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Scientific Opinion of the Scientific Panel on Animal Health and Welfare on a request from the Commission regarding the

ASSESSMENT OF THE RISK OF ECHINOCOCCOSIS INTRODUCTION INTO THE UK, IRELAND, SWEDEN, MALTA AND FINLAND AS A CONSEQUENCE OF ABANDONING NATIONAL RULES

EFSA-Q-2006- 112

Adopted by the AHAW panel by written procedure on 18h of January 2007

SUMMARY

Regulation (EC) No 998/2003[1] lays down the rules for the non-commercial movements of pet animals (dog, cat, ferrets) both within the community as well as from third countries into the EU. The United Kingdom, Ireland and Malta have maintained their national rules as regards the control of echinococcosis and ticks, while Sweden and Finland have maintained their national rules as regards the control of echinococcosis. The derogations will be reviewed at the end of a transitional period of 5 years, on the basis of a report on the need to maintain such additional requirements. This opinion addresses the risk of introduction of *Echinococcus multilocularis* into free MS, by pet movements, if the treatment in place is abandoned.

The principal definitive hosts for *E. multilocularis* are canids consuming rodents as prey, e.g. foxes (*Vulpes* spp., *Alopex lagopus*) and coyotes (*Canis latrans*). The metacestodes of *E. multilocularis* are adapted to small rodents (usually species of Arvicolidae). Human beings can become accidentally infected (dead-end host) by ingesting tapeworm eggs excreted by the final hosts. The resulting disease, alveolar echinococcosis (AE) typically presents as an infiltrative tumour-like growth in the liver, with a poor prognosis. Domestic dogs and cats can also be infected by the worms, although with a low prevalence.
The parasite is found in foxes in central Europe, from the north to Denmark, the Netherlands and Belgium, in the east to the Baltic States and Slovakia, in the south to north eastern Italy and Hungary, and in the west to central France. There is evidence of an increase in the parasite density in many areas, probably correlated to an increase in the fox population. Also, foxes have adapted to urban environments. Infection of domestic carnivores by *E. multilocularis* appears to be a rare event, but may, however, play a key role in transmission to humans due to close contact. Very few studies exist on prevalence of *E.multilocularis* in domestic carnivores. The low infection rates in domestic dogs in Europe are most likely due to low exposure to the parasite and to routine worming of domestic pets. In humans, data point to an apparent increase of AE cases.
Praziquantel and Epsiprantel may be used for effective treatment of *E. multilocularis* infection in definitive hosts. Both are safe and well tolerated in dogs and cats. However, none of these products is ovicidal. Parasiticidal effect is short lived (around 24 hours), allowing for re-infection after treatment. Also, due to the lack of ovicidal activity, infected pets treated with Praziquantel may shed infectious tapeworm eggs for several hours after treatment.
There are very few data on the prevalence or incidence of infections with E. multilocularis in pets, in particular in pets to be moved into an area considered free of this parasite. Therefore it was considered that the risk assessment should be qualitative.
From the RA it was concluded that the risk of dogs and cats to become infected with *E. multilocularis* as final hosts in endemic areas is greater than negligible. The regional prevalence in wildlife and access to intermediate hosts influence the infection risk of pets and dogs. Therefore, a proportion of dogs and cats to be moved from an endemic area into a country considered free of *E. multilocularis* will be infected, and the abandoning of additional measures will increase the risk of introducing the parasite into an area considered free of *E. multilocularis*.
From the three current treatment protocols used by the UK, Republic of Ireland, Malta, Finland and Sweden it was concluded that the probability of re-infection in the country of origin, and the probability of viable egg elimination in the importing country is reduced to a negligible level when a suitable treatment with Praziquantel is given between 24 and 48hours prior to departure...

Key words: echinococcosis, hydatidosis, Alveolar echinococcosis, *Echinococcus multilocularis*, Praziquantel, risk assessment, *Echinococcus multilocularis* distribution, Fox tapeworm.

[1] OJ L 146/1, 13.06.2003, p. 1-9.

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ABREVIATIONS AND DEFINITIONS

AE	Alveolar Echinococcosis
CE	Cystic Echinococcosis
EM	*Echinococcus multilocularis*
EU	European Union
MS	Member States
OIE	World Organisation for Animal Health
PETS	UK Pet Travel Scheme
RA	Risk Assessment
UK	United Kingdom
WHO	World Health Organisation

Pet Animals: for the purpose of this assessment are dogs and cats.

Final hosts: animal species that harbor the adult phase of the parasite.

Intermediate hosts: animal species that harbor the larval stages of the parasite.

1. TERMS OF REFERENCE

1.1. Background

Regulation (EC) No 998/2003[2] lays down the rules for the non-commercial movements of pet animals (dog, cat, ferrets) both within the community as well as from third countries into the EU.
Article 16 of the above Regulation provides that Member States may maintain their national provisions for a transitional period of 5 years from the entry into force of this Regulation, i.e. until July 2008. This derogation provides for additional guarantees to prevent the risk of introduction of echinococcosis and ticks, before entry of pet animals into their territory.
The United Kingdom, Ireland and Malta have maintained their national rules as regards the control of echinococcosis and ticks, while Sweden and Finland have maintained their national rules as regards the control of echinococcosis. The Regulation further states that the above derogations will be reviewed at the end of this transitional period of 5 years.
To this end, the Commission has to submit to the European Parliament and to the Council, before the 1st February 2007, a report on the need to maintain such additional requirements, and with appropriate proposals for determining the regime to be applied after this period. This report shall be based on the experience gained so far and on a risk evaluation, following receipt of a scientific opinion of the European Food Safety Authority (Article 23).
As a consequence, the Commission requests EFSA to issue a scientific opinion in order to assist the Commission in proposing appropriate amendments to the above Regulation that are scientifically justified.

1.2. Mandate

In view of the above, the Commission requests EFSA, in accordance with Article 29 (1) (a) of Regulation (EC) No 178/2002[3], to issue a scientific opinion on an assessment of the risk of echinococcosis and ticks introduction into the UK, Ireland and Malta and echinococcosis introduction into Sweden and Finland, as a consequence of abandoning the national rules.
In particular, the scientific opinion should address the following questions:

- To what extent the abandoning of such additional guarantees (treatments prior to movement) could be envisaged, taking into account the different epidemiological situations with regard to these diseases prevailing in third countries and the Member States other than UK, Sweden, Ireland, Finland and Malta, without increasing the risk of introducing those diseases into these latter countries from the remainder of the EU territory and third countries.

- If the assessment reveals that in certain circumstances the need to maintain such treatments prior to movement is scientifically justified (in other words, if the consequential risk is higher than negligible), what would be the appropriate protocol (treatments / movement) to be considered as giving equivalent assurances for the protection of these Member States. To this end, the different national rules that are currently in force could be considered.

[2] OJ L 146/1, 13.06.2003, p. 1-9.

[3] OJ L 31, 1.2.2002, p. 1.

1.3. Scope and objectives of the opinion

According to Article 16 of Regulation (EC) No 998/2003, for a transitional period of five years from the day of entry of the regulation, Member States which previously had special rules for the control of echinococcosis may maintain their national rules, such as the request for treatment containing Praziquantel against Echinococcus tapeworms prior to the entry of pets into their territories.

The MS that requested special guarantees were: United Kingdom, Ireland, Finland, Sweden and Malta. In these countries *Echinococcus multilocularis* has never been reported and these MS have been considered free of the infection.

The scope of this opinion is to assess the risk of introduction of *E. multilocularis* into the above mentioned MS by pet movement. The risk of introduction of *E. multilocularis* by wild hosts is not in the scope of this opinion.

Infection of pets can be through ingestion of infected wild intermediate hosts (mainly rodent species). After infection, dogs and cats harbour the adult tapeworm in their digestive tract, and are then able to introduce the infection into the intermediate host population, or to directly infect humans, via egg-containing faeces. Treatment of pets with Praziquantel is considered to be a highly effective deworming medication.

The risks associated with *E. multilocularis* infected pets will depend on various estimates.

1. Prevalence of *E. multilocularis* in the wild final and intermediate reservoirs in the country of origin.
2. Prevalence of *E .multilocularis* in pets in endemic countries.
3. Numbers of infected pets coming into a free country.
4. Effectiveness of deworming drugs and treatment protocols.
5. Level of compliance with the prescribed / demanded treatment.

The final risk of introducing the disease by pets can be expected to be proportional to the total number of pets being moved into the member states considered to be free of the disease, from endemic areas. Unfortunately, no accurate information is presently available on both numbers and movements of pet animals between countries with exception of movements to UK and Ireland and even those provide no indication of the animal's origin
http://www.defra.gov.uk/animalh/quarantine/pets/procedures/stats.htm (Accessed 21 January 2007)

Whereas data on prevalence of *E. multilocularis* in its wild final host are available from different surveys in several MS, data on prevalence of *E. multilocularis* in dogs and cats in the different countries are scarce. Moreover, no surveillance diagnostic data were found for dogs and cats entering MS with additional protection measures in place. Therefore, only a qualitative risk assessment was possible. *Echinococcus granulosus* infection is present in most MS and this parasitic infection is not within the scope of this opinion.

2. HAZARD IDENTIFICATION

Echinococcus multilocularis is the hazard.

2.1 Description of E. multilocularis infection

2.1.1. Transmission and reservoir

The fox tapeworm *Echinococcus multilocularis* (Cestoda, Taeniidae) is one of several species of the genus *Echinococcus* (Jenkins et al., 2005), all of them exploiting predator-prey systems between carnivores and their prey species for transmission. Worldwide, the principal definitive hosts for *E. multilocularis* are canids, e.g. foxes (*Vulpes* spp., *Alopex lagopus*) and coyotes (*Canis latrans*) consuming rodents as prey (Eckert et al., 2001). The metacestodes of *E. multilocularis* are adapted to small rodents (usually species of Arvicolidae). The characteristic vesicular growth form of the metacestode seems to be caused by the limited space available in such small mammals. Most of the mature metacestode is eventually filled with protoscolices, in contrast to other *Echinococcus* species whose metacestodes contain large amounts of cyst fluid. Humans are not part of the lifecycle, but can become accidentally infected (dead-end host) by ingesting tapeworm eggs excreted by the final hosts, dogs and cats can also be infected the same way (Deplazes and Eckert, 2001). The resulting disease, alveolar echinococcosis (AE), typically presents as an infiltrative tumour-like growth in the liver which at later stages, may invade neighbouring organs and form metastases. Surgical treatment is successful only at the early stages when the infection is still asymptomatic and, therefore, rarely recognized. For later stages, treatment is unsatisfactory. Chemotherapy with benzimidazoles (albendazole and mebendazole) causes at best retarded or arrested growth of the parasite, but there is no cure as yet and treatment has to be continued life long.

E. multilocularis occurs throughout the northern hemisphere, although its scale distribution and frequency is not completely known. Due to the zoonotic potential of this parasite, AE is considered one of the most severe human parasitoses in non-tropical regions. It has received considerable attention in recent years, particularly in Europe, Japan and, most recently, in China. Although risk factors are still incompletely understood, it is apparent that environmental parameters, including climatic conditions, play a key role for the transmission intensity of the parasite and for the infection risk of humans. These factors are thought to act in two ways: sufficient ground moisture will increase the survival period of eggs in the environment, and certain vegetation types will provide the habitat for large densities of suitable intermediate host species.

The typical transmission cycle in Europe is wildlife-based. It involves red foxes (*Vulpes vulpes*) as final hosts, and rodents (especially the common vole *Microtus arvalis* and the water vole *Arvicola terrestris*) as intermediate hosts (see Fig.1). For endemic areas of west-central Europe, most of the parasite's biomass is estimated to be present in this wildlife cycle. While domestic dogs and cats can also be infected by the worms (Crellin et al., 1981; Thompson and Eckert, 1983) and natural infections acquired under field conditions have been observed (Eckert et al., Worbes, 1992; Deplazes et al., 1999; Gottstein et al., 2001), the absolute number of infected animals in Europe is small and they appear to be of secondary importance for the lifecycle's persistence (Kapel et al., 2006; Thompson et al., 2006), they may, however, play a key role in transmission to humans due to close contact. Other wildlife species with confirmed susceptibility like the raccoon dog (*Nyctereutes procyonoides*), wolf (*Canis lupus*), lynx (*Lynx* spp.), wild cat (*Felis silvestris*) and jackal (*Canis aureus*) are of limited or no importance as final hosts in Europe. There are numerous records of *E. multilocularis* infection in the arctic fox (*Alopex lagopus*) outside Europe, e.g. in Siberia and Alaska (Rausch, 1995), in Europe the first record of EM in arctic fox came recently from the Norwegian arctic island of Spitsbergen (Svalbard), where the parasite life cycle was established with an accidentally

introduced vole species, *Microtus rossiaemeridionalis*, as the intermediate host (Henttonen et al., 2001).

Apart from rodents, metacestodes of *E. multilocularis* are recorded from a number of 'dead end' hosts which do not play any role in the transmission. Infections in wild boars (*Sus scrofa*) and domestic pigs appear to be self-limiting without development of protoscolices (Sydler et al., 1998), while various species of non-human primates kept in zoos have been reported to succumb rapidly to the disease (Deplazes and Eckert, 2001).

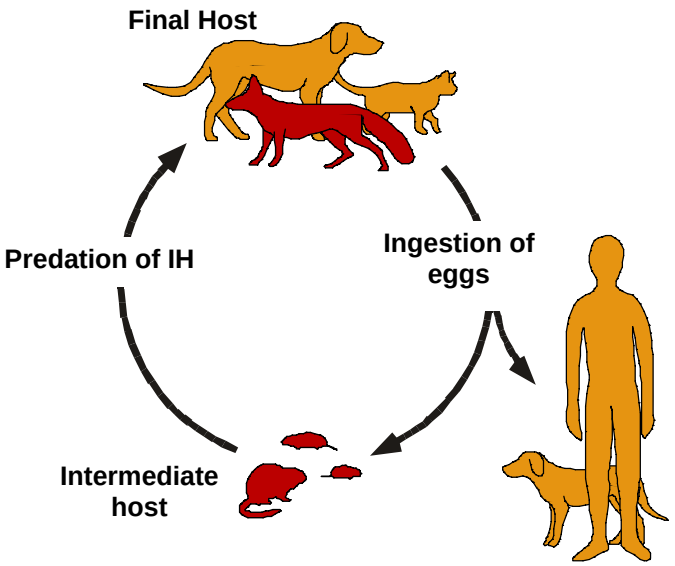

Figure 1: Life Cycle of *Echinococcus multilocularis* (pets can be infected as dead end hosts)

2.1.2. Pathogenesis and clinical signs in definitive hosts

The adult worms of *E. multilocularis* live in the lumen of the small intestine of their carnivore hosts. They are temporarily attached to the intestinal mucosa with their scolex (head), which possesses adhesive structures (suckers, hooklets). The worms do not feed on blood or tissue, but take up nutrients from the intestinal content through their integument. There seems to be no damage to the mucosa at the adhesion sites, even in the presence of thousands of worms. Consequently, there are no clinical signs of infection. There seems to be a certain degree of immunity induced by the worms, which may give partial protection from re-infection, but the available data on that are contradictory (Torgerson, 2006).

2.1.3. Prepatent and patent periods in definitive hosts

After ingestion of protoscolices (larvae), usually together with the intermediate host, a minimum of 28 days is needed for the development of the worms and shedding of infectious eggs into the environment in the faeces. There seems to be no significant variation in the prepatent period between foxes, dogs, raccoon dogs and cats (Kapel et al., 2006). The life span of adult *E. multilocularis* is not well-known perhaps, in part, because of biohazard associated with studies involving patent parasite infection. However, the patent period may not be long. In one experiment with red foxes, egg excretion was seen between days 29 and 84 post-infection (Nonaka et al., 1996). The raccoon dog, recently recognised as a good definitive host for *E. multilocularis* (Yimam et al., 2002, Thompson et al., 2006), can sustain a patent infection for slightly longer than foxes (Thompson et al., 2006). This may be an important factor in the trans-boundary spread of infection as raccoons

are expanding their range in Europe. The effective patent period of *E. multilocularis*, time taken for 95% of eggs to be excreted, was 17-42 days in red foxes, and 22-47 days in raccoon dogs. Domestic dogs showed a prolonged excretion of eggs with an effective patent period of 22-93 days post-infection (Kapel et al., 2006).

2.2 E. multilocularis distribution

2.2.1. In EU Member States, Switzerland and Norway

Wild animals

Surveys for *E. multilocularis* have been conducted in recent years in the majority of EU countries, providing a broad picture of range and density of the parasite in wild animals in different regions.

In addition to anecdotal reports demonstrating the presence of *E. multilocularis* in certain regions, several surveys have been conducted in wildlife in European countries since the 1980s (Zeyhle, 1982, Martynenko et al., 1988; Petavy et al., 1990; Ballek et al., 1992; Ewald et al., 1992; Wessbecher et al., 1994; Tackmann, 1996; Tackmann et al., 1998; Gottstein et al., 2001; Raoul et al., 2001; Berke et al., 2002; Stieger et al., 2002; Losson et al., 2003; Smith et al., 2003; Deplazes et al., 2004; Van der Giessen et al., 2005; Denzin et al., 2005; Moks et al., 2005; Duscher et al., 2006; Manfredi et al., 2006; Saeed et al., 2006). These studies assess, with different accuracy, prevalence in various regions or countries (for a review, see Deplazes, 2006; Romig et al., 2006). However they do not cover the entire area of the European Union and only a few allow conclusions on the development of prevalence over time. It is also difficult to draw conclusions on the spatial development of echinococcosis in wildlife.

Due to the variety of sampling strategies and diagnostic methods inter-study comparisons are extremely difficult. Moreover, prevalence and host density show strong temporal dynamics, which needs to be considered when comparing data from different regions obtained in different periods. In Table 1, recent prevalence data for *E. multilocularis* in foxes from Europe are presented (obtained by necropsy). The question of whether or not the geographical range of *E. multilocularis* has been expanding in Europe since the 1980s was addressed in several recent reviews (Eckert et al., 2000; Romig, 2002). Prior to 2000, the range of the infection was thought to be restricted to south-central Europe (Fig. 2) an assumption largely based on the historical occurrence of human cases. Today the parasite (in foxes) is recorded from an apparently coherent area in central Europe (Fig.2), extending in the north to Denmark, the Netherlands and Belgium, in the east to the Baltic states and Slovakia, in the south to north eastern Italy and Hungary, and in the west to central France (Romig, 2002; Sreter et al., 2004; Manfredi et al., 2006). Although fox prevalence data from within this coherent area differ greatly in number and quality, transmission seems to be most intense in the northern pre-alpine regions, the high Tatra mountains between Poland and Slovakia, the French, Swiss and German Jura mountains, and the mountainous areas stretching from southern Belgium to central Germany where prevalence rates in foxes often exceed 50% and approach 100% in restricted areas (Martinek et al., 2001b; Dubinsky et al., 2001; Vervaeke et al., 2003; König et al., 2005). In contrast, prevalence rates are usually <5% in the area north of this region (The Netherlands, northern and eastern Germany, Denmark, western Poland). There is no record of *E. multilocularis* infection in the Iberian Peninsula, in the British Isles, or in Fennoscandia (in Norway, the parasite was introduced only into the arctic islands of Svalbard, see Section 2.1). No positive animals were detected in surveys of 587 red foxes in Great Britain (Smith et al., 2003) or in 854 red foxes and 335 raccoon dogs in Finland (Oksanen and Lavikainen, 2004). The reasons for the unequal prevalence are not yet clear, but appear to be linked to agricultural land use and landscape patterns. The presence of permanent grassland (meadows, pastures) favours populations of the parasite's most important intermediate hosts (common voles and water voles) and is likely to be of primary importance for transmission (Giraudoux et al., 2002).

Table 1: Observed prevalence of *E. multilocularis* in foxes in several European regions

Country	**Region (state, province)**	**Sample size (n)**	***E. multilocularis* observed prevalence (%)**	**Reference**
Austria	Vienna and vicinity	94	6.3	Duscher et al., 2005°
Austria	Lower Austria	337	11.0	EchinoRisk, 2005
Austria	Carinthia	605	0.5	EchinoRisk, 2005
Austria	Upper Austria	357	12.0	EchinoRisk, 2005
Belgium	Entire area	1018	16.1	Vervaeke et al., 2006
Czech Republic	Klatovy, Pilsen	50	60.0	Martinek et al., 2001b
Czech Republic	Entire area	1052	33.6	EchinoRisk, 2005
Denmark	Entire area	1040	0.3	Saeed et al., 2006
Finland		854	0.0	Oksanen and Lavikainen, 2004
France	Franche-Comté	222	49.0	Raoul et al., 2001
France	Meurthe, Moselle	74	44.6	Robardet et al., 2005
Germany	Lower Saxony	2617	11.4	Berke et al., 2002
Germany	Bavaria	268	51.1	König et al., 2005
Germany	Stuttgart (urban area)	492	16.8	Deplazes et al., 2004
Hungary	Northern Hungary	156	15.4	Sréter et al., 2004
Italy	Trentino-Alto Adige	360	0.6	Manfredi et al., 2002
Netherlands	Limburg	196	12.8	Van der Giessen et al., 2005
Poland	SW-Poland	380	0.3	Ramisz et al., 2004
Poland	Pomerania	719	7.9	EchinoRisk, 2005
Poland	Warmia / Mazuria	376	39.6	EchinoRisk, 2005
Poland	Carpathians	419	36.8	EchinoRisk, 2005
Slovak Republic	Entire area	662	24.8	Dubinsky et al., 2001
Sweden	Entire area	280	0.0	Christensson, personal comm.
Switzerland	Graubünden	543	6.4	Tanner et al., 2006
Switzerland	Zurich (urban area)	388	44.3	Deplazes et al., 2004
Switzerland	Geneva (urban area)	160	43.1	Deplazes et al., 2004
UK	Great Britain	588	0.0	Smith et al., 2003

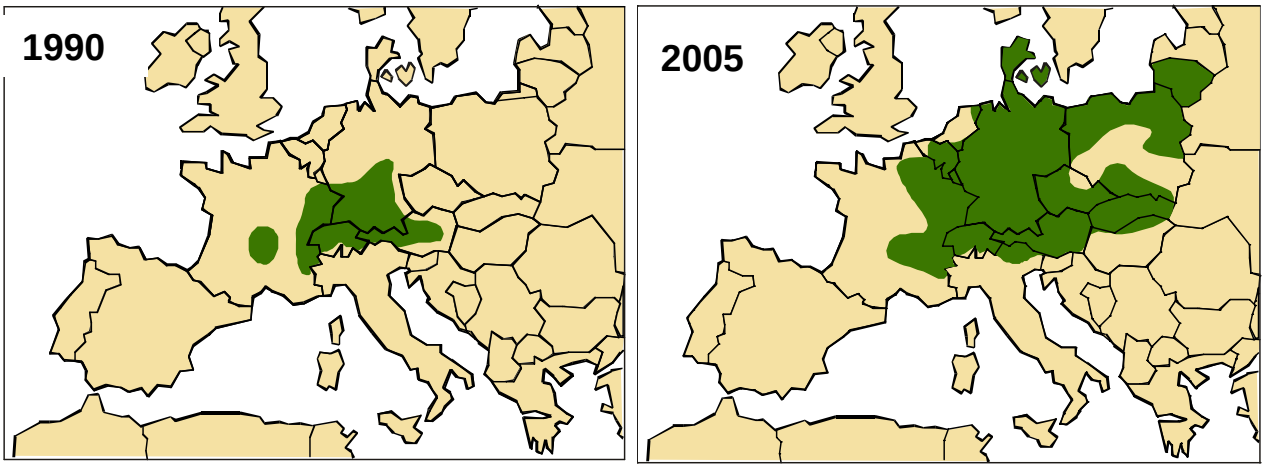

Figure 2: Known distribution of *E. multilocularis* in Europe in 1990 and in 2005.

Data on *E. multilocularis* surveys in foxes conducted in MS have also been collected for the EFSA's Community Summary Reports on Trends and Sources of Zoonoses, Zoonotic Agents and Antimicrobial resistance in the European Union in 2004 and 2005 (Table 2). The proportion of positive samples in foxes ranged between 5.3 to 37.4 in seven MS. In animals, *Echinococcus* detection is notifiable in most MS except for Czech Republic, Hungary and The United Kingdom, and non-MS. Cyprus, France, Germany, Luxembourg, Malta and Poland provided no information. (EFSA 2006).

Table 2: Reporting of *E. multilocularis* findings in foxes. (EFSA, 2005 and 2006).

	2005		**2004**		**2003**		**2002**	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Austria	19	5.3	86	8.1	807	5.6	592	6.8
Czech Republic	833	7.4						
Germany	7764	21.6	5398	20.2	4483	33.4	7860	28.4
France	172	5.8	986	7.6	-		-	
Luxembourg	329	20.9	35	14.3	29	27.6	58	37.9
Netherland	45	6.6						
Slovakia	289	37.4	490	30.2	-		-	

N = number of foxes sampled; **%** = % infected.

In accordance to Regulation 998/2003/EC the European Commission requested information from the MS experience on the implementation of Article 16. Responses were received from Sweden, Finland, and Ireland regarding *E. multilocularis* in wildlife and are summarised in Table 3. To date, the limited number of surveys conducted in these MS indicated the absence of *E. multilocularis* in wild foxes. There are no wildlife surveillance data on EM infection available for Malta or UK.

Table 3: Reporting of *E. multilocularis* findings in foxes. (MS reports received and reviewed by EFSA)

	2005			2004			2003			2002			2001		
	N	**Test**	**Pos**	**N**	**Test**	**Pos**	**N**	**Test**	**Pos**	**N**	**Test**	**Pos**	**N**	**Test**	**Pos**
Sweden***	1800	CAg	0			0			0			0			0
Ireland **	220	Ne	0												
Finland	281	CAg	0	355	CAg	0	297	Ne	0	300	Ne	0	257	Ne	0
							166	CAg	0	109	CAg	0	12	CAg	0
							335*	Ne	0						
	218*	CAg	0	242*	CAg	0	101*	CAg	0						

Ne = Necropsy examination; **CAg** = Coproantigen; N=number of tested animals; **Pos** = number of infected animals.

*** Sweden have tested approximately 1800 foxes during the years 2001-2005 by coproELISA and of these 280 were also examined by necropsy / sedimentation and counting technique.

**Murphy - unpublished results (it is not stated when the study was conducted)

* Survey in racoon dogs

The various isolated surveys show great variability from one country to another and even between regions in the same country. Therefore comparisons between various epidemiological situations are extremely difficult. This variability and the numerous factors have to be considered in any definition of the status of the countries, i.e. free or endemic.

It cannot be decided whether the increased range of *E. multilocularis*, recognized today, is the result of expansion, or the result of intensified investigations due to the lack of appropriate retrospective data. However, there is evidence of an increase in the parasite density (increase in prevalence and/or increase of host populations) in many areas, e.g. several regions of Germany (Romig et al., 1999a, Berke et al., 2002, König et al., 2005), the High Tatra mountains in Poland and Slovakia (Echinorisk, 2005), Belgium (Vervaeke et al., 2006) and the Netherlands (van der Giessen et al., 2005). For some regions and countries, an increase in the occurrence of the parasite cannot be proven, but there has not been a decrease in any region. In central Europe there is an obvious temporal correlation between the prevalence of *E. multilocularis* and an increase in the fox population; the successful immunization of foxes against rabies has largely removed it as a significant mortality factor since the early 1990s. As a consequence, the parasite density (biomass) in south-western Germany is estimated to be 10 times higher than before 1990 (Romig et al., 1999a; Chautan et al., 2000). This intensified transmission is reflected by data from intermediate hosts in the same region, where the infection rates of muskrats (*Ondatra zibethicus*) with *E. multilocularis* metacestodes increased from 2% in the period 1980-1989 to 26% in the period 1995-2000 (Romig et al., 1999a).

The adaptation of foxes to urban environments (observed in Britain since the 1940s) occurred rather more recently in continental Europe, possibly being previously prevented by lower fox populations prior to the rabies control programme (Chautan et al., 2000). Today ‘urban foxes’ are seen in many towns and cities in south-central Europe, e.g. southern Germany and Switzerland (Gloor et al., 2001). In these locations fox population densities can be much higher than in rural habitats due to abundant availability of anthropogenic food (Contesse et al., 2004). Infection rates in foxes with *E. multilocularis* can be high (e.g. 44% in Zurich, 43% in Geneva, 17% in Stuttgart) (Deplazes et al., 2004), but are generally lower than in surrounding rural areas, probably due to the limited presence of habitats suitable for voles in the urban areas. However, due to the high population density the absolute number of infected foxes may still be higher than in rural areas, and the close proximity between foxes and humans poses a considerable infection risk. Transmission to humans may not only occur directly from infected foxes, but also from pet dogs and cats which become infected by catching infected rodents in city parks and gardens (9% of water voles were found to be infected in the urban to peri-

urban areas of Zurich) (Stieger et al., 2002). As is known from other high endemic areas outside Europe (parts of Alaska and China), the prevalence of human AE can be extremely high where humans are in close contact with infected domestic dogs. Therefore, the increasingly close association between fox and humans in urban areas is cause for concern.

In Poland and eastern Germany, the raccoon dog (*Nyctereutes procyonoides*), a neozootic species introduced from eastern Asia, appears to have drastically increased its population density in recent years. Since this species is highly susceptible to infection, and does not seem to compete directly with foxes, an additional pool of definitive hosts may be developing in central Europe (Thiess et al., 2001; Machnicka-Rowinska et al., 2002). Coypu (*Myocastor coypus*), a neozootic rodent originating from South America which has established feral populations in Europe, was shown to be less susceptible to *E. multilocularis* infection than microtine rodents (voles), and plays only a marginal role for transmission. In a recent survey in western Germany only 1 of 119 feral coypu harboured fertile metacestodes, compared with 13 of 92 muskrats (*Ondatra zibethicus*) from the same habitat (Hartel et al., 2004).

Domestic animals

Infection of domestic carnivores by *E. multilocularis* appears to be a rare event that is difficult to detect, as large numbers of samples per geographical unit must be analysed to obtain an accurate estimate of the prevalence of infection. While domestic dogs and cats are sporadically naturally infected, they appear to be of secondary importance for the lifecycle which is typically wildlife based (Eckert, 1996). They may, however, play a key role in transmission to humans due to close contact. Dogs are highly suitable hosts with an even longer patent period than foxes (Kapel et al., 2006; Thompson et al., 2006).

The low infection rates in domestic dogs in Europe are most likely due to low exposure to the parasite and to routine worming of domestic pets. The suitability of cats as final hosts is less clear. Although some cats show high infection intensities, average worm burdens of experimentally infected cats are much lower than those of canids, rendering their contribution to the transmission cycle doubtful (Deplazes et al., 1999; Jenkins and Romig, 2000; Deplazes et al., 2004; Kapel et al., 2006; Thompson et al., 2006). However at the moment there is not sufficient evidence to completely exclude cats as possible infection source. A limited number of surveys regarding infection in pets have been published (Table 4). Individual surveys may be biased as they often rely on the testing of animals that are not randomly sampled. Furthermore no data are known to exist from surveillance of imported pets into MS considered free from the infection either prior to or after the implementation of Regulation 998/2003.

Table 4: Surveys for *E. multilocularis* in domestic dogs and cats in some European Countries

Dogs	**Number animals**	**% infected**	**Reference**
Kanton Fribourg (Switzerland)	86	7.0	Gottstein et al., 2001
Northeastern Switzerland	660	0.3	Deplazes et al., 1999
Auvergne (France)	9	11.1	Petavy et al., 1991
Prignitz and Ostprignitz-Ruppin Counties (Germany)*	588	0,0	Tackmann, K. & Conraths, F., Personal. Comm., 2006
Finland	867	0.0	Evira (Finish Food Safety Authority), 2006 (surveillance results from 2001 to 2005, tested by CoproAntigen)
Cats			
Rhineland-Palatinate (Germany)	254	0.0	Jonas and Hahn, 1984
Baden-Württemberg (Germany)	11	45.5	Meyer and Svilenov, 1985
Baden-Württemberg (Germany)	162	1.9	Fesseler et al., 1989
Baden-Württemberg (Germany)	498	1.0	Zeyhle et al., 1990
Baden-Württemberg (Germany)	53	0.0	Ewald, 1990
Brandenburg (Germany)	10	0.0	Tackmann and Beier, 1993
Thuringia (Germany)	178	1.7	Worbes and Hoffmann, 1996
Northeastern Switzerland	263	0.4	Deplazes et al., 1999
Kanton Fribourg (Switzerland)	33	3.0	Gottstein et al., 2001
Ht Savoie et Ain (France)	81	3.1	Petavy et al., 2000
Prignitz and Ostprignitz-Ruppin Counties (Germany)*	731	0,0	Tackmann, K. & Conraths, F., Personal Comm., 2006

* The area has been examined between 1992 and 2006 and the prevalence in foxes was approximately 10 to 30 % during that period. It should be noted that between 1996 and 1998 foxes were treated with baits containing praziquantel and during that period, the prevalence was lower (0 to 5%).

To date, surveys conducted in Finland to detect *E. multilocularis* in dogs (the sampling strategy was not indicated) have yielded negative results (Evira - Finish Food Safety Authority, 2006 - surveillance results from 2001 to 2005). Neither UK, Ireland, Sweden or Malta provided any information on domestic animals surveillance..

Humans

Data on the distribution and prevalence of human AE cases in Europe are scarce (Eckert et al., 2001b; Kern et al., 2003; see Fig. 3). Prevalence of human AE in high endemic areas of central Europe has been estimated to range between 2 and 40 per 100,000 (Romig et al., 1999; Eckert et al., 2001b). The highest published value of AE prevalence was reported from eastern France, with 152 per 100,000. This study included cases of inactive AE and concentrated on farmers, a recognised group with higher infection risk (Bresson-Hadni et al., 1994). In France, from 1948 to 1983 (a period of 35 years), around 200 cases of AE were recorded; between 1981 and 2000, (a period of 19 years), 455 cases were recorded in Europe, including 212 cases in France (Kern et al, 2003). More recently from 2000 to 2004, a total of 85 new AE cases were detected in France. These data could point to an increase of AE cases (at least in France) during this period, perhaps as a result of the extension of *E. multilocularis* infection in its wild host, and the increase of the host population in Europe (Screter et al., 2003), although part of it could also be due to improved diagnosis.

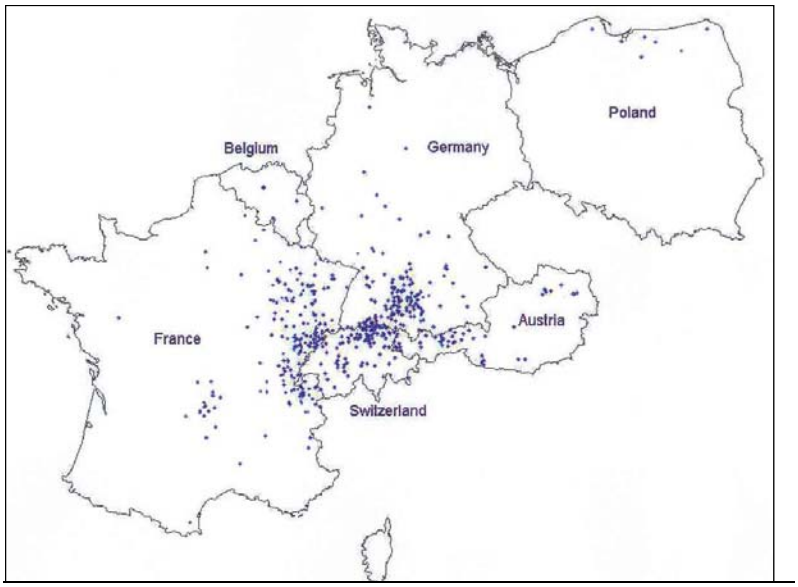

Figure 3: Distribution of human cases in some MS between 1983 and 2000 (Kern et al, 2003). Each point is the location of the 532 patients at the time of diagnosis.

Echinococcosis is notifiable in humans in all MS except for Denmark, France, The Netherlands, Switzerland and The United Kingdom, and non-MS. Cyprus, Luxembourg, Malta and Poland provided no information whether echinococcosis is notifiable in humans. These data are collected and published as the EFSA's Community Summary Report on Trends and Sources of Zoonoses, Zoonotic Agents, Antimicrobial resistance and Food Borne Outbreaks in the European Union. However, for the year 2005, Luxembourg, Malta, Belgium, Estonia, Finland, Greece, Ireland, Italy and Slovenia provided no information for the report (EFSA, 2006).

According to the 2004 EFSA's Community Summary Report on Trends and Sources of Zoonoses, Zoonotic Agents and Antimicrobial resistance in the European Union the incidence of human echinococcosis (calculated without distinguishing between *E. multilocularis* and *E. granulosus*) ranged from less than 0.1 per 100,000 in Belgium, France and Spain to 0.5 per 100,000 in Portugal (EFSA, 2005; see Table 5). Regarding Alveolar Echinococcosis (AE), 49 cases were reported in the 25 MS but the distribution between the two types of human echinococcosis (Alveolar echinococcosis and Cystic Echinococcosis) differs between countries. For example, in Portugal 100%

of human cases were caused by *E. granulosus*, whereas in France, Spain[4] and Belgium 100% were caused by *E. multilocularis*. Overall, the majority of echinococcosis cases are due to *E. granulosus*. In 2005 the number of reported human cases was similar to 2004 (47 cases). The annual incidence ranged from <0.1 to 0.4 per 100,000 population. *E multilocularis* was reported in 15.5% of the confirmed echinococcosis cases, but in 45.1% the causal species was unknown.

Table 5: Reported cases of Echinococcosis in humans in 2004/2005 (EFSA, 2005, 2006)

	2005			**2004**		
	Cases / 100,000 Population	**Case due to *E. multilocularis***		**Cases / 100,000 Population**	**Case due to *E. multilocularis***	
		Number	**%**		**Number**	**%**
Austria	0.1	0	-	0.3	4	16
Belgium	0	-	-	<0.1	1	100
Cyprus	0.1	0	-	-		-
Czech Republic	-	0	-	-		-
Denmark	-	-	-	0.2	1	11
Estonia	0	-	-	-		-
Finland	-	-	-	0.1	0	-
France	<0.1	17	100	<0.1	17	100
Germany	0.1	20	18	0.1	16	16
Greece	-	-	-	0.2	0	-
Hungary	<0.1	0	-	0.1	0	-
Ireland	0	-	-	-		-
Italy	-	-	-	-		-
Latvia	0.2	1	20	0.1	0	-
Lithuania	0.4	4	26	0.4	1	7
Luxembourg	0	-	-	-		-
Malta	0	-	-	-		-
Poland	<0.1	4	11	0.1	3	14

[4] *E .multilocularis* infection in wild final or intermediate host has not been described up to now in Spain. Attribution of 100% cases of human echinococcosis to *E. multilocularis* (cases of alveolar Echinococcosis) should be reviewed, as it seems epidemiologically improbable.

Portugal	<0.1	0	-	0.5	0	-
Slovakia	<0.1	1	50	-		-
Slovenia	-	-	-	0.1	0	-
Spain	0.2	0	-	<0.1	6	100
Sweden	<0.1	0	-	0.1	0	-
Netherlands	-	-	-	0.2		-
United kingdom	<0.1	0	-	<0.1	0	-
EU Total	<0.1	47	15.5%	0.1	49 cases	7%

(-) = no data available.

Prevalence data on AE are difficult to evaluate, because of the low prevalence levels. Even in regions where *E. multilocularis* prevalence in wildlife is high the few human cases do not allow recognition of temporal developments or even differences in spatial distribution with any satisfactory probability. Obtaining data on epidemiologically relevant routes of infection is hampered by the low number of patients available for analysis. In a review of 210 AE cases from central Europe, 61.4% of patients were engaged in professional or part-time farming, gardening or other outdoor activities, and 70.5% owned dogs or cats (Kern et al., 2003). A recent case-control study in Germany with 40 AE cases and 120 matched controls showed the strongest associations with ownership of free roaming dogs, farming, and living on or near farms (Kern et al., 2004). These difficulties are exacerbated by the long asymptomatic period of AE (which also varies considerably among individual patients; Pawlowski et al., 2001), making identification of time and place of infection uncertain. Furthermore a diagnosis of Cystic Echinococcosis (CE) is often not achieved or is unreliable, especially with retrospective data.

2.2.2. In Third Countries

In Europe, no reliable recent data are available from regions east of the Baltic States and Slovakia, or from the Balkan Peninsula. Old records from different hosts suggest that *E. multilocularis* is present in most of these regions (see reviews by Eckert et al., 2000; Romig et al., 2002).

In Asia, *E. multilocularis* is widespread across the arctic, sub-arctic and temperate climate zones of Asia, and from Turkey to Japan (Eckert et al., 2001b). From most regions where the parasite is known to be present (e.g. the Russian Federation and the newly independent states of central Asia), few recent data on distribution and frequency are available. In Turkey, cases of human AE are most frequent in central and eastern Anatolia, but there is no information on the local transmission patterns (Altintas, 1998). The latter is also true for the newly independent states of Central Asia, *E. multilocularis* is present, but data on the prevalence of *E. multilocularis* in humans and domestic animals is largely unknown. Some human cases are thought to have occurred in patients in Kazakstan (Shaikenov and Torgerson 2004) but identification of most lesions is uncertain. *E. multilocularis* infection has been identified in domestic dogs in a mountainous region of Kazakstan (Almaty Oblast) (Stefanic et al., 2004), but the prevalence in humans in that area has yet to be determined. The role of wildlife in the transmission of *E. multilocularis* in Central Asia is completely unknown.

In China, eight provinces covering the entire western and northern part of the country are known to be endemic for *E. multilocularis* (Vuitton et al., 2003). AE is a serious public health problem

mainly in the more sparsely populated regions, including the Tibetan plateau and Inner Mongolia, and is often associated with pastoral communities. The domestic dog, wolf (*Canis lupus*) and foxes (*V. vulpes, V. corsac, V. ferrilata*) were confirmed as definitve hosts, and a large number of small mammal species serve as intermediate hosts (Vuitton et al., 2003). Far more human cases than from any other country are reported from China, with prevalence exceeding 5% locally in Gansu Province, western Sichuan Province and Ninxia Hui Autonomous Region (reviewed in Vuitton et al., 2003). Such foci of human AE seem always to be associated with "domestic" lifecycles involving dogs as definitive hosts. The particular risk seems to be the keeping dogs which feed on grassland-associated intermediate hosts. In several foci of human AE, the epidemiological situation appears to have drastically changed some time ago due to eradication of dogs and wild canids by secondary poisoning with rodenticides (Vuitton et al., 2003). In other regions, large-scale deforestation producing vast areas of grassland or scrubland (e.g. on the slopes of the Tibetan plateau) seems to have exacerbated the problem by creating habitats for intermediate host rodents (Giraudoux et al., 2003). Overgrazing pastures by livestock (e.g. yak) was found to favour populations of intermediate hosts (*Ochotona* spp.), and was associated with a higher risk for human AE (Wang et al., 2004). Overall, knowledge on the epidemiological situation in China is still very limited. In a recent survey in Inner Mongolia (China), two "forms" of *E. multilocularis* were reported to be occurring sympatrically, utilising the same host species (*Vulpes corsac* and *Microtus brandti*) (Tang et al., 2004). Based on minor morphological differences, they were tentatively allocated by the authors to *E. m. multilocularis* and *E. m. sibiricensis*. However, without any molecular data to support this assertion, no conclusions can be drawn, and the simultaneous occurrence of two subspecies is a contradiction in itself.

In Japan, human AE is restricted to the northern island of Hokkaido where it was probably introduced accidentally with infected foxes from the Kurile Islands early in the 20th century. Since the early 1980s the parasite has rapidly spread from the easternmost part of Hokkaido through the entire island, and has recently entered a phase of rapid prevalence increase in animal hosts (Ito et al., 2003). In contrast to Europe and continental Asia, no rodent species is adapted to grassland in northern Japan. Grey-sided voles (*Clethrionomys rufocanus*) form large populations in dense bamboo undergrowth of forests and scrubland of northern Japan and are the most important intermediate hosts. It appears that the parasite in Japan is exploiting a predator-prey situation which is rather different from other regions. The number of human AE cases is moderate with 373 records between 1937 and 1997, with approximately 10 new cases diagnosed annually (Eckert et al., 2001b). As in Europe, *E. multilocularis* has taken advantage of the increasingly urban lifestyle of foxes, and a transmission cycle has been established in urban areas e.g. in the outskirts of Sapporo (Ito et al., 2003). A recent case-control study with 134 human AE patients identified cattle and pig farming and the use of well water as risk factors for human infection (Yamamoto et al., 2001).

The distribution of *E. multilocularis* in North America appears to be irregular. In the northern tundra region it is present between western Alaska and the Hudson Bay, including some of the sub-arctic and arctic islands. While its principal final host, the arctic fox (*Alopex lagopus*), is widespread, the local occurrence of *E. multilocularis* appears to be limited by the presence of suitable intermediate hosts, mainly *Microtus oeconomus* (Rausch, 1995). In this northern range, human AE cases are rare, not a single case has been reported from the entire tundra region of Canada. However, human AE can be extremely frequent where domestic dogs are substantially involved in the lifecycle. This is the case in some villages on St. Lawrence Island (Alaska) from where an annual incidence of 98 per 100,000 has been reported (Schantz et al., 1995; Eckert et al., 2001b).

A second endemic area exists in the temperate zone of southern Canada to the central USA. There, red foxes (*Vulpes vulpes*) and coyotes (*Canis latrans*) are the most important final hosts, main intermediate hosts being the meadow vole *(Microtus pennsylvanicus)* and the deer mouse *(Peromyscus maniculatus)* (Eckert et al., 2001b). No records of *E. multilocularis* exist from the interspersed Canadian taiga zone which is either a non-endemic area, or prevalence levels are still too low to allow infection to be detected (Schantz et al., 1995). The endemic region in central North America may be of rather recent origin, after becoming suitable for *E. multilocularis* transmission due to anthropogenic deforestation. In this central region, both the geographical range and the prevalence levels in animal hosts are increasing. While a survey of red foxes in South Dakota during the late 1960s resulted in one

infected fox out of 222, prevalence in the period 1987-1991 had increased to 74.5% of 137 red foxes and, in addition, 4 of 9 coyotes were found to be infected (Schantz et al., 1995; Hildreth et al., 2000; Storandt et al., 2002). It is believed that the parasite will spread further, since suitable hosts for *E. multilocularis* are widespread, especially coyotes, which migrate over much larger distances than foxes and are suspected to be important in facilitating the spread of this parasite (Storandt et al., 2002). Curiously, only two human AE cases are known to have originated from central North America since 1939. This is in stark contrast with the situation in Europe and Asia, and no conclusive explanation for this almost complete absence of human infection has been given. Factors under discussion include the genotype of the parasite, behavioural differences of the human population, and misdiagnosis of the disease (Hildreth et al., 2000).

2.3 Description of trans-boundary wild life movements

Wild animals, including definitive and intermediate hosts of *E. multilocularis*, do not recognise political boundaries without clear physical barriers. The most effective physical barriers are open seas, such as those surrounding the UK and Ireland. However, as the example of Spitsbergen illustrates, both definitive and intermediate hosts can make extensive voyages.

One hundred years ago, the *E. multilocularis* life cycle could not be completed on the Norwegian high arctic island of Spitsbergen (Svalbard) because there were no native rodents (Henttonen et al., 2001). Between the 1920s and the early 1960s the Sibling vole *(Microtus rossiaemeridionalis)* appears to have been introduced with animal fodder, brought in from Russia to the Grumant mining community, and this enabled the *E. multilocularis* life cycle. The parasite may have been introduced either with the Sibling voles or, more likely, with strolling arctic foxes. It is most likely that the voles came from the St Petersburg (Leningrad) area which is considered free from *E. multilocularis* infection, although the evidence is scarce. Arctic foxes, on the other hand, run over vast areas of ice fields, e.g. fox marked on Svalbard was later killed on Novaya Zemlya, some 1000 km away. Therefore, the most plausible explanation for the introduction of the parasite probably is that it came in with a strolling arctic fox, perhaps from Novaya Zemlya or the Taimyr Peninsula.

For the disease to become established, the trans-boundary movement would have to be relatively fast as the life span of adult parasites is not long (see 2.1.3.). The raccoon dog is a good definitive host for *E. multilocularis* (Thompson et al., 2006) as after it was introduced from eastern Siberia into western parts of the Soviet Union during the 1930s it subsequently spread into Finland, and more recently Germany, and its range in Europe is still increasing (Kauhala and Saeki, 2004).

Accidental introduction of intermediate hosts may take place in the same way as that of the Sibling vole to Spitsbergen. Most of the potential intermediate hosts have a rather short lifespan (months to a few years), which may be further shortened by parasite-induced mortality. However, both lactating and pregnant sibling vole females have been found with massive infections (Henttonen et al., 2001) which might indicate that infection does not always necessarily shorten the intermediate host life span significantly. In addition to voles and muskrats, mice, rats, hamsters, squirrels, shrews and moles can also serve as intermediate hosts (Rausch, 1995) and, more recently, European beavers have been found to be infected (Janovsky et al., 2002).

It can be concluded that the trans-boundary movement of many different species, acting as the final host or as an intermediate host, may be relevant for *E. multilocularis* introduction into free zones.

2.4 Conclusions

1. *E. multilocularis* is widely distributed in most of Europe. However it has never been recorded in the British Isles, Fennoscandia, and the Iberian Peninsula.
2. The typical transmission cycle in Europe is wildlife based, involving red foxes as the main final host and rodents, mainly common voles and water voles, as intermediate hosts.
3. Pets can be infected and although their significance for the life cycle persistence might be small they may play a key role in transmission to humans.
4. Humans can become accidentally infected by ingesting tapeworm eggs but are dead-end hosts. The resulting disease, alveolar Echinococcosis is considered to be one of the most severe human parasitic diseases in non-tropical areas.
5. Obtaining data on epidemiologically relevant routes of infection is hampered by the low number of human patients with AE available for analysis and by the long asymptomatic period of the disease.
6. Human cases do not reflect the epidemiological situation of the disease in animals in certain countries.
7. No coordinated surveillance of the infection in wildlife is in place in any country
8. The available data originate from individual surveys often conducted in small areas over a short period. Where longitudinal data exist, there appears to be an increase in parasite prevalence over time and there are indications that the parasite is extending its range.
9. Factors favourable for the spread of the parasitic infection are increased population density of foxes and the adaptation of foxes to urban environments.
10. In all surveyed endemic countries, the prevalence of the infection in foxes differs drastically among regions so that that no uniform infection risk can be given for individual countries.
11. Very few data on infection rates of pets (dogs and cats) are available, and the existing ones are difficult to interpret due to the lack of information on the sampling strategies
12. Pets can be naturally infected but no data exist on the quantitative relationships between fox and pet infection rates.
13. Trans-boundary wildlife movements can constitute an important route for the introduction of the disease in certain countries
14. The low infection rates in domestic dogs in Europe are most likely due to low exposure to the parasite and to routine worming of domestic pets
15. Although some cats show high infection intensities, worm burdens of experimentally infected cats are much lower than those of canids, rendering their contribution to the transmission cycle doubtful. However, at the moment there is not sufficient evidence to completely exclude cats as possible source of infection.

2.5 Recommendations

1. Surveillance systems for *E. multilocularis* infections in domestic and wild animals in Europe should be urgently established. This will lead to better recognition of the geographical risk areas, will provide information on change over time, and will allow the development of countermeasures.
2. Information on both the number and origin of imported pets should be collected.

3. The reporting of infection in humans, such as the one presented by the EFSA's Community Summary Report on Trends and Sources of Zoonoses, Zoonotic Agents, Antimicrobial resistance and Foodborne Outbreaks in the European Union (EFSA, 2006), should clearly distinguish between *E.granulosus* and *E. multilocularis* infections. The report should also state the source of information and the level of control in the country that have infections.
4. Reporting of infection should include details of the sampling and diagnostic methods used.

2.6 Areas and Recommendations for Future Research

1. To further understand the risk factors for transmission between animal hosts and from animals to humans

3. DIAGNOSTIC

3.1. Diagnostic methods in the definitive host

The diagnostic methods for *E. multilocularis* infection in the definitive host are difficult to interpret because the eggs of all *Echinococcus* and taenia species are morphologically indistinguishable, and the characteristic segment of *Echinococcus* spp may be absent from faeces or can be easily overlooked as it is so small. *E. multilocularis* is located in the distal part (ileum) of the small intestine of foxes or dogs. However, in the case of heavy infection the parasite can be found throughout the intestine. The diagnostic techniques represent a considerable hazard for the staff involved. In order to eliminate the infection risk for the laboratory personnel, all the samples (faeces and intestine) should be inactivated by deep freezing at -80 C for one week before any analysis as this kills the eggs (Veit et al., 1995). Analysis should be done in a specific necropsy room.

3.1.1. Parasitological diagnosis at necropsy

Three parasitological techniques are currently used for the detection of the *E. multilocularis* adult form in the small intestine.

1. Intestinal scraping (Deplazes and Eckert, 1996; Eckert et al., 2001)
2. Sedimentation (Mathis et al., 1996)
3. Sedimentation and filtration (Duscher et al., 2005)

All these techniques, currently used for diagnosis, require the use of small intestine collected at necropsy, and are not suitable for *in vivo* diagnosis. The mucosal scraping is taken from the small intestine using microscope slides. The material adhering to the slide is squashed in a thin layer and then examined in a transmission light with a stereoscopic microscope at high magnification: 15 slides are read and the intensity of infection is determined subjectively as low (+), medium (++), or high (+++) based on the number of parasites found.

In sedimentation techniques, the intestine fragments are shaken vigorously in saline solution, and then the mucosa is stripped between two fingers. The intestinal material removed in the washing fluid is decanted to obtain the sediment. The sediment is then examined under a stereomicroscope in small aliquots and the number of parasites counted. This technique is highly specific due to the visual identification of the worm, and the sensitivity is also high. However, it is a laborious and time consuming. Alternatively, a filtration step can be added, with a high-grade steel mesh (500µm). After filtration the sediment is read using a stereomicroscope. A positive sample is evaluated as low (+),

medium (++), or high (+++) based on the number of parasites found. This technique has high specificity and sensitivity, similar to sedimentation.

Compared with sedimentation techniques, the intestinal scraping is faster, but is of lower sensitivity (Hofer et al., 2000). Sedimentation techniques are the WHO reference method (Eckert et al, 2001) due its high sensitivity (one worm per intestine).

3.1.2. Detection of circulating antibodies

Antigens derived from Echinococcus worms at different stages of development can induce an immune response with the production of specific antibodies and is well documented in foxes (Gottstein et al., 1991). But it has also been shown that an animal can have circulating antibodies without having worms in the intestine probably reflecting an earlier *E. multilocularis* infection. The detection of antibodies by ELISA can be recommended only for pre-screening in areas in which the status of foxes regarding *E. multilocularis* infection is unknown, but not as a routine method for diagnosis.

3.1.3. Coproantigen detection

Coproantigen ELISA methods can detect excreted or secreted antigens by the adult worm in the intestine (Kohno et al., 1995; Sakai et al., 1998a, 1998b; Deplazes et al., 1999). Methods using polyclonal or monoclonal antibodies (anti Em9) are available (Nonaka et al., 1996; Sakai et al., 1998a, 1998b). All these techniques have a high specificity, around 95%, and sensitivity between 85% and 95% (Eckert and Deplazes, 2001). Nevertheless this sensitivity is lower when there is a weak parasitic burden (<100 worms) (Nonaka et al., 1998; Raoul et al., 2001). The coproantigen ELISA using antibodies against excretory/secretory antigens of the intestinal stages of *E. multilocularis* allows for an individual diagnosis on a faecal sample from a live animal. Experimentally, coproantigens are detected five days after infection until the elimination of the parasite.

3.1.4. CoproDNA detection

Parasite DNA excreted with eggs, proglottids or parasite cells can be detected in faeces after amplification by PCR. The main targets for amplification are the genes of the RNAsn U1 and the 12S rRNA. The specificity is 100% whereas the sensitivity varies between 89% and 94% according to the method (Bretagne et al., 1993; Mathis et al., 1996; Monnier et al., 1996; Dinkel et al., 1998; Van Der Giessen et al., 1999).

Table 6: Characteristic of test systems for diagnosis of *E. multilocularis* in definitive hosts (Deplazes et al., 2003)**.**

Techniques	Test characteristics	Approximate Number of animals/samples investigated per person per day
Sedimentation (Eckert et al., 2001)	SE and SP 100% reference method in WHO. Application at necropsy, laborious for routine screening but quantitative and precise	10 intestines
Sedimentation and filtration (Duscher et al., 2005b)	SE 96% and SP 100% Application at necropsy, laborious for routine, semi-quantitative	ND
Intestinal scraping (Hofer et al., 2000)	SE 78% and SP 100% Application at necropsy, laborious, semi-quantitative. Routine test at necropsy	15 to 20 intestines
Copro-antigen ELISA (Deplazes et al., 1999)	SE 80% and SP 95-99% *In vivo* and post mortem diagnosis and testing of field faecal samples, rapid and easy, infection detectable in pre-patent stage. Routine test for mass screening	200 Faecal samples
Copro-antigen ELISA (Sakai et al., 1998a)	SE 87% and SP 70% Test characteristics see above	200 Faecal samples
Coproantigen ELISA (CHEKIT Echinotest, Dr. Bommeli AG, CH-3097 Bern)	SE 60-80% and SP 80-95% Test characteristics see above	200 Faecal samples
PCR (Mathis et al, 1996)	SE 94% and SP 100% Target : RNAsn U1 *In vivo* or post mortem diagnosis and testing field faecal samples, laborious, PCR detect only eggs. Confirmation test for coproantigen-positive results and for identification of taeniid eggs	15 Faecal samples
PCR (Monnier et al, 1996)	SE 82% and SP 96% Target : RNAsn U1 *In vivo* or post mortem diagnosis and testing field faecal samples, laborious total DNA isolation from faeces allows detection of eggs and parasite tissue. Alternative method to necropsy and for confirmatory purposes	15 Faecal samples
PCR (Dinkel et al, 1998)	SE 89% and SP 100% Test characteristics as above	15 Faecal samples
PCR (Van der Giessen et al, 1999)	SE ND and SP 100% Test characteristics as above	15 Faecal samples

SE = Sensitivity; **SP** = Specificity

For live domestic animals, such as cats and dogs, few techniques are available for diagnosis of Echinococcosis and is done on faeces using ELISA coproantigen detection or by coproDNA detection using PCR.

3.2. Diagnostic methods in the intermediate and aberrant host

3.2.1 In vivo diagnosis

Specific antibodies against *E. multilocularis* antigens (Em2, EmG11, II/3-10) could be detected in the majority of intermediate and aberrant hosts (Deplazes and Eckert, 2001; Eckert and Deplazes, 2001). After biopsy, Em2 and EmG11 antigens, specific to the metacestode stage, can be detected by ELISA and fragments of metacestode cuticle can be demonstrated by immunohistochemistry using the monoclonal antibody EmG11 (Deplazes and Gottstein, 1991).

3.2.2. Post-mortem diagnosis

In voles, the natural intermediate host of the parasite, as well as in aberrant hosts, the examination of the liver and the abdominal cavity allow the detection of lesions due to the parasite. Histopathology is required for the confirmation of the aetiology of the lesions observed (Houin et al., 1982). Development of the larva is incomplete (no protoscolex) in some intermediate or aberrant hosts, as has been reported in pig and wild boar (Pfister et al., 1993; Sydler et al., 1998; Boucher et al., 2005; Deplazes et al., 2005). As an aid to diagnosis, identification of small or atypical lesions can be done using molecular biology or immunohistochemistry (Lightowlers and Gottstein, 1995; Boucher et al., 2005).

3.3. Conclusions

1. The diagnostic methods available at the moment are not adapted to disease surveillance on a large scale.
2. Most of the diagnostic methods available are laborious, require specialised laboratories, and are not adapted to live domestic animals
3. Diagnostic methods can represent a hazard for the staff**.**

3.4. Areas and Recommendations for Future Research

A rapid, easy and validated surveillance and diagnostic techniques that could be used for asymptomatic as well as clinically diseased live animals should be developed.

4. TREATMENT

4.1. Treatment for tapeworms in pets

Currently two substances are available for treatment *E. multilocularis* infection in definitive hosts, praziquantel and epsiprantel (Manger et al., 1989 ; Arru et al., 1990), which are requested by national authorities under the pet importation schemes . Both molecules have an efficacy near 100% against mature and immature forms *E. multilocularis* in a single administration (Andersen et al., 1981; Jenkins & Romig, 2000, Eckert et al., 2001). However none of the drugs is ovicidal (Thakur et al., 1979). The two substances are well tolerated in dog and cat. Praziquantel is available different

pharmaceutical forms whereas epsiprantel exist only in tablets for oral administration. With praziquantel, 100% efficacy is achieved after a single administration; however, occasionally low residual worm burden may persist. In this case a second dose of praziquantel should be administrated within 7 days (Andersen et al., 1981).

Studies on pharmacokinetics of praziquantel in animals (Coles, 1979) and humans (Leopold et al., 1978) show a short half life of the drug. All investigated animal species excrete praziquantel and its metabolites rapidly. Within 24 hours of administration of radiolabelled praziquantel the radioactivity in the serum was in the same order of magnitude as the detection limit (EMEA, 1996). The possibility of re-infection after treatment and before entry into an area considered free from the infection has to be taken into account due to the short half life of the drug.

Due to the lack of ovicidal activity, infected pets treated with praziquantel may shed infectious tapeworm eggs for several hours after treatment. A period of 24 hours between treatment and entry of the pet into a country free from *E. multilocularis* is considered sufficient to prevent the shedding of infectious tapeworm eggs with the faeces taking into account the rapid intestinal transit observed in cats and dogs.

4.2. Treatment of wildlife

It is possible to administer parasitic treatment to foxes using baits containing praziquantel. This treatment destroys the larva and the adult worm in the intestine of the definitive host, but it has no effect on the eggs from patent adults. Since the 1980s different field assays have been done with baits containing 50 mg of Praziquantel. The baits have been distributed by hand or by air-drop and a diminution of the prevalence of the parasite in definitive host has been observed. In Germany the prevalence decreased from 32% to 4% in the experimental area (Schelling et al., 1997). In an experimental trial of 5000 km2, the observed prevalence decreased from 26% to 3% (Tackman et al., 2001) but after stopping the praziquantel treatment the prevalence increased again, so it did not totally eliminate the parasite on the treated area. In Switzerland, a similar experiment done in an urban area (Hegglin et al. 2004) showed that faecal samples positive for the parasite decreased from 38.6% to 5.5% with a similar decline in the intermediate host population (Hegglin et al., 2003).

These experimental studies demonstrate that the treatment of wildlife with baits containing praziquantel is possible both in rural and urban conditions. Nevertheless, when fox population density is high, the treatment may be effective only if the density of baits is high and if the duration of baiting is long and repeated throughout the year.

4.3. Requirements in relation to non-commercial movements of pet animals

The national authorities in UK, Ireland, Sweden, Finland, Malta and Cyprus require specific procedures for free movement of pets. These requirements concern only pets which accompany their owner or person responsible for them on behalf of the owner, and which are not intended to be sold or transferred to another owner.

Identification

The animal must be identified by a microchip or clearly readable tattoo. As of 3 July 2011 only a microchip will be approved as identification. The animal must be identified before the rabies vaccination.

Vaccination against rabies

The animal must have been vaccinated against rabies with an inactivated vaccine of at least one antigenic unit per dose (WHO standard).

Pet passport

A uniform model for the pet passport is applied in the whole EU. When travelling, the animal must be accompanied by this pet passport including the information on the identification of the animal, and an entry by the veterinarian concerning a valid rabies vaccination and that the pet has been treated against the tapeworm Echinococcus multilocularis using a veterinary medicine whose active ingredient is praziquantel or epsiprantel.

Treatment against tapeworms

The United Kingdom, Ireland and Malta have maintained their national rules as regards the control of echinococcosis and ticks, while Sweden and Finland have maintained their national rules as regards the control of Echinococcosis (see Table 7).

For UK Ireland and Malta:

Dogs and cats must be treated by a veterinarian against tapeworm not less than 24 hours and not more than 48 hours before the pet is checked-in with an approved transport company. The treatment must contain the active ingredient: praziquantel. The treatment must be carried out every time the pet enters the UK.
The pet treatment must be recorded in the appropriate section VI & VII of the EU pet passport or the third country official veterinary certificate.

http://www.defra.gov.uk/animalh/quarantine/pets/procedures/support-info/parasites.htm (Accessed 21 January 2007)
http://www.agriculture.gov.ie/index.jsp?file=pets/travel.xml (Accessed 21 January 2007)

For Finland

Not more than 30 days before they arrive in Finland, dogs and cats must be given an appropriate dose of praziquantel or epsiprantel against tapeworms causing Echinococcosis approved for the species concerned. A record of the treatment against Echinococcosis has to be entered on the pet passport by the veterinarian. Medication against Echinococcosis is not required for animals which are less than three months old. The animal must be accompanied by a pet passport carrying the identification information on the animal and a record of the Echinococcus treatment (parts I-IV and VII).
http://www.evira.fi/portal/en/animals_and_health/import_and_export/dogs__cats_and_ferrets/import_from_eu_countries_and_norway/ (Accessed 21 January 2007)

For Sweden

Sweden also requires that the pet will have been treated against tapeworms using a product containing praziquantel. A veterinarian shall treat the animal against tapeworm (Echinococcus) 1-10 days before bring it to Sweden. A passport is also required.
http://www.sjv.se/home/amnesomraden/animalhealthwelfare/importexportofliveanimals/dogsandcats.4.7502f61001ea08a0c7fff126754.html (Accessed 21 January 2007)

In summary, three different treatment protocols prior to movement currently exist (Table 7). In two protocols, praziquantel must be applied; one protocol also allows the use of epsiprantel. One protocol (P1) stipulates that the treatment with praziquantel must be applied no less than 24 hours and no more than 48 hours before the pet is moved into a country considered free of E. multilocularis. The second protocol (P2) allows treating pets with praziquantel between 1 to 10 days before entry into a country considered free of E. multilocularis and the third protocol (P3) allows treatment with praziquantel or epsiprantel no more than 30 days before entry into the area considered free. None of the protocols specifies the dosage although UK rules specifically advise treatment to be effectuated in accordance to manufacturer instructions. All five MS require that the treatment is performed and certified by a Veterinary surgeon.

Table 7: Protocols of treatment against tapeworms for pets

	Country				
	United Kingdom (P1)	**Ireland (P1)**	**Malta (P1)**	**Finland (P3)**	**Sweden (P2)**
Used treatment	praziquantel	praziquantel	Praziquantel	praziquantel or epsiprantel	praziquantel
Day of treatment	> 24 h [1] < 48 h [1]	> 24 h [1] < 48 h [1]	> 24 h [1] < 48 h [1]	< 30 days [2]	1- 10 days [3]
[1] treatment has to be repeated every time pet enters the country; [2] before pet entry in the country; not required for animals less than three months old; [3] before pet entry in the country.					

4.4. Conclusions

1. The treatments used are effective for the adult forms of the parasite but lack ovicidal properties.

2. The parasite is usually eliminated from the definitive host within 24h. Some data show that residual worm burden can persist after a single treatment.
3. Considering the different treatment regimes of MS, for **P2** (Sweden) and **P3** (Finland) and the short half -life of the drugs, the risk of re-infection with *E. multilocularis* after treatment cannot be excluded.

4.5. Recommendations

The treatment should be administered between 24 and 48h prior to departure so that the probability of re-infection in the country of origin, and the probability of viable egg elimination in the importing country are reduced.

4.6. Areas and Recommendations for future research

1. To investigate the importance of possible residual parasite presence after a single administration of the drug.
2. Develop baiting strategies for wild life treatment.
3. To develop research on drugs with ovicidal properties for *E. multilocularis*.

5. REPORTS BY MS

Finland submitted a RA elaborated by the National Veterinary and Food Research Institute (EELA), Helsinki, in 2001. It is a qualitative RA, and no numerical data are provided in the report. The main conclusions of the report is that the risk for transmission of *E. multilocularis* to Finland exists both through movements of the wild final and (to a lesser extent) intermediate hosts, as well as from the entry of domestic dogs and cats coming from endemic areas. No statistics on the number of dogs entering Finland, or on their origin are given. The population of susceptible wild carnivores is probably increasing in the country, but no numerical data are provided. A second RA, dated 2006, was provided with information on surveys conducted in red foxes, raccoon dogs, and domestic dogs. From 2001-2005, 923 red foxes were investigated by necropsy and/or coproantigen ELISA and all yielding negative results. Similarly, from 2003-2005, 896 racoon dogs were necropsied and investigated by coproantigen ELISA, with negative results. At least 2000 wild rodents have been examined annually by necropsy for *E. multilocularis*, with negative results. The report concludes that the risk of introduction by pet movement is still higher than negligible, and that the situation has not changed

from the report of 2001 or that the risk is even higher due to the apparent increase in *E. multilocularis* infection of wild animals.

The UK RA has been produced by the Veterinary Surveillance Team (Central Science Laboratory) in August 2006, and is also qualitative. The document identifies 250 exotic cat and dog diseases, and considers the risk of their introduction into UK. Infections are categorized by risk depending on their zoonotic potential, the presence of intermediate hosts and/or vectors in UK, the risk of spread into UK, and disease risk to humans, pets, farm animals and wild fauna. Using these criteria, *E. multilocularis* is categorized as a high risk disease due to its high pathogenicity for humans, its endemic presence in many countries commonly visited by travelling pets, the presence of intermediate hosts in UK, and the high likelihood of establishment if introduced in UK.

The Swedish report has been prepared by the National Veterinary Institute, and uses both qualitative and quantitative approaches. The most important uncertainties in this assessment were the number of dogs entering Sweden every year from EM endemics areas. Approximately 30,000 import permits for dogs entering Sweden were issued during 2003 by the Swedish Board of Agriculture. Approximately 50 to 200 dogs came from MS where *E. multilocularis* is endemic (Germany, Switzerland, France, Italy, Austria), and 1000 dogs were registered annually by the Swedish Kennel Club originating from other countries with possibly EM infected rodents. The EM prevalence was assumed to be around 0.3% in domestic dogs from endemic countries. The release assessment outputs show an expected number of 29 infected dogs per year entering Sweden if no treatment is implemented. To achieve a low probability of EM introduction (0.05-0.3), the efficacy of treatment measures must be at least 99.9%. The report, therefore, concludes that the probability of at least one infected dog entering Sweden is high (>0.7) unless the current anthelmintic treatment is maintained and followed with high compliance.

Ireland has submitted a qualitative RA, without numeric data on pet travels, or on *E. multilocularis* surveys. The conclusion in the report is that treatment should be maintained due to the risk of introduction by pets, and the consequent risk for human.

6. RISK ASSESSMENT

6.1. Method of risk assessment

Risk assessment is recognised by the World Organisation for Animal Health (OIE) as a transparent and scientific method for determining the risk of unwanted events occurring. It is being used, in particular, for animal importation and food safety and the results serve as a decision support for risk managers.

Before a RA Hazard identification must be undertaken (OIE)

The components of the risk assessment are:

- Release assessment;
- Exposure assessment;
- Consequence assessment; and
- Risk estimate

The hazard identification and its description are presented in Chapter 2. According to the mandate, the aim of the present risk assessment is to assess the risk of introducing *Echinococcus multilocularis* through non-commercial movement of pets (section 2) hence, the focus of this risk assessment is on the release assessment.

Risk assessments can be conducted in a qualitative or a quantitative manner. A qualitative assessment presents data in a logical way and aims at summing up the risk in words using terms like negligible, low, moderate and high without allocating exact numerical values to probabilities, costs and consequences. For *E. multilocularis* there is a lack of regular surveillance programmes in pets and wildlife in the EU, differences in the studies undertaken to obtain data concerning infections in wildlife, and limited availability of data on the prevalence or incidence of infections with *E.*

multilocularis in pets, in particular in pets to be moved into an area considered free of this parasite. Therefore it was considered that until that data was available this risk assessment should be qualitative.

On the other hand, a quantitative assessment is built upon mathematical and statistical methods and the result is presented numerically. The uncertainty of the result reflects variation and uncertainty in our knowledge of the process. At this time, it was considered that the lack of data preclude a quantitative risk assessment. As an orientation, a model of estimation of risk of introduction *E. multilocularis* by pets is provided in Annex 1.

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6.2. Risk Questions

The following questions are raised in the mandate for the risk assessment.

- To what extent the abandoning of such additional guarantees (treatment prior to movement) could be envisaged, taking into account the different epidemiological situations with regard to these diseases prevailing in third countries and the Member States other than in the UK, Sweden, Ireland, Finland and Malta, without increasing the risk of introducing those diseases into these latter countries from the remainder of the EU territory and third countries?

- If the assessment reveals that in certain circumstances the need to maintain such treatments prior to movement is scientifically justified (in other words, if the consequential risk is higher than negligible), what would be the appropriate protocol (treatments / movement) to be considered as giving equivalent assurances for the protection of these Member States? To this end, the different national rules that are currently in force could be considered.

6.3. Hazard identification

See Chapter 2. The hazard is *E. multilocularis*.

6.4. Risk Assessment

Risk Pathway

The risk of introduction of *E. multilocularis* into a **country considered free** of this parasite is outlined in a schematic view by presenting the available information in a logical order and identifying the respective risks (Fig. 4).

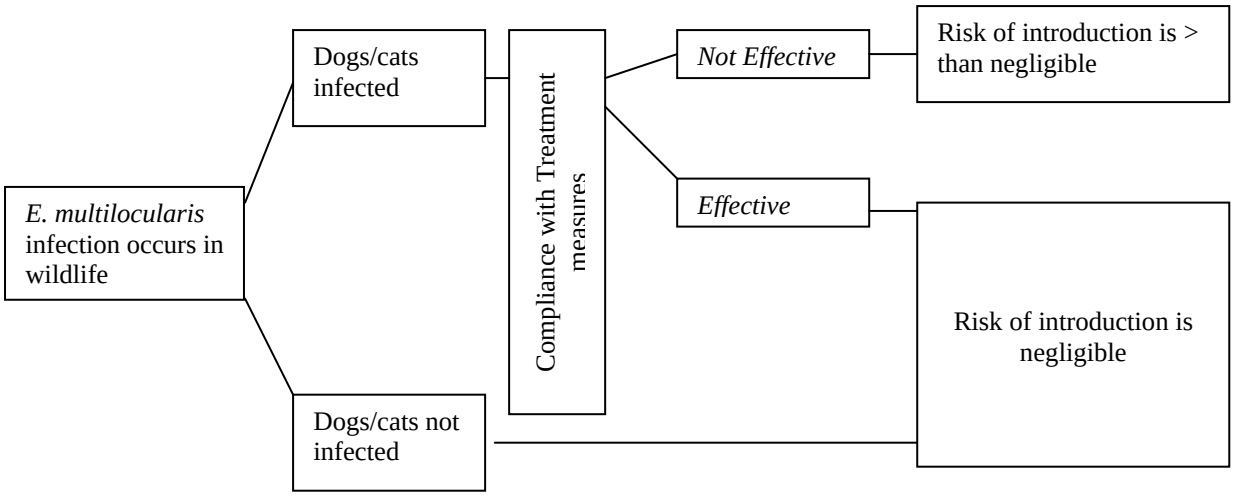

Figure 4: Schematic view of the risk of introducing *E. multilocularis* into an area considered free of the parasite

Release Assessment (no safeguards in place)

1. *E. multilocularis* is widely distributed in most of Europe. However it has never been recorded in the British Isles, Fennoscandia, and the Iberian Peninsula.
2. The typical transmission cycle in Europe is wildlife based and involves red foxes as the main final host and rodents, mainly common voles and water voles as intermediate hosts.
3. Pets can be infected and although their significance for the life cycle persistence might be small they may play a key role in transmission to humans.

From the available information the following conclusions may be drawn.

1. The risk of dogs and cats becoming infected with *E. multilocularis* as final hosts in endemic areas is **greater than negligible**.
2. It can be assumed that the regional prevalence in wildlife and access to intermediate hosts influence the risk of infection to cats and dogs.
3. A proportion of dogs and cats to be moved from an endemic area into a country considered free of *E. multilocularis* will be infected. The probability of infection for an individual animal will depend on the originating country, the area visited the period of residency and the host susceptibility.
4. Abandoning the additional measures will increase the risk of introducing the parasite into an area considered to be free of *E. multilocularis*

Release Assessment (effect of safeguards)

1. To reduce the risk of introduction, dogs and cats can be treated.
2. The treatments available are effective for the live parasite but lack ovicidal properties.
3. A period of at least 24 hours between treatments and entry of the pet into a country free from *E. multilocularis* is more likely to prevent the possibility of post-treatment faecal contamination that is due to the lack of ovicidal activity of the compounds used for treatment.
4. The risk of re-infection with *E. multilocularis* after treatment cannot be excluded, due to the short half-life of the drugs.

The following conclusions can be drawn.

1. To reduce the risk of introduction, dogs and cats should be treated.
2. If compliance can be assured, the risk of introducing *E. multilocularis* into an area free of the parasite after treatment of infected pets is lowest for a treatment done not less than 24 hours and not more than 48 hours prior to movement so that the probability of re-infection in the country of origin, as well as the probability of viable egg elimination in the importing country, are reduced.
3. The risk of introducing *E. multilocularis* into an area free of the parasite after successful treatment of infected pets with P1 (treatment no less than 24 hours and not more than 48 hours prior to movement) is negligible.

The actual / present level of compliance with requirements cannot be addressed in this document due to lack of data.

6.5. Conclusions of release assessment

1. If *E. multilocularis* is present in wildlife in a country, then it is assessed that the prevalence of *E. multilocularis* in dogs and cats in that country whether native or visiting is greater than negligible. Therefore on import into countries considered free from the infection, it follows that the probability of a proportion being infected is also greater than negligible.

2. Abandoning the additional measures will increase the risk of introducing the parasite into an area considered free of *E. multilocularis.*

3. Currently, three different protocols (P1, P2, P3, see Table 7) for treatments prior to movement exist in the respective countries. The risk of introducing *E. multilocularis* into an area free of the parasite, after treatment of infected pets with P2 or P3, is greater than negligible. The risk of introducing *E. multilocularis* into an area free of the parasite after treatment of infected pets with P1 is negligible.

6.6. Recommendations

1. Surveillance programmes should be introduced to provide data for a better risk estimation.

2. Data should be collected on the number of pets being imported, their country/area of origin, and their duration of stay or residence for a better estimate of the risk.

3. The epidemiological status of various countries should be better defined in relation to the prevalence of infection in both wild and domestic animals.

4. The disease should be notifiable in both humans and animals to give a more accurate epidemiological evaluation of the disease.

5. In order not to increase the risk of introduction of EM into free countries, the treatment of pets prior to importation with appropriate drug and treatment protocol should be carried out.

6. From the different treatments of pets in place in the concerned MS, administration of praziquantel not less than 24 hours and not more than 48 hours prior to movement is the preferred treatment protocol for reducing the risk of introduction and spread of Echinococcosis by non-commercial movement of pets within EU, provided that compliance is high.

7. Compliance with the treatment protocols should be ensured.

8. Countries such as Finland with extensive borders can be more exposed to the risk of introduction of EM by wildlife movements than islands such as UK, Ireland or Malta, where the major factor for introduction of the disease is the importation of infected domestic pets. This risk should be monitored

9. Public awareness should be raised by providing information for dog and cat owners about this parasitic infection.

6.7. Areas and Recommendations for future research

1. To further understand the risk factors for transmission between animal hosts and from animals to humans.
2. To develop rapid, easy and validated diagnostic techniques that could be used for healthy live animals.
3. To investigate the importance of the possible residual parasite presence after a single administration of the drug.
4. Develop baiting techniques for wild life treatment.
5. To develop research on drugs with ovicidal properties for *Echinococcus multilocularis*.

7. ANNEX I

A qualitative RA was performed due to lack of data on prevalence of *E. multilocularis* in pets, and on the number of pets entering concerned MS from endemic areas. To assess the effect of factors like time of treatment, efficacy of treatment, and compliance of measures on the overall risk of introduction of *E. multilocularis*, a simulation model is provided based on assumptions on the former parameters. This model could be the basis for a quantitative risk assessment if data on the different parameters were available in the future. In this simulation model, the risk of introduction of *E. multilocularis* by pets into a **country considered free** of this parasite is outlined in a schematic view identifying the respective risks (Fig. 1). Four scenarios were considered leading to the introduction of infected dogs:

A: Dog becomes infected during the waiting period after a successful treatment;
B: Unsuccessful treatment of an infected dog;
C: Dog is not infected at time of treatment and becomes infected after the treatment;
D: Untreated infected dogs (problem of non-compliance).

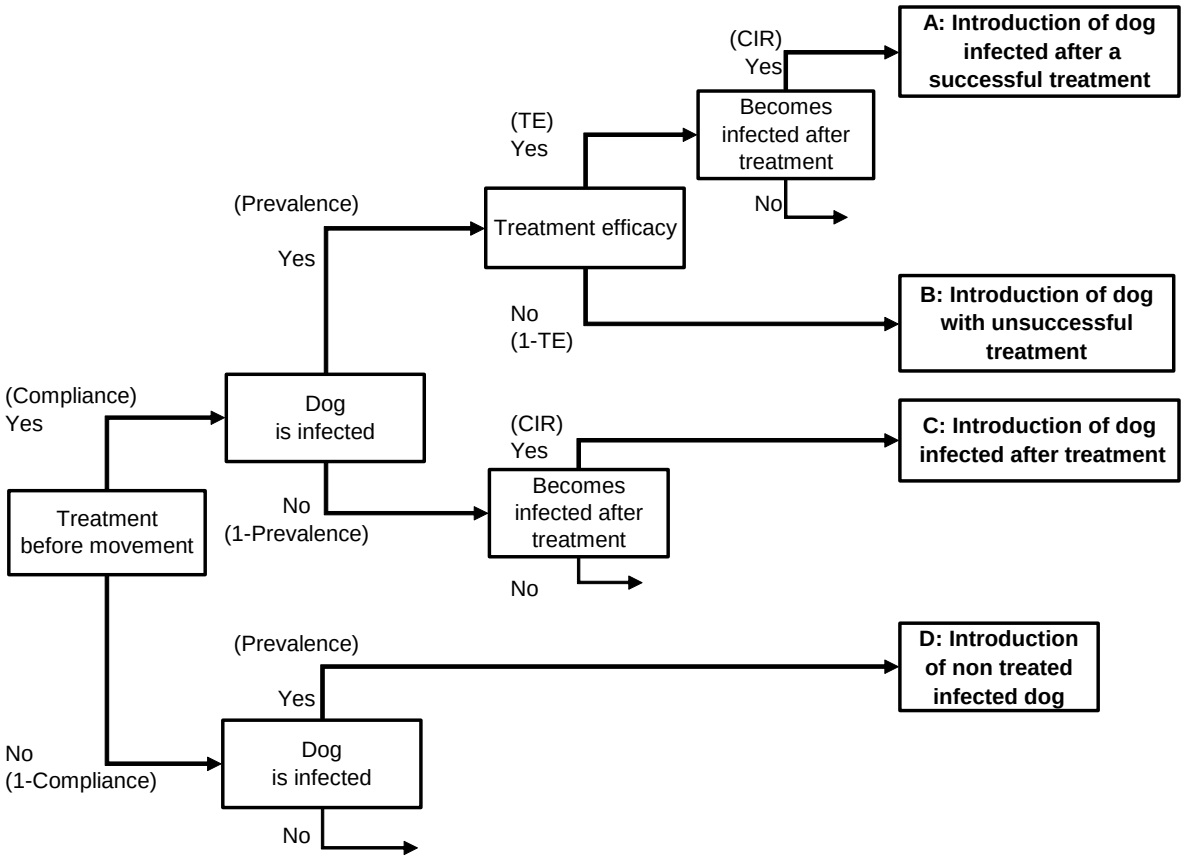

Figure 1: Flow diagram outlining the pathways leading to the introduction of *E. multilocularis* into an area considered free of the parasite by infected dogs and the different risk situations.

Using this model, the risk of introduction of EM to a free country through movements of pets from abroad could be estimated using different assumptions on the number of dogs entering the free country, the prevalence of infected dogs in the country of origin, treatment efficacy and the average duration of infection (Table 1). The prevalence figures of 0.01 to 0.5 are based on the results available from literature (see Table 4 in the Opinion). The duration of infection has been assumed to be of 90 days based on references published on the patent and pre-patent periods of dogs and foxes. The

waiting period is the time framework stipulated for the treatments in the different MS. The numbers of dogs entering from endemic areas or countries are probably different between MS, but for the purpose of simulation, data provided in the Swedish report (around 1100 pets coming each year from infected areas) have been used; other MS such as UK or Ireland described the total number of pets imported but provided no data about their country of origin. Compliance levels are assumptions. The value 0 for compliance would be an estimation of risk of introduction without any treatment. As the available data (see section on treatment on the opinion) indicate that the efficacy of treatment is very high, close to 100%, the effect of three different values 90%, 99%, and 99.9% has been assessed.

Parameters	Notation	Assumptions / formulas
Prevalence: probability of selecting an infected animal at a given point in time	P	from 0.01% to 0.5%
Patent and pre-patent periods	D	90
Incidence rate per day	IR	$IR = \frac{P}{D}$ (a)
Waiting period in days	WP	0 to 2, 1 to 10, 0 to 30
Cumulative incidence rate: probability for one dog to becomes infected during the waiting period	CIR	$CIR = IR \times \frac{WP}{2}$ (b)
Compliance	C	0%, 50%, 75%, 99%, 99.9%
Treatment efficacy	TE	90%, 99%, 99.9%
Risk A: Dog becomes infected during the waiting period after a successful treatment	RA	$RA = C \times P \times TE \times CIR$
Risk B: Unsuccessful treatment of an infected dog	RB	$RB = C \times P \times (1 - TE)$
Risk C: Dog is not infected at time of treatment and becomes infected after the treatment	RC	$RC = C \times (1 - P) \times CIR$
Risk D: Untreated infected dogs (problem of non compliance)	RD	$RB = (1 - C) \times P$
Overall risk	R	$R = RA + RB + RC + RC$
Number of dogs entering per year	N	500, 1000, 1500, 2000
Risk of introduction: probability that at least one out of the N entering animals is infected	RI	$RI = 1 - (1 - R)^N$
Expected number of EM infected dogs introduced per year	I	$I = N \times R$

Table 1: Different formulae and assumptions used in this simulation model.

(a): It is assumed that the disease incidence is regularly distributed throughout the year.

(b): There is no data on the average number of days between treatment and animal movement. It is assumed here that the number of days between treatment and animal movement is distributed uniformly between 0 and the WP.

Results of calculations are shown in Table 2, using as example a situation with a prevalence of 0.3 and compliance and treatment efficacy of 99.9%, and a waiting period of 24-48 hours.

Parameters	notation	Values
Prevalence: probability of selecting an infected animal at a given point in time	P	0.30%
Average duration of infection in days (average period during which an animal can be expected to carry the agent)	D	90
Incidence rate per day	IR	0.0033%
Waiting period in days	WP	2
Cumulative incidence rate: probability for one dog to become infected during the waiting period	CIR	0.0033%
Compliance	C	99.9%
Treatment efficacy	TE	99.9%
Risk A: Dog becomes infected during the waiting period after a successful treatment	RA	0.0000100%
Risk B: Unsuccessful treatment of an infected dog	RB	0.0002997%
Risk C: Dog is not infected at time of treatment and becomes infected after the treatment	RC	0.0033200%
Risk D: Untreated infected dogs (problem of non compliance)	RD	0.0003000%
Overall risk	R	0.0039297%
Number of dogs entering per year	N	1000
Risk of introduction: probability that at least one out of the N entering animals is infected	RI	3.85%
Expected number of EM infected dogs introduced per year	I	0.04

Table 2: Example of calculation of risk of introduction of EM infected dogs in a free country.

The model can be used to illustrate various situations, and how the different factors influence the risk to introduce EM in free countries.

Risk of Introduction RI as a function of compliance and waiting period

Compliance	Waiting period		
	2	10	30
0.0%	95.0%	95.0%	95.0%
50.0%	78.1%	79.5%	82.7%
75.0%	54.0%	58.4%	67.6%
99.0%	6.4%	18.0%	41.0%
99.9%	3.9%	15.8%	39.7%

Prevalence = 0.003 Number of dogs entering /year = 1000
Treatment efficacy = 0.999

Expected number of EM infected dogs introduced per year function of compliance and waiting period

Compliance	Waiting period		
	2	**10**	**30**
0.0%	3.00	3.00	3.00
50.0%	1.52	1.58	1.75
75.0%	0.78	0.88	1.13
99.0%	0.07	0.20	0.53
99.9%	0.04	0.17	0.51

Prevalence = 0.003 Number of dogs entering /year =1000
Treatment efficacy= 0.999

Risk of Introduction RI as a function of compliance and prevalence

	Compliance				
Prevalence	**0.0%**	**50.0%**	**75.0%**	**99.0%**	**99.9%**
0.01%	9.5%	4.9%	2.6%	0.2%	0.1%
0.02%	18.1%	9.6%	5.0%	0.4%	0.3%
0.03%	25.9%	14.1%	7.5%	0.7%	0.4%
0.04%	33.0%	18.3%	9.8%	0.9%	0.5%
0.05%	39.4%	22.4%	12.2%	1.1%	0.7%
0.06%	45.1%	26.2%	14.4%	1.3%	0.8%
0.07%	50.4%	29.8%	16.6%	1.5%	0.9%
0.08%	55.1%	33.3%	18.7%	1.7%	1.0%
0.09%	59.4%	36.6%	20.8%	2.0%	1.2%
0.10%	63.2%	39.7%	22.8%	2.2%	1.3%
0.15%	77.7%	53.2%	32.2%	3.2%	1.9%
0.20%	86.5%	63.7%	40.4%	4.3%	2.6%
0.25%	91.8%	71.8%	47.7%	5.3%	3.2%
0.30%	95.0%	78.1%	54.0%	6.4%	3.9%

Treatment efficacy=0.999 Number of dogs entering /year=1000

Expected number of EM infected dogs introduced per year as a function of prevalence and compliance

Prevalence	Compliance				
	0.0%	50.0%	75.0%	99.0%	99.9%
0.01%	0.10	0.05	0.03	0.00	0.00
0.02%	0.20	0.10	0.05	0.00	0.00
0.03%	0.30	0.15	0.08	0.01	0.00
0.04%	0.40	0.20	0.10	0.01	0.01
0.05%	0.50	0.25	0.13	0.01	0.01
0.06%	0.60	0.30	0.16	0.01	0.01
0.07%	0.70	0.35	0.18	0.02	0.01
0.08%	0.80	0.40	0.21	0.02	0.01
0.09%	0.90	0.46	0.23	0.02	0.01
0.10%	1.00	0.51	0.26	0.02	0.01
0.15%	1.50	0.76	0.39	0.03	0.02
0.20%	2.00	1.01	0.52	0.04	0.03
0.25%	2.50	1.27	0.65	0.05	0.03
0.30%	3.00	1.52	0.78	0.07	0.04

Treatment efficacy=0.999 Number of dogs entering /year=1000

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UK:
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Ireland:
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Sweden:
Ivar Vågsholm National Veterinary Institute, Sweden (2006). An assessment of the risk that EM is introduced with dogs entering Sweden from other EU countries without and with antihelmintic treatments. Ivar Vågsholm, National Veterinary Institute, S 751 89, Uppsala, Sweden. http://www.sva.se/pdf/ask/qra_emdogsaug06.pdf. (Accessed 21 January 2007)

* The project EchinoRisk was conducted in the period 2001-2004 with 12 participants from Austria, the Czech Republic, France, Germany, Italy, the Netherlands, Poland, the Sloval Republic, Switzerland and the UK (coordinator: P. Kern from the University of Ulm, Germany). Main conclusions of the project were:

- During this study, new endemic regions were identified, and in all countries where retrospective data are available, prevalence levels either increased (Germany, Poland, Austria, Slovak Republic) or remained stable (Netherlands, Switzerland). In none of the countries, any prevalence decrease could be observed. This suggests that transmission of this parasite has increased in many regions of Europe. This calls for an ongoing monitoring in the endemic regions and near (within and without) the known range limits of *E. multilocularis*.
- The influence of landscape is evident in most surveys. However, the influence of individual parameters on transmission appears to vary among regions. This must be further investigated in order to achieve reliable tools for prospective risk assessment. As a hypothesis, landscape parameters do not define precise prevalence levels, but provide a broader frame within which other parameters (climatic variation, host animal population densities etc.) are likely to influence transmission. Therefore, prevalence rates should be monitored in selected areas longitudinally to identify long term (within 10 years and more) temporal and spatial variability in transmission intensity.
- Various data sets (environmental faecal samples, shot foxes …) which have been collected during the current study will in future be used to evaluate models (frequencists vs. bayesians) predicting prevalence rate distribution over time and space. These models will be used both to evaluate the prediction power of landscape parameters, and to test if human prevalence rates (i.e. EurEchinoReg human register) are correlated with prevalence rates in foxes (human morbidity rates are unlikely to reflect short term prevalence levels in animals, but rather the long term capacity of a certain region for transmission).
- The increasing presence of synathropic fox populations in European cities, towns and villages, and their high rate of infection with *E. multilocularis*, calls for countermeasures against this apparent infection risk for the human population. Anthelmintic baiting was demonstrated to be a viable option both in rural and urban areas, although total eradication is likely to be difficult to achieve, and the countermeasure have to be adapted to local situations. A surveillance of the transmission in urban and peri urban areas is strongly recommended, and antihelmintic treatment needs to be optimized and combined with other measures (e.g. information campaigns), particularly with regard to cost-benefit considerations.

- First results of genetic characterization of European isolates with the newly developed micro satellite marker EmsB suggest the usefulness to assess the *E. multilocularis* genetic polymorphism at a highly sensitive level. However, full analysis of all collected samples could not be achieved during the time of this project. Consequently, a continuing study, financed from other sources, was developed to finalize this promising investigation.

- The results of the telephone survey call for the need of country-specific approaches to information campaigns, taking into account levels of information and attitudes. While there is a clear need for more baseline information e.g. in France, the emphasis e.g. in Germany or Switzerland should be on the promotion of realistic risk perception, avoidance of over-reactions and correction of misinformation. Inhabitants of urban areas should be a target group for information due to their lower levels of knowledge, and in view of the increasing importance of urban areas for transmission of the parasite. The country-specific differences underline the need for corresponding surveys in other countries prior to the decision on information measures.

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The working group drafted the scientific risk assessment, which was then reviewed and revised by Panel. The working group was chaired by Dr. Mariano Domingo on behalf of the AHAW Panel. The members of the working group were:

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The Panel wishes to thank Marion Wooldridge and Moez Sanaa, members of the AHAW Panel for their support and thorough review to the risk assessment. The Panel also wishes to thank Mike Taylor (Central Veterinary Laboratory, UK) for the support provided on the later stages of the drafting of the opinion.

European Medicines Agency
Veterinary Medicines and Inspections

London, 15 March 2007
Doc. Ref. EMEA/CVMP/EWP/82649/2007

To
Ana Afonso Polyviou
Scientific Panel on Animal Health and Welfare
European Food Safety Authority (EFSA)
Largo N. Palli 5/A
43100 Parma
Italy

Dear Dr Polyviou,

Subject: Comments by the CVMP on the Opinion of the EFSA Scientific Panel on Animal Health and Welfare on the assessment of the risk of *Echinococcus* introduction into the UK, Ireland, Sweden, Malta and Finland as a consequence of abandoning national rules.

Following a request by the EFSA Secretariat, the CVMP has reviewed the above opinion in relation to Chapter 4 ("Treatment") in consultation with its Efficacy Working Party (EWP). In general the conclusions and recommendations made by EFSA can be supported; in particular, with EFSA's recommendation for future research to investigate possible residual parasite presence after a single treatment was supported.

CVMP recognises that the EFSA panel adopts opinions based on the best available scientific advice and limiting their scope to risk assessment rather than risk management. Nevertheless, in the case of recommendations, the CVMP considers that it is important to ensure that when the recommendations would result in the use of veterinary medicinal products outside the terms of their authorisation, this "off-label use" should be highlighted in the opinion. It is important for risk mangers to be aware in these cases that these recommendations are not based on data which have been independently verified by licensing authorities as part of the process of approving a marketing authorisation. The following comments are made in light of these concerns:

- Veterinary medicinal products containing praziquantel, which are indicated for the treatment against all stages of *E. multilocularis* are not authorised in all Member States. Therefore, off-license use of veterinary medicinal products might occur, i.e. the use of medicines not licensed for this particular indication. Such off-license use might result in using an inadequate dosage for the treatment against *E. multilocularis.*
  EFSA should therefore consider including an additional sentence under Section 4.5 Recommendations that 'risk managers will need to take into account the availability of suitably authorised products for the treatment regime proposed to avoid off-label use'.

- Efficacy of a single dose of praziquantel may not be 100% for *E. multilocularis* and recommendations for repeated administration are included in some SPCs (summary of product characteristics) and package leaflets of authorised products. The optimal treatment programme would be to repeat treatment after 7 days with the final administration being 24 – 48 hours prior to entry into the country. Treatment against *E. multilocularis* with an authorised

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veterinary medicinal product for this claim and according to the approved labelling instructions should therefore be recommended. However, the CVMP acknowledged that this recommendation might be difficult to implement in the field situation, e.g. when travelling with pets.

- The efficacy documentation for epsiprantel is limited as compared to praziquantel. It appears that epsiprantel in dogs is only indicated to be effective for adult stages (while praziquantel is effective against immature and mature stages) of *E. multilocularis*. The EWP, therefore, does not support the systematic use of epsiprantel in the treatment of *E. multilocularis*.

We hope that you will be able to accommodate these changes and please contact the EMEA if further discussion is necessary.

Yours sincerely,

Gerard Moulin
Chairman of the CVMP

European Food Safety Authority

Parma, August 3, 2007
Ref / (2007) – out - **2302206**

Dr. Gerard Moulin
EMEA
Chairman of the CVMP
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Subject: Comments by the CVMP and Corrigendum on the Opinion of the EFSA Scientific Panel on Animal Health and Welfare on the assessment of the risk of Echinococcus introduction into the UK, Ireland, Sweden, Malta and Finland as a consequence of abandoning national rules.

Dear Dr. Moulin,

Concerning your letter on the above subject (Ref EMEA/CVMP/EWP82649/2007) received on the 19th March. First of all we should like to express our appreciation for the good collaboration and help provided by EMEA during the preparation of this scientific opinion and now after its publication.

We are pleased to acknowledge that the CVMP in consultation with its Efficacy Working Party (EWP) has supported the EFSA AHAW Panel's conclusions and recommendations in Chapter 4 regarding treatment.

We do recognise the need to make a clear distinction between "authorised" and "off-label use". However, we would like to point out that the Scientific Opinion had as its mandate the evaluation of the various protocols requested by the five Member States and, therefore, the policy to be applied in the country of origin was not within our terms of reference. Nevertheless the Panel agreed that a sentence concerning the availability of suitably authorised products for the treatment regime proposed, to avoid off-label use, should be included in section 4.5.as follows.

"The anti-parasitic treatment for *E. multilocularis* should be administered between 24 and 48h prior to departure from the country of origin so that the probability of re-infection in the country of origin, and the probability of viable egg elimination in the importing country are reduced. The anti-parasitic treatment should be performed with a drug approved for this indication or a drug where sufficient scientific evidence for its efficacy is given. The availability of suitable authorized products for the treatment regime proposed should be taken into account to avoid off label use "

Concerning the repeated administration, the panel opinion was that there is not sufficient scientific information for a recommendation to be made.

Yours sincerely,

Dr. Philippe Vannier
Chairman of EFSA- AHAW Panel

Copy: C. Geslaine-Lanéelle, H. Koeter, AHAW team, H. Deluyker, D. Mackay (EMEA)