Attachment XIII

Guidance note on the licensing of discharges of Panacur (fenbendazole) at marine cage fish farms

Version 1.0
28 May 2007

Introduction

Panacur (active ingredient fenbendazole) has been developed by Hoechst Roussel Vet Limited as a broad spectrum anthelmintic for the removal and control of gastrointestinal parasites and lungworm in cattle. The EC safety data sheets for fenbendazole (Hoechst Roussel Vet Limited) describe the chemical as not readily degradable, and of low acute toxicity to fish and bacteria (e.g. EC50 > 500 mg/L). As a general precaution the documentation advises against uncontrolled release to soil or water ways. Panacur does not have a marketing authorisation as a fish medicine but SEPA understands that is being prescribed by vets under the cascade principle on the rare occasions it is required.

SEPA has received a small number of applications for consent under the Control of Pollution Act 1974 (COPA) and will receive applications under the Water Environment (Controlled Activities) (Scotland) Regulations 2005 (CAR) for the use of Panacur in the treatment of salmon in marine cage salmon farms. SEPA's predecessor bodies the Scottish RPAs authorised occasional use by issuing specific letters of authorisation however this approach was thought not fully to meet the requirements of the COPA or CAR and SEPA requires to follow closely the procedure laid down by the Regulations.

This report provides an initial assessment of the toxicity risk to marine life associated with the use of Panacur for the treatment of salmon in marine salmon farms.

Usage of Panacur (fenbendazole) in marine salmon farming

Panacur has been used on an occasional basis for the treatment of *Eubothrium* (a stomach cestode) outbreaks in marine salmon farms and applications have generally been made for 'one-off' treatments. Furthermore, SEPA's records indicate that the total quantity used in marine salmon farming has been small. For example, during the period 1990-99, there has only been 308 kg Panacur (equivalent to 12kg fenbendazole) use based on record returns (to 12-04-99) in SEPA's South-West Area.

Treatment regimen

Panacur 4% Powder is a powder formulation of fenbendazole for incorporation into feedstuffs for oral administration (i.e. 1g Panacur 4% powder contains 0.04g active ingredient fenbendazole). SEPA does not have detailed information on the treatment regimen. Panacur 4% Powder has been used in the few (3) cases examined. It is understood that this is mixed with feed as required on a case-by-case basis.

Toxicity of fenbendazole to marine organisms

The following is an extract from unpublished work carried out by a PhD student (Maurice Clarke) under the supervision of Ian Davies, FRS Marine Laboratory, Aberdeen.

The drug Panacur has been shown to be effective for the control of cestode infections in salmonids and is currently being used for this purpose. However its eco-toxicity in the marine environment is poorly understood. Panacur is a commercial formulation containing fenbendazole, a member of the benzimidazole group of anthelmintics, the primary action of which is the inhibition of the formation of the microtubule complex in eukaryotic cells. Panacur is administered as a feed additive in aquaculture.

The toxicity of Panacur 2.5% suspension was investigated by means of static toxicity tests on a suite of species. The lethal and sub-lethal toxicity of the drug was determined by exposure to increasing concentrations of the drug suspended in filtered seawater. The following tests were carried out:

- Acute toxicity in seawater to *Corophium volutator*.
- Acute toxicity in sediments to *Corophium volutator*.
- Sub-lethal toxicity to *Littorina littorea*.
- Acute and sub-lethal toxicity to *Mytilus edulis*.
- Sub-lethal toxicity to *Patella vulgata*.
- Acute and sub-lethal toxicity to *Asterias rubens*.

The data (see Table 1) illustrate that fenbendazole is of very low acute toxicity to a range of marine invertebrates. This is reinforced by the environmental data sheets of Hoechst Roussel Vet Limited which demonstrate low acute toxicity to fish and bacteria (EC50 > 500 mg/L).

The most sensitive of the species tested was *Corophium volutator* where respective 9-day LC50 and NOEC values of 46 mg/L and 8 mg/L were determined. *Mytilus* byssal attachment was of similar sensitivity to fenbendazole with a 72 hour EC50 value for detachment of 41 mg/L.

Derivation of Predicted No Effect Concentrations (PNECs)
From this small data set it may be appropriate to derive a water column MAC value of 0.1 - 1 mg/L for the protection of marine life. This should be taken as a provisional limit however and used with caution. PNEC (acute, water) = 0.1 - 1 mg/L

There is very little data on the toxicity of fenbendazole to sediment-dwelling organisms. The data for the *Corophium* sediment test suggest that levels as high as 400 mg/kg are not acutely toxic. From these data, it is tentatively proposed that a PNEC of 50 mg/kg be adopted for preventing acute sediment toxicity arising from the presence of fenbendazole. PNEC (acute, sediment) = 50 mg/kg wet sediment.

Derivation of Predicted Environmental Concentrations (PECs)
The following predictions have been made using DEPOMOD.

Modelling Site
- Case Study Site: Farm situated in Loch Slapin, Isle of Skye. 18 cages on site.
- Low energy site; hydrographic measurements indicate low current velocities, little re-suspension predicted.
- Seabed survey data have highlighted a significant benthic impact.
- This farm is assumed to represent sites at which the highest concentrations of Fenbendazole (FBDZ) would be found following treatment.

Modelling Assumptions
- 6 kg of FBDZ is assumed to be discharged over 2 consecutive days during neap tidal forcing. This was the mass applied for by Marine Harvest McConnell (MHM) for use at their Ardnish site (ref. letter received by SEPA - Fort William Office, dated 17/04/97).
- Ardnish has a biomass limit of 1000 tonnes and 36 cages on site.
- The mass of compound is assumed to be released evenly throughout the 18 cages at Slapin. Based on the mass applied for by MHM, this is twice the amount likely to be used at Slapin.
- The compound is released directly. No conversion from compound mass per kg of food to mass of compound per kg of faeces is modelled. Compound attached to waste feed is not modelled. Therefore, the mass of the compound released is associated exclusively with particles which have faecal settling velocities.

- Model output, in compound mass per unit area, is converted to compound mass per kg of wet sediment using an assumed wet sediment density value of 2416 kgm^{-3}. In addition, the compound is assumed to be mixed throughout the top 5 cm of the bed sediment.

Modelling Results

- Allowable 25 m and 100m impact zones (AZE) for Slapin are 14800 m^2 and 77050 m^2 respectively.
- **Maximum PEC** = 8.7 mg FBDZ per kg wet sediment.
- **Average PEC** within 25 m AZE = 3.6 mg FBDZ per kg wet sediment.
- **PEC at edge of 100 m AZE** = 0.001 mg FBDZ per kg wet sediment.

Environmental risk assessment

It is expected that the use of Panacur in marine salmon farming (as an in-feed treatment) will pose little risk of toxicity to species living in the water column and that the main risk is that arising from the potential accumulation in sediment and the effects on benthic organisms. Attention therefore focuses on the assessment of the PEC:PNEC ratio in sediments below treated cages.

The PEC:PNEC data are summarised as follows:

Maximum PEC = 8.7 mg FBDZ per kg wet sediment.
Average PEC within 25 m AZE = 3.6 mg FBDZ per kg wet sediment.
PEC at edge of 100 m AZE = 0.001 mg FBDZ per kg wet sediment.

PNEC (acute, water) = 0.1-1 mg/L.
PNEC (acute, sediment) = 50 mg/kg wet sediment.

PEC:PNEC ratio: even based on the maximum PEC of 8.7 mg/kg, the PEC:PNEC ratio is less than 0.2 and that the use of Panacur poses little risk to marine life.

Conclusions and Recommendations

The information on the behaviour, fate and effects of fenbendazole in the marine environment is sparse. This has been compensated for by the use of a very precautionary approach to the risk assessment of fenbendazole (e.g. low energy site, large safety factors in derivation of sediment PNEC).

Based on a low energy (thus poor-case) site, and a 'one-off' farm treatment, it is concluded that the use of Panacur (fenbendazole) in the treatment of *Eubothrium* in marine salmon farms poses little risk of toxicity to marine life.

It is thus recommended that, based on existing information, 'one-off' treatments of Panacur be authorised without recourse to detailed environmental risk assessment and the use of a site-specific modelling approach. Water use licences should include the following requirement in Appendix 1 of the licence:

"This medicine/chemical shall not be discharged from the premises unless the discharger has given SEPA not less than 2 working days notice of its intended use and received approval in writing from SEPA of each specific use or course of treatment. Details of its actual use shall be recorded and reported in accordance with Schedule 6 of this licence."

Detailed records/returns on the use of Panacur by each farm will allow usage to be reviewed periodically with respect to the re-assessment of environmental risk. It is also recommended that such use be reported to the VMD such that they can assess the requirement for residue surveillance.

The assistance of SEPA's National Centre for Eco-toxicology and Marine Science Section is acknowledged in the preparation of this report.

Table 1: Toxicity of Panacur (fenbendazole) to marine invertebrates
(Data provided by Ian Davies, Marine Laboratory Aberdeen. Data are based on nominal rather measured concentrations).

Species/test/endpoint	**Concentration (mg/L)**
(a) Corophium volutator (in water):	
24h NOEC	15.9
72h NOEC	1.0
9 day LC50	45.7
9 day NOEC	8.4
(b) Corophium volutator (in sediment): over 5 days, highest test concentration of 400 mg/L (approx 400 mg/kg) did not cause significantly higher mortality than control.	5 day NOEC > 400
(c) *Littorina littorea (in water):* over 4 days, no mortalities at highest test concentration of 223 mg/L: behavioural response (avoidance) observed at concentrations of 137 and 223 mg/L.	4 day NOEC > 223
(d) Mytilus edulis (in water):	
24h EC50 (behaviour)	> 223
48h EC50 (behaviour)	> 136
72h EC50 (bysal detachment)	41
(e) Patella vulgata (in water):	
24h NOEC (detachment)	223
48h NOEC (detachment)	136