



# FISH DISEASES LACKING TREATMENT

Gap Analysis Outcome  
FINAL

FishMed + Coalition  
Federation of Veterinarians of Europe (FVE)





## Contents

Gap Analysis Outcome.....	0
EXECUTIVE SUMMARY:.....	2
Background:.....	4
 Methodology .....	4
<input checked="" type="checkbox"/>  Gap Analysis survey .....	4
Similar gap analyses .....	4
 Laboratory hit list.....	5
 Literature research .....	5
 Aquaculture in Europe (data from FEAP Annual Report 2015).....	6
 Results .....	6
Salmon.....	7
Trout      ( <i>Oncorhynchus spp</i> ).....	8
Seabass/Seabream .....	9
Flatfish.....	10
(Turbot, Halibut, ..).....	10
Cleaner fish .....	10
(Wrasse, lumpfish).....	10
Emerging species .....	11
Lack in groups of medication in all species .....	11
Emerging diseases mentioned: .....	11
<b>1. Annex 1: Products with Marketing Authorisation in some countries, mentioned in the survey (wished) to be used under the cascade in other countries .....</b>	<b>12</b>
<b>Annex II: Biocides used mentioned in the survey .....</b>	<b>14</b>
ACKNOWLEDGEMENTS.....	15
Correspondence .....	15



## EXECUTIVE SUMMARY:

The availability of veterinary medicinal products, including vaccines, for use in farmed aquatic animals is extremely low. This situation is a serious constraint on the prevention and treatment of disease, leading to welfare problems and hampering the growth of European Aquaculture. More than 60% of the aquaculture products eaten in the EU are imported. To prevent further use of non-authorized products, the FishMedPlus Coalition aims to increase the greater availability of authorized veterinary medicinal products for aquaculture on the market of European Union and EFTA countries.

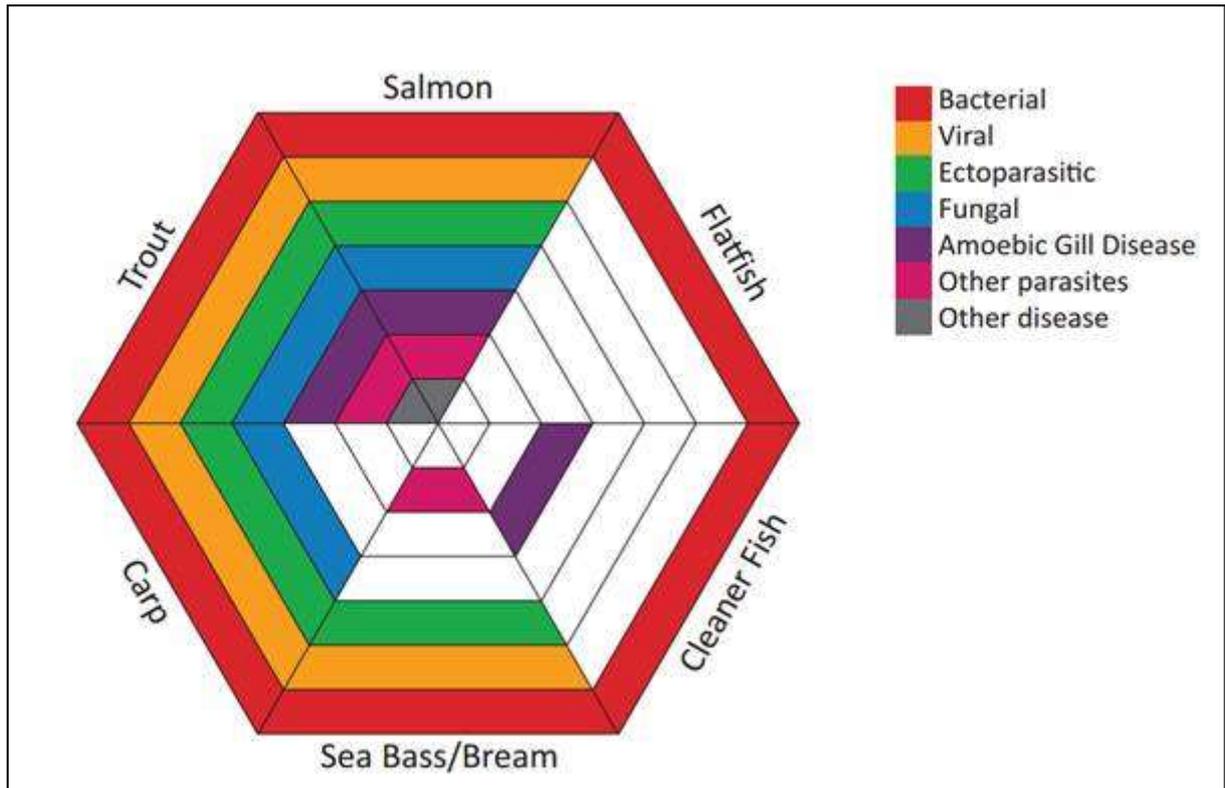
In order to know which veterinary medicines are urgently needed, in 2016 the Coalition undertook an initial gap analysis. The aim was to identify the critical diseases or indications for which little or no treatment options are available. Four sources of information was used: a dedicated survey to fish producers and veterinarians, similar gap analyses done in a selected number of countries, the laboratory "hit lists" showing the most frequently diagnosed diseases in aquatic animals and scientific research.

The Coalition focused on Salmon, Trout, Seabass, Seabream and Carp, which together are making up more than 94% of the weight of production in Europe.

The main priority diseases/indications identified were:

<b>PRIORITY LIST OF IDENTIFIED DISEASES/INDICATIONS</b>
<b>Ectoparasites</b> - Ich (Ichthyophthirius or Ichthyophthiriosis), costia (Ichthyobodosis), Sea/salmon lice, Monogenea infestation – All species
<b>Bacterial diseases</b> - Aeromonas - All species
<b>Fungal and Oomycotic infections</b> – All species
<b>Amoebic gill disease (AGD)</b> – Mostly Salmon
<b>Rainbow Trout Fry syndrome (RTFS)</b> – Flavobacteriosis – Trout and Carp
<b>Sedation and anaesthesia</b> - All species
<b>Viral diseases</b> – all species (see OIE list)
<b>Hormones</b> for broodstock management/maturation/ovulation induction
<b>Endoparasites</b> - in all species (mostly secondary effects, lower production parameters and food quality aspect)

In conclusion, parasite infections are a main cause of concern in all the fish species examined. Treatment to common parasites often lacks efficacy or is not available. Secondary bacterial infection can occur between parasitic and bacterial diseases. To prevent bacterial diseases occurring (and the need to treat with antibiotics) it is necessary to be able to effectively treat parasitic infections.





## Background:

The FishMedPlus Coalition, composed of many organisations and institutions active in the aquaculture sector and led by the Federation of Veterinarians of Europe (FVE), was established in December 2015. The aim of this Coalition is to increase the greater availability of authorized veterinary medicinal products for aquaculture to prevent further use of non-authorized products on the market of European Union and EFTA countries.

As a first step, this coalition undertook an initial gap analysis, to identify the critical diseases for which little or no treatment options are available and to identify where medicinal products are missing.

## Methodology

This gap analysis was done between May and July 2016. Four sources of information were used to do the gap analysis, namely

- A dedicated survey both available online as in MS Word.
- Similar gap analyses done in a selected number of countries
- Laboratory “hit lists’ showing the most frequently diagnosed diseases in aquatic animals.
- Scientific literature metadata analysis

This gap analysis only focuses on fin fish. It does not include shellfish or crustacean aquaculture. It is recognised that also in these species gaps exist and that a future gap analysis would also be beneficial.



### Gap Analysis survey

The **dedicated survey** was active between 1 May to 31 July 2016 and was available both via online survey via SurveyMonkey and via an MS Word survey. In total, 54 institutes/individuals answered the survey out of 19 European countries. This resulted in a total number of 178 species/disease/gap indications. Participants were asked to score on the basis of reasons of animal health and welfare, productivity loss and economic loss.

### Similar gap analyses

**Similar gap analyses** were found to already have been done in a selected number of countries, namely:



- In France, done by the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) in 2014
- In Spain, done by the Agencia Espanola de Medicamentos y Productos Sanitarios (AEMPS) (last revised in January 2016)
- In Norway, by the Norwegian Veterinary Institute in its Fish Health report 2015



### Laboratory hit list

The **laboratory hit list** of the EU reference lab in Denmark was used. See <http://www.eurl-fish.eu/>

In addition, the outcome report of the 20th Annual Workshop of the National Reference Laboratories for Fish Diseases Copenhagen, Denmark May 31st – June 1st 2016 was used.



### Literature research

The **scientific literature metadata analysis** showed relative significance/occurrence of the different types of fish diseases in literature. It does not reflect the severity of the impact or the economic impact.

Fish diseases* most researched are:	Relative Significance of Fish Disease Types in Scientific Literature 2000-2015										
<ol style="list-style-type: none"> <li>1. Nematoda (P)</li> <li>2. Monogenea (P)</li> <li>3. Myxozoa (myxobolus) (P)</li> <li>4. Digenea (P)</li> <li>5. Cestoda (P)</li> <li>6. Flavobacterium (B)</li> <li>7. Herpesvirus (V)</li> <li>8. Acantocephala (P)</li> <li>9. Infectious salmon anaemia (ISA), (V)</li> <li>10. Streptococcus (B)</li> <li>11. Saprolegniasis (F)</li> <li>12. Salmonid alphavirus (V)</li> <li>13. Ichthyophthirius (P)</li> <li>14. Furunculosis (B)</li> <li>15. Viral haemorrhagic septicaemia (VHS) (V)</li> </ol>	<table border="1"> <caption>Relative Significance of Fish Disease Types in Scientific Literature 2000-2015</caption> <thead> <tr> <th>Disease Type</th> <th>Relative Significance (%)</th> </tr> </thead> <tbody> <tr> <td>Parasitic (P)</td> <td>43,8</td> </tr> <tr> <td>Bacterial (B)</td> <td>30,6</td> </tr> <tr> <td>Viral (V)</td> <td>21,8</td> </tr> <tr> <td>Fungal (F)</td> <td>3,7</td> </tr> </tbody> </table>	Disease Type	Relative Significance (%)	Parasitic (P)	43,8	Bacterial (B)	30,6	Viral (V)	21,8	Fungal (F)	3,7
Disease Type	Relative Significance (%)										
Parasitic (P)	43,8										
Bacterial (B)	30,6										
Viral (V)	21,8										
Fungal (F)	3,7										

\*The disease names and/or etiological agent were taken from PTK Woo Fish Diseases and Disorders vol. 1-3 (2<sup>nd</sup> Ed).



## Aquaculture in Europe (data from FEAP Annual Report 2015)

The EU is a major consumption market of fish products in the world and the first importer worldwide (>60% of fish eaten is imported).

In Europe, 3 types of fish production takes place:

- Marine Cold Water (71%) – mostly Atlantic Salmon 93%, Trout 7%
- Fresh Water Production (15%) – mostly Trout 78%, Carp 17%, Catfish 2% and Eel 2%
- Marine Mediterranean species (13%)- mostly Sea Bass 49% , Sea Bream 45%, and Flatfish 4%

So the most important species in Europe farmed are Salmon, Trout, Seabass, Seabream and Carp making up more than 94% of the weight of production.

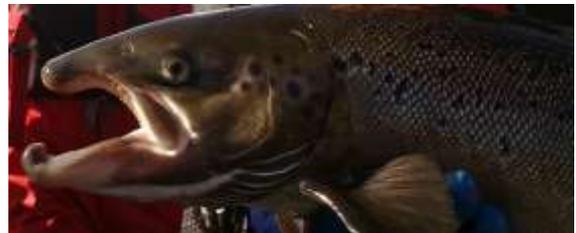
Looking at the increasing demand for fish products and the stable fisheries sector it is clear that there is a strong role that European aquaculture can play in filling the gap between EU consumption and domestic supply. To increase EU's self-sufficiency level, European aquaculture needs to grow substantially. To do so, the sector needs authorized veterinary medicines to prevent and treat the most common diseases and secure animal welfare.

### Results

Underneath you can find the results of the gap analysis, listing per species the gaps in order of importance.

## Salmon

(*Salmo* or *Oncorhynchus* spp)



1. **Ectoparasitic infections:** Salmon/sea lice (problems with increasing levels of resistance to medicines, combined with off label use, e.g. increased doses/holding times and ineffective combination treatments, which is leading to rising mortality to treatments), MRLs have been established for hexaflumuron and lufenuron but no product is yet on the market
2. **Viral infections:** Pancreas Disease (PD<sup>1</sup>) by Salmonid Alphavirus (SAV), Heart and skeletal muscle inflammation (HSMI), Salmon Gill Poxvirus, Infectious Pancreatic Necrosis (IPN)<sup>2</sup>, Infectious Salmon Anemia (ISA)<sup>3</sup>
3. **Fungal infections** especially during all fresh water stages from eggs to smolts
4. **Amoebic gill disease (AGD)** e.g. *Neoparamoeba perurans* and other gill disease
5. **Bacterial disease** (vaccines are already widely used for several diseases but there is a need for further vaccine development to reduce reliance on antimicrobials)
6. **Tape worms** (praziquantel, is currently used, but increase resistance is seen, both fenbendazole and praziquantel have established MRLs for other species but not for fish, are used under the cascade)
7. **Other parasites**

---

<sup>1</sup> Both Intervet/MSD and Pharmac have single component PD vaccines holding MA in Norway (and Ireland, UK). Intervet/MSD also has a multivalent vaccine with PD component holding MA in Norway. Although Pharmac have MAs for PD vaccine, patent dispute with MSD has prevented its use. On EU level, in 2016 a positive CVMP opinion was given for a marketing authorisation for CLYNAV, a biotechnological vaccine based on a DNA plasmid that protects Atlantic salmon against pancreas disease caused by infection with salmonid alphavirus subtype 3.

<sup>2</sup> IPN was big problem in the past but less now due to successful breeding programs.

<sup>3</sup> Vaccines exists, but not licensed in Europe yet and only in Norway available upon special prescription..

## Trout

(*Oncorhynchus spp*)



1. **Ectoparasitic infections:** *Ichthyophthirius multifiliis* (Ick, white spot), *Ichthyobodo spp.* (ichthyobodiasis or costiasis), *Trichodina spp.*, *Gyrodactylus spp.* (gill and skin fluke), *Dactylogyrus spp* (gill fluke), *Diplostomum spathaceum* (diplostomiasis - eye fluke)
2. **Bacterial infections:** such as *Aeromonas spp. e.g. salmonicida*, *Flavobacterium* <sup>4</sup>spp. e.g. *psychrophilum* (Rainbow Trout Fry syndrome (RTFS) - flavobacteriosis), Lactococcosis (especially need for vaccine development to reduce reliance on antimicrobials, Lactococcus vaccine is available via HIPRA Spain (ICTHIOVAC® LG)), *Yersinia ruckerii* (Enteric Red Mouth – ERM), bacterial kidney disease (BKD)
3. **Viral infections:** Infectious Pancreatic Necrosis (IPNV), rhabdovirus IHNV and VHSV
4. **Parasitic myxozoan infections:** Proliferative Kidney Disease (PKD)
5. **Fungal and oomycotic infections:** *Saprolegnia sp.* (saprolegniosis)
6. **Amoebic gill disease (AGD - *Neoparamoeba perurans*)**
7. **Aetiology unknown:** Red Mark Disease (RMD), Puffy Skin disease, (warm water) Strawberry disease, Rainbow Trout Gastroenteritis (RTGE, gastro)

---

<sup>4</sup> Zoetis/Pharmaq has developed a *Flavobacterium*-component vaccine in Norway via a special permit. The permit was granted with a condition that the company should establish documentation for this vaccine with the aim to apply for a marketing authorisation.

## Carp

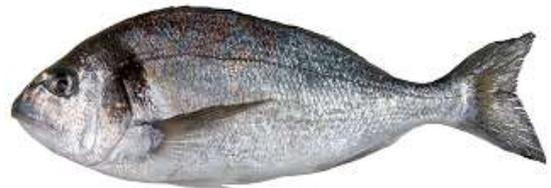
(*Cyprinidae spp*)



1. **Ectoparasitic infections:** *Ichthyophthirius multifiliis* (Ich, white spot), *Ichthyobodo spp.* (ichthyobodiasis or costiasis), *Argulus spp.* (fish louse), *Lernea sp.* (anchor worm), *Trichodina spp.*, *Gyrodactylus spp.* (gill and skin fluke), *Dactylogyrus spp* (gill fluke),...
2. **Fungal and Oomycotic infections:** *Saprolegnia sp.* (saprolegniosis, oomycota), *Branchiomyces* (gill rot disease, branchiomycosis, fungus).
3. **Bacterial infections:** *Aeromonas hydrophilla* (septicaemia, erythrodermatitis); *Aeromonas salmonicida* (furunculosis), *Flavobacterium columnare* (columnaris disease or flavobacteriosis),...
4. **Viral infections:** Cyprinid Herpesvirus 3 (koi herpes virus, KHV), Carp oedema virus (koi sleeping disease), Spring viremia of carp virus (SVC), Cyprinid herpesvirus 1 (carp pox).
5. **Aetiology unknown:** Carp oedema virus or Koi sleeping disease

## Seabass/Seabream

(*Sparus Aurata*)



1. **Internal Parasites infections:** *Enteromyxum leei*, *Enterospora nucleophile*,...
2. **Ectoparasitic infections:** *Sparicotyle spp* e.g. *chrysophrii* (sparicotylosis, gill anemia)
3. **Bacterial infections:** *Vibrio spp* (e.g. *Vibrio Anguillarum* and *Vibrio harveyi*, vibriosis), *Aeromonas spp*, *Photobacterium damsela* (pasteurellosis), *Mycobacteriosis* (zoonosis), *Flavobacterium columnare* (columnaris disease or flavobacteriosis),...
4. **Viral infections:** Viral Nervous Necrosis virus (VNN), Nodavirus infection (seems to play an increasing role, before resistant, now susceptible).

### Flatfish

(Turbot, Halibut, ..)



The gap analysis did not give a lot of information on flatfish. If anybody has additional info, please let us know.

Bacterial infections<sup>5</sup>: *Vibrio logei*, *Vibrio splendidus*, *Listonella (vibrio), anguillarum O2*, *Aeromonas salmocida* (atypical)

### Cleaner fish

(Wrasse, lumpfish)



1. **Bacterial infections:** *Aeromonas salmonicida* (atypical), *Vibrio ordalii*, *Vibrio logei*, *Vibrio splendidus*, *Listonella (vibrio) anguillarum O1 and O2*
2. **Amoebic Gill Disease** (*Neoparamoeba perurans*)

#### Remark:

- Cleaner fish at this moment are generally not eaten (no MRL needed). It is possible to treat them during breeding (ideally via vaccination), before they are put in the final cages. Nevertheless, it is important to maintain healthy populations as they are essential for control of sea lice. Also for sustainability reasons and to prevent food waste, slaughter of cleaner fish should be considered in the long run.
- Cleaner fish may be a vector to other diseases

---

<sup>5</sup> For several of these bacterial diseases, applications have been made to develop autogenous vaccines



### Emerging species

In marine: meagre (*Argyrosomus regius*), common dentex (*Dentex dentex*), tuna (*Thunnus spp*), yellow tail (*Seriola spp*).

In freshwater: Tilapia (*Oreochromis spp*) - already produced in a small amount in Europe, Pike-Perch (*Sander lucioperca*), African catfish (*Clarias spp.*), different sturgeon species (white sturgeon (*Acipenser transmontanus*), sterlet sturgeon (*Acipenser ruthenus*)), jade perch (*Scortum barcoo*), ...

### Lack in groups of medication in all species

1. Sedation and anaesthesia
2. Hormones for broodstock management/maturation/ovulation induction<sup>6</sup>

### Emerging diseases mentioned:

1. Sturgeon: viral infections such as herpesviridae e.g. acipenser herpesvirus, and iridoviruses
2. Lumpfish: iridoviruses, VHSV genotype IV

---

<sup>6</sup> Only few hormones are licensed such as Buserelin (Receptal by Intervet UK)



## 1. Annex 1: Products with Marketing Authorisation in some countries, mentioned in the survey (wished) to be used under the cascade in other countries

FVE and FEAP has created a list of aquatic medicines authorised in the different European countries ([link](#)). The underneath table lists a selective number of products with marketing authorisation in fish in certain countries, for which broader availability was suggested by the survey respondents. It is crucially important that veterinarians can easily import aquatic products licensed in other European countries, in order that they do not have to resort to non-authorised products. In some countries, for environmental reasons, veterinarians are not given consent to use certain authorised aquatic medicinal products via the cascade.

Active substance	Trade name	Licensed in	Notes
Florfenicol	Florocol, Aquaflor–MSD	Austria, Bulgaria, Czech Republic, Croatia, France, Italy, Norway, UK, ...	against <i>Aeromonas salmonicida</i> infection in Atlantic Salmon
Oxytetracycline hydrochloride	Aquatet– Pharmaq Ltd	Ireland and UK	against <i>Aeromonas salmonicida</i> and columnaris disease in Atlantic salmon, and furunculosis and enteric redmouth disease in Rainbow trout
Amoxicillin trihydrate	Vetremox Fish - Pharmaq	UK	against <i>Aeromonas salmonicida</i> in Atlantic salmon
Formaldehyde	Aquacen formaldehyda - Cenavisa SL	Spain, Portugal and Greece	Formaldehyde is licensed as VMP in some countries but also used as a biocide. Active applications are on the way in other countries.  In Norway, it can be used under the cascade for eggs and fry, although not for sea lice as this would require massive volumes and gives environmental concerns.
H2O2	Paramove -Solvay” Hydrogenperoxid - Akzo Nobel”	UK, Ireland and Norway	For use in Salmon ( <i>Salmo salar</i> ). Used both against AGD and Sea Lice)



Tricaine methane sulphate	Finquel vet - Scan Aqua Tricaine – Pharmaq Ltd Nytox – Neptune Pharma Ltd	Norway, UK, Ireland, Iceland, Spain, Italy and Greece	Sedative but difficult to buy in many countries, etc
Benzocaine	Benzoak vet - ACD Pharmaceuticals AS	Norway	Sedative
Isoeugenol	Aqui-S vet - Scan Aqua	Norway	Sedative
Emamectin benzoate	Slice - MSD Animal Health	Norway, UK	Against <i>some</i> stages of sea lice
Azamethiphos	Salmosan Vet - Fish Vet Group  Azasure – Neptune Pharma	Norway and UK	against Sea Lice
Teflubenzuron	Calicide - Trouw Ltd Ektobann (medicated pellets) – Skretting AS	Norway, UK	Against sea lice
Deltamethrin	Alpha Max/AMX – Pharmaq AS	Norway, UK	Against sea lice
Enrofloxacin	Baytril - Bayer	Romania	Enrofloxacin is used in some countries as broad spectrum antibiotic against bacterial infections. It should be noted that this is a critically important antibiotic and has a long depletion time.
Diflubenzuron (in the group of benzoylureas)	Releeze vet. "EWOS AS" (medicated pellets), authorized for use in Atlantic salmon ( <i>Salmo salar</i> )	Norway	Against some stages of Salmon Lice ( <i>Lepeophtheirus salmonis</i> )
Buserelin	Receptal - Intervet UK Ltd	UK	

Some products have an MRL set for fish, but no products have a marketing authorisation such as Erythromycin (important against Lactococcosis (trout). Gram +), Doxycycline (many uses) and Tylosin (Gastroenteritis syndrome (trout)). It would be good if products with these active substances could get a marketing authorisation.



Products with only an MRL in other species, for which fish experts would like to see an MRL extension for fish

- Flubendazole (Flubenol) - dewormer
- Praziquantel (eg Cestocur)

Other products

- 17-alpha-methyltestosterone (this is a hormone<sup>7</sup> used for broodstock management/maturation/ovulation induction, it does not have an MRL)
- Ovaplant (sGnRHa)

## Annex II: Biocides used mentioned in the survey

Note: Biocides are used as water disinfectant or disinfectant in general (equipment, tank sides and so on). According to legislation, if biocides are used not only for routine disinfection but for direct treatment/metaphylaxis/prophylaxis (medicinal claim), the product falls under the EU definition of a Veterinary Medicinal Product. In some countries, it is allowed to treat the water without the fish in it, as biocide. If you treat water with fish on it, it needs to be a VMP.

- Potassium permanganate (KMnO<sub>4</sub>) – disinfectant that also is active against parasites
- Chloramine T – biocide and mild disinfectant, used in some public water supplies instead of active chlorine, some countries/local wastewater regulations may require water treated to be “neutralized” with thiosulphate or similar compound until residual chlorine level falls under certain value (e.g. 0.01 mg/L)
- Copper Sulphate – is used to disinfect the nets (exists as VMP for cattle, so has MRL set)
- Organophosphates are used to treat monogenean flukes, *Gyrodactylus* spp. (skin fluke) and *Dactylogyrus* spp. (gill fluke), as well as leeches and crustacean ectoparasites *Argulus* (fish lice) and *Lernaea* (anchor worm). Example of products are Soldep - Trichlorfon (Bayer) was taken from the market. Azamethiphos in Norway and the UK is replacing the older product.
- Other biocides used commonly in some countries are sodium percarbonate, quaternary ammonium compounds (QACs, used e.g. against bacterial gill disease, licensed in some countries such as under Vetark’s Ark-Klens’ and NT Labs ‘Gill Wash’ in the UK) and Peracetic acid (used against ectoparasites, licensed under ‘Wofasteril’).

---

<sup>7</sup> Regulated by Council Directives 96/22/EC and 96/23/EC related to the prohibition of use, use under specific conditions and monitoring of residues of such kind of substances



#### **Banned products:**



- Malachite Green - used as an antimycotic and antiparasitic substance, effective against Ichthyophthirius, has no MRL established, and is banned in the EU due to carcinogenic properties. Based on Council Directive 96/23/EC, Malachite Green and Leuco-malachite Green are included in VMPs residues monitoring program in the group B3 (other substances and environmental contaminants), dyes (B3e).

## ACKNOWLEDGEMENTS

FVE is grateful to the many experts who completed the gap analysis and provided valuable comments and expert advice during the production of this report. They also thank all members of the FishMed+ Coalition [Peter Jones (UK, FVE -Chair), Rick Clayton (IFAH), Tonje Høy (Norway –CVMP observer), Jordi Lopes (ES, FEAP), Leona Nepejchalová (CZ -Institute State Control of Veterinary Biologicals & Medicines/Research Institute Fisheries and Hydrobiology), Kari Norheim (NO -FVE), Ariane van de Moer (FR -IFAH/Virbac), Dusan Palić (DE - Ludwig-Maximillians-Universität Muchen/WAVMA), Jason Partridge (UK -Elanco/IFAH), Veronika Piačková (CZ), Patrick Smith (UK -EAFP), Kenneth Stapleton (UK – CVMP observer), Jimmy Turnbull (UK - Stirling) and Nancy De Briyne (FVE)].

Prof. Dušan Palić, Dr. Kari Norheim and Mrs. Nancy De Briyne are gratefully acknowledged for the preparation of the report.

## Correspondence

Any correspondence relating to this report should be sent by e-mail to: [nancy@fve.org](mailto:nancy@fve.org)