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Rapport

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Diergeneesmiddelen in aquacultuur

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Inhoudsopgave

Samenvatting

1. Inleiding

De Nederlandse visteelt heeft nog niet de beschikking over toegestane diergeneesmiddelen, terwijl de noodzaak om bepaalde middelen te gebruiken in de praktijk bestaat. Deze middelen zijn met name: flumequine, mebendazole, oxolinezuur, oxytetracycline, praziquantel en trimethosulfmix.

Het gebruik van de genoemde middelen staat ook beschreven in de handleiding opgesteld door het ID-DLO, om viskwekers te helpen bij het herkennen van visziekten en het behandelen van vissen tegen die ziekten(Haenen et al., 1996).

Wat op dit moment niet duidelijk is is de farmacokinetiek van deze middelen voor de vissoorten die in Nederland gekweekt worden. Deze informatie is van belang om te voorkomen dat residuen van de geneesmiddelen in voor consumptie bestemde visproducten terecht komen.

Om meer inzicht te krijgen in bestaande farmacokinetische data voor de meest gebruikte middelen heeft het Visserijcentrum opdracht gegeven aan het Nederlands Instituut voor Visserij Onderzoek om een literatuuronderzoek uit te voeren.

2. Doel

Beschikbare bestaande data over farmacokinetiek en veilige wachttijd in vis species voor flumequine, mebendazole, oxolinezuur, oxytetracycline, praziquantel en trimethosulfmix verzamelen, evalueren en samenvatten.

3. Zoekstrategie

Informatie over de farmacokinetiek van flumequine, mebendazole, oxolinezuur, oxytetracycline, praziquantel en trimethosulfmix in verschillende vissoorten werd verzameld met behulp van online literatuur zoekopdrachten. Hierbij zijn de volgende literatuurbestanden gebruikt:

- ISI Web of Science (bestaat uit vijf databestanden met duizenden wetenschappelijke tijdschriften in alle onderzoeksrichtingen vanaf 1945),
- ASFA (Aquatic Sciences and Fisheries Abstracts vanaf 1971),
- Aqualine (publicaties vanaf 1960) en
- Oceanic Abstracts (publicaties vanaf 1981).

Zoekopdrachtcriteria en aantal hits zijn opgenomen in Annex 1. Omdat verwacht werd dat de meest relevante informatie niet ouder dan 20 jaar zou zijn, werden de zoekopdrachten uitgevoerd voor de periode van 1985 tot 2005. Ondanks het gebruik van aanvullende keywords om de zoekopdracht te beperken tot relevante artikelen en om het aantal hits te verminderen, moest een groot aantal artikelen handmatig doorgespit worden. Dit was noodzakelijk omdat de target diergeneesmiddelen ook veel gebruikt worden in de humane geneeskunde en daardoor regelmatig voorkomen in abstracts.

Het middel 'Trimethosulfmix' is niet terug te vinden in de gebruikte literatuurbestanden. Trimethosulfmix blijkt een mengsel van trimethoprim en sulfadiazine natrium (1:5) te zijn, die geproduceerd wordt door Eurovet Nederland. Hierom werd de zoekopdrachten toegespitst op trimethoprim in combinatie met sulfadiazine/sulphadiazine, maar ook trimethoprim en sulfadiazine/sulphadiazine apart.

4. Resultaten zoekopdracht en dataoverzicht

Een aantal publicaties is gevonden voor elk van de diergeneesmiddelen in de target set. De volledige referenties hiervoor zijn weergegeven in Annexen 2 t/m 7.
Publicaties werden in drie categorieën verdeeld, afhankelijk van hun relevantie voor de doelen van deze opdracht:

1. **Depletie in vis:** deze zeer relevante artikelen zijn toegespitst op of besteden aandacht aan depletie of veilige wachttijd (*'withdrawl time*) van de geneesmiddel in vis. Concentratie-tijd profielen van het middel in verschillende weefsels worden gepresenteerd gedurende lange periodes.
2. **Farmacokinetische:** deze artikelen beschrijven de farmacokinetische profielen van de middelen en zijn met name bedoeld om de optimale dosering van het middel te bepalen, of om de efficiëntie van het middel te toetsen. De depletie of wachttijden zijn niet expliciet behandeld, hoewel er een mogelijkheid bestaat om deze parameters te schatten op basis van eliminatie halfwaardetijden (als dit gerapporteerd is voor spier en huid, en niet alleen voor plasma).
3. **Overige:** artikelen waarin farmacokinetische gegevens van de middelen beschreven staan, maar niet in voldoende mate om iets te kunnen zeggen over depletie of veilige wachttijd in vis.

Verder is een aantal review artikelen gevonden dat de target middelen en hun farmacokinetische gedrag beschrijft. Hoewel er geen informatie over depletie van de middelen

in vissoorten gerapporteerd wordt, zijn ze wellicht nuttig als algemene informatie en zijn daarom weergegeven in Annex 8.
Voor elk middel zijn de belangrijkste resultaten van de verschillende soorten artikelen samengevat in de tabellen in Annexes 9 t/m 14. Deze tabellen geven de parameters en informatie weer die van belang zijn, zoals temperatuur, farmacokinetiek, weefsel type, manier van toediening, dosis, halfwaardetijden, depletie/eliminatie informatie. Een korte beschrijving van de data per middel volgt in de tekst.

Flumequine

De artikelen die voor flumequine zijn gevonden zijn opgenomen in Annex 2 en de onderzoeksresultaten van de artikelen in Annex 9. In zes artikelen kwam de depletie van flumequine aan bod. De vissoorten waarin depletie werd bestudeerd zijn tarbot (*Scophthalmus maximus*), heilbut (*Hippoglossus hippoglossus*), europese aal (*Anguilla anguilla*), (gilthead) zee brasem (*Sparus aurata*), channel catfish (*Ictalurus punctatus*) en Atlantische zalm (*Salmo salar*). In deze studies wordt de verplaatsing van het middel in het vislichaam (spier, huid, lever, plasma) bediscussieerd en concentratie-tijd profielen worden weergegeven. De farmacokinetiek van flumequine in vis is vaker onderzocht; in totaal zijn 21 artikelen gevonden. Voor de volgende vissoorten is farmacokinetische data beschikbaar: europese aal (*Anguilla anguilla*), zalm forel (*Salmo gairdneri R.*), zee brasem (*Sparus aurata*), atlantische zalm (*Salmo salar L.*), orange-spotted grouper (*Epinephelus coioides*), heilbot (*Hippoglossus hippoglossus*), tarbot (*Scophthalmus maximus*), kabeljauw (*Gadus morhua*), gold wrase (*Ctenolabrus rupestris*), regenboor forel (*Oncorhynchus mykiss*), zee baars (*Dicentrarchus labrax L.*), corkwing wrasse (*Symphodus melops*) and karper (*Cyprinus carpio*).

Mebendazole

Een lijst met artikelen over mebendazole is weergegeven in Annex 3 met uitgebreider inhoudelijke informatie uit de artikelen in Annex 10. Een relevant artikel werd gevonden voor dit middel, waarin de concentratie profiel van het middel en de metabolieten ervan in spier, huid, lever, nier en vetweefsel van europese aal (*Anguilla anguilla*) wordt gepresenteerd na een badbehandeling. Andere artikelen gaan over effectiviteit van mebendazole tegen parasieten in europese aal, tarbot en andere vissoorten, maar deze geven geen informatie die bruikbaar is voor het schatten van depletie.

Oxolinezuur

De artikelen over oxolinezuur zijn weergegeven in Annex 4 met gedetailleerde data in Annex 11. Zes artikelen zijn relevant voor deze studie. De depletie van oxolinezuur is beschreven voor drie soorten, namelijk regenboog forel (*Oncorhynchus mykiss*), gilthead sea bream (*Sparus aurata*) and sharpsnout sea bream (*Diplodus puntazzo*). Concentratie-tijd profielen van het middel in

plasma, spier, lever, huid en gall worden gerapporteerd. Enige depletie data is beschikbaar voor zalm.

De farmacokinetiek van oxolinezuur in vis is goed beschreven in de literatuur (17 artikelen gevonden). Farmacokinetische data zijn beschikbaar voor: regenboog forel (*Oncorhynchus mykiss*), atlantische zalm (*Salmo salar L.*), channel catfish (*Ictalurus punctatus*), tarbot (*Scophthalmus maximus*), zee baars (*Dicentrarchus labrax*), gilthead sea bream (*Sparus aurata L.*), sharpsnout sea bream (*Diplodus puntazzo*), kabeljauw (*Gadus morhua L.*), heilbot (*Hippoglossus hippoglossus L.*) and corkwing wrasse (*Symphodus melops*).

Oxytetracycline

Een lijst van artikelen is opgenomen in Annex 5, met verdere data in Annex 12. Oxytetracycline is het meest onderzocht geneesmiddel in vis, met 45 gepubliceerde artikelen. Hiervan zijn er 18 die informatie rapporteren over depletie of veilige wachttijd voor de volgende soorten: chinnook zalm (*Oncorhynchus tshawytscha*), coho zalm (*Oncorhynchus kisutch*), Atlantische zalm (*Salmo salar*), snoek (*Esox lucius*), walleye (*Stizostedion vitreum*), walley (*Sander vitreus*), sea urchin (*Psammechinus miliaris*), zalm forel (*Salmo gairdneri R.*), regenboog forel (*Oncorhynchus mykiss*), perch (*Lateolabras janopicus*), black sea bream (*Sparus macrocephalus*), zee baars (*Dicentrarchus labrax*), gilthead sea bream (*Sparus aurata*), channel catfish (*Ictalurus punctatus*), summer flounder (*Paralichthys dentatus*), nijl tilapia (*Oreochromis niloticus*), Japanse aal (*Anguilla japonica*), ayu (*Plecoglossus altivelis*) en karper.

In totaal zijn 21 artikelen gevonden die farmacokinetische data rapporteren voor de soorten: chinnook zalm (*Oncorhynchus tshawytscha*), Atlantische zalm (*Salmo salar*), regenboog forel (*Oncorhynchus mykiss*), zee baars (*Dicentrarchus labrax*), gilthead sea bream (*Sparus aurata*), Japanse aal (*Anguilla japonica*), ayu (*Plecoglossus altivelis*), karper (*Cyprinus carpio* L.), red pacu (*Colossoma brachypomum*), afrikaanse meerval (*Clarias gariepinus*), yellowtail (*Seriola quinqueradiata*), sharpsnout sea bream (*Diplodus puntazzo*), beekridder (*Salvelinus alpinus* L.), zeelt (*Tinca tinca* L.) en amago zalm.

Praziquantel

Een lijst van artikelen zijn in Annex 6 opgenomen, met in Annex 13 de aanvullende data. Drie relevante artikelen werden gevonden. Twee hiervan gaan in op de depletie van het middel in plasma, spier en huid van cultured rockfish (*Sebastes schlegelli*). De derde gaat over de farmacokinetiek van praziquantel in regenboog forel (*Salmo gairdneri* R.). Overige artikelen over praziquantel zijn met name gefocused op effectiviteit van het middel tegen bepaalde ziektes.

Trimethosulfmix

Trimethosulfmix artikelen zijn in Annex 7 opgenomen, met aanvullende data in Annex 14. In drie artikelen wordt de depletie van het middel beschreven. Twee ervan gaan over depletie van

trimethoprim in regenboog forel (*Salmo gairdneri R.*) en heilbot (*Hippoglossus hippoglossus L.*). De derde gaat over depletie van trimethorpim en sulfadiazine in regenboog forel (*Salmo gairdneri R.*). Wat betreft farmacokinetische studies, een vijftal artikelen werden gevonden. Twee ervan beschrijven de farmacokinetische parameters van trimethoprim in carp, regenboog forel (*Oncorhynchus mykiss*) en zee baars. Twee anderen beschrijven de parameters van trimethoprim en sulfadiazine in Atlantische zalm en karper (*Cyprinus carpio L.*).

5. Bestaande adviezen voor de visteelt.

Het handboek 'visziekten: voorkomen, herkennen en bestrijden' (Haenen et al., 1996), geeft adviezen over wachttermijnen voor een aantal middelen en vissoorten (Tabel 1). Omdat ons literatuuronderzoek geen wetenschappelijke onderbouwing geeft voor deze genoemde wachttermijnen, hebben wij contact opgenomen met de auteurs van deze handleiding, te weten Dr.ir. Olga Haenen en Drs.ing. Peter Werkman. Beide auteurs bevestigden onze bevindingen, namelijk dat een goede onderbouwing voor de wachttermijnen ontbreekt, en dat de richtlijnen zijn opgesteld op basis van ruwe inschattingen en uit combinaties van verschillende onderzoeken. Ook zijn zij het er mee eens dat er op dit moment geen wetenschappelijke basis is voor een advies over de wachttermijnen, en dat het niet mogelijk is gegevens voor de ene soort rechtstreeks te gebruiken voor een andere soort. De 500 daggraden norm, die zij eerder zagen als een veilige norm, blijkt door nieuwe recente ervaringen niet altijd voldoende voor het volledig verdwijnen van de middelen uit de vis. Zij stellen dan ook dat gericht onderzoek voor de Nederlandse visteelt sector gewenst is.

Tabel 1. Overzicht van wachtermijnen zoals vermeld in: "Visziekten: voorkomen, herkennen en bestrijden" (Haenen et al., 1996)

	Wachttermijn (dagen) per soort				Daggraden* voor
Middel	Meerval bij 25°C	Paling bij 25°C	Forel bij >10°C	Forel bij <10°C	Overige
Flumequine	30	-	90	-	500
Mebendazole	-	28	-	-	-
Oxolinezuur	30	-	30	60	500
Oxytetracycline	30	50	40	-	500
Trimethosulfmix	30	-	40	80	500

* daggraden = aantal dagen x de gemiddelde watertemperatuur

6. Conclusie

Voor de Nederlandse aquacultuur zijn de soorten European eel (*Anguilla anguilla*), Afrikaanse meerval (*Clarias gariepinus*), Nijl tilapia (*Oreochromis niloticus*), tarbot (*Scophthalmus maximus*) en tong (*Solea solea*) van belang. Uit de literatuur die onderzocht is voor dit verslag blijkt enige farmacokinetische informatie voor aal beschikbaar voor flumequine en mebendazole, voor tarbot voor de middelen flumequine, mebendazole en oxolinezuur, en voor de Afrikaanse meerval voor oxytetracycline. Voor de andere vissoorten en middelen zijn geen data gevonden.

Voor wat betreft aal is de eliminatie (verwijdering van middelen uit het dier) van mebendazole na badbehandeling uitgebreid beschreven en lijkt daardoor geen nader onderzoek nodig te zijn. Flumequine data zijn minder bruikbaar, omdat er uitsluitend over distributie van residuen in aalweefsel is gerapporteerd, zonder het concentratieprofiel dat nodig is voor het berekenen van een veilige wachttijd. Voor tilapia is een goed onderzoek uitgevoerd naar de eliminatie van oxytetracycline uit zowel serum, spierweefsel als organen. Dit onderzoek kon echter voor tilapia geen goede conclusies opleveren als gevolg van te weinig data.

Met uitzondering van mebendazole in aal na badbehandeling, wordt nader experimentele onderzoek naar het gedrag van de zes target diergeneesmiddelen nodig geacht voor alle soorten die van belang zijn voor de Nederlandse aquacultuur.

De data die beschikbaar zijn kunnen voor andere soorten niet gebruikt worden, omdat uit de literatuur blijkt dat er aanzienlijke verschillen zijn in de farmacokinetiek van de diergeneesmiddelen in de verschillende vissoorten. Daarom is extrapolatie geen betrouwbare methode om MRLs en veilige wachttijden te schatten.

In het rapport “Visziekten: voorkomen, herkennen en bestrijden” staan voor verschillende vissoorten en middelen wachttermijnen beschreven. Deze wachttermijnen berusten niet op wetenschappelijke data, maar op een combinatie van diverse bronnen, praktijkervaring en een inschatting van wat redelijk zou zijn. Op basis van de huidige kennis kunnen wij niet stellen dat de genoemde wachttermijnen juist zijn. Voor een gefundeerde uitspraak over veilige wachttermijnen moet soortspecifiek onderzoek naar ieder afzonderlijk middel worden uitgevoerd.

Annex 1. Literatuur zoekopdracht criteria en aantal hits in ISI Web of Science databestand voor periode 1985–2005.

- Flumequine

Gebruikte keywords	Aantal hits	
flumequine	292	reviewed

- Mebendazole

Gebruikte keywords	Aantal hits	
mebendazole	786	not reviewed
mebendazole and depletion	6	reviewed
mebendazole and withdrawal	5	reviewed
mebendazole and residue*	16	reviewed
mebendazole and tissue distribution	0	reviewed
mebendazole and elimination	13	reviewed
mebendazole and disposition	9	reviewed
mebendazole and metabolism	28	reviewed
mebendazole and pharmacokinetic*	52	reviewed
mebendazole and excretion	10	reviewed
mebendazole and fish	18	reviewed
mebendazole and eel	16	reviewed
mebendazole and catfish	0	reviewed
mebendazole and sole	3	reviewed
mebendazole and anguilla anguilla	11	reviewed
mebendazole and silurus glanis	0	reviewed
mebendazole and solea solea	0	reviewed

- Oxolinic acid

Gebruikte keywords	Aantal hits	
oxolinic acid	534	not reviewed
oxolinic acid and depletion	17	reviewed
oxolinic acid and withdrawal	23	reviewed
oxolinic acid and residue*	153	reviewed
oxolinic acid and tissue distribution	32	reviewed
oxolinic acid and elimination	71	reviewed
oxolinic acid and disposition	20	reviewed
oxolinic acid and metabolism	10	reviewed
oxolinic acid and pharmacokinetic*	109	reviewed
oxolinic acid and excretion	18	reviewed
oxolinic acid and fish	285	reviewed
oxolinic acid and eel	21	reviewed
oxolinic acid and catfish	33	reviewed
oxolinic acid and sole	0	reviewed
oxolinic acid and anguilla anguilla	13	reviewed
oxolinic acid and silurus glanis	0	reviewed
oxolinic acid and solea solea	0	reviewed

- Oxytetracycline

Gebruikte keywords	Aantal hits	
oxytetracycline	2359	not reviewed
oxytetracycline and depletion	34	reviewed
oxytetracycline and withdrawal	64	reviewed
oxytetracycline and residue	439	not reviewed
oxytetracycline and tissue distribution	33	reviewed
oxytetracycline and elimination	118	reviewed
oxytetracycline and disposition	55	reviewed

oxytetracycline and metabolism	44	reviewed
oxytetracycline and pharmacokinetic*	234	reviewed
oxytetracycline and excretion	40	reviewed
oxytetracycline and fish	100	reviewed
oxytetracycline and eel	17	reviewed
oxytetracycline and catfish	49	reviewed
oxytetracycline and sole	8	reviewed
oxytetracycline and anguilla anguilla	7	reviewed
oxytetracycline and silurus glanis	0	reviewed
oxytetracycline and solea solea	1	reviewed

- Praziquantel

Gebruikte keywords	**Aantal hits**	
praziquantel	2004	not reviewed
praziquantel and depletion	5	reviewed
praziquantel and withdrawal	2	reviewed
praziquantel and residue*	5	not reviewed
praziquantel and tissue distribution	2	reviewed
praziquantel and elimination	28	reviewed
praziquantel and disposition	2	reviewed
praziquantel and metabolism	53	reviewed
praziquantel and pharmacokinetic*	55	reviewed
praziquantel and excretion	42	reviewed
praziquantel and fish	41	reviewed
praziquantel and eel	1	reviewed
praziquantel and catfish	2	reviewed
praziquantel and sole	3	reviewed
praziquantel and anguilla anguilla	2	reviewed
praziquantel and silurus glanis	0	reviewed
praziquantel and solea solea	0	reviewed

- Trimethosulfmix

Gebruikte keywords	**Aantal hits**	
trimethoprim and sulphadiazine	71	reviewed
trimethoprim and sulfadiazine	315	not reviewed
and depletion	4	reviewed
and withdrawal	13	reviewed
and residue*	26	reviewed
and tissue distribution	2	reviewed
and elimination	15	reviewed
and disposition	13	reviewed
and metabolism	10	reviewed
and pharmacokinetic*	63	reviewed
and excretion	8	reviewed
and fish	20	reviewed
and eel	0	reviewed
and catfish	1	reviewed
and sole	0	reviewed
and anguilla anguilla	0	reviewed
and silurus glanis	0	reviewed
and solea solea	0	reviewed
trimetoprim	38	reviewed
trimethoprim	7115	not reviewed
trimethoprim and depletion	26	reviewed
trimethoprim and withdrawal	46	reviewed
trimethoprim and residue*	54	reviewed

trimethoprim and tissue distribution	7	reviewed
trimethoprim and elimination	105	reviewed
trimethoprim and disposition	75	reviewed
trimethoprim and metabolism	141	reviewed
trimethoprim and pharmacokinetic*	413	reviewed
trimethoprim and excretion	84	reviewed
trimethoprim and fish	81	reviewed
trimethoprim and eel	3	reviewed
trimethoprim and catfish	7	reviewed
trimethoprim and sole	17	reviewed
trimethoprim and anguilla anguilla	2	reviewed
trimethoprim and silurus glanis	0	reviewed
trimethoprim and solea solea	0	reviewed
sulfadiazine	1286	not reviewed
sulfadiazine and depletion	10	reviewed
sulfadiazine and withdrawal	20	reviewed
sulfadiazine and residue*	90	reviewed
sulfadiazine and tissue distribution	30	reviewed
sulfadiazine and elimination	23	reviewed
sulfadiazine and disposition	17	reviewed
sulfadiazine and metabolism	24	reviewed
sulfadiazine and pharmacokinetic*	97	reviewed
sulfadiazine and excretion	17	reviewed
sulfadiazine and fish	25	reviewed
sulfadiazine and eel	0	reviewed
sulfadiazine and catfish	1	reviewed
sulfadiazine and sole	0	reviewed
sulfadiazine and anguilla anguilla	0	reviewed
sulfadiazine and silurus glanis	0	reviewed
sulfadiazine and solea solea	0	reviewed

Annex 2. Literatuurlijst voor flumequine (onderverdeeld in drie categorieen)

1. Depletie en veilige wachttijd artikelen

Hansen, M. K.*, et al.* (2001). "Disposition of C-14-flumequine in eel *Anguilla anguilla*, turbot *Scophthalmus maximus* and halibut *Hippoglossus hippoglossus* after oral and intravenous administration" *Diseases Of Aquatic Organisms* 47, 183-191.

Malvisi, J.*, et al.* (1997). "Tissue distribution and depletion of flumequine after in-feed administration in sea bream (*Sparus aurata*)" *Aquaculture* 157, 197-204.

Plakas, S. M.*, et al.* (2000). "Pharmacokinetics, tissue distribution, and metabolism of flumequine in channel catfish (*Ictalurus punctatus*)" *Aquaculture* 187, 1-14.

Sohlberg, S.*, et al.* (2002). "Flumequine in Atlantic salmon *Salmo salar*: disposition in fish held in sea water versus fresh water" *Diseases Of Aquatic Organisms* 49, 39-44.

Steffenak, I.*, et al.* (1991). "Reservoir Of Quinolone Residues In Fish" *Food Additives And Contaminants* 8, 777-780.

Tyrpenou, A. E.*, et al.* (2003). "Flumequine depletion from muscle plus skin tissue of gilthead seabream (Sparus aurata L.) fed flumequine medicated feed in seawater at 18 and 24 degrees C" *Aquaculture* 220, 633-642.

2. Farmacokinetiek

Boon, J. H.*, et al.* (1991). "Disposition of Flumequine In Plasma of European Eel (Anguilla-Anguilla) After A Single Intramuscular Injection" *Aquaculture* 99, 213-223.

Chevalier, R. G., J.P.; Michel, C. (1981). "Distribution and Tissular Kinetics of Flumequin in the Salmon Trout (Salmo gairdneri, Richardson). Research of Residues" *Revue de Medecine Veterinaire* 132, 831-837.

Della Rocca, G. M., J.; Anfossi, P.; Giorgetti, G. (1996). "Tissue and residue kinetics of oxytetracycline and flumequine in sea bream (*Sparus aurata*) following in feed administration" *Bollettino Societa Italiana di Patologia Ittica* 8, 8-16.

Elema, M. O.*, et al.* (1994). "Multiple-Dose Pharmacokinetic Study Of Flumequine In Atlantic Salmon (*Salmo salar* L)" *Aquaculture* 128, 1-11.

Elema, M. O.*, et al.* (1995). "Bioavailability of flumequine after oral administration to Atlantic salmon (*Salmo salar* L)" *Aquaculture* 136, 209-219.

Guo, J.-J. H., Yueh-O; Liao, I Chiu (1997). "Pharmacokinetics of flumequine in orange-spotted grouper, *Epinephelus coioides*, after a single oral administration" *Reports on fish disease research* (18), 71-78.

Hansen, M. K. & Horsberg, T. E. (1999). "Single-dose pharmacokinetics of flumequine in halibut (*Hippoglossus hippoglossus*) and turbot (*Scophthalmus maximus*)" *Journal Of Veterinary Pharmacology And Therapeutics* 22, 122-126.

Hansen, M. K. & Horsberg, T. E. (2000a). "Single-dose pharmacokinetics of flumequine in cod (*Gadus morhua*) and goldsinny wrasse (*Ctenolabrus rupestris*)" *Journal Of Veterinary Pharmacology And Therapeutics* 23, 163-168.

Hansen, M. K. & Horsberg, T. E. (2000b). "Single-dose pharmacokinetics of flumequine in the eel (*Anguilla anguilla*) after intravascular, oral and bath administration" *Journal Of Veterinary Pharmacology And Therapeutics* 23, 169-174.

Malvis, J. G., G.; Raspa, M.; Giuliani, A.; Tomasi, L.; Roncada, P. (1994). "Kinetics of flumequine in rainbow trout (*Oncorhynchus mykiss*) tissue" *Rivista italiana di acquacoltura* 29, 121-128.

Martinsen, B. & Horsberg, T. E. (1995). "Comparative Single-Dose Pharmacokinetics Of 4 Quinolones, Oxolinic Acid, Flumequine, Sarafloxacin, And Enrofloxacin, In Atlantic Salmon (*Salmo salar*) Held In Seawater At 10-Degrees-C" *Antimicrobial Agents And Chemotherapy* 39, 1059-1064.

Rigos, G.*, et al.* (2002). "A pharmacokinetic study of flumequine in sea bass, *Dicentrarchus labrax* (L.), after a single intravascular injection" *Journal Of Fish Diseases* 25, 101-105.

Rigos, G.*, et al.* (2003). "Pharmacokinetics of flumequine and in vitro activity against bacterial pathogens of gilthead sea bream *Sparus aurata*" *Diseases Of Aquatic Organisms* 54, 35-41.

Rogstad, A.*, et al.* (1993). "Pharmacokinetics And Bioavailability Of Flumequine And Oxolinic Acid After Various Routes Of Administration To Atlantic Salmon In Seawater" *Aquaculture* 110, 207-220.

Samuelsen, O. B. (2003). "Administration of the antibacterial agents flumequine and oxolinic acid to small turbot (*Scophthalmus maximus* L.) by bath" *Journal Of Applied Ichthyology* 19, 55-58.

Samuelsen, O. B. & Ervik, A. (1997). "Single dose pharmacokinetic study of flumequine after intravenous, intraperitoneal and oral administration to Atlantic halibut (*Hippoglossus hippoglossus*) held in seawater at 9 degrees C" *Aquaculture* 158, 215-227.

Samuelsen, O. B. & Lunestad, B. T. (1996). "Bath treatment, an alternative method for the administration of the quinolones flumequine and oxolinic acid to halibut *Hippoglossus hippoglossus*, and in vitro antibacterial activity of the drugs against some Vibrio sp" *Diseases Of Aquatic Organisms* 27, 13-18.

Samuelson, O. B. & Ervik, A. (2001). "Absorption, tissue distribution and excretion of flumequine and oxolinic acid in corkwing wrasse (Symphodus melops) following a single intraperitoneal injection or bath treatment" *Journal Of Veterinary Pharmacology And Therapeutics* 24, 111-116.

Sohlberg, S.*, et al.* (1994). "Temperature-Dependent Absorption And Elimination Of Flumequine In Rainbow-Trout (*Oncorhynchus mykiss* Walbaum) In Fresh-Water" *Aquaculture* 119, 1-10.

Sohlberg, S.*, et al.* (1990). "Plasma-Concentrations Of Flumequine After Intraarterial And Oral-Administration To Rainbow-Trout (*Salmo gairdneri*) Exposed To Low Water Temperatures" *Aquaculture* 84, 355-361.

Vanderheijden, M. H. T.*, et al.* (1994). "Plasma Disposition Of Flumequine In Common Carp (*Cyprinus carpio* L, 1758), African Catfish (*Clarias gariepinus* Burchell, 1822) And European Eel (*Anguilla anguilla* L, 1758) After A Single Peroral Administration" *Aquaculture* 123, 21-30.

3. Overige

geen

Annex 3. Literatuurlijst voor mebendazole

1. ***Depletie en veilige wachttijd artikelen***

Iosifidou, E. G.*, et al.* (1997). "Residue study of mebendazole and its metabolites hydroxy-mebendazole and amino-mebendazole in eel (*Anguilla anguilla*) after bath treatment" *Drug Metabolism And Disposition* 25, 317-320.

2. ***Pharmacokinetiek***

geen papers

3. ***Overige***

geen

Annex 4. Literatuurlijst voor oxolinezuur

- ***Depletie en veilige wachttijd artikelen***
  - Bjorklund, H. V.*, et al.* (1992). "Temperature-Related Absorption And Excretion Of Oxolinic Acid In Rainbow-Trout (*Oncorhynchus mykiss*)" *Aquaculture* 102, 17-27.
  - Bjorklund, H. V.*, et al.* (1991). "Residues Of Oxolinic Acid And Oxytetracycline In Fish And Sediments From Fish Farms" *Aquaculture* 97, 85-96.
  - Ishida, N. (1992). "Tissue-Levels Of Oxolinic Acid After Oral Or Intravascular Administration To Fresh-Water And Seawater Rainbow-Trout" *Aquaculture* 102, 9-15.
  - Jacobsen, M. D. (1989). "Withdrawal Times Of Fresh-Water Rainbow-Trout, *Salmo gairdneri* Richardson, After Treatment With Oxolinic Acid, Oxytetracycline And Trimetoprim" *Journal Of Fish Diseases* 12, 29-36.
  - Rigos, G.*, et al.* (2003). "Tissue distribution and residue depletion of oxolinic acid in gilthead sea bream (*Sparus aurata*) and sharpsnout sea bream (*Diplodus puntazzo*) following multiple in-feed dosing" *Aquaculture* 224, 245-256.
  - Steffenak, I.*, et al.* (1991). "Reservoir Of Quinolone Residues In Fish" *Food Additives And Contaminants* 8, 777-780.
- ***Pharmacokinetiek***
  - Bjorklund, H. V. & Bylund, G. (1991). "Comparative Pharmacokinetics And Bioavailability Of Oxolinic Acid And Oxytetracycline In Rainbow-Trout (*Oncorhynchus mykiss*)" *Xenobiotica* 21, 1511-1520.
  - Hustvedt, S. O. (1992). "Pharmacokinetics Of Oxolinic Acid In Atlantic Salmon (*Salmo salar* L) And In Rainbow-Trout (*Oncorhynchus mykiss* Walbaum)" *Acta Pharmaceutica Nordica* 4, 111-112.
  - Hustvedt, S. O. & Salte, R. (1991). "Distribution And Elimination Of Oxolinic Acid In Rainbow-Trout (*Oncorhynchus mykiss* Walbaum) After A Single Rapid Intravascular Injection" *Aquaculture* 92, 297-303.
  - Hustvedt, S. O.*, et al.* (1991). "Absorption, Distribution And Elimination Of Oxolinic Acid In Atlantic Salmon (*Salmo salar* L) After Various Routes Of Administration" *Aquaculture* 95, 193-199.
  - Kleinow, K. M.*, et al.* (1994). "Comparative Pharmacokinetics And Bioavailability Of Oxolinic Acid In Channel Catfish (*Ictalurus punctatus*) And Rainbow-Trout (*Oncorhynchus mykiss*)" *Canadian Journal Of Fisheries And Aquatic Sciences* 51, 1205-1211.
  - Martinsen, B. & Horsberg, T. E. (1995). "Comparative Single-Dose Pharmacokinetics Of 4 Quinolones, Oxolinic Acid, Flumequine, Sarafloxacin, And Enrofloxacin, In Atlantic Salmon (*Salmo salar*) Held In Seawater At 10-Degrees-C" *Antimicrobial Agents And Chemotherapy* 39, 1059-1064.
  - Poher, I. & Blanc, G. (1998). "Pharmacokinetics of a discontinuous absorption process of oxolinic acid in turbot, Scophthalmus maximus, after a single oral administration" *Xenobiotica* 28, 1061-1073.
  - Poher, I.*, et al.* (1997). "Pharmacokinetics of oxolinic acid in sea-bass, *Dicentrarchus labrax* (L, 1758), after a single rapid intravascular injection" *Journal Of Veterinary Pharmacology And Therapeutics* 20, 267-275.
  - Rigos, G.*, et al.* (2002a). "Temperature-dependent pharmacokinetics and tissue distribution of oxolinic acid in sea bass, *Dicentrarchus labrax* L., after a single intravascular injection" *Aquaculture Research* 33, 1175-1181.
  - Rigos, G.*, et al.* (2002b). "Pharmacokinetics of oxolinic acid in gilthead sea bream, *Sparus aurata* L" *Journal Of Fish Diseases* 25, 401-408.
  - Rigos, G.*, et al.* (2004). "The kinetic profile of oxolinic acid in sharpsnout sea bream, *Diplodus puntazzo* (Cetti 1777)" *Aquaculture Research* 35, 1299-1304.
  - Rogstad, A.*, et al.* (1993). "Pharmacokinetics And Bioavailability Of Flumequine And Oxolinic Acid After Various Routes Of Administration To Atlantic Salmon In Seawater" *Aquaculture* 110, 207-220.

Samuelsen, O. B. (2003). "Administration of the antibacterial agents flumequine and oxolinic acid to small turbot (*Scophthalmus maximus* L.) by bath" *Journal Of Applied Ichthyology* 19, 55-58.
Samuelsen, O. B.*, et al.* (2003). "A single-dose pharmacokinetic study of oxolinic acid and vetoquinol, an oxolinic acid ester, in cod, *Gadus morhua* L., held in sea water at 8 degrees C and in vitro antibacterial activity of oxolinic acid against *Vibrio anguillarum* strains isolated from diseased cod" *Journal Of Fish Diseases* 26, 339-347.
Samuelsen, O. B. & Ervik, A. (1999). "A single-dose pharmacokinetic study of oxolinic acid and vetoquinol, an oxolinic acid ester, in Atlantic halibut, *Hippoglossus hippoglossus* L., held in sea water at 9 degrees C" *Journal Of Fish Diseases* 22, 13-23.
Samuelsen, O. B.*, et al.* (2000). "Single-dose pharmacokinetic study of oxolinic acid and vetoquinol, an oxolinic acid ester, in Atlantic salmon (*Salmo salar*) held in seawater and in vitro antibacterial activity against *Aeromonas salmonicida*" *Aquaculture* 187, 213-224.
Samuelson, O. B. & Ervik, A. (2001). "Absorption, tissue distribution and excretion of flumequine and oxolinic acid in corkwing wrasse (*Symphodus melops*) following a single intraperitoneal injection or bath treatment" *Journal Of Veterinary Pharmacology And Therapeutics* 24, 111-116.

- ***Overige***

Coyne, R.*, et al.* (2004a). "Attempt to validate breakpoint MIC values estimated from pharmacokinetic data obtained during oxolinic acid therapy of winter ulcer disease in Atlantic salmon (*Salmo salar*)" *Aquaculture* 238, 51-66.
Coyne, R.*, et al.* (2005). "A question of temperature related differences in plasma oxolinic acid concentrations achieved in rainbow trout (*Oncorhynchus mykiss*) under laboratory conditions following multiple oral dosing" *Aquaculture* 245, 13-17.
Coyne, R.*, et al.* (2004b). "A comparison of oxolinic acid concentrations in fanned and laboratory held rainbow trout (*Oncorhynchus mykiss*) following oral therapy" *Aquaculture* 239, 1-13.
Kasuga, Y.*, et al.* (1984). "Oxolinic Acid Residues In Tissues Of Cultured Rainbow-Trout And Ayu Fish" *Journal Of The Food Hygienic Society Of Japan* 25, 512-516.

Annex 5. Literatuurlijst voor oxytetracycline

- ***Depletie en veilige wachttijd artikelen***

  Aoyama, R. G.*, et al.* (1991). "High-Performance Liquid-Chromatographic Analysis Of Oxytetracycline In Chinook Salmon Following Administration Of Medicated Feed" *Journal Of Chromatography* 588, 181-186.

  Bernardy, J. A.*, et al.* (2003). "Residue depletion of oxytetracycline from fillet tissues of northern pike and walleye" *Aquaculture* 221, 657-665.

  Bjorklund, H. & Bylund, G. (1990). "Temperature-Related Absorption And Excretion Of Oxytetracycline In Rainbow-Trout (*Salmo gairdneri* R)" *Aquaculture* 84, 363-372.

  Bjorklund, H. V.*, et al.* (1991). "Residues Of Oxolinic Acid And Oxytetracycline In Fish And Sediments From Fish Farms" *Aquaculture* 97, 85-96.

  Brocklebank, J. R.*, et al.* (1997). "An oxytetracycline residue depletion study to assess the physiologically based pharmokinetic (PBPK) model in farmed Atlantic salmon" *Canadian Veterinary Journal-Revue Veterinaire Canadienne* 38, 645-646.

  Campbell, D. A.*, et al.* (2001). "Impact and residence time of oxytetracycline in the sea urchin, *Psammechinus miliaris*, a potential aquaculture species" *Aquaculture* 202, 73-87.

  Chen, C. Y.*, et al.* (2004). "Oxytetracycline residues in four species of fish after 10-day oral dosing in feed" *Journal Of Aquatic Animal Health* 16, 208-219.

  Jacobsen, M. D. (1989). "Withdrawal Times Of Fresh-Water Rainbow-Trout, Salmo-Gairdneri Richardson, After Treatment With Oxolinic Acid, Oxytetracycline And Trimetoprim" *Journal Of Fish Diseases* 12, 29-36.

  Lapinska, K.*, et al.* (2005). "Oxytetracycline acquisition and time of disposal in the rainbow trout" *Medycyna Weterynaryjna* 61, 466-470.

  Luzzana, U.*, et al.* (1994). "Effect Of Temperature And Diet Composition On Residue Depletion Of Oxytetracycline In Cultured Channel Catfish" *Analyst* 119, 2757-2759.

  Malvisi, J.*, et al.* (1996). "Tissue distribution and residue depletion of oxytetracycline in sea bream (*Sparus aurata*) and sea bass (*Dicentrarchus labrax*) after oral administration" *Aquaculture* 147, 159-168.

  Maruyama, R. & Uno, K. (1997). "Oxytetracycline residues in tissues of cultured eel and ayu and the effect of cooking procedures on the residues" *Journal Of The Food Hygienic Society Of Japan* 38, 425-429.

  Meinertz, J. R.*, et al.* (2001). "Oxytetracycline depletion from skin-on fillet tissue of coho salmon fed oxytetracycline medicated feed in freshwater at temperatures less than 9 degrees C" *Aquaculture* 198, 29-39.

  Namdari, R.*, et al.* (1996). "Tissue distribution and elimination of oxytetracycline in seawater chinook and coho salmon following medicated-feed treatment" *Aquaculture* 144, 27-38.

  Namdari, R.*, et al.* (1999). "A comparative tissue distribution study of oxytetracycline in rainbow trout, *Oncorhynchus mykiss* (Walbaum), and chinook salmon, *Oncorhynchus tshawytscha* (Walbaum)" *Aquaculture Research* 30, 279-286.

  Romvary, A.*, et al.* (1991). "Residues Investigation In Carps Treated With Oxytetracycline" *Magyar Allatorvosok Lapja* 46, 463-466.

  Salte, R. & Liestol, K. (1983). "Drug Withdrawal From Farmed Fish - Depletion Of Oxytetracycline, Sulfadiazine, And Trimethoprim From Muscular Tissue Of Rainbow-Trout (*Salmo gairdneri*)" *Acta Veterinaria Scandinavica* 24, 418-430.

  Wang, Q.*, et al.* (2004). "Tissue distribution and elimination of oxytetracycline in perch *Lateolabras janopicus* and black seabream (*Sparus macrocephalus*) following oral administration" *Aquaculture* 237, 31-40.

- ***Pharmacokinetiek***

  Abedini, S.*, et al.* (1998). "Comparative pharmacokinetics and bioavailability of oxytetracycline in rainbow trout and chinook salmon" *Aquaculture* 162, 23-32.

  Bjorklund, H. V. & Bylund, G. (1991). "Comparative Pharmacokinetics And Bioavailability Of Oxolinic Acid And Oxytetracycline In Rainbow-Trout (*Oncorhynchus mykiss*)" *Xenobiotica* 21, 1511-1520.

Black, W. D.*, et al.* (1991). "Pharmacokinetic And Tissue Distribution Study Of Oxytetracycline In Rainbow-Trout Following Bolus Intravenous Administration" *Journal Of Veterinary Pharmacology And Therapeutics* 14, 351-358.

Dagoglu, G.*, et al.* (2004). "Bioavailability and pharmacokinetics of oxytetracycline in cultured rainbow trout following intramusicular administration" *Indian Veterinary Journal* 81, 989-992.

Doi, A. M.*, et al.* (1998). "Pharmacokinetics of oxytetracycline in the red pacu (*Colossoma brachypomum*) following different routes of administration" *Journal Of Veterinary Pharmacology And Therapeutics* 21, 364-368.

Elema, M. O.*, et al.* (1996). "Bioavailability of oxytetracycline from medicated feed administered to Atlantic salmon (*Salmo salar* L) in seawater" *Aquaculture* 143, 7-14.

Grondel, J. L.*, et al.* (1987). "Pharmacokinetics And Tissue Distribution Of Oxytetracycline In Carp, *Cyprinus carpio* L, Following Different Routes Of Administration" *Journal Of Fish Diseases* 10, 153-163.

Grondel, J. L.*, et al.* (1989). "Comparative Pharmacokinetics Of Oxytetracycline In Rainbow-Trout (*Salmo gairdneri*) And African Catfish (*Clarias gariepinus*)" *Journal Of Veterinary Pharmacology And Therapeutics* 12, 157-162.

Haug, T. & Hals, P. A. (2000). "Pharmacokinetics of oxytetracyline in Arctic charr (*Salvelinus alpinus* L.) in freshwater at low temperature" *Aquaculture* 186, 175-191.

Keck, G.*, et al.* (1984). "Fish Pharmacology - A Pharmacokinetic Study Of Oxytetracycline (Otc) In Rainbow-Trout - Therapeutic And Hygienic Consequences - Influence Of A Proteolytic-Enzyme (Fradiase Nd)" *Revue De Medecine Veterinaire* 135, 217-228.

Law, F. C. P. (1998). "A physiologically based pharmacokinetic (PBPK) model of oxytetracycline (OTC) for withdrawal period (WP) estimation in cultured salmon" *Abstracts Of Papers Of The American Chemical Society* 215, U54-U54.

Reja, A.*, et al.* (1996). "Concentration-time profiles of oxytetracycline in blood, kidney and liver of tench (*Tinca tinca* L) after intramuscular administration" *Veterinary And Human Toxicology* 38, 344-347.

Rigos, G.*, et al.* (2002). "Pharmacokinetics and tissue distribution of oxytetracycline in sea bass, *Dicentrarchus labrax*, at two water temperatures" *Aquaculture* 210, 59-67.

Rigos, G.*, et al.* (2003). "Pharmacokinetics and bioavailability of oxytetracycline in gilthead sea bream (*Sparus aurata*) after a single dose" *Aquaculture* 221, 75-83.

Rigos, G.*, et al.* (2004). "Poor bioavailability of oxytetracycline in sharpsnout sea bream *Diplodus puntazzo*" *Aquaculture* 235, 489-497.

Rogstad, A.*, et al.* (1991). "Pharmacokinetic Study Of Oxytetracycline In Fish.1. Absorption, Distribution And Accumulation In Rainbow-Trout In Fresh-Water" *Aquaculture* 96, 219-226.

Turel, I.*, et al.* (2003). "Pharmacokinetics of oxytetracycline in rainbow trout (*Oncorhynchus mykiss*) following administration of medicated feed" *Turkish Journal Of Veterinary & Animal Sciences* 27, 223-227.

Ueno, R.*, et al.* (2004). "Comparative pharmacokinetics of oxytetracycline in eel and its fate in a closed aquatic environment" *Aquaculture* 235, 53-63.

Uno, K. (1996). "Pharmacokinetic study of oxytetracycline in healthy and vibriosis-infected ayu (*Plecoglossus altivelis*)" *Aquaculture* 143, 33-42.

Uno, K.*, et al.* (1992). "Pharmacokinetic Study Of Oxytetracycline In Cultured Rainbow-Trout, Amago Salmon, And Yellowtail" *Nippon Suisan Gakkaishi* 58, 1151-1156.

Uno, K.*, et al.* (1997). "Pharmacokinetics of oxytetracycline in rainbow trout *Oncorhynchus mykiss* following bolus intravenous administration" *Fisheries Science* 63, 90-93.

- ***Overige***

Brown, M. L.*, et al.* (2002). "In-transit oxytetracycline marking, nonlethal mark detection, and tissue residue depletion in yellow perch" *North American Journal Of Fisheries Management* 22, 236-242.

Du, W. X.*, et al.* (1995). "Oxytetracycline, sulfadimethoxine, and ormetoprim residues in channel catfish by HPLC" *Journal Of Food Science* 60, 1220-&.

Du, W. X.*, et al.* (1997). "Retention of oxytetracycline residues in cooked channel catfish fillets" *Journal Of Food Science* 62, 119-122.

Ohara, T. M.*, et al.* (1997). "Oxytetracycline residues in channel catfish: A feeding trail" *Veterinary And Human Toxicology* 39, 65-70.
Rigos, G.*, et al.* (2004). "Bioavailability of oxytetracycline in sea bass, *Dicentrarchus labrax* (L.)" *Journal Of Fish Diseases* 27, 119-122.
Tantillo, G.*, et al.* (1997). "Research about the persistence of oxytetracycline residue in breeding trout (*Salmo gairdneri*) experimentally treated" *Industrie Alimentari* 36, 1483-1485.

Annex 6. Literatuurlijst voor praziquantel

- ***Depletie en veilige wachttijd artikelen***

  Bjorklund, H. & Bylund, G. (1987). "Absorption, Distribution And Excretion Of The Anthelmintic Praziquantel (Droncit) In Rainbow-Trout (*Salmo gairdneri* R)" *Zeitschrift Fur Parasitenkunde-Parasitology Research* 73, 240-244.

  Kim, C. S.*, et al.* (2003). "Depletion of praziquantel in muscle tissue and skin of cultured rockfish (*Sebastes schlegeli*) under the commercial culture conditions" *Aquaculture* 219, 1-7.

  Kim, K. H.*, et al.* (2001). "Depletion of praziquantel in plasma and muscle tissue of cultured rockfish *Sebastes schlegeli* after oral and bath treatment" *Diseases Of Aquatic Organisms* 45, 203-207.

- ***Pharmacokinetiek***

  geen

- ***Overige***

  geen

Annex 7. Literatuurlijst voor trimethosulfmix

- ***Depletie en veilige wachttijd artikelen***

Jacobsen, M. D. (1989). "Withdrawal Times Of Fresh-Water Rainbow-Trout, Salmo-Gairdneri Richardson, After Treatment With Oxolinic Acid, Oxytetracycline And Trimetoprim" *Journal Of Fish Diseases* 12, 29-36.

Salte, R. & Liestol, K. (1983). "Drug Withdrawal From Farmed Fish - Depletion Of Oxytetracycline, Sulfadiazine, And Trimethoprim From Muscular Tissue Of Rainbow-Trout (Salmo Gairdneri)" *Acta Veterinaria Scandinavica* 24, 418-430.

Samuelsen, O. B.*, et al.* (1997). "Pharmacokinetic and efficacy studies on bath-administering potentiated sulphonamides in Atlantic halibut, *Hippoglossus hippoglossus* L" *Journal Of Fish Diseases* 20, 287-296.

- ***Pharmacokinetiek***

Heinze, W. & Weirowski, F. (1991). "Pharmacokinetics Of Sulfamerazine And Trimethoprim In Carp, With Particular Reference To Age And Pond Temperature" *Monatshefte Fur Veterinarmedizin* 46, 843-848.

Horsberg, T. E.*, et al.* (1997). "Potentiated sulfonamides: In vitro inhibitory effect and pharmacokinetic properties in Atlantic salmon in seawater" *Journal Of Aquatic Animal Health* 9, 203-210.

Nouws, J. F. M.*, et al.* (1993). "Pharmacokinetics Of Sulfadiazine And Trimethoprim In Carp (*Cyprinus-Carpio* L) Acclimated At 2 Different Temperatures" *Journal Of Veterinary Pharmacology And Therapeutics* 16, 110-113.

Tan, W. P. & Wall, R. A. (1995). "Disposition Kinetics Of Trimethoprim In Rainbow-Trout (*Oncorhynchus-Mykiss*)" *Xenobiotica* 25, 315-329.

Touraki, M.*, et al.* (1999). "Bioaccumulation of trimethoprim, sulfamethoxazole and N-acetyl-sulfamethoxazole in *Artemia nauplii* and residual kinetics in seabass larvae after repeated oral dosing of medicated nauplii" *Aquaculture* 175, 15-30.

- ***Overige***

Chair, M.*, et al.* (1996). "Accumulation of trimethoprim, sulfamethoxazole, and N-acetylsulfamethoxazole in fish and shrimp fed medicated *Artemia franciscana*" *Antimicrobial Agents And Chemotherapy* 40, 1649-1652.

Gapasin, R. S. J.*, et al.* (1996). "Drug assimilation in the tissue of European sea bass (*Dicentrarchus labrax*) fry delivered orally through bioencapsulation" *Journal Of Applied Ichthyology-Zeitschrift Fur Angewandte Ichthyologie* 12, 39-42.

Gehring, T. A.*, et al.* (1996). "HPLC determination of sulfadiazine residues in coho salmon (Oncorhynchus kisutch) with confirmation by liquid chromatography with atmospheric pressure chemical ionization mass spectrometry" *Journal Of Agricultural And Food Chemistry* 44, 3164-3169.

Hormazabal, V. & Rogstad, A. (1992). "Simultaneous Determination Of Sulfadiazine And Trimethoprim In Plasma And Tissues Of Cultured Fish For Residual and Pharmacokinetic Studies" *Journal Of Chromatography-Biomedical Applications* 583, 201-207.

Annex 8. Algemente reviewartikelen

Burka, J. F.*, et al.* (1997). "Drugs in salmonid aquaculture - A review" *Journal Of Veterinary Pharmacology And Therapeutics* 20, 333-349.

Dayan, A. D. (2003). "Albendazole, mebendazole and praziquantel. Review of non-clinical toxicity and pharmacokinetics" *Acta Tropica* 86, 141-159.

Pouliquen, H. & Le Bris, H. (2002). "Residues of antibacterial drugs in foodstuff of fish origin: risk assessment" *Revue De Medecine Veterinaire* 153, 675-678.

Rigos, G. & Troisi, G. M. (2005). "Antibacterial agents in mediterranean finfish farming: A synopsis of drug pharmacokinetics in important euryhaline fish species and possible environmental implications" *Reviews In Fish Biology And Fisheries* 15, 53-73.

Annex 9. Dataoverzicht - flumequine (1/4)

No.	Species		Reference	Rating	Availability	Administration	
	English name	Latin name				Type	Dose
1	African catfish	*Clarias gariepinus*	van der Heijden, M.H.T. et al. (1994)	Pharmacokinetics	paper	single oral	18 mg/kg
2	Atlantic halibut	*Hippoglossus hipoglossus*	Samuelsen, O.B. & Ervik, A. (1997)	Pharmacokinetics	paper	single intravenously	12 mg/kg
3	Atlantic halibut	*Hippoglossus hipoglossus*	Samuelsen, O.B. & Ervik, A. (1997)	Pharmacokinetics	paper	single intraperitoneal	25 mg/kg
4	Atlantic halibut	*Hippoglossus hipoglossus*	Samuelsen, O.B. & Ervik, A. (1997)	Pharmacokinetics	paper	single oral	25 mg/kg
5	Atlantic salmon	*Salmo salar L.*	Sohlberg, S. et al. (2002)	Depletion	paper	single intravenously	5 mg/kg
6	Atlantic salmon	*Salmo salar L.*	Sohlberg, S. et al. (2002)	Depletion	paper	single intravenously	5 mg/kg
7	Atlantic salmon	*Salmo salar L.*	Sohlberg, S. et al. (2002)	Depletion	paper	single oral	5 mg/kg
8	Atlantic salmon	*Salmo salar L.*	Sohlberg, S. et al. (2002)	Depletion	paper	single oral	5 mg/kg
9	Atlantic salmon	*Salmo salar L.*	Elema, M.O. et al. (1994)	Pharmacokinetics	paper	orally - medicated feed for 6 or 8 d	22 mg/kg/day
10	Atlantic salmon	*Salmo salar L.*	Elema, M.O. et al. (1994)	Pharmacokinetics	paper	orally - medicated feed for 6 or 8 d	22 mg/kg/day
11	Atlantic salmon	*Salmo salar L.*	Elema, M.O. et al. (1994)	Pharmacokinetics	paper	orally - medicated feed for 6 or 8 d	22 mg/kg/day
12	Atlantic salmon	*Salmo salar L.*	Elema, M.O. et al. (1994)	Pharmacokinetics	paper	orally - medicated feed for 6 or 8 d	22 mg/kg/day
13	Atlantic salmon	*Salmo salar L.*	Rogstad, A. et al. (1993)	Pharmacokinetics	paper	single oral	25 mg/kg
14	Atlantic salmon	*Salmo salar L.*	Rogstad, A. et al. (1993)	Pharmacokinetics	paper	single oral	50 mg/kg
15	Atlantic salmon	*Salmo salar L.*	Rogstad, A. et al. (1993)	Pharmacokinetics	paper	single intravenously	4,9 mg/kg
16	Atlantic salmon	*Salmo salar L.*	Elema, M.O. et al. (1995)	Pharmacokinetics	paper	single intravenously	10 mg/kg
17	Atlantic salmon	*Salmo salar L.*	Martinsen, B. and Horsberg, T.E. (1995)	Pharmacokinetics	paper	single intravenously	25 mg/kg
18	Channel catfish	*Ictalurus punctatus*	Plakas, S.M. et al. (2000)	Depletion	paper	single intravascular	1 mg/kg
19	Channel catfish	*Ictalurus punctatus*	Plakas, S.M. et al. (2000)	Depletion	paper	single oral	5 mg/kg
20	Cod	*Gadus morhua*	Hansen, M.K. and Horsberg, T.E. (2000a)	Pharmacokinetics	paper	single intravenously	5 mg/kg
21	Cod	*Gadus morhua*	Hansen, M.K. and Horsberg, T.E. (2000a)	Pharmacokinetics	paper	single oral	10 mg/kg
22	Common carp	*Cyprinus carpio L.*	van der Heijden, M.H.T. et al. (1994)	Pharmacokinetics	paper	single oral	18 mg/kg
23	Corkwing wrasse	*Symphodus melops*	Samuelsen, O.B. and Ervik, A (2001)	Pharmacokinetics	paper	single intraperitoneal	25 mg/kg
24	Corkwing wrasse	*Symphodus melops*	Samuelsen, O.B. and Ervik, A (2001)	Pharmacokinetics	paper	single intraperitoneal	25 mg/kg
25	Corkwing wrasse	*Symphodus melops*	Samuelsen, O.B. and Ervik, A (2001)	Pharmacokinetics	paper	single intraperitoneal	25 mg/kg
26	Corkwing wrasse	*Symphodus melops*	Samuelsen, O.B. and Ervik, A (2001)	Pharmacokinetics	paper	bath	
27	European eel	*Anguilla anguilla*	Hansen, M.K. et al. (2001)	Depletion	paper	single intravenously	5 mg/kg
28	European eel	*Anguilla anguilla*	Hansen, M.K. et al. (2001)	Depletion	paper	single oral	5 mg/kg
29	European eel	*Anguilla anguilla*	Boon, R. (1996)	Pharmacokinetics	paper	single intramuscular	9 mg/kg
30	European eel	*Anguilla anguilla*	van der Heijden, M.H.T. et al. (1994)	Pharmacokinetics	paper	single oral	18 mg/kg
31	European eel	*Anguilla anguilla*	Hansen, M.K. and Horsberg, T.E. (2000b)	Pharmacokinetics	paper	single intravenously	10 mg/kg
32	European eel	*Anguilla anguilla*	Hansen, M.K. and Horsberg, T.E. (2000b)	Pharmacokinetics	paper	single oral	10 mg/kg
33	Gilthead seabream	*Sparus aurata L.*	Tyrpenou, A.E. et al. (2003)	Depletion	paper	5 days	35 mg/kg/day
34	Gilthead seabream	*Sparus aurata L.*	Tyrpenou, A.E. et al. (2003)	Depletion	paper	5 days	35 mg/kg/day
35	Gilthead seabream	*Sparus aurata*	Rigos, G. et al. (2003)	Pharmacokinetics	paper	single intravascular	10 mg/kg
36	Goldsinny wrasse	*Ctenolabrus rupestris*	Hansen, M.K. and Horsberg, T.E. (2000a)	Pharmacokinetics	paper	single intravenously	10 mg/kg
37	Goldsinny wrasse	*Ctenolabrus rupestris*	Hansen, M.K. and Horsberg, T.E. (2000a)	Pharmacokinetics	paper	single oral	10 mg/kg
38	Halibut	*Hippoglossus hipoglossus*	Hansen, M.K. et al. (2001)	Depletion	paper	single intravenously	5 mg/kg

Annex 9. Dataoverzicht - flumequine (vervolg 2/4)

No.	Species	Temp. held	Pharmacokinetics		Tissue	Depletion
	English name	(C)	elimination half-lives (h)	terminal elim. half-lives		
1	African catfish	24	59,5		plasma	
2	Atlantic halibut	9	7	43 h	plasma	
3	Atlantic halibut	9	n.a.	n.a.	plasma	
4	Atlantic halibut	9	n.a.	n.a.	plasma	
5	Atlantic salmon	11,9 (fresh water)			muscle, blood, kidney, liver, skin	Radiolabelled compound was present in blood and muscle for more than 8
6	Atlantic salmon	11,9 (fresh water)			muscle, blood, kidney, liver, skin	weeks in fresh water group. In the seawater group, however, no radioactivity
7	Atlantic salmon	11,1 (sea water)			muscle, blood, kidney, liver, skin	was detected in the blood after 4 d and in the muscle after 2 weeks.
8	Atlantic salmon	11,1 (sea water)			muscle, blood, kidney, liver, skin	Elimination is substantially faster in sea water than in fresh water
9	Atlantic salmon	8	22,8 or 20,6		plasma	steady-state level was achieved after 70 h = 3 days
10	Atlantic salmon	8	21,2 or 23,5		liver	steady-state level was achieved after 70 h = 3 days
11	Atlantic salmon	8	17,6 or 21,3		muscle	steady-state level was achieved after 70 h = 3 days
12	Atlantic salmon	8	32,8 or 33,2		skin	steady-state level was achieved after 110 h = 4,5 days
13	Atlantic salmon	5	n.a.		plasma	
14	Atlantic salmon	5	n.a.		plasma	
15	Atlantic salmon	5	23		plasma	
16	Atlantic salmon	6-8	33-40		plasma	
17	Atlantic salmon	10	22,8		plasma	
18	Channel catfish	24	24,6		plasma	
19	Channel catfish	24	21,8		plasma, muscle	after 336 h conc. in muscle was < LOD (5 ng/g); elimination in tissue slower
20	Cod	8	75		plasma	
21	Cod	8	74		plasma	
22	Common carp	24	104,3		plasma	
23	Corkwing wrasse	12	26		plasma	
24	Corkwing wrasse	12	24		muscle	
25	Corkwing wrasse	12	29		liver	
26	Corkwing wrasse					
27	European eel	23 (fresh water)		232 h	plasma	
28	European eel	23 (fresh water)				Substantial amounts of flumequine remained in all majpr organs for 7 days.
29	European eel	23	255,6		plasma	145 days to achieve LOD of 0,002 ug/ml
30	European eel	24	451,2		plasma	
31	European eel	23 (fresh water)	314		plasma	
32	European eel	23 (fresh water)	208		plasma	
33	Gilthead seabream	18	22,14		muscle plus skin	Withdrawal period for MRL of 600 ug/kg at 95 tolerance limit was 106,08 h
34	Gilthead seabream	24	21,43		muscle plus skin	Withdrawal period for MRL of 600 ug/kg at 95 tolerance limit was 75,84 h
35	Gilthead seabream	19		30 h	plasma	
36	Goldsinny wrasse	14,5	31		plasma	
37	Goldsinny wrasse	14,5	41		plasma	
38	Halibut	16		62 h	plasma	

Annex 9. Dataoverzicht - flumequine (vervolg 3/4)

No.	Species		Reference	Rating	Availability	Administration	
	English name	Latin name				Type	Dose
39	Halibut	*Hippoglossus hipoglossus*	Hansen, M.K. et al. (2001)	Depletion	paper	single oral	5 mg/kg
40	Halibut	*Hippoglossus hipoglossus*	Hansen, M.K. and Horsberg, T.E. (1999)	Pharmacokinetics	paper	single intravenously	10 mg/kg
41	Halibut	*Hippoglossus hipoglossus*	Hansen, M.K. and Horsberg, T.E. (1999)	Pharmacokinetics	paper	single oral	10 mg/kg
42	Halibut	*Hippoglossus hipoglossus*	Samuelsen, O.B. & Lunestad, B.T. (1996)	Pharmacokinetics	abstract	bath for 72 h	150 mg/l
43	Orange-spotted grouper	*Epinephelus coioides*	Guo, J.-J. et al. (1997)	Pharmacokinetics	abstract	single oral	20 mg/kg
44	Rainbow trout	*Oncorhynchus mykiss W.*	Sohlberg, S. et al. (1994)	Pharmacokinetics	paper	single intraarterial	5 mg/kg
45	Rainbow trout	*Oncorhynchus mykiss W.*	Sohlberg, S. et al. (1994)	Pharmacokinetics	paper	single intraarterial	5 mg/kg
46	Rainbow trout	*Oncorhynchus mykiss W.*	Sohlberg, S. et al. (1994)	Pharmacokinetics	paper	single oral	5 mg/kg
47	Rainbow trout	*Oncorhynchus mykiss W.*	Sohlberg, S. et al. (1994)	Pharmacokinetics	paper	single oral	5 mg/kg
48	Rainbow trout	*Salmo gairdneri*	Sohlberg, S. et al. (1990)	Pharmacokinetics	paper	single intraarterial	5 mg/kg
49	Rainbow trout	*Salmo gairdneri*	Sohlberg, S. et al. (1990)	Pharmacokinetics	paper	single oral	5 mg/kg
50	Rainbow trout	*Oncorhynchus mykiss W.*	Malvis, J.G. et al. (1994)	Pharmacokinetics	title		
51	Salmon		Steffenak, I. et al. (1991)	Depletion	paper	orally for 10 days	10 mg/kg/day
52	Salmon trout	*Salmo gairdneri*	Chevalier, R.G. et al. (1981)	Pharmacokinetics	abstract	5 days	6 or 12 mg/kg/day
53	Sea bass	*Dicentrarchus labrax L.*	Rigos, G. et al. (2002)	Pharmacokinetics	paper	single intravascular	10 mg/kg
54	Sea bream	*Sparus aurata*	Malvisi, J. et al. (1997)	Depletion	paper	5 days	12 mg/kg/day
55	Sea bream	*Sparus aurata*	Malvisi, J. et al. (1997)	Depletion	paper	5 days	12 mg/kg/day
56	Sea bream	*Sparus aurata*	Malvisi, J. et al. (1997)	Depletion	paper	5 days	12 mg/kg/day
57	Sea bream	*Sparus aurata*	Della Rocca, G.M. et al. (1996)	Pharmacokinetics	abstract	orally for 5 days	12 mg/kg/day
58	Turbot	*Scophthalmus maximus*	Hansen, M.K. et al. (2001)	Depletion	paper	single intravenously	5 mg/kg
59	Turbot	*Scophthalmus maximus*	Hansen, M.K. et al. (2001)	Depletion	paper	single oral	5 mg/kg
60	Turbot	*Scophthalmus maximus*	Hansen, M.K. and Horsberg, T.E. (1999)	Pharmacokinetics	paper	single intravenously	10 mg/kg
61	Turbot	*Scophthalmus maximus*	Hansen, M.K. and Horsberg, T.E. (1999)	Pharmacokinetics	paper	single oral	10 mg/kg
62	Turbot	*Scophthalmus maximus*	Samuelsen, O.B. (2003)	Pharmacokinetics	paper	bath for 72 h	150 mg/l

Annex 9. Dataoverzicht - flumequine (vervolg 4/4)

No.	Species	Temp. held	Pharmacokinetics		Tissue	Depletion
	English name	(C)	elimination half-lives (h)	terminal elim. half-lives		
39	Halibut	16				Significant levels were observed over 96 h in bile, skin, intestine and eye
40	Halibut	10,3	32		plasma	
41	Halibut	10,3	43		plasma	
42	Halibut		10 h		muscle	elimination from muscle 6,5 days
43	Orange-spotted grouper	23	7,32-7,94		serum, muscle, liver, kidney	predicted withdrawal period 16 days
44	Rainbow trout	3	52,5		plasma	
45	Rainbow trout	13	10,3		plasma	
46	Rainbow trout	3	736		plasma	
47	Rainbow trout	13	285		plasma	
48	Rainbow trout	6,8-1,8			plasma	Extremely slow elimination at such low temperature: 0,3 ug/ml was present
49	Rainbow trout	6,8-1,8			plasma	in the plasma 300 h after the intraarterial and 600 h after the oral aministration
50	Rainbow trout					
51	Salmon	14			muscle, liver, skin, bone, fat	concentration profile measured over 70 days
52	Salmon trout	12			muscle	drug disappeared after 49-72 h
53	Sea bass	18	10,71		plasma	
54	Sea bream	25-28			vertebrae	after 240 h conc. was 179,4 ng/g
55	Sea bream	25-28			muscle	after 240 h conc. was < LOD (2,0 ng/g)
56	Sea bream	25-28			skin	after 240 h conc. was 101,5 ng/g
57	Sea bream	>20			muscle, skin, bone, liver	
58	Turbot	16		38 h	plasma	
59	Turbot	16				Significant levels observed over 96 h in bile, urine, bone, skin, intestine and eye
60	Turbot	18	34		plasma	
61	Turbot	18	42		plasma	
62	Turbot	16	10		muscle	

Annex 10. Dataoverzicht - mebendazole

No.	Species		Reference	Rating	Availability	Administration	
	English name	Latin name				Type	Dose
1	European eel	Anguilla anguilla	Iosifidou, E.G. et al. (1996)	Depletion	paper	bath	1 mg/l
2	European eel	Anguilla anguilla	Iosifidou, E.G. et al. (1996)	Depletion	paper	bath	1 mg/l
3	European eel	Anguilla anguilla	Iosifidou, E.G. et al. (1996)	Depletion	paper	bath	1 mg/l
4	European eel	Anguilla anguilla	Iosifidou, E.G. et al. (1996)	Depletion	paper	bath	1 mg/l
5	European eel	Anguilla anguilla	Iosifidou, E.G. et al. (1996)	Depletion	paper	bath	1 mg/l

No.	Species	Temp.	Pharmacokinetics		Tissue	Depletion
	English name	held (C)	elimination half-lives	terminal elim. half-lives		
1	European eel	25		3,2 h	muscle	Concentration profile was measured over 13 days after treatent
2	European eel	25		21,7 h	skin	Concentration profile was measured over 13 days after treatent
3	European eel	25		4,5 h	liver	Concentration profile was measured over 13 days after treatent
4	European eel	25		6,1 h	kidney	Concentration profile was measured over 13 days after treatent
5	European eel	25		3,6 h	fat	Concentration profile was measured over 13 days after treatent

Annex 11. Data overview for oxoliniczuur (1/4)

No.	Species		Reference	Rating	Availability	Administration	
	English name	Latin name				Type	Dose
1	Atlantic halibut	*Hippoglossus hippoglossus*	Samuelsen, O.B. & Ervik, A. (1999)	Pharmacokinetics	paper	single intravenous	10 mg/kg
2	Atlantic halibut	*Hippoglossus hippoglossus*	Samuelsen, O.B. & Ervik, A. (1999)	Pharmacokinetics	paper	single intraperitoneal	25 mg/kg
3	Atlantic halibut	*Hippoglossus hippoglossus*	Samuelsen, O.B. & Ervik, A. (1999)	Pharmacokinetics	paper	single oral	25 mg/kg
4	Atlantic salmon	*Salmo salar L.*	Hustvedt, S.O. et al. (1991)	Pharmacokinetics	paper	single intravascular	20 mg/kg
5	Atlantic salmon	*Salmo salar L.*	Hustvedt, S.O. (1992)	Pharmacokinetics	title		
6	Atlantic salmon	*Salmo salar L.*	Rogstad, A. et al. (1993)	Pharmacokinetics	paper	single intravascular	
7	Atlantic salmon	*Salmo salar L.*	Rogstad, A. et al. (1993)	Pharmacokinetics	paper	single oral	25 mg/kg
8	Atlantic salmon	*Salmo salar L.*	Martinsen, B. & Horsberg, T.E. (1995)	Pharmacokinetics	paper	single intravascular	25 mg/kg
9	Atlantic salmon	*Salmo salar L.*	Martinsen, B. & Horsberg, T.E. (1995)	Pharmacokinetics	paper	single oral	25 mg/kg
10	Atlantic salmon	*Salmo salar L.*	Samuelsen, O.B. et al. (2000)	Pharmacokinetics	paper	single intravenous	20 mg/kg
11	Atlantic salmon	*Salmo salar L.*	Samuelsen, O.B. et al. (2000)	Pharmacokinetics	paper	single oral	40 mg/kg
12	Atlantic salmon	*Salmo salar L.*	Coyne, R. et al. (2004a)	Some information	paper	orally for 13 days	
13	Ayu		Kasuga, Y. et al. (1984)	Some information	title		
14	Channel catfish	*Ictalurus punctatus*	Kleinow, K.M. et al. (1994)	Pharmacokinetics	abstract	oral	
15	Channel catfish	*Ictalurus punctatus*	Kleinow, K.M. et al. (1994)	Pharmacokinetics	abstract	oral	
16	Cod	*Gadus morhua L.*	Samuelsen O.B. et al. (2003)	Pharmacokinetics	paper	single intravenous	12,5 mg/kg
17	Cod	*Gadus morhua L.*	Samuelsen O.B. et al. (2003)	Pharmacokinetics	paper	single oral	25 mg/kg
18	Cod	*Gadus morhua L.*	Samuelsen O.B. et al. (2003)	Pharmacokinetics	paper	single oral	25 mg/kg
19	Cod	*Gadus morhua L.*	Samuelsen O.B. et al. (2003)	Pharmacokinetics	paper	single oral	25 mg/kg
20	Corkwing wrasse	*Symphodus melops*	Samuelsen, O.B. and Ervik, A (2001)	Pharmacokinetics	paper	single intraperitoneal	25 mg/kg
21	Corkwing wrasse	*Symphodus melops*	Samuelsen, O.B. and Ervik, A (2001)	Pharmacokinetics	paper	single intraperitoneal	25 mg/kg
22	Corkwing wrasse	*Symphodus melops*	Samuelsen, O.B. and Ervik, A (2001)	Pharmacokinetics	paper	single intraperitoneal	25 mg/kg
23	Corkwing wrasse	*Symphodus melops*	Samuelsen, O.B. and Ervik, A (2001)	Pharmacokinetics	paper	bath	
24	Gilthead sea bream	*Sparus aurata*	Rigos, G. et al. (2003)	Depletion	paper	orally with medicated feed for 10 d	
25	Gilthead sea bream	*Sparus aurata*	Rigos, G. et al. (2002b)	Pharmacokinetics	paper	single intravascular	20 mg/kg
26	Gilthead sea bream	*Sparus aurata*	Rigos, G. et al. (2002b)	Pharmacokinetics	paper	single oral	30 mg/kg
27	Rainbow trout	*Salmo gairdneri R.*	Jacobsen, M.D. (1989)	Depletion	title		
28	Rainbow trout	*Oncorhynchus mykiss*	Bjorklund, H.V. et al. (1992)	Depletion	paper	single oral	75 mg/kg
29	Rainbow trout	*Oncorhynchus mykiss*	Bjorklund, H.V. et al. (1992)	Depletion	paper	single oral	75 mg/kg
30	Rainbow trout	*Oncorhynchus mykiss*	Bjorklund, H.V. et al. (1992)	Depletion	paper	single oral	75 mg/kg
31	Rainbow trout	*Oncorhynchus mykiss*	Bjorklund, H.V. et al. (1991)	Depletion	paper	orally with medicated feed for 10 d	85 mg/kg/day
32	Rainbow trout	*Oncorhynchus mykiss*	Bjorklund, H.V. and Bylund, G. (1991)	Pharmacokinetics	abstract	single intravascular	10 mg/kg
33	Rainbow trout	*Oncorhynchus mkiss*	Bjorklund, H.V. and Bylund, G. (1991)	Pharmacokinetics	abstract	single oral	75 mg/kg
34	Rainbow trout	*Oncorhynchus mykiss*	Hustvedt, S.O. & Ragnar, S. (1991)	Pharmacokinetics	paper	single intravascular	10 mg/kg
35	Rainbow trout	*Oncorhynchus mykiss*	Hustvedt, S.O. (1992)	Pharmacokinetics	title		
36	Rainbow trout	*Oncorhynchus mykiss*	Kleinow, K.M. et al. (1994)	Pharmacokinetics	abstract	oral	
37	Rainbow trout	*Oncorhynchus mykiss*	Coyne, R. et al. (2005)	Some information	paper	orally with medicated feed for 9 d	50 mg/kg/day
38	Rainbow trout	*Oncorhynchus mykiss*	Coyne, R. et al. (2004b)	Some information	paper	orally for 6 days	50 mg/kg/day

Annex 11. Dataoverzicht - oxoliniczuur (vervolg 2/4)

No.	Species	Temp.	Pharmacokinetics		Tissue	Depletion
	English name	held	elimination	terminal elim.		
		(C)	half-lives	half-lives		
1	Atlantic halibut	9	52 h		plasma	
2	Atlantic halibut	9	48 h		plasma	
3	Atlantic halibut	9	50 h		plasma	
4	Atlantic salmon	9	60,3 h		plasma	
5	Atlantic salmon					
6	Atlantic salmon	5	10 h		plasma	
7	Atlantic salmon	5			muscle, plasma, liver	
8	Atlantic salmon	10	18,2 h			
9	Atlantic salmon	10				
10	Atlantic salmon	10	15 h		plasma, muscle, liver	
11	Atlantic salmon	10			plasma, muscle, liver	
12	Atlantic salmon	5,7-7,2			plasma, muscle, liver, kidney	concentr. measured just once - 24 h after last treatment
13	Ayu					
14	Channel catfish	24	40,9 h		plasma	
15	Channel catfish	14	939 h		plasma	
16	Cod	8	84 h		plasma	
17	Cod	8	82 h		plasma	
18	Cod	8	58 h		muscle	
19	Cod	8	82 h		liver	
20	Corkwing wrasse	12		57 h	plasma	
21	Corkwing wrasse	12		59 h	muscle	
22	Corkwing wrasse	12		72 h	liver	
23	Corkwing wrasse					
24	Gilthead sea bream	19	11-14 h		muscle, skin, liver	conc. profile measured for 7 days post-treatment
25	Gilthead sea bream	20	12,6 h		plasma	
26	Gilthead sea bream	20			plasma, muscle	
27	Rainbow trout					
28	Rainbow trout	5	6,1 d		serum, muscle, liver, kidney	predicted withdrawal time 140 d to reach LOD (0,01ug/g)
29	Rainbow trout	10	4 d		serum, muscle, liver, kidney	predicted withdrawal time 60 d to reach LOD (0,01ug/g)
30	Rainbow trout	16	24 h		serum, muscle, liver, kidney	predicted withdrawal time 28 d to reach LOD (0,01ug/g)
31	Rainbow trout	17			muscle	concentration profile measured for 25 days
32	Rainbow trout	16	69,7 h		plasma	
33	Rainbow trout	16	69,7 h		plasma	
34	Rainbow trout	8,5	52,6 h	29,1 h	plasma	
35	Rainbow trout					
36	Rainbow trout	14	16,3 h		plasma	
37	Rainbow trout	6			plasma	concentr. measured just once - 24 h after last treatment
38	Rainbow trout	12			plasma	concentr. measured just once - 24 h after last treatment

Annex 11. Dataoverzicht - oxoliniczuur (vervolg 3/4)

No.	Species		Reference	Rating	Availability	Administration	
	English name	Latin name				Type	Dose
39	Rainbow trout		Kasuga, Y. et al. (1984)	Some information	title		
40	Rainbow trout (freshwater)		Ishida, N. (1992)	Depletion	paper	single intravascular	20 mg/kg
41	Rainbow trout (freshwater)		Ishida, N. (1992)	Depletion	paper	single oral	40 mg/kg
42	Rainbow trout (seawater)		Ishida, N. (1992)	Depletion	paper	single intravascular	20 mg/kg
43	Rainbow trout (seawater)		Ishida, N. (1992)	Depletion	paper	single oral	40 mg/kg
44	Salmon		Steffenak, I. et al. (1991)	Depletion	paper	orally for 10 days	25 mg/kg/day
45	Sea bass	*Dicentrarchus labrax*	Poher, I. et al. (1997)	Pharmacokinetics	paper	single intravascular	10 mg/kg
46	Sea bass	*Dicentrarchus labrax*	Rigos, G. et al. (2002a)	Pharmacokinetics	paper	single intravascular	15 mg/kg
47	Sea bass	*Dicentrarchus labrax*	Rigos, G. et al. (2002a)	Pharmacokinetics	paper	single intravascular	15 mg/kg
48	Sea bass	*Dicentrarchus labrax*	Rigos, G. et al. (2002a)	Pharmacokinetics	paper	single intravascular	15 mg/kg
49	Sea bass	*Dicentrarchus labrax*	Rigos, G. et al. (2002a)	Pharmacokinetics	paper	single intravascular	15 mg/kg
50	Sea bass	*Dicentrarchus labrax*	Rigos, G. et al. (2002a)	Pharmacokinetics	paper	single intravascular	15 mg/kg
51	Sea bass	*Dicentrarchus labrax*	Rigos, G. et al. (2002a)	Pharmacokinetics	paper	single intravascular	15 mg/kg
52	Sharpsnout sea bream	*Diplodus puntazzo*	Rigos, G. et al. (2003)	Depletion	paper	orally with medicated feed for 10 d	
53	Sharpsnout sea bream	*Diplodus puntazzo*	Rigos, G. et al. (2004)	Pharmacokinetics	paper	single intravascular	20 mg/kg
54	Turbot	*Scophthalmus maximus*	Poher, I. & Blanc, G. et al. (1998)	Pharmacokinetics	paper	single oral	10 mg/kg
55	Turbot	*Scophthalmus maximus*	Samuelsen, O.B. (2003)	Pharmacokinetics	paper	bath for 72 h	200 mg/l

Annex 11. Dataoverzicht - oxoliniczuur (vervolg 4/4)

No.	Species	Temp.	Pharmacokinetics		Tissue	Depletion
	English name	held (C)	elimination half-lives	terminal elim. half-lives		
39	Rainbow trout					
40	Rainbow trout (freshwater)	16			serum, muscle	conc. near LOD after 244 h
41	Rainbow trout (freshwater)	16			serum, muscle	conc. near LOD after 244 h
42	Rainbow trout (seawater)	16			serum, muscle	conc. near LOD after 72 h
43	Rainbow trout (seawater)	16			serum, muscle	conc. near LOD after 72 h
44	Salmon	6-14			muscle, liver, skin, bone	conc. profile measured over 180 days
45	Sea bass	15,2		86,64 h	plasma	
46	Sea bass	13	297,6 h		plasma	
47	Sea bass	13	146,4 h		liver	
48	Sea bass	13	141,6 h		muscle	
49	Sea bass	22	60 h		plasma	
50	Sea bass	22	40,8 h		liver	
51	Sea bass	22	38,4 h		muscle	
52	Sharpsnout sea bream	19	11-19 h		muscle, skin, liver	conc. profile measured for 7 days post-treatment
53	Sharpsnout sea bream	19	10 h		Plasma & muscle	
54	Turbot	16	20,4 h		serum	
55	Turbot	16			muscle	

Annex 12. Data overview for oxotetracycline (1/4)

No.	Species		Reference	Rating	Availability	Administration	
	English name	Latin name				Type	Dose
1	African catfish	*Clarias Gariepinus*	Grondel, J.L. et al. (1989)	Pharmacokinetics	title	single intravascular	60 mg/kg
2	Amago salmon		Uno, K. et al. (1992)	Pharmacokinetics	abstract	single oral	100 mg/kg
3	Arctic charr	*Salvelinus alpinus L.*	Haug, T. and Hals, P.A. (2000)	Pharmacokinetics	paper	single intravascular	10 or 20 mg/kg
4	Arctic charr	*Salvelinus alpinus L.*	Haug, T. and Hals, P.A. (2000)	Pharmacokinetics	paper	single oral	50 or 100 mg/kg
5	Atlantic salmon		Brocklebank, J.R. et al. (1997)	Depletion	title		
6	Atlantic salmon	*Salmo salar L.*	Elema, M.O. et al. (1996)	Pharmacokinetics	paper	single intravascular	20 mg/kg
7	Atlantic salmon	*Salmo salar L.*	Elema, M.O. et al. (1996)	Pharmacokinetics	paper	single oral	50 mg/kg
8	Ayu	*Plecoglossus altivelis*	Maruyama, R. and Uno, K. (1997)	Depletion	abstract	single oral	50 mg/kg
9	Ayu	*Plecoglossus altivelis*	Uno, K. (1996)	Pharmacokinetics	paper	single intravascular	25 mg/kg
10	Ayu	*Plecoglossus altivelis*	Uno, K. (1996)	Pharmacokinetics	paper	single oral	100 mg/kg
11	Black seabream	*Sparus macrocephalus*	Wang, Q. et al. (2004)	Depletion	paper	oral for 5 days	100 mg/kg/day
12	Carp		Romvary, A. et al. (1991)	Depletion	abstract	orally for 7 days	75 mg/kg/day
13	Carp		Romvary, A. et al. (1991)	Depletion	abstract	orally for 7 days	75 mg/kg/day
14	Carp	*Cyprinus carpio L.*	Grondel, J.L. et al. (1987)	Pharmacokinetics	title	different routes	
15	Channel catfish	*Ictalurus punctatus*	Luzzana, U. et al. (1994)	Depletion	paper	orally with medicated feed for 7 days	
16	Channel catfish		Du, W.X. et al. (1997)	Some information	paper	oraly for 10 days	150 mg/kg/day
17	Channel catfish		Du, W.X. et al. (1997)	Some information	paper	oraly for 10 days	37,5 mg/kg/day
18	Channel catfish		Du, W.X. et al. (1995)	Some information	paper	orally - medicated feed for 4 or 8 wks	12,5/25/50 mg/kg
19	Channel catfish		Ohara, T.M. et al. (1997)	Some information	abstract	orally - medicated feed for 2 or 3 wks	
20	Chinook salmon		Aoyama, R.G. et al. (1991)	Depletion	paper	orally - medicated feed for 10 days	80 mg/kg/day
21	Chinook salmon	*Oncorhynchus tshawytscha*	Namdari, R. et al. (1996)	Depletion	paper	orally - medicated feed for 21 days	75 mg/kg/day
22	Chinook salmon	*Oncorhynchus tshawytscha*	Namdari, R. et al. (1996)	Depletion	paper	orally - medicated feed for 21 days	75 mg/kg/day
23	Chinook salmon	*Oncorhynchus tshawytscha (W)*	Namdari, R. et al. (1999)	Depletion	paper	single intraarterially	5 or 50 mg/kg
24	Chinook salmon	*Oncorhynchus tshawytscha*	Abedini, S. et al. (1998)	Pharmacokinetics	paper	single intraarterially	50 mg/kg
25	Chinook salmon	*Oncorhynchus tshawytscha*	Abedini, S. et al. (1998)	Pharmacokinetics	paper	single intraarterially	50 mg/kg
26	Coho salmon	*Oncorhynchus kisutch*	Namdari, R. et al. (1996)	Depletion	paper	orally - medicated feed for 42 days	100 mg/kg/day
27	Coho salmon	*Oncorhynchus kisutch*	Meinertz, J.R. et al. (2001)	Depletion	paper	orally - medicated feed for 10 days	88,2 mg/kg/day
28	Gilthead sea bream	*Sparus aurata*	Rigos, G. et al. (2003)	Pharmacokinetics	paper	single intravascular	40 mg/kg
29	Japanese eel	*Anguilla japonica*	Maruyama, R. and Uno, K. (1997)	Depletion	abstract	single oral	50 mg/kg
30	Japanese eel	*Anguilla japonica*	Ueno, R. et al. (2004)	Pharmacokinetics	paper	single intravascular	50 mg/kg
31	Japanese eel	*Anguilla japonica*	Ueno, R. et al. (2004)	Pharmacokinetics	paper	orally with medicated feed for 6 days	
32	Nile tilapia	*Oreochromis niloticus*	Chen, C.Y. et al. (2004)	Depletion	paper	oral for 10 days	82,8 mg/kg/day
33	northern pike	*Esox lucius*	Bernardy, J.A. et al. (2003)	Depletion	paper	orally - medicated feed for 10 days	82.7 mg/kg/day
34	Perch	*Lateolabras janopicus*	Wang, Q. et al. (2004)	Depletion	paper	oral for 5 days	100 mg/kg/day
35	Rainbow trout	*Salmo gairdneri Richardson*	Jacobsen, M.D. (1989)	Depletion	title		
36	Rainbow trout	*Salmo gairdneri R.*	Bjorklund, H. and Bylund, G. (1990)	Depletion	paper	single oral	75 mg/kg
37	Rainbow trout	*Salmo gairdneri R.*	Bjorklund, H. and Bylund, G. (1990)	Depletion	paper	single oral	75 mg/kg
38	Rainbow trout	*Salmo gairdneri R.*	Bjorklund, H. and Bylund, G. (1990)	Depletion	paper	single oral	75 mg/kg

Annex 12. Dataoverzicht - oxotetracycline (vervolg 2/4)

No.	Species	Temp.	Pharmacokinetics		Tissue	Depletion
	English name	held (C)	elimination half-lives	terminal elim. half-lives		
1	African catfish	25	80,3 h		plasma	
2	Amago salmon		16 h		serum	elimination time from muscle was 21 days
3	Arctic charr	6,3		266,3 / 326,9h	plasma	
4	Arctic charr	6,3	367 / 444,2 h		plasma	
5	Atlantic salmon					
6	Atlantic salmon	7,0-8,0			plasma	bioavailability, no description of elimination phase
7	Atlantic salmon	7,0-8,0			plasma	bioavailability, no description of elimination phase
8	Ayu	18	5-6 days		serum, muscle, skin, bone, liver	Concentration profile for all tissues measured for 30 days
9	Ayu	18	53,1-125 h		plasma, muscle, liver, kidney	
10	Ayu	18			plasma, muscle, liver, kidney	
11	Black seabream	17,3			blood, muscle, liver, kidney	levels below LOD (0,05 ug/g) after 30 days
12	Carp	20			muscle, liver, kidney, fat	Concentration profile for all tissues measured for 80 days
13	Carp	11			muscle, liver, kidney, fat	Concentration profile for all tissues measured for 80 days
14	Carp					
15	Channel catfish	18 or 23			muscle	concentration profile measured over 40 days
16	Channel catfish	24,4				conc. After 18 hours - 1,14 ppm
17	Channel catfish	24,4				conc. After 18 hours - 0,48 ppm
18	Channel catfish	28				after 3 week withdrawal period no detectable residues
19	Channel catfish				muscle, liver	
20	Chinook salmon	7,8-10,3	5,4 h		muscle	levels were below LOD (0.05 ppm) 35 days after last dose (measured for 42 days)
21	Chinook salmon	9			liver, kidney, muscle, skin, bone	levels were below LOD (0.05 ug/g) 65 days after last dose (measured for 63 days)
22	Chinook salmon	15			liver, kidney, muscle, skin, bone	levels were below LOD (0.05 ug/g) 41 days after last dose (measured for 63 days)
23	Chinook salmon	10			All possible tissues	Concentration profile for all tissues measured for 30 days
24	Chinook salmon			88,29 h	plasma	
25	Chinook salmon		428,19 h		plasma	
26	Coho salmon	10			liver, kidney, muscle, skin, bone	(measured for 63 days)
27	Coho salmon	4,1-8,5		4,9 days	fillet with skin	Concentration profile measured for 19 days
28	Gilthead sea bream	20	53 h		plasma	muscle concentration profile for 180 h
29	Japanese eel	28	4-11 days		serum, muscle, skin, bone, liver	Concentration profile for all tissues measured for 30 days
30	Japanese eel	28	115 h		plasma	
31	Japanese eel	28			plasma	after 7 days no residues were detected
32	Nile tilapia	25 or 30			serum, liver, muscle+skin	concentration profile measured over 31 days
33	northern pike	14	5,9-6,7 h		fillet and skin	0 withdrawal time for FDA tissue tolerance limit 2000 ng/g (measured for 14 days)
34	Perch	20,4			blood, muscle, liver, kidney	levels below LOD (0,05 ug/g) after 8 days
35	Rainbow trout					drug was detected at the level 0.05 ppm 22 days after the last dose
36	Rainbow trout	5	8,9 h		plasma, muscle, liver	predicted withdrawal times varied from 27 to 135 days depending on
37	Rainbow trout	10	6,1 h		plasma, muscle, liver	temperature and tissue studied
38	Rainbow trout	16	4,8 h		plasma, muscle, liver	

Annex 12. Dataoverzicht - oxotetracycline (vervolg 3/4)

No.	Species		Reference	Rating	Availability	Administration	
	English name	Latin name				Type	Dose
39	Rainbow trout	*Oncorhynchus mykiss (W)*	Namdari, R. et al. (1999)	Depletion	paper	single intraarterially	5 or 50 mg/kg
40	Rainbow trout	*Oncorhynchus mykiss*	Bjorklund, H.V. et al. (1991)	Depletion	paper	orally - medicated feed for 10 days	85 mg/kg/day
41	Rainbow trout		Lapinska, K. et al. (2005)	Depletion	abstract		
42	Rainbow trout	*Salmo gairdneri*	Salte, R. and Liestol, K. (1983)	Depletion	title		
43	Rainbow trout	*Oncorhynchus mykiss*	Abedini, S. et al. (1998)	Pharmacokinetics	paper	single oral	50 mg/kg
44	Rainbow trout	*Oncorhynchus mykiss*	Abedini, S. et al. (1998)	Pharmacokinetics	paper	single oral	50 mg/kg
45	Rainbow trout		Rogstad, A. et al. (1991)	Pharmacokinetics	paper	single oral	150 mg/kg
46	Rainbow trout	*Oncorhynchus mykiss*	Bjorklund, H. and Bylund, G. (1991)	Pharmacokinetics	abstract	single intravascular	10 and 20 mg/kg
47	Rainbow trout	*Oncorhynchus mykiss*	Bjorklund, H. and Bylund, G. (1991)	Pharmacokinetics	abstract	single oral	75 mg/kg
48	Rainbow trout		Black, W.D. et al. (1991)	Pharmacokinetics	abstract	single intravenous	5 mg/kg
49	Rainbow trout	*Oncorhynchus mykiss*	Dagoglu, G. et al. (2004)	Pharmacokinetics	abstract	single intramuscular	
50	Rainbow trout		Keck, G. et al. (1984)	Pharmacokinetics	title		
51	Rainbow trout	*Oncorhynchus mykiss*	Turel, I. et al. (2003)	Pharmacokinetics	abstract	single intravascular	5 mg/kg
52	Rainbow trout	*Oncorhynchus mykiss*	Turel, I. et al. (2003)	Pharmacokinetics	abstract	single oral with medicated feed	100 mg/kg
53	Rainbow trout		Uno, K. et al. (1992)	Pharmacokinetics	abstract	single oral	100 mg/kg
54	Rainbow trout	*Oncorhynchus mykiss*	Uno, K. et al. (1997)	Pharmacokinetics	abstract	single intravenous	50 mg/kg
55	Rainbow trout	*Salmo gairdneri*	Tantillo, G. et al. (1997)	Some information	abstract	orally with medicated feed for 6 days	
56	Red pacu	*Colossoma brachypomum*	Doi, A.M. et al. (1998)	Pharmacokinetics	paper	single intravenous	5 mg/kg
57	Red pacu	*Colossoma brachypomum*	Doi, A.M. et al. (1998)	Pharmacokinetics	paper	single intramuscular	5 mg/kg
58	salmon		Law, F.C.P. et al. (1998)	Pharmacokinetics	title		
59	Sea bass	*Dicentrarchus labrax*	Malvisi, J. et al. (1996)	Depletion	paper	orally - medicated feed fo 14 days	
60	Sea bass	*Dicentrarchus labrax*	Rigos, G. et al. (2002)	Pharmacokinetics	paper	single intravascular	40 mg/kg
61	Sea bass	*Dicentrarchus labrax*	Rigos, G. et al. (2002)	Pharmacokinetics	paper	single intravascular	40 mg/kg
62	Sea bass	*Dicentrarchus labrax (L.)*	Rigos, G. et al. (2004a)	Some information	paper	single oral	50 mg/kg
63	Sea bream	*Sparus aurata*	Malvisi, J. et al. (1996)	Depletion	paper	orally - medicated feed fo 14 days	
64	Sea urchin	*Psammevhinus miliaris*	Campbell, D.A. et al. (2001)	Depletion	paper	orally - medicated feed for 12 days	
65	Sharpsnout sea bream	*Diplodus puntazzo*	Rigos, G. et al. (2004b)	Pharmacokinetics	paper	single intravascular	40 mg/kg
66	Summer flounder	*Paralichthys dentatus*	Chen, C.Y. et al. (2004)	Depletion	paper	oral for 10 days	82,8 mg/kg/day
67	Sunshine bass		Chen, C.Y. et al. (2004)	Depletion	paper	oral for 10 days	82,8 mg/kg/day
68	Tench	*Tinca tinca L.*	Reja, A. et al. (1996)	Pharmacokinetics	abstract	single intramuscular	
69	walleye	*Stizostedion vitreum*	Bernardy, J.A. et al. (2003)	Depletion	paper	orally - medicated feed for 10 days	82.7 mg/kg/day
70	Walleye	*Sander vitreus*	Chen, C.Y. et al. (2004)	Depletion	paper	oral for 10 days	82,8 mg/kg/day
71	Yellow perch	*Perca flavescens*	Brown, M.L. et al. (2002)	Some information	paper	immersed (for marking) for 6h	600 mg/l
72	Yellowtail	*Seriola quinqueradiata*	Ueno, R., et al.	Pharmacokinetics	other paper	single intravascular	50 mg/kg
73	Yellowtail		Uno, K. et al. (1992)	Pharmacokinetics	abstract	single oral	100 mg/kg

Annex 12. Dataoverzicht - oxotetracycline (vervolg 4/4)

No.	Species	Temp.	Pharmacokinetics		Tissue	Depletion
	English name	held (C)	elimination half-lives	terminal elim. half-lives		
39	Rainbow trout	10			All possible tissues	Concentration profile for all tissues measured for 30 days
40	Rainbow trout	17			muscle	concentration profile measured for 25 days
41	Rainbow trout	18			various	Disposal times varied between 9-20 days depending on dose and tissue
42	Rainbow trout					
43	Rainbow trout			94,22 h	plasma	
44	Rainbow trout		479,43 h		plasma	
45	Rainbow trout	7	278,4 h		plasma	muscle, skin, liver, bones concentration profile for 336 h
46	Rainbow trout	16	60,3 h		plasma	
47	Rainbow trout	16			plasma	
48	Rainbow trout		81,5 h		serum	
49	Rainbow trout				plasma	
50	Rainbow trout					
51	Rainbow trout	10,5	33,5 h		plasma	
52	Rainbow trout	10,5	27 h		plasma	
53	Rainbow trout		23 h		serum	elimination time from muscle was 22 days
54	Rainbow trout		52 h		serum	
55	Rainbow trout				muscle	concentration profile measured for 60 days
56	Red pacu	23	50,97 h		plasma	
57	Red pacu	23	62,25 h		plasma	
58	salmon					Withdrawal period estimate
59	Sea bass	19-28			muscle, liver, vertebrae, skin	concentration profile measured over 60 days
60	Sea bass	13,5	69 h		plasma	liver, muscle concentration profile for 128 h
61	Sea bass	22	9,65 h		plasma	liver, muscle concentration profile for 128 h
62	Sea bass	22			plasma	plasma concentration profile for 120 h - bioavailability study
63	Sea bream	19-28			muscle, liver, vertebrae, skin	concentration profile measured over 60 days
64	Sea urchin	11,0-13,0	24,6 h		gonad tissue	concentration profile measured over 70 days
65	Sharpsnout sea bream	19	35 h		plasma	
66	Summer flounder	17 or 20			serum, liver, muscle+skin	concentration profile measured over 31 days
67	Sunshine bass	20 or 25			serum, liver, muscle+skin	concentration profile measured over 31 days
68	Tench		21,2 h		plasma	
69	walleye	16	10,5 h		fillet and skin	0 withdrawal time for FDA tissue tolerance limit 2000 ng/g (measured for 14 days)
70	Walleye	15 or 20			serum, liver, muscle+skin	concentration profile measured over 31 days
71	Yellow perch	18			muscle	depletion below 2,0 ug/g reached after 2h
72	Yellowtail	21	22,5 h		plasma	
73	Yellowtail		28 h		serum	elimination time from muscle was 21 days

Annex 13. Dataoverzicht - praziquantel

No.	Species		Reference	Rating	Availability	Administration	
	English name	Latin name				Type	Dose
1	Rainbow trout	Salmo gairdneri R.	Bjorklund, H. & Bylund, G. (1987)	Depletion	title		
2	Rockfish	Sebastes schlegeli	Kim, C.S. et al. (2003)	Depletion	paper	orally for 3 days	200 mg/kg/day
3	Rockfish	Sebastes schlegeli	Kim, C.S. et al. (2003)	Depletion	paper	orally for 3 days	400 mg/kg/day
4	Rockfish	Sebastes schlegeli	Kim, K.H. et al. (2001)	Depletion	paper	single oral	400 mg/kg
5	Rockfish	Sebastes schlegeli	Kim, K.H. et al. (2001)	Depletion	paper	bath for 4 min	100 ppm

No.	Species	Temp.	Pharmacokinetics		Tissue	Depletion
	English name	held (C)	elimination half-lives	terminal elim. half-lives		
1	Rainbow trout					
2	Rockfish	19-20			muscle and skin	Conc. profile measuerd for 8 days
3	Rockfish	19-20			muscle and skin	Conc. profile measuerd for 8 days
4	Rockfish				plasma and muscle	Conc. profile measuerd for 168 h
5	Rockfish				plasma and muscle	Conc. profile measuerd for 168 h

Annex 14. Dataoverzicht - trimethosulfmix (1/2)

Species		Reference	Rating	Availability	Administration
English name	**Latin name**				**Type**
Atlantic halibut	*Hippoglossus hipoglossus L.*	Samuelsen, O.B. et al. (1997)	Pharma + depl	paper	bath treatment for 72 h
Atlantic halibut	*Hippoglossus hipoglossus L.*	Samuelsen, O.B. et al. (1997)	Pharma + depl	paper	bath treatment for 72 h
Atlantic salmon	*Salmo salar*	Horsberg, T.E. et al. (1997)	Pharmacokinetics	paper	single oral
Atlantic salmon	*Salmo salar*	Horsberg, T.E. et al. (1997)	Pharmacokinetics	paper	single intravenously
Atlantic salmon		Hormazabal, V. and Rogstad, A. (1992)	Some information	paper	single oral medicated feed pellets
Carp	*Cyprinus carpio*	Nouws, J.F.M. et al. (1993)	Pharmacokinetics	title	
Carp-198 yearling		Heinze, W. and Weirowski, F. (1991)	Pharmacokinetics	abstract	n.a.
Carp-198 yearling		Heinze, W. and Weirowski, F. (1991)	Pharmacokinetics	abstract	n.a.
Carp-2 years old		Heinze, W. and Weirowski, F. (1991)	Pharmacokinetics	abstract	n.a.
Carp-2 years old		Heinze, W. and Weirowski, F. (1991)	Pharmacokinetics	abstract	n.a.
Coho salmon	*Oncorhynchus kisutch*	Gehring, T.A. et al. (1996)	Some information	paper	orally - mediacted feed for 10 d
Coho salmon	*Oncorhynchus kisutch*	Gehring, T.A. et al. (1996)	Some information	paper	orally - mediacted feed for 10 d
Coho salmon	*Oncorhynchus kisutch*	Gehring, T.A. et al. (1996)	Some information	paper	orally - mediacted feed for 10 d
Rainbow trout	*Salmo gairdneri*	Salte, R. and Liestol, K. (1983)	Depletion	title	
Rainbow trout	*Salmo gairdneri Richardson*	Jacobsen, M.D. (1989)	Depletion	title	
Rainbow trout	*Oncorhynchus mykkis*	Tan, W.P. and Wall, R.A. (1995)	Pharmacokinetics	abstract	single intraaortic
Sea bass	*Dicentarchus labrax*	Gapasin, R.S.J., et al. (1996)	Some information	abstract	orally - encaps. at 20% w/w
Sea bass	*Dicentarchus labrax*	Gapasin, R.S.J., et al. (1996)	Some information	abstract	orally - encaps. at 40% w/w
Sea bass (52 d old)		Chair, M. et al. (1996)	Some information	paper	orally - encaps.
Seabass larvae		Touraki, M. et al. (1999)	Pharmacokinetics	paper	orally - encaps.
Turbot (32 days old)		Chair, M. et al. (1996)	Some information	paper	orally - encaps.

Annex 14. Dataoverzicht - trimethosulfmix (vervolg 2/2)

No.	Species	Administration	Temp.	Pharmacokinetics		Tissue	Depletion
	English name	Dose	held (C)	elimination half-lives	terminal elim. half-lives		
1	Atlantic halibut	200 ug/ml	12	98 h		muscle	Calculated elimination time 40 days to reach MRL of 0,05 ug/g using 95% confidence limit
2	Atlantic halibut	200 ug/ml	12	116 h		liver	Calculated elimination time 55 days to reach MRL of 0,05 ug/g using 95% confidence limit
3	Atlantic salmon	5 mg + 25 mg	10			plasma	Concentration profile in plasma for both drugs was measured over 168 hours
4	Atlantic salmon	5 mg + 25 mg	10			plasma	Concentration profile in plasma for both drugs was measured over 168 hours
5	Atlantic salmon	100 mg/kg	8			plasma	Concentration profile in plasma for both drugs was measured over 300 hours
6	Carp		2				
7	Carp-198 yearling	n.a.	15	43,5 h			
8	Carp-198 yearling	n.a.	20	13,7 h			
9	Carp-2 years old	n.a.	15	16,8 h			
10	Carp-2 years old	n.a.	20	20,6 h			
11	Coho salmon	33,3 mg SDZ/kg/day	n.a.				Muscle conc. of SDZ varied significantly among the fishes sampled at the same day
12	Coho salmon	33,3 mg SDZ/kg/day	n.a.				Day 0 (conc. 9,07-10200 ng/g), day 5 (2,57-8180 ng/g), day 15 (0,2-855 ng/g)
13	Coho salmon	33,3 mg SDZ/kg/day	n.a.				This indicates problems with determination
14	Rainbow trout						Drug withdrawal study
15	Rainbow trout						
16	Rainbow trout				36,1 h	plasma	
17	Sea bass	n.a.	n.a.				TMP peak levels (8,74 ug/g dw) reached after 5 hours; TMP persisted in the tissue up to 72 h
18	Sea bass	n.a.	n.a.				TMP peak levels (19,3 ug/g dw) reached after 2 hours; TMP persisted in the tissue up to 72 h
19	Sea bass (52 d old)	300 nauplii/animal	opt.				Slow elimination; trimethoprim detectable above 1 ug/g up to 80 h postdosage
20	Seabass larvae	34,51 mg/kg		50 h		body tissue	
21	Turbot (32 days old)	300 nauplii/animal	opt.				Slow elimination; trimethoprim detectable above 1 ug/g up to 80 h postdosage