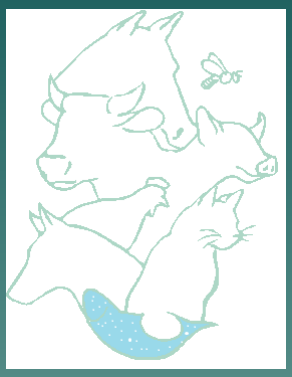
Veterinary Medicinal Products in Aquaculture



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Topics

- Active ingredients with MRL for fish
- VMPs licensed for fish
- Changes since 2007
- Needs
- Costs for registration and RoI
- Consequences and proposals

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Background:

- Mission is to promote a predictable, harmonised, science-based and innovative market place for the provision of quality animal medicines, vaccines and other animal health products, and so contribute to a healthy and safe food supply, and to a high standard of health and welfare for animals and people (IFAH mission).
- Any product must be safe and efficacious based on controlled studies in the target species. Any claim made must be substantiated / justified (Dir. 2001/82).

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MRLs for fish

Species	Actives with MRL (year MRL granted)
Fish	Azamethiphos (2012) Deltamethrin (2000) Emamectin (2001) Florfenicol (1997) Isoeugenol (2011) Thiamphenicol (1998)
Extension to Salmonidae	Benzocain (2001) Cypermethrin (1998)
	Oxytetracyclin Amoxicillin Sulfadimethoxine
Desinfectants	Iodine complex Chloramine T
Products listed in Annex 2 of former Reg. 2377/90 (MRL)	e.g. Bronopol (fin fish, farmed fertilised fish eggs)

Non-exclusive list: www.ema.europa.eu

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Authorised Products

Species	Product (Active)	Indication	Country
Pharma ceuticals	Alpha Max 10 mg/ml	Salmon, Trout, Fish: Sea lice	NO, MRP
	AMX 10 mg/ml	Fish: Furunculosis, ERM	
	Aquatet 100 % w/w Premix	Salmon, Trout: Furunculosis	Chile
	Birnagen Forte	Salmon: Furunculosis	UK
	Excis 10 mg/ml	Salmon: Furunculosis	UK, IR
	Alphacol Premix (Florfenicol)	Salmon: Furunculosis	UK
	Paramove	Fish: Fungal Infection	Many
	Pyceze 500 mg/ml	Salmon, Trout: Fungal Inf.	UK
	Receptal	Salmon: Sea Lice	UK
	Salmosan Powder for Susp (Azamethiphos)	Trout: facilitate stripping Salmon, Trout: Sea Lice	UK
	Slice	Breeding fish:	UK
	Tricaine (MRP)	Trout: Furunculosis	UK
	Terramycin Sol Powder	Fish: Furunculosis	CY
	Vetremox Fish 100 %		UK

Non-complete list

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Authorised Products

Species	Product (Active)	Indication	Country
Vaccines	Alpha Ject 2-2	Fish:	NOR, UK,
	Aquavac Vibrio	Salmon, Trout: Virbriosis	NOR, MRP
	Aquavac ERM	Trout: Enteric Redmouth D	MRP
	Aquavac Relera	Fish: Enteric Redmouth D	UK, MRP
	Aquavac FNM	Salmon: Furunculosis	Various (14)
	Ermogen	Trout: Enteric Redmouth D	Various (14)
	Norvax Compact PD	Salmon: Pancreas disease	PT, UK, FR, DK

More fish species kept for food production than actives with MRL or products licensed

Non-complete list

As searched on national product libraries

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Situation

- Use of many products not evaluated for safety and efficacy in the target species/indication
  - Significant use of the Cascade (useful, but should be the exemption rather than the rule)
  - Significant use of other products (chemicals)
- Lack of VMPs forces vets/producers into use of non licensed products
  - Concerns regarding safety (fish, user, consumer, environment)
- Lack of enforcement of current regulations

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Changes since 2007

- Some changes
  - MUMS guidelines introduced
  - List of relevant diseases established (Discontools, OIE)
- Just few new MRLs
- Few new products: mainly for salmonidae
- MUMS not applicable for salmon, but trout (EMA)
- MUMS does often not generate sufficient reduction of requirements as to bring development back into a positive investment balance

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Need for VMPs to treat disease

- Lice in salmon (due to emerging resistance of current products) and lice in other species
- Vaccines: viral, bacterial, parasitological
  - E.g. ISE, SAV-PD, AGD
  - As outlined yesterday in Session 2
- VMPs for other species and indications
  - e.g. sturgeon, catfish, talapia, carp, eel etc.
  - Others: e.g. crustaceae, oyster

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Need for VMPs to treat diseases

- If aquaculture production shall grow in Europe, health of such fish must be assured
- Beneath improved husbandry and management, Veterinary Medicinal Products required to prevent and treat disease safely and efficaciously
- Need for products in different species and indications
- Nothing changed in EU:
  - Production of aquaculture not increasing
  - Availability of VMPs not increasing
- But: global fish production/consumption has grown double digit

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Current requirements to obtain a Marketing Authorisation for a VMP

1. MRL (Regulation 470/2009)
2. Marketing Authorisation (MA)
   (Dir. 2001/82 as amended)
   a) Quality (formulation) for the target species
   b) Safety for the user, consumer, environment and target species
   c) Efficacy in the target disease as confirmed by studies (PK, PD, dose titration, confirmation, field studies)

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MRLs for products used in Salmonidae and other fin fish

- Normally, costs for MRL dossier 250-500.000 €
- EMEA/CVMP/153b/97 FINAL
- "an extrapolation can be considered acceptable, whereby if a MRL has been established for a substance in muscle in a major mammalian species it may be applied to salmonidae and other fish."
- "The parent compound is normally acceptable as a valid marker residue in salmonidae and other fin fish."

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Cost for new MA (Dir 2001/82, Art. 12)

Part of Dossier		Costs in 1.000 €
Part I: administrative data		~25-35
Part II: Quality of the product		~200-300
Part III:	Toxicology Target Animal Safety User and Environmental Safety	~250 ~150 ~500-1.000
Part IV:	Efficacy	~250-1.000
Fees at Authorities		~ 50-200
Project Management, Dossier Preparation, Meetings etc.		100-250
Total development costs:		**1.000-2.500**

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Market Evaluation

Annual EU Market	Turnover in 1.000 €
VMPs for Aquaculture (2009)	~ 30.000
Total Vaccine Sales (2009)	> 3.500
Average turnover per product	< 200.000
Use of non-licensed products (Cascade and others)	At least as the official market

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Cost Benefit Analysis

- Return of investment too low to justify investment
  - Costs of registration are too high versus the potential sales and risks to be taken
  - Legislation too rigorous for the multiple fish/aquaculture species and provisions for extrapolation not sufficient

→ Lacking investment into VMPs for fish in Europe

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Example: Reproduction of Tuna

- Product stimulates ovulation in capture, currently major problem
- Product applied once to females to generate sufficient number of roes for years of production
- Will solve a major problem of over-fishing for one of the most attractive fish
- Without public funding of the complete development, will never reach the RoI

→ Public interest (environment, protein production)

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Obstacles of current EU Legislation on VMP Registration

- The need for animal species specific Maximum Residue Levels
  - Extrapolation by commission
- The burden of Environmental Impact Assessment: high costs, non-predictable outcome

→ Interest of public in environment versus interest in food protein production

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Consequences of current EU legislation on availability of VMPs for fish in the EU

- Defence of licensed products swallows >30 % of R&D budgets of industry
- Investments have been directed to high Return of Investment markets like South America, Asia, Africa as they are less regulated
- The current attractive situation for generics
- Consolidation of industry: less players

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Consequences of current EU legislation on availability of VMPs for fish in the EU

- Less VMPs in general, but especially for "minor species" like fish or bees
  - Significant gaps to prevent and treat diseases
- Animal welfare of fish threatened
- Broad use of non-licensed products

→ Are consumers better protected, if 90 % of products are imported from less regulated markets or treated with products, not-licensed in Europe?

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Proposals for change

- The new animal drug legislation should provide:
  - Legally authorised transparent procedure to extend MRLs to other fish species,
  - Provide options to apply/find models to extrapolate MRLs from other food producing animals
  - Options for easier import of VMPs for aquaculture that are registered in non-EU countries and imported to EU via the food chain anyway (e.g. US, CAN)
  - Risk based reduced requirements for environmental risk assessment assuring a balanced Return of Investment
  - Provide opportunities for funding the above mentioned steps and also the development of products for minor, but relevant diseases (not limited to highly contagious)

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Most important

- MUMS is not enough, but a first, but non-sufficient step on a long way
- We must bring back to balance:
  - Costs needed to comply with regulatory requirements and
  - Return of investment and opportunities
- Fish and aquaculture is just one example, other animal species similar problems

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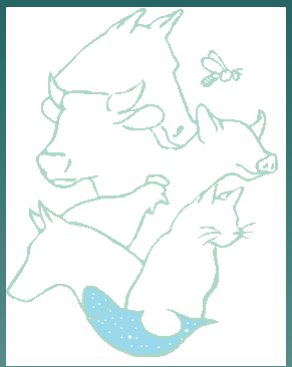
Thank you



- Commission and FVE for invitation
- Irish council presidency to orgainse this conference
- Dr. Gabriel Beechinor (IMB) for addressing MUMS and the availability of VMPs

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