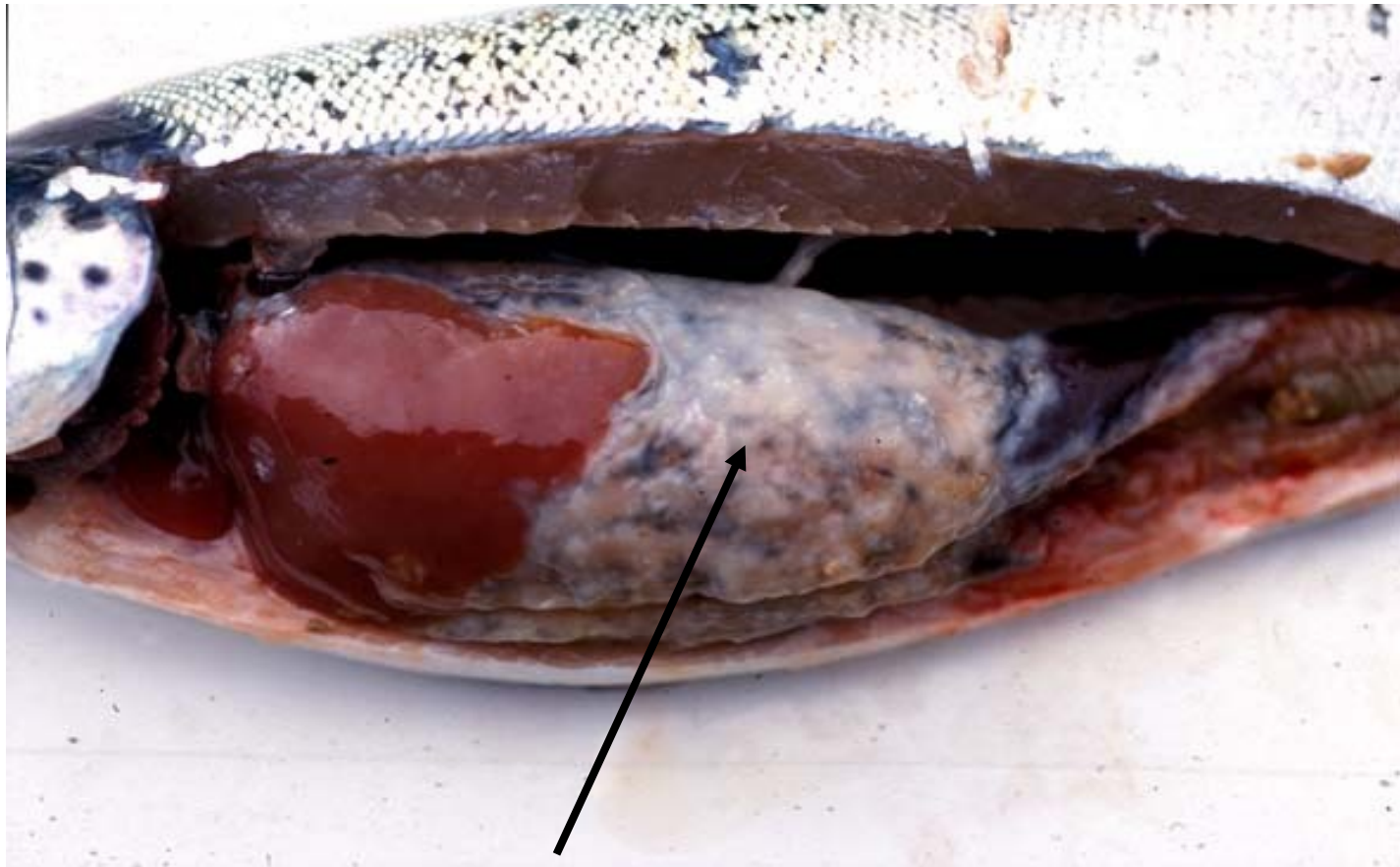


**Because:**

**Over the years fish farmers in Norway (and strangely enough to a very limited extent in other countries) have experienced severe and unacceptable side-effects in vaccinated fish.**

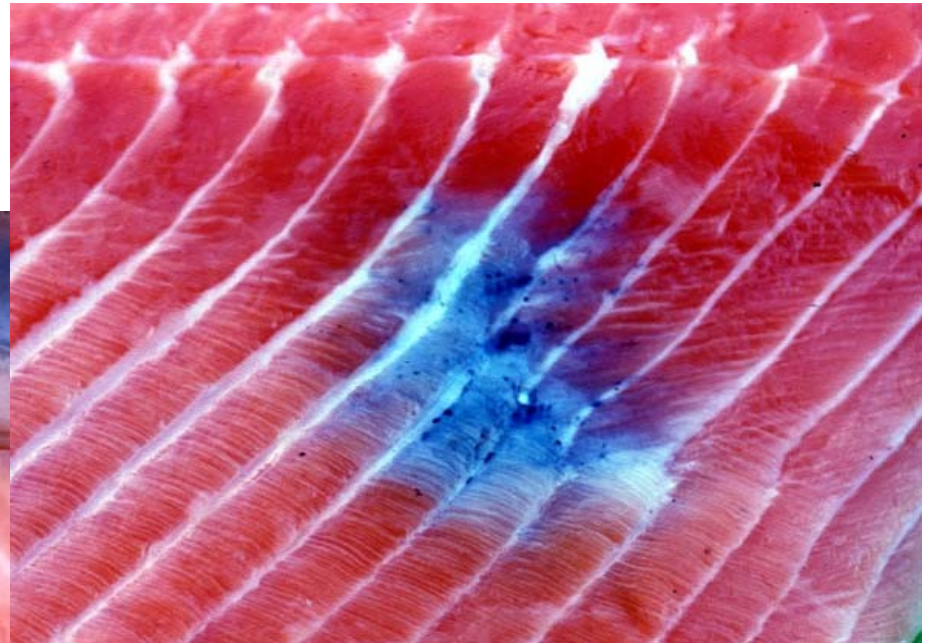
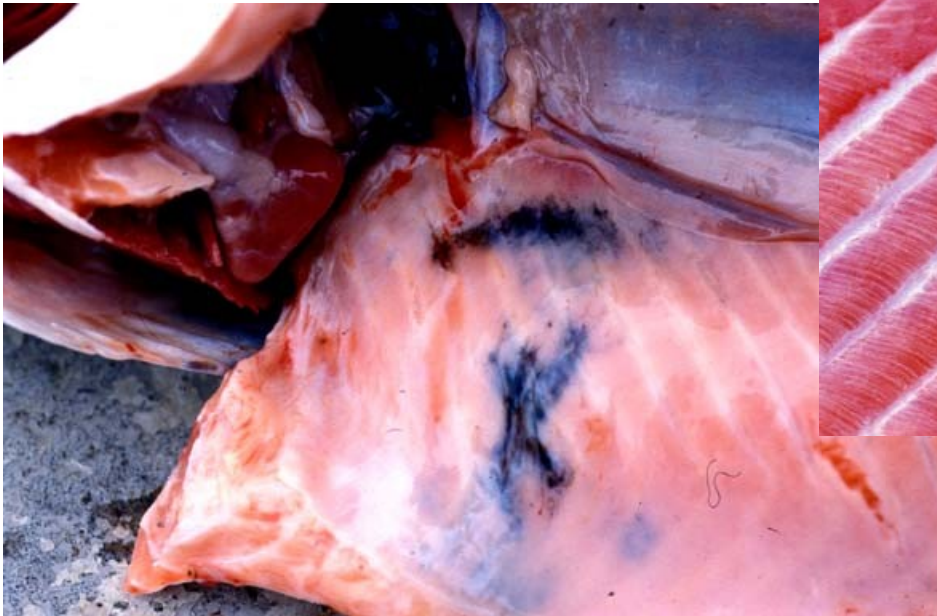


**In such cases, severe adhesions and a generalized granulomatous peritonitis causes retarded growth and increased mortality**





**Sometimes, lesions are not restricted to the abdominal cavity and internal organs, but may also affect the end product (i.e. the fillets), often with heavy melanization.**





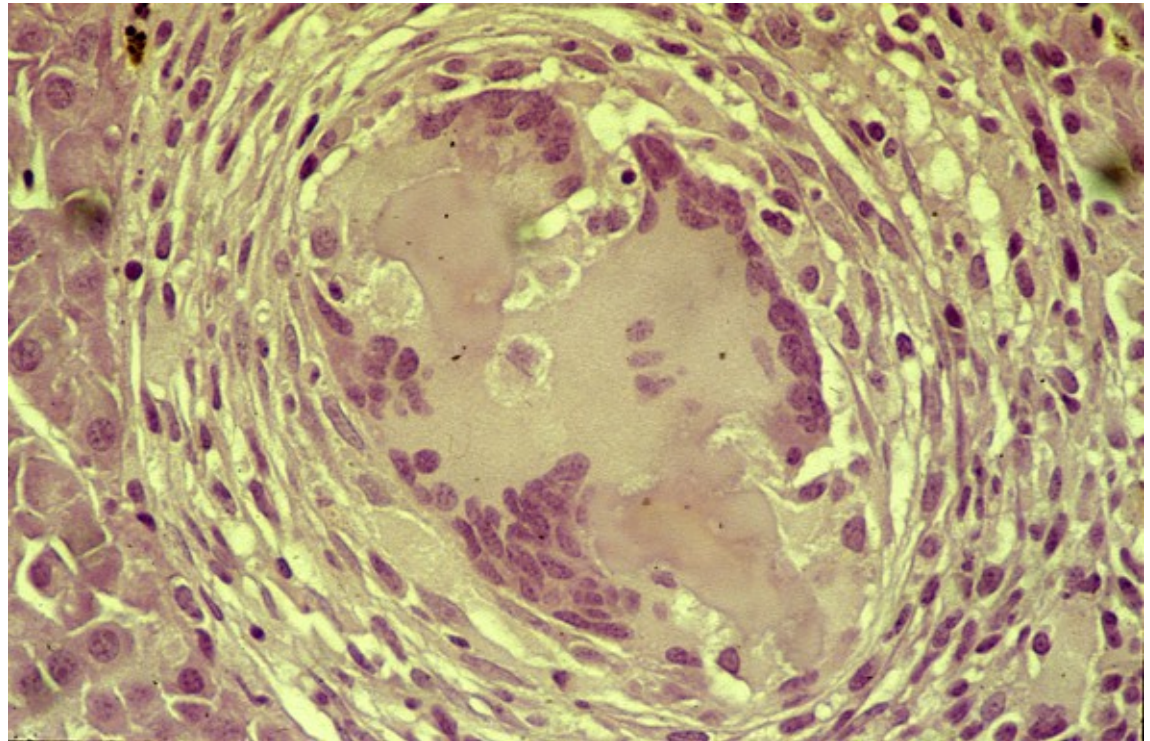


**Provocation: We save the majority of the fish from acute death caused by bacterial infections, but we sentence some to life-long suffering due to severe pathological lesions in internal organs.**



**At the present time, we have no consensus about pain perception in fish, but anorexia and retarded growth are good indicators.**

**Liver granuloma with multinucleated giant cell**





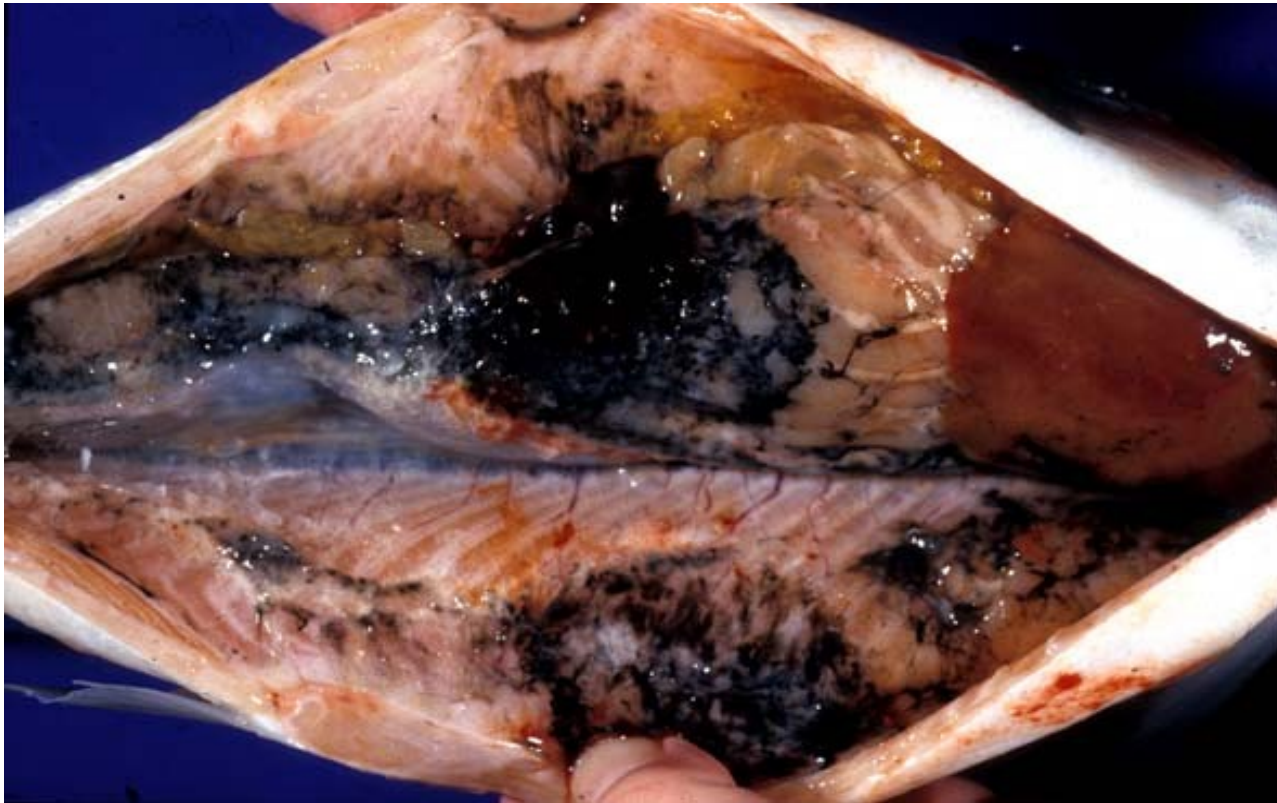
**Who can define the ethical and economical cost/benefit borderline?**







**Such cases have occurred at irregular and unpredictable intervals over the last 10-12 years. All vaccine producers on the Norwegian market have been represented in these cases.**





**The magnitude and significance of these cases are not known and are certainly underreported as most cases have been closed in agreement between the fish farmers and the vaccine manufacturer. This is confirmed by The Norwegian Medicines Agency (NMA).**

**The following data have been provided by NMA. It should be emphasized that the number of affected fish is VERY inaccurate and represent a MINIMUM**

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## Reported side-effects from fish health veterinarians to Norwegian Medicines Agency, 1996 to 2004

<b>Year</b>	<b>No. of fish in pop.</b>	<b>Remarks</b>
<b>1996</b>	<b>500.000</b>	<b>Plus 2 cases with unknown no. fish</b>
<b>1997</b>	<b>1 million</b>	<b>Plus 3 cases with unknown no. fish</b>
<b>1998</b>	<b>635 000</b>	<b>Plus 1 case with unknown no. fish</b>
<b>1999</b>	<b>0</b>	
<b>2000</b>	<b>42 700</b>	
<b>2001</b>	<b>275 000</b>	<b>25% of pop. with severe lesions</b>
<b>2002</b>	<b>920 000</b>	<b>Plus 1 case with unknown no. fish</b>
<b>2003</b>	<b>200 000</b>	
<b>2004</b>	<b>1.9 million</b>	<b>Plus 1 case with unknown no. fish</b>





# **How should we interpret these (very inaccurate) figures?**

**The problem is still present**

**Is this an example of testing where results obtained in experiments are far from what happens in real life?**

**Is this good enough? (acceptable)**

**Possible problems are not addressed well enough prior to release of the products?**



**How can this happen as long as these vaccines are approved by NMA following their testing protocols (since 2001)?**

**Explanations from the producers typically include:**

- **Temperature was too high during and after immunization**
- **The fish were too small**
- **Poor water quality**
- **Something went wrong in the production of one particular batch...**
- **Combination of factors above**



**Would this be acceptable in  
pets and traditional farm  
animals?**

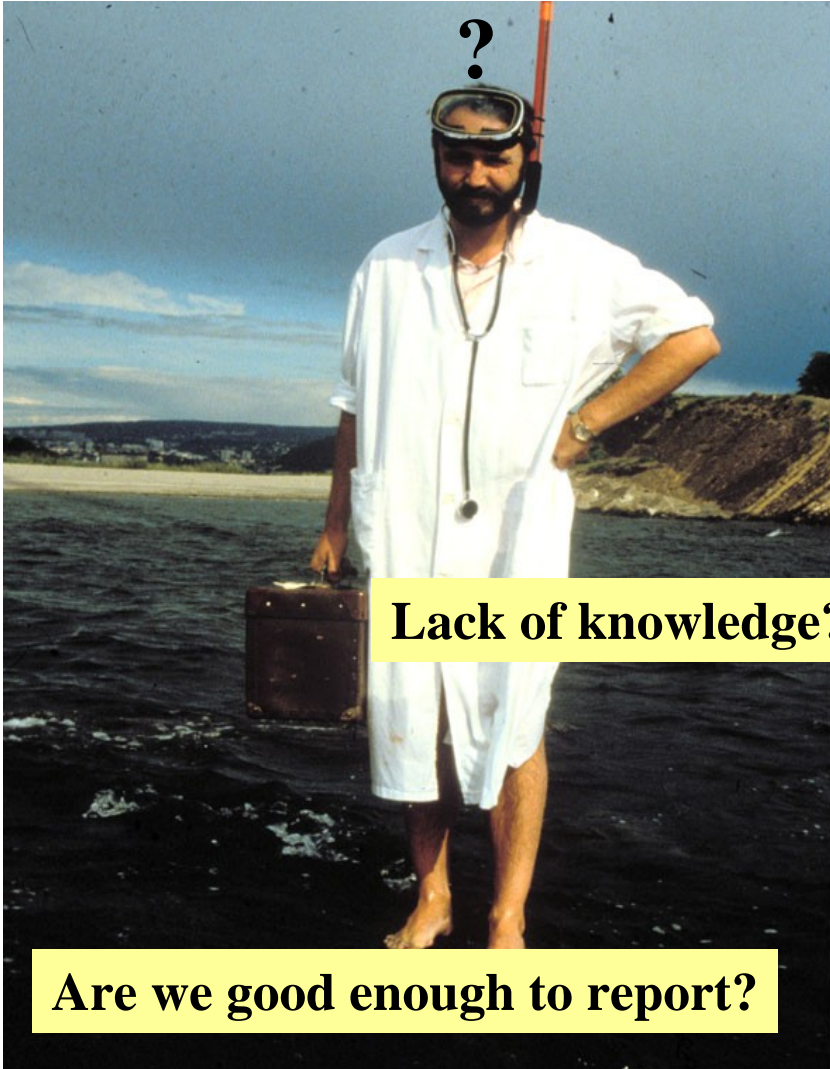


**No !**





# Why do we accept this in fish?



**Lack of knowledge?**

**Are we good enough to report?**



**”Fish is fish” (tradition)**



**Lack of ”bambi-appeal”?**



## **Provocation:**

**Should we INCREASE the number of experimental fish for vaccine testing prior to release in order to reduce the number of side-effects? (or how should we REFINE present testing?)**





**We are here to discuss the  
FISH.**

**A bonus for addressing this in  
a proper and decent way is  
the fact that consumers are  
very concerned about animal  
welfare and the "quality of  
life" for the fish prior to  
slaughter.**







## Summary:

- Vaccination is a "fact of life" for fish and modern fish farming is probably impossible without vaccines.
- Side-effects are still occurring after 12 years of extensive use of vaccines.
- Knowledge about chronic pain and suffering to affected fish is lacking
- Postulate: Field testing of vaccines is not adequate.
- How should we refine present testing to reduce side-effects?
- Feedback and reporting from farmers, fish health personell and producers must be improved and standardized.



**Thank you for your attention**