

# The probability of rabies entry to Norway through dogs, cats and wild fauna

### Norwegian Scientific Committee for Food Safety

Panel on Biological Hazards

**July 2005** 

### CONTENTS

EXECUTIVE SUMMARY	3
Norsk Sammendrag	
TERMS OF REFERENCE	5
BACKGROUND	5
Regulations	6
Importation of dogs and cats	7
Aetiology	7
Clinical appearance	8
Diagnosis	8
Disease transmission and reservoirs	8
Sylvatic (wildlife) rabies	9
Úrban rabies	
Bat rabies	9
Vaccination and serological tests	9
Eradication in wild carnivores	
PROBABILITY OF RABIES ENTRY THROUGH WILD ANIMALS THAT FREELY CROSS THE BORDER	10
PROBABILITY OF RABIES ENTRY THROUGH DOGS AND CATS	11
Methodology	11
Results	
Number of infected dogs and cats imported each year	13
Yearly probability of importing at least one infected pet	13
Ten-year probability of importing at least one infected pet	
Expected number of years between the importation of an infected dog or cat	
Effect of uncertain values used in the model	
ANSWERS TO THE QUESTIONS ASKED BY THE NORWEGIAN FOOD SAFETY AUTHORITY (MATTILSYNET)	
References	
SCIENTIFIC PANEL MEMBERS	
ACKNOWLEDGMENTS	
Appendix A - List of third countries from which the importation to Norway of dogs, cats and ferrets is allowed without quarantine	24
Appendix B - Country summaries of reported rabies cases in Europe in 2003 and 2004	25

#### **EXECUTIVE SUMMARY**

The Norwegian Scientific Committee for Food Safety was asked by the Norwegian Food Safety Authority (Mattilsynet) to evaluate the probability of introduction of rabies to Norway through:

- 1) the importation of young dogs and cats under the present regulations;
- 2) the importation of young dogs and cats if the regulations are changed to allow importation of unvaccinated animals younger than three months from certain EEA countries;
- 3) the importation of dogs or cats from an EEA country when the animals are both identified, vaccinated and have valid serology tests;
- 4) the free passage of wild animals across the Norwegian border?

The first three questions were answered by a quantitative approach using a simulation model. The EEA countries were classified into 4 groups based on the estimated prevalence of rabies in dogs and cats, with the estimate increasing from Group 1 up to Group 4. The estimates for the prevalence of rabies were based upon the number of reported cases of rabies in dogs and cats for the years 2003-2004 and corrected for possible underreporting.

**Group 1** - No rabies cases reported during the last two years (except in bats), AND negligible probability of importation of rabies cases from close areas: Cyprus, Iceland, Ireland, UK, Sweden, Denmark, (Norway).

**Group 2** - No rabies cases reported during the last two years (except in bats or in imported animals), but non-negligible probability of importation from close areas: Italy, France, Spain, Greece, Portugal, Belgium, Liechtenstein, Luxembourg, Netherlands, Finland and Malta.

**Group 3** - Low-prevalence endemic area, with few rabies cases reported: Germany, Austria, Slovenia, and Czech Republic.

**Group 4** - Large number of rabies cases reported in domestic and wild animals: Slovak Republic, Poland, Lithuania, Latvia, Estonia, and Hungary.

Any significant change in the prevalence of rabies in exporting countries will cause a change in the probability of introduction of rabies to importing countries. Therefore, continuous surveillance of rabies is necessary and the probability of the introduction of rabies should be re-evaluated if significant changes in the prevalence of rabies occur in exporting countries.

The number of imported cats and dogs is important for assessing the probability of introducing rabies. In this report, three scenarios based upon different numbers of imported cats and dogs from each of the different groups of countries have been considered (100, 1000 or 10 000).

Provided that the current rabies situation in the different groups of countries remained constant, it was estimated that, with an annual importation of 10 000 vaccinated and tested dogs and cats from countries in Group 3, this would, on average, cause the importation of one rabies infected animal approximately every 11 000 years. With similar importation scenarios from countries in Groups 1 and 2, the number of years between every estimated imported case of rabies would be even higher. By annual importation of 10 000 vaccinated and tested dogs/cats from countries in Group 4, it was estimated that on average one rabies infected animal would be imported every 58 years with a 95% confidence interval of 16-194 years.

With an annual importation of 10 000 unvaccinated dogs and cats younger than three months from countries in Group 3, it was estimated that this would, on average, cause the importation of one rabies infected animal every 2 000 years. With similar importation scenarios from the countries in Groups 1 and 2, the number of years between every estimated rabies import would be even higher. With an annual importation of 10 000 unvaccinated dogs and cats younger than three months from countries in Group 4, it was estimated that, on average, one rabies infected animal would be imported every 21 years with a 95% confidence interval of 11-35 years.

By reducing the number imported in each category to 1000 or 100, the number of years would increase by a factor of 10 or 100, respectively, for each group.

The probability of introducing rabies to Norway via wild fauna is most likely very low. There are two different ways that rabies could be introduced by wildlife; either by migrating carnivores or through bats. Migration of wild carnivores (in this context red fox, raccoon dog, wolf and Arctic fox) is buffered by the geographical separation of Norway from the epidemic areas. The probability of introduction of rabies to Norway through bats is unknown and could be higher than through wild carnivores.

#### **NORSK SAMMENDRAG**

Mattilsynet gav Vitenskapskomiteen for mattrygghet i desember 2004 (Ref 2004/50372) spørsmål som omhandlet sannsynligheten for introduksjon av rabiessmitte til Norge ved

- 1) import av hund/katt ved dagens regler;
- 2) import av hund/katt dersom dagens regler endres til å tillate import av uvaksinerte hunder/katter yngre enn 3 mnd fra diverse EØS land;
- 3) import fra EØS land av hund/katt som både er identifisert, vaksinert og har gyldig serologitest;
- 4) kvalitativ vurdering av sannsynligheten for introduksjon av rabiessmitte med ville dyr som fritt passerer grensen.

Spørsmålene, med unntak av det siste, er besvart ved hjelp av en kvantitativ beregningsmodell. EØS land ble gruppert i 4 grupper basert på prevalensen av rabies blant hunder og katter, økende fra gruppe 1 til 4. Estimatene bygger på rapporterte rabiestilfeller i hunder og katter i 2003 og 2004. Det ble korrigert for underrapportering.

**Gruppe 1** - Ingen rabiestilfeller de to siste årene (unntatt hos flaggermus), OG neglisjerbar sannsynlighet for import av rabiestilfeller fra grenseområder: Kypros, Island, Irland, Storbritannia, Sverige, Danmark, (Norge).

**Gruppe 2** - Ingen rabiestilfeller de to siste årene (unntatt hos flaggermus og importerte husdyr), MEN ikke neglisjerbar sannsynlighet for import av rabiestilfeller fra grensende områder: Italia, Frankrike, Spania, Hellas, Portugal, Belgia, Liechtenstein, Luxemburg, Nederland, Finland, Malta.

**Gruppe 3** - Lav-prevalens endemisk område, med få rabiestilfeller rapportert: Tyskland, Østerrike, Slovenia, Tsjekkia.

**Gruppe 4** - Stort antall rabiestilfeller rapportert hos husdyr og vill fauna: Slovakia, Polen, Litauen, Latvia, Estland, Ungarn.

En eventuell signifikant endring i rabiesprevalensen i eksporterende land vil gi en endring i sannsynligheten for introduksjon av rabies. Derfor bør rabiessituasjonen overvåkes kontinuerlig og sannsynligheten for introduksjon av rabies estimeres på nytt dersom det finner sted større endringer i rabiesprevalensen i eksporterende land.

Antallet hunder/katter som importeres er av vesentlig betydning for sannsynligheten for introduksjon av rabies. I rapporten ble tre ulike scenarioer for antallet importerte hunder/katter benyttet, henholdsvis 100, 1000 eller 10 000 hunder/katter per år fra de enkelte grupper av land.

For vaksinerte og testede dyr ble det ved import av 10 000 hunder/katter årlig estimert at det gjennomsnittlig vil gå mer enn 11 000 år mellom hvert tilfelle av rabies importert fra gruppe 3. For gruppene 1 og 2 var det estimerte antall år mellom hver import enda høyere. For gruppe 4 ble det estimert at det gjennomsnittlig vil gå 58 år, med et 95 % konfidensintervall på 16-194 år, mellom hver import av rabies ved import av 10 000 vaksinerte og testede dyr.

For uvaksinerte unge dyr ble det ved import av 10 000 hunder/katter årlig estimert at det vil gjennomsnittlig gå 2 000 år mellom hvert tilfelle av rabies importert fra gruppe 3. For gruppene 1 og 2 var det estimerte antall år mellom hver import enda høyere. For gruppe 4 ble det estimert at det gjennomsnittlig vil gå 21 år, med et 95 % konfidensintervall på 11-35 år, mellom hver import av rabies ved import av 10 000 hunder/katter årlig.

Ved import av 1000 eller 100 hunder/katter fra de ulike gruppene av land vil antall år øke med en faktor på henholdsvis 10 og 100.

Sannsynligheten for introduksjon av rabies med ville dyr anses for å være veldig lav. Det er to antatte mulige introduksjonsveier; via rovdyr eller flaggermus. Norges geografiske separasjon fra områder med rabies hos rovdyr, det vil i denne sammenhengen si rødrev, mårhund, ulv og fjellrev, gjør at sannsynligheten for introduksjon via disse dyrene anses for å være meget lav. Sannsynligheten for introduksjon av rabies via flaggermus er ukjent, og kunne være noe større enn via rovdyr.

#### **TERMS OF REFERENCE**

The Norwegian Scientific Committee for Food Safety was asked by the Norwegian Food Safety Authority (Mattilsynet) to evaluate the probability of introducing rabies to Norway through the importation of young dogs and cats (< 3 months) not vaccinated against rabies. The specific questions asked are listed below:

Questions from the Norwegian Food Safety Authority (Mattilsynet):

- 1. What is the probability that a puppy or kitten infected with rabies virus is imported to Norway under the current regulations? (the current regulations allow import of unvaccinated animals younger than three months from a small number of rabies-free countries)
- 2. What is the probability that a puppy or kitten infected with rabies virus is imported to Norway if the importation of unvaccinated animals younger than three months from the following countries is allowed in addition to those allowed by the current regulations?
  - a. Denmark and Finland
  - b. EEA countries from which Sweden allows importation, i.e. countries with no cases of rabies (with the exception of rabies in bats) in the last two years, according to International Office of Epizootics (OIE)
  - c. All EEA countries
- 3. What is the probability that a dog or cat infected with rabies virus is imported to Norway from an EEA country when the animal is both identified, vaccinated and has a valid serology test?
- 4. What is the probability of the introduction of rabies to Norway through wild animals that freely cross the border?<sup>1</sup>

#### **BACKGROUND**

Rabies is a fatal zoonotic viral infection of the central nervous system. Late in infection the virus is present in saliva and the disease is then generally transmitted via the bite of infected animals. Rabies has been known as a deadly human disease associated with rabid dogs and to a lesser extent with cats, since ancient times (Steel *et al.* 1991). According to the World Health Organization (WHO), more than 30,000 people die from rabies each year and more than 10 million undergo post-exposure treatment (Dreesen 1997). Dogs account for 99% of all human rabies deaths and 90% of all human post-exposure treatments (Anonymous 1991).

<sup>1.</sup> Hvor stor er sannsynligheten for at en valp/kattunge med rabiessmitte blir importert til Norge med dagens regler? (Det er tillatt å importere uvaksinerte dyr yngre enn tre måneder fra et fåtall rabiesfrie land.) (land med overgangstiltak i følge Forskrift om dyrehelsemessige betingelser for ikke-kommersiell transport av kjæledyr (FOR-2004-07-01-1105)

<sup>2.</sup> Hvor stor vil sannsynligheten være for at en valp/kattunge med rabiessmitte vil bli innført til Norge hvis vi i tillegg tillater import av uvaksinerte dyr yngre enn 3 mnd fra følgende land?:

a. Danmark og Finland

b. EØS-land som Sverige tillater import av yngre dyr fra, dvs. land uten tilfeller av rabies de to siste årene i følge OIE (det vil si med unntak av flaggermus-rabies)

c. Alle EØS-land

<sup>3.</sup> Hvor stor er sannsynligheten for at en hund/katt med rabiessmitte blir innført til Norge fra EØS land gjennom dyr som både er identifisert, vaksinert og har gyldig serologitest?

<sup>4.</sup> Hvor stor er sannsynligheten for introduksjon av rabiessmitte med ville dyr som fritt passerer grensen? (kvalitativ vurdering)

#### Regulations

WHO defines a rabies-free area as one in which an effective import policy is implemented and, in the presence of adequate disease surveillance, no case of indigenously acquired rabies infection has been confirmed in humans or any animal species at any time during the previous 2 years. Conversely, an area can be considered to be rabies-infected if an indigenously acquired rabies infection has been confirmed in humans or any animal at any time during the previous two years (WHO Expert Committee on Rabies 1992).

However, according to the International Office of Epizootics (OIE) (<a href="www.oie.int">www.oie.int</a>), a country is considered free from rabies when all the following criteria are fulfilled: 1- the disease is notifiable:

- 2- an effective system of disease surveillance is operational;
- 3- all regulatory measures for the prevention and control of rabies have been implemented, including effective importation procedures;
- 4- no case of indigenously acquired rabies infection has been confirmed in man or any animal species during the past 2 years; however, this status would not be affected by the isolation of a European Bat *Lyssavirus* (EBLV1 or EBLV2);
- 5- no imported case in carnivores has been confirmed outside a quarantine station for the past 6 months.

The difference between these two definitions mainly concerns the inclusion or exclusion of European Bat *Lyssavirus*, which has regularly been recorded in Europe since the 1980s. The two definitions of rabies-free areas by WHO and OIE cannot at present be combined. As rabies has not been detected in bats in Norway, the disadvantage of using the WHO definition of rabies-free areas or countries, which does not exclude those where bat rabies has been detected, is of minor importance for the purposes of this document.

Mainland Norway is a rabies-free area. Of the countries bordering Norway, Russia is considered as a high-risk country for occurrence of rabies, while Sweden is defined as a rabies-free country (www.sjv.se). The last case of rabies in Finland was on 11 June 2003, in a two-year-old horse imported from a Baltic country. Rabies occurs in Finland's neighbouring areas in the Baltic States and Russia. The Finnish Ministry of Agriculture and Forestry recommends that people travelling overseas ensure the appropriate legally-required rabies vaccinations for their dogs and cats. Rabies vaccines are also recommended for horses travelling to and from the areas in question (http://www.mmm.fi/el/julk/pdf/Import%20of%20pets%203.7.2004.pdf).

The European Union aims for a common legislation with regard to health and animal health requirements for the transport of pet animals (<a href="http://europa.eu.int/eurlex/en/consleg/pdf/2003/en\_2003R0998\_do\_001.pdf">http://europa.eu.int/eurlex/en/consleg/pdf/2003/en\_2003R0998\_do\_001.pdf</a>). Article 5 (2) of the new Pet Regulation, (2003/998/EF) on the animal health requirements applicable to the non-commercial movement of pet animals and amending Council Directive 92/65/EEC provides that:

"Member States may authorise the movement of animals listed in parts A and B of Annex I which are under three months old and unvaccinated, if they are accompanied by a passport and have stayed in the place in which they were born since birth without contact with wild animals likely to have been exposed to the infection or are accompanied by their mothers on whom they are still dependent".

Furthermore, Decision 2004/839/EC provides:

"Member States may authorise the introduction onto their territory of dogs and cats less than three months of age and not vaccinated against rabies from third countries listed respectively in part B and C of Annex II to Regulation (EC) No 998/2003 under conditions at least equivalent to those laid down in Article 5(2) of that Regulation."

The importation of dogs and cats younger than three months not vaccinated against rabies is formally regulated similarly in Norway and Sweden (2003/998/EF). However, Norway has maintained a more restrictive policy than Sweden for the importation of dogs and cats not vaccinated against rabies. Until recently, the importation of non-rabies-vaccinated dogs and cats (< 3 months) to Norway was restricted to rabies-free countries comprising Sweden, Australia, New Zealand, the United Kingdom, Ireland, Mauritius, and Hawaii.

The Swedish Board of Agriculture allows the importation of dogs and cats younger than three months not vaccinated against rabies from certain countries considered as free from rabies (http://www.sjv.se/amnesomraden/djurveterinar/inutforselavlevandedjur/sammanfattningreglerforinforselavsallskapsdjur.4.7502f61001ea08a0c7fff49990.html#Text10. For list of rabies-free countries

http://www.sjv.se/download/18.17e53c910471ed6a6a80001085/Rabiesfria%20l%E4nder%20enl%20OI E%201a%20kvartalet%202004%2016%20juni%2005%20SVE.doc).

The importation/exportation of dogs and cats between Norway and Sweden takes place freely, which makes such differences in implementation problematic.

#### Importation of dogs and cats

According to the Norwegian Food Safety Authority, approximately 25,000 pets, mostly dogs, are at present introduced to Norway every year from countries other than Sweden (Arild Pettersen, personal communication 2005). These consist of Norwegian pets returning to Norway as well as foreign pets entering Norway for a period or permanently. Denmark, Germany and Finland are considered the main countries of origin. There are no complete data about how many are permanently imported. However, the Norwegian Kennel Club registered 1057 imported dogs in 2000. The countries of origin were Sweden (748), Denmark (43), Finland (45) and Great Britain (87). In 2004, the corresponding number was 1250 (Arild Pettersen, personal communication 2005).

Pets originating outside the EEA and certain third countries (see Appendix A) can be imported with quarantine. The number of cats and dogs kept in the quarantine system during the last 5 years in Norway ranged between 70-154 (Table 1). Based on the new Pet Regulation, which has been operational in Norway since 03.07.2004, it is also possible to import dogs and cats from countries that are not recognized as rabies-free. The number of applications for importation of unvaccinated dogs and cats from countries not considered as rabies-free has increased.

Table 1- the number of cats and dogs in quarantine system in Norway 2000-2004 (Arild Pettersen, Norwegian Food Safety Authority).

Year	Dogs	Cats
2000	42	28
2001	90	37
2002	63	52
2003	88	66
2004	68	40

#### **Aetiology**

Taxonomically, rabies and rabies-related viruses comprise the genus *Lyssavirus* in the family of *Rhabdoviridae* (Brown *et al.* 1979). Of the other six rabies-related viruses, all but Lagos bat virus have caused fatal encephalitis in people. *Lyssavirus*es are genetically related viruses, adapted for replication in the mammalian central nervous system (Bahloul *et al.* 2000). The genus has seven recognised genotypes (Gt) (Amengual *et al.* 1997;Bourhy *et al.* 1992;Bourhy *et al.* 1993;Bourhy *et al.* 1999;Gould *et al.* 1998), but the number of genotypes is likely to increase (Kuzmin *et al.* 2005):

- -Genotype 1 include the classical rabies virus (RV) strains,
- -Genotype 2-7 comprises the rabies-related viruses, described more specifically as follows:
  - -Lagos bat virus (LBV), (Gt2)
  - -Mokola (MOK) virus, (Gt3)
  - -Duvenhage virus, (Gt4)
  - -European bat lyssavirus 1 (EBLV-1), (Gt5)
  - -European bat lyssavirus 2 (EBLV-2), (Gt6)
  - -Australian bat lyssavirus (ABLV), (Gt7).

The reservoir of classical rabies virus is mammals, the particular species differing with geographical area. Mokola virus also has mammals as its reservoir, mainly cats, but is localised in Southern Africa. The other genotypes have different species of bats (Order *Chiroptera*) as reservoirs (Warrell and Warrell 2004), but in rare circumstances may induce spill-over infections to terrestrial mammals

including domestic livestock, wildlife and man. Although spill-over infections have occurred, there is, as yet, no evidence that these viruses have adapted to a new host (Fooks *et al.* 2003). Rabies virus has a linear, single-stranded, negative sense RNA genome. The genome encodes five viral proteins as follows:

- the N gene encodes the nucleoprotein that encapsulates the genomic RNA;
- the P gene, encodes phosphoprotein which has an important function in transcription and replication, and interactions with the cellular protein components during axoplasmic transport;
- the M gene encodes for the matrix protein;
- the G gene encodes the single surface glycoprotein (glycoprotein G) that mediates receptor recognition and fusion of the viral envelope with the cell membrane, and which induces neutralizing antibodies;
- the L gene encodes the viral RNA dependent RNA polymerase (Wunner et al. 1988).

The virus particle has a bullet shaped structure of about 75 nm by 200 nm with a helical nucleocapsid surrounded by matrix protein, and an outer envelope acquired through the budding process. Uptake of the virus in a host cell occurs as fusion of the viral envelope with the cell membrane following recognition of several possible cellular receptors such as the nicotinic acetylcholine receptor and the low-affinity nerve-growth-factor receptors (Hemachudha *et al.* 2002;Tuffereau *et al.* 2001).

#### Clinical appearance

The incubation period is usually between 14-90 days, but may vary from a week to up to one year, depending on viral strain and dose, host species, and site of inoculation (Anonymous 1991). Animal and human rabies have several similar clinical features. There is a prodromal phase prior to the clinical disease that in animals may be overlooked or is recalled only in retrospect. Two clinical forms of the disease are recognized; the excitatory or "furious" form with hydrophobia, which continues for a few days until the patient lapses into coma and dies, and the paralytic or "dumb" form, which manifest itself as depression and paralysis followed by a coma. In the stages of excitation, many animals become aggressive. They frequently snap at imaginary objects and may attempt to bite any animal or human that approaches. Within a short time, these signs give way to those of the final stage, which usually lasts for only a day or two and ends in death (Anonymous 1991).

#### **Diagnosis**

The immunofluorescent antibody (IFA) test is the technique most frequently used to diagnose rabies, and is recommended by both WHO and OIE. The test requires brain tissue from the animal suspected of being rabid (Kaplan *et al.* 1986) and thus, the test can only be performed *post-mortem*. The rabies virus RNA in brain tissue, in the saliva and the cerebrospinal fluid (CSF) of infected individuals can be amplified by reverse transcriptase polymerase chain reaction (RT-PCR) (Wacharapluesadee and Hemachudha 2001; Wacharapluesadee and Hemachudha 2002). This method reduces the diagnosis time to a few hours. RT-PCR can confirm IFA results and can detect rabies virus in a greater variety of samples, some of which need not require autopsy.

#### Disease transmission and reservoirs

Rabies virus infects warm-blooded animals, although different animal species show different susceptibilities. The probability of introducing rabies in meat or meat products is considered to be negligible (Anonymous 1991). The probablity of rabies acquisition after contact with a rabid animal is at least 50 times higher after a bite than with scratches (5-80% vs 0.1-1.0%) (Hattwick 1974). Rabies virus in an animal's saliva can infect across mucosal membranes or through skin lesions. Intact skin is protective, but minute lesions caused by bats may result in infection (Warrell and Warrell 2004). In countries in which rabies is endemic, the disease is maintained by two interrelated ecological niches: an urban niche limited to stray dogs, and a sylvatic (wildlife) niche, which varies according to different regions of the world (Kaplan *et al.* 1986). The number of cases reported in 2003 and 2004 in Europe in different animal species is reported in Appendix B.

#### Sylvatic (wildlife) rabies

The main wildlife reservoir and vector of rabies in Europe is the red fox (*Vulpes vulpes*) followed by the raccoon dog (*Nyctereutes procyonoides*) in Central and Baltic Europe (Cliquet and Picard-Meyer 2004). The raccoon dog is considered an important vector in Poland and the Baltic countries (Bourhy *et al.* 1999). Also the Russian wolf population is regularly infected with rabies virus (Cherkasskiy 1988). The incidence of rabies in foxes shows a peak every 2-4 years and a seasonal increase in the incidence in regions with fox-mediated rabies may be due to an increase in the contact rate in the population due to the dispersal of young foxes born in spring (Muller *et al.* 1998). Sporadic cases occur in unvaccinated dogs and cats (in about equal proportions) that come into contact with infected wild animals.

In the Arctic, circumpolar region, the major reservoir of rabies is the Arctic fox (*Alopex lagopus*) (Johnson and Fong 1992). However, this virus variant has also been found in the red fox (*Vulpes vulpes*), raccoon dog (*Nyctereutes procyonoides*), skunk (*Meohitis mephitis*) and wolf (*Canis lupus*) in sub-Arctic areas (Nyberg *et al.* 1992;Selimov *et al.* 1994;Webster *et al.* 1986). As with other variants of rabies virus, untreated infections are fatal to humans (Kuzmin 1999).

#### Urban rabies

Urban rabies has a transmission cycle sustained principally in stray dogs and occurs in communities where there are a high proportion of unvaccinated and stray dogs. Urban rabies has been virtually eliminated from Europe and North America. Dogs may spread the disease to new areas. Other species, including cats, do not contribute significantly to the perpetuation of urban transmission cycles.

Turkey is the only European country in which the domestic dog is a main vector of rabies. Spill-over from the domestic dog to the fox in Turkey has been indicated by studies of virus isolates which suggest that there has been transmission of virus between these two species (Johnson *et al.* 2003).

#### Bat rabies

The first case of bat rabies in Europe was diagnosed in 1954 and the virus isolate was referred to as European bat lyssavirus (EBLV). Since then, EBLV-1 and EBLV-2 have been detected in several parts of Europe (Cliquet and Picard-Meyer 2004). Since 1977, four human deaths from EBLV infection have been reported. None of them had a record of prophylactic rabies immunization. Only fragmentary data exist about the effectiveness of current rabies vaccines in cross-protection against EBLVs. It is clear that EBLV in bats cannot be eliminated by using conventional strategies similar to the control programmes, based on vaccine baits, used for fox rabies in Europe. Due to the protected status of bats in Europe, the knowledge of EBLV prevalence and epidemiology is limited. It is possible that EBLV is under-reported and that the recorded cases of EBLV represent only a small proportion of the actual number of infected bats (Fooks *et al.* 2003). Information on the pathogenesis of lyssaviruses in bats is scarce. However, in general, mortality in bats infected *via* a natural route appears to be low, and sero-conversion occurs in many of those that survive (McColl *et al.* 2000).

Of the 34 bat species recognised in Europe, EBLV has been found in 13 (Brass 1994). *Eptesicus serotinus* (sørflaggermus) appears to be the principal reservoir for EBLV1 and *Myotis dasycneme* (damflaggermus) and *M. daubentonii* (vannflaggermus) the reservoirs for EBLV2 (Amengual *et al.* 1997). There are two different genetic lineages of EBLV1; EBLV1a has an east-west occurrence while EBLV1b has a north-south occurrence. On Prince Edward Island, Canada it has been tentatively suggested that transmission to, and restricted establishment of bat rabies in, a fox population has occurred (Amengual *et al.* 1997).

#### Vaccination and serological tests

The control of urban rabies in endemic areas mainly depends on the prevention of infection in dogs and cats by vaccination. The conventional vaccines currently used for the vaccination of humans and domestic animals are derived from classical rabies virus (genotype 1). The vaccines contain inactivated virus produced from cell cultures. These vaccines give good protection against classical rabies virus (Lodmell *et al.* 1995), but the protection against other genotypes is uncertain (Herzog *et al.* 1991;Perrin *et al.* 1991).

The acquired humoral response induced by rabies vaccination may neutralize the rabies virus. Neutralizing antibodies bind to the virus surface glycoprotein G and interfere with the infection of a target cell (Cox 1982). In Europe, serological tests that are used to evaluate the efficacy of vaccination of dogs and cats are conducted by laboratories which have been approved by one of three competent authorities, i. e. the Brussels European Commission, the UK Veterinary Authorities, or the Scandinavian Veterinary Authorities (Cliquet et al. 2003). Two different neutralization tests are used; the rapid fluorescent focus inhibition test (RFFIT) (Smith et al. 1973; Zalan et al. 1979) and the fluorescent antibody virus neutralization (FAVN) test (Briggs et al. 1998; Cliquet et al. 1998). The titre of the serum is measured by calculating the dilution of serum at which 50% of a constant viral dose on a given type of cell culture is neutralized. The minimum protective antibody level is suggested to be a titre of 0.5 IU/ml serum (Tuffereau et al. 2001; WHO Expert Committee on Rabies 1992). Above this threshold the rabies virus is neutralized.

#### Eradication in wild carnivores

Bait vaccines based on replicating vaccine agent, (attenuated virus and recombinant vaccinia virus expressing parts of the rabies virus genome), have been used to immunize wild carnivores. Both types of vaccines have been used with success in Western and Central Europe to reduce and ultimately eliminate rabies in the wild fox population (Brochier 2001; Selhorst *et al.* 2005).

#### PROBABILITY OF RABIES ENTRY THROUGH WILD ANIMALS THAT FREELY CROSS THE BORDER

In temperate regions of the world, rabies in wildlife is more common than urban rabies (see Appendix B). In tropical countries, urban rabies is common, but the occurrence of wildlife rabies may not have been studied or assessed in detail.

Introduction of rabies to Norway by a wild animal does not necessary imply the establishment of rabies in the Norwegian wild animal population. The density, population dynamics, migration, social behaviour, and susceptibility of the particular wild animal species are among the many factors that have implications for the further transmission and establishment of the infection. The potential implications of these factors are not discussed further.

In a recent Master of Science thesis, published by the Norwegian University of Science and Technology (NTNU), the possibility of introduction of sylvatic rabies to Norway is discussed (Willa Hansen 2005). Introduction of rabies to mainland Norway by Arctic fox, red fox, raccoon dog and wolf is considered improbable. Due to the geographical separation of Norway from areas where non-bat wildlife rabies is enzootic, the long-distance dispersal of wild carnivore species infected with rabies to Norway is unlikely to occur.

The red fox and raccoon dog are the main vectors for rabies in Central- and East-Europe. Spill-over infections to other wild carnivores such as wolves happen sporadically. Both the red fox and wolves can be long-distance wanderers. However, potentially rabid animals would then be approaching Norway from southeast and Finland will be a buffer zone. The lack of occurrence of rabies in Finland, although it is close to the Baltic countries that have a relatively high prevalence of rabies, indicates that such long-distance transport is not a common occurrence.

The principal host for Arctic rabies is the Arctic fox, although this virus variant may cause spill-over infection and possible epidemics in other carnivore species, such as the red fox and the raccoon dog (Mørk and Prestrud 2004;Nyberg *et al.* 1992). The population of Arctic foxes in Finland/Sweden/Norway is estimated to be approximately 120 individuals. In Norway, this population is found in small isolated groups. The Russian regions Arkangelsk and Nenets, east of the White Sea (Kvitsjøen), have Arctic fox populations with endemic rabies. As the White Sea freezes during the winter, it is possible for carnivores to cross it for travelling westwards. It is possible that this was the origin of the rabies epidemics on the Kola Peninsula in the late 1980s. Between 1987-89 rabies was detected in the Kola Peninsula in 20 red foxes, 6 Arctic foxes, 4 dogs, 1 wolverine and 1 mink. One of the rabid red foxes was found in the Petchenga-district that borders Norway and Finland (Mørk 2001). As the Arctic fox tends to avoid forested areas, and this occurs along the Russian, Finish and Norwegian borders, forestation could be a barrier for further migration (Willa Hansen 2005).

Wolves may migrate long distances but are not considered an independent rabies reservoir in areas close to Norway. Infections in wolves have usually been considered as spill-over from infections in red fox or Arctic fox (Mørk 2001). In a review of attacks by wolves on humans worldwide that have been documented throughout history, the majority appear to concern rabid wolves (Linnell and Bjerke 2002). However, most of these incidents documented from Europe are from previous centuries. If the Scandinavian wolf population were to be strengthened by the intentional introduction of wolves from other areas, the use of quarantine and possibly vaccination of those wolves could reduce the probability of introducing rabies.

The probability of introducing rabies via bats may be higher, since bats may migrate over long distances. The prevalence of rabies in bats is uncertain, because most insectivorous bat species in Europe are protected, and most examinations have been performed in animals found dead or diseased. In general, mortality in bats infected *via* a natural route appears to be low and EBLV may thus have a very low prevalence (<1%) in bat populations without being detected (Brookes *et al.* 2005;McColl *et al.* 2000). It is possible that EBLV is under-reported and that the recorded cases of EBLV represent only a small proportion of the actual number of infected bats. Some of the bat species found in Norway, trollflaggermus (*Pipistrellus nathusii*), dvergflaggermus (*Pipistrellus pygmaeus*), skimmelflaggermus (*Vespertilio murinus*), storflaggermus (*Nyctalus noctula*) and vannflaggermus (*Myotis daubentonii*) may migrate over long distances (Willa Hansen 2005) and thus come in contact with Central-European populations. EBLV may also be transported with bat species, which expand their northern distribution borders, due to favourable environmental changes. Although spill-over of EBLV infections to other species, including humans, has occurred, there has been no evidence that these viruses have adapted to non-bat hosts (Fooks *et al.* 2003).

In summary, the probability of introducing rabies via wild carnivores is considered very low because of the geographical separation of Norway from the epidemic areas. The probability of introduction through insectivorous bats is difficult to estimate and could be higher. However, there is little contact between insectivorous bats and domestic animals or humans.

#### PROBABILITY OF RABIES ENTRY THROUGH DOGS AND CATS

#### Methodology

To quantify the probability of introducing rabies to Norway through the importation of dogs and cats, a simulation model was built. This model uses Monte Carlo simulation, which allows the inclusion of a number of elements of uncertainty, for example the level of underreporting of rabies in the exporting country and the compliance of imported dogs and cats with existing regulations. Details related to the model and the results are presented in the report entitled "Probability of rabies entry to Norway through dogs and cats. Quantitative model, description and results", by DVM, PhD Helga R. Høgåsen, at the National Veterinary Institute, 30.06.2005, and the main elements are summarized below.

The model does not distinguish between dogs and cats, assuming that the probabilities are of the same order of magnitude in both species.

#### The model estimates:

- The number of rabies infected dogs and cats imported each year
- The probability that at least one rabies infected dog or cat will be imported each year or each ten-year period
- -The expected number of years between the importations of each rabies infected dog or cat.

The proportion of dogs and cats that carry the rabies virus in the exporting country, termed the prevalence of infection in the exporting country, is first estimated. The number of reported cases in 2003 and 2004, as reported to the WHO-collaborating centre for rabies surveillance and research (http://www.who-rabies-bulletin.org/index.html), has been used as main input. It is assumed that the actual number of rabies cases is probably 50 % higher than the reported number, and could be as much as five times higher. In the absence of reported cases, a minimum level, which is called the "detection level" for rabies, is assumed, based on geographical situation and reported cases in other countries. The lowest prevalence used in the model was 0.005 per million, accounting for the

lowest probability estimates. The total pet population is estimated from the human population, assuming that there is approximately one dog or cat per every five person.

The number of reported rabies cases in domestic animals and wild fauna differs significantly between the EEA countries (see Appendix B). Therefore, the countries have been classified into four risk groups, based on the number of reported cases as well as on the proximity to areas in which rabies is endemic. The definitions of the country groups are as follows:

**Group 1** - No rabies cases reported during the last two years (except in bats), AND negligible probability of importation of rabies cases from close areas

Cyprus UK
Iceland Sweden
Ireland Denmark

Group 2 - No rabies cases reported during the last two years (except in bats or in imported

ItalyLiechtensteinFranceLuxembourgSpainNetherlandsGreeceFinlandPortugalMalta

Belgium

Group 3 - Low-prevalence endemic area, with few rabies cases reported

Germany Slovenia

Austria Czech Republic

Group 4 - Large number of rabies cases reported in domestic and wild animals

Slovak Republic Latvia
Poland Estonia
Lithuania Hungary

Each of these groups is considered as a homogenous entity, from which a given number of dogs and cats are imported. From each country group, the probability associated with two categories of importation is considered: the importation of young (<3 months) unvaccinated dogs or cats, and the importation of vaccinated and tested dogs and cats.

For the importation of vaccinated and tested dogs and cats, the probability is reduced by the effect of vaccination and testing. However, the possibility that imported individuals are not really vaccinated and tested is also considered and included in the model. Young unvaccinated dogs or cats are considered to have no particular protection.

Since it is difficult to predict how many dogs and cats of the two categories will be imported from the different country groups, six different scenarios are considered for each country group: the importation of 100, 1000 or 10,000 unvaccinated young (<3 month) dogs and cats, and the importation of 100, 1000 or 10,000 vaccinated and tested dogs and cats. Future monitoring of the importation of dogs and cats may allow better assessment of which scenarios are most appropriate. The total probability for Norway can be deduced by adding the different probability in the four country groups and two categories of imports.

#### Results

A mathematical model is always a simplification of reality, and the results are therefore valid only as long as the assumptions made remain valid. The present results are based on the current situation of rabies, as reported by international organisations. If major changes in the rabies situation, or in our knowledge about the disease, occur, the conclusions need to be re-evaluated.

A model based on Monte Carlo simulation produces a range of values that could occur in a real life situation. These values can be reported as a mean (average of all values), median (middle value),

mode (the value occurring most frequently), and 95% confidence interval (CI) (interval containing 95% of the values). Main results for the different scenarios are presented here, and discussed in the next section. Details are reported in the appended document.

The term "very rare" is used when the value occurs in less than 1% of the situations, and the term "rare" when it occurs in less than 5% of situations.

#### Number of infected dogs and cats imported each year

The number of infected dogs and cats which may be imported when importing up to 10,000 dogs and cats, was in most scenarios found to be zero in all iterations.

A very rare occurrence of one infected pet was found in the following scenarios:

- Importation of 10 000 unvaccinated or vaccinated dogs and cats from Group 3 countries
- Importation of 100 or 1000 unvaccinated or vaccinated dogs and cats from Group 4 countries A rare occurrence of one infected pet, and very rare occurrence of two infected dogs or cats, were found in the following scenario:
  - Importation of 10 000 dogs and cats from Group 4 countries

Table 2: Comparison of mean values of occurrence of infected dogs and cats, by country group and number of dogs and cats imported annually.

Number of animals imported/ye	ar	100	1 000	10 000
	Group 1	0	0	0
Vaccinated and tested	Group 2	0	0	0
vaccinated and tested	Group 3	0	0	0.0002
	Group 4	0.0002	0.002	0.03
	Group 1	0	0	0
Unvaccinated puppies/kittens	Group 2	0	0	0
onvaccinated pupples/kitteris	Group 3	0	0	0.0004
	Group 4	0.0008	0.005	0.05

#### Yearly probability of importing at least one infected pet

This value indicates how likely it is that rabies will be imported in a given year, through one or more infected dogs or cats.

Table 3: Comparison of mean values of the yearly probability of infected dogs and cats, by country group and number of dogs and cats imported annually

and number of dogs and dats imported annually									
Number of animals imported/ye	ar	100	1 000	10 000					
	Group 1	0.000009%	0.00009%	0.0009%					
Vaccinated and tested	Group 2	0.000026%	0.00026%	0.0026%					
vaccinated and tested	Group 3	0.00012%	0.0012%	0.012%					
	Group 4	0.026%	0.26%	2.6%					
	Group 1	0.00005%	0.0005%	0.005%					
Unvaccinated puppies/kittens	Group 2	0.00011%	0.0011%	0.011%					
onvaccinated pupples/kitteris	Group 3	0.0005%	0.005%	0.05%					
	Group 4	0.052%	0.52%	5.1%					

As shown in table 3, the probability is proportional to the number of imported dogs and cats. When the number of dogs and cats increases by a factor of ten (from 100 to 1000, or from 1000 to 10 000), the probability also increases by a factor of ten.

There is a major difference in probability between importing cats and dogs from countries in Groups 1 to 3 and from Group 4 countries. Using Group 1 countries as a reference, the probability of importing unvaccinated dogs and cats increases by a factor of two if the dogs and cats are imported from Group 2 countries, a factor of ten if they are imported from Group 3 countries, and notably a factor of 1000 if they are imported from Group 4 countries. For vaccinated adults, the probability

increases by a factor of three if the dogs and cats are imported from Group 2 countries, a factor of thirteen if they are imported from Group 3 countries, and a factor of 3000 if they are imported from Group 4 countries.

The probability of importing rabies through unvaccinated young dogs and cats is 2-5 times higher than the probability of importing vaccinated and tested adults. This result is based on the assumption that only a fraction of the dogs and cats imported as vaccinated and tested, are actually vaccinated and tested. Moreover, it is based on the assumption that a large proportion of the dog and cat population in the country of origin is vaccinated, since these countries have declared to the OIE that a mandatory vaccination programme is in place.

For Group 4 countries, the 95% confidence intervals for the probability of importing at least one infected pet when importing 1000 unvaccinated young dogs and cats and 1000 vaccinated adults are respectively 0.3-0.9% and 0.1-0.6%. When importing 10 000 dogs and cats, corresponding values are 3-9% and 1-6%.

#### Ten-year probability of importing at least one infected pet

This value indicates how likely it is that rabies would be imported in a ten-year period. It is approximately ten times higher than the yearly probability, as long as the values are small enough. Average values obtained during simulation are listed in table 4.

Table 4: Comparison of mean values of the ten-year probability of infected dogs and cats, by

country group and number of dogs and cats imported annually

y group and number or dogs and eats imported annually										
Number of animals imported /y	ear	100	1 000	10 000						
	Group 1	0.00009%	0.0009%	0.009%						
Vaccinated and tested	Group 2	0.0026%	0.0026%	0.026%						
vaccinated and tested	Group 3	0.0012%	0.012%	0.12%						
	Group 4	0.26%	2.6%	22.2%						
	Group 1	0.0005%	0.005%	0.05%						
Unvaccinated puppies/kittens	Group 2	0.0011%	0.011%	0.11%						
Unvaccinated pupples/kittens	Group 3	0.005%	0.05%	0.5%						
	Group 4	0.52%	5.1%	39.9%						

The ten-year probability of introducing rabies is as high as 5.1% (95% CI of 2.8-8.8%) if only 1000 unvaccinated dogs and cats are imported each year from Group 4 countries. As long as the number of imported dogs and cats is lower than 100 per year, the ten-year probability remains lower than 1% for dogs and cats imported from Group 4 countries, whether vaccinated or not.

#### Expected number of years between the importation of an infected dog or cat

This value indicates how many years will, on average, pass between the successive importations of two infected dogs or cats, provided the situation remained constant. It is a value that is often easier to understand and relate to than probabilities, but since disease situations or importation numbers rarely remain constant over a large number of years, it remains theoretical. Average values obtained are shown in table 5.

Table 5: Comparison of mean values of expected number of years between importation of 2 infected cats or dogs, by country group and number of dogs and cats imported annually

Number of animals imported/year	100	1 000	10 000	
Vaccinated and tested	Group 1	15 486 757	1 548 676	154 868
	Group 2	5 612 991	561 299	56 130
	Group 3	1 169 204	116 920	11 692
	Group 4	5 766	577	58
	Group 1	2 000 000	200 000	20 000
Unvaccinated puppies/kittens	Group 2	960 014	96 001	9 600
Onvaccinated pupples/kitteris	Group 3	200 000	20 000	2 000
	Group 4	2 119	212	21

These results indicate that the importation of rabies through dogs and cats remains a rare event in all of the scenarios considered. Even if 10 000 unvaccinated dogs and cats were imported from Group 4 countries each year, 21 years could still be expected to pass between each occasion that an infected pet was imported. The 95% confidence interval for this value is 11-35 years, i.e. we are 95% confident that the expected value is between 11 and 35 years. If the dogs and cats are vaccinated, 58 years could be expected to pass between the importations of each infected pet, with a 95% confidence interval of 16-194 years.

#### Effect of uncertain values used in the model

A Monte Carlo simulation model allows the evaluation of the impact of the uncertain variables used during simulation, through a sensitivity analysis. This is useful to decide whether acquisition of more knowledge about these variables would reduce the uncertainty of the result significantly or not. It also indicates whether management options directed towards these variables might have a significant impact on the probability.

In this simulation, the greatest impact was shown to be associated with the proportion of imported dogs and cats that were actually vaccinated. Controls at the border cannot ensure that 100% of imported dogs and cats are vaccinated, even if the regulation requires it. This is particularly true for dogs and cats arriving by car. Therefore, although vaccines and tests themselves are efficient, the protective effect of requiring vaccination and testing is weakened by the fact that a number of animals might not be vaccinated. A conservative estimate was used in the model, assuming that of the dogs and cats that are imported as "vaccinated and tested", most probably 89% were actually vaccinated. Since this value is uncertain, it was allowed to decrease down to 56% and increase up to 100%, with the values becoming less and less probable (triangular distribution). To test the effect of this value, the importation of vaccinated and tested dogs and cats from Group 4 countries, with either 100% vaccination coverage, or 50% vaccination coverage, was simulated. The probability of importing at least one infected pet increased by a factor of almost 30 between the 100% and 50% vaccination coverage, which illustrates that increased border controls might have a significant impact on the probability. With a 100% compliance, the yearly probability of importing rabies when importing 10 000 vaccinated and tested dogs and cats from Group 4 countries was 0.11%, with a 95% confidence interval of 0.01-0.7%. The expected number of years between the importations of rabies cases was 2955 years, with a 95% confidence interval of 143-8614.

The probability of rabies entry was directly related to the true number of cases in the exporting country. If the true number increased by a factor of ten, then the probability also increased by a factor of ten. Acquisition of more information about the level of underreporting in the various countries will reduce our uncertainty about the probability of rabies entry.

## ANSWERS TO THE QUESTIONS ASKED BY THE NORWEGIAN FOOD SAFETY AUTHORITY (MATTILSYNET)

Based on the quantitative model developed, in which countries are classified into 4 risk groups, Group 1 having the lowest incidence of rabies in dogs and cats, and Group 4 the highest, the following answers can be given:

Question 1. What is the probability that a puppy or kitten infected with rabies virus will be imported to Norway under the current regulations? (the current regulations allow import of unvaccinated animals younger than three months from a small number of rabies-free countries.)

Answer: The number of countries currently considered rabies-free and covered by the current regulations include Sweden, Australia, New Zealand, the United Kingdom, Ireland, Mauritius, Hawaii and Malta. All these were classified as Group 1 countries, except for Malta, which was considered as belonging to Group 2 due to its proximity to North Africa and its high level of tourism. The probability related to Group 2 countries was estimated to be twice as high as the probability from Group 1 countries. Nevertheless, the yearly probability that a puppy or kitten infected with rabies virus will be imported to Norway was estimated to be lower than 0.02 %, even when up to 10 000 unvaccinated puppies or kittens are imported from any one of these countries. If all were imported from the country considered representing the highest risk (Malta), the probability would be 0.011%, with a 95% confidence interval of 0.010-0.016%. The expected number of years between the importation of one infected puppy or kitten would be around 10 000 years.

Question 2. What is the probability that a puppy or kitten infected with rabies virus will be imported to Norway if we allow the importation of unvaccinated animals younger than three months from the following countries in addition to those allowed by the current regulations?

- a. Denmark and Finland
- b. EEA-countries from which Sweden allows imports, i.e. countries with no cases of rabies (with the exception of rabies in bats) in the last two years, according to International Office of Epizootics (OIE)
- c. All EEA countries

#### Answer:

2.a. Denmark was classified as belonging to risk Group 1, and Finland to Group 2. The probability related to Group 2 countries was estimated to be twice as high as the probability from Group 1 countries. Nevertheless, the yearly probability that a puppy or kitten infected with rabies virus will be imported to Norway was estimated to be lower than 0.02 %, even when up to 10 000 unvaccinated puppies or kittens are imported from any one of these countries. If all were imported from the country considered as the highest risk (Finland), the probability would be 0.011%, with a 95% confidence interval of 0.010-0.016%. The expected number of years between the importation of one infected puppy or kitten would be about 10 000 years.

2.b. The countries covered by this section of the question include, in addition to Denmark, Finland, and the countries considered in question 1, Belgium, Cyprus, Greece (including islands), The Netherlands, Italy, Luxembourg, Portugal (including islands) and Spain (excluding Ceuta and Melilla).

All these countries were classified as belonging to either Group 1 or Group 2, and the same upper limit for the probability described in the answer to 2.a. is valid. The yearly probability that a puppy or kitten infected with rabies virus will be imported to Norway was estimated to be lower than 0.02 %, even when up to 10 000 unvaccinated puppies or kittens are imported from anyone of these countries. If all were imported from the countries considered as the highest risk countries (Malta, Finland, Italy, Spain, Greece, Portugal, Belgium, Luxembourg or Netherlands), the probability would be 0.011%, with a 95% confidence interval of 0.010-0.016%. The expected number of years between the importation of one infected puppy or kitten would be around 10 000 years.

2.c. When considering the importation from all EEA countries, countries classified into Groups 3 and 4 must also be considered. There is a major difference in probability between importing dogs and

cats from countries from Groups 1 to 3 and importing dogs and cats from countries classified as belonging to Group 4. For Group 3 countries (Germany, Austria, Slovenia, Czech Republic), the probability was estimated to be ten times higher than the probability for Group 1 countries and five times higher than for Group 2 countries. For Group 4 countries (Latvia, Lithuania, Estonia, Poland, Hungary and Slovak Republic), the probability was estimated to be approximately one thousand times higher than the probability from Group 1 countries.

The yearly probability that a puppy or kitten infected with rabies virus will be imported to Norway from country groups 1, 2 or 3 was estimated to be lower than 0.05 %, even when up to 10 000 unvaccinated puppies or kittens are imported from any one of these countries. If all were imported from the countries considered as the highest risk (Group 3 countries), the probability would be 0.05%. The expected number of years between the importation of one infected puppy or kitten would be around 2 000 years.

The yearly probability that a puppy or kitten infected with rabies virus will be imported to Norway from a country classified in Group 4 was estimated to be 5.1 %, with a 95% confidence interval of 2-8.8%, when 10 000 unvaccinated puppies or kittens are imported. The expected number of years between the importation of one infected puppy or kitten would be 21 years, with a 95% confidence interval of 11-35 years.

The probability of rabies entry changes proportionally with the number of imported puppies or kittens. If only 1000 unvaccinated puppies or kittens are imported from Group 4 countries, the probability decreases to 0.5%, with a 95% confidence interval of 0.3-0.9%. The expected number of years between the importation of one infected puppy or kitten is 212 years, with a 95% confidence interval of 108-352 years. With only 100 animals the probability decreases to 0.05%, and the expected number of years between the importation of one infected puppy or kitten is 2119 years, with a 95% confidence interval of 1083-3516 years.

It is presently unknown where imported puppies or kittens come from, and future estimates are uncertain. The total probability for Norway would be the sum of the probabilities for the four country groups. Since the probability associated with the importation from country Group 4 is 100-1000 times higher than for the others, it will have a major impact on the final probability. Future monitoring of the country of origin of imported puppies and kittens would allow improved estimation of the associated probability of rabies entry.

The probability of introducing rabies remains below 1% per year as long as less than 1000 unvaccinated puppies or kitten are imported from Group 4 countries (with 95% confidence). In a ten-year period, the probability remains below 10%.

# Question 3. What is the probability that a dog or cat infected with rabies virus will be imported to Norway from an EEA country when the animal is both identified, vaccinated and has a valid serology test?

The answer to this question is directly dependent on which country an animal is imported from, and whether the animal is indeed vaccinated and has a valid serology test.

With a conservative approach, where we assume that most likely 89% of imported dogs or cats are actually vaccinated, the probability is shown to be 3000 times higher if the animal is imported from Group 4 countries (Latvia, Lithuania, Estonia, Poland, Hungary and Slovak Republic) as compared to Group 1 countries (Sweden, Denmark, Iceland, United Kingdom, Ireland, Cyprus). If 1000 dogs and cats are imported from Group 4 countries each year, the annual probability of introducing rabies is 0.3%, with a 95% confidence interval of 0.1-0.6%. The expected number of years between two introductions of rabies is 577, with a 95% confidence interval of 161-1938. If 1000 dogs and cats are imported from Group 1 countries each year, the annual probability of introducing rabies is 0.0001%, with a 95% confidence interval of 0.00002-0.0002%. From Group 2 countries (Finland, Belgium, Netherlands, France, Spain (excluding Melilla and Ceuta), Portugal, Greece, Italy, Liechtenstein, Luxembourg, Malta), the probability of introducing rabies when importing 1000 vaccinated and tested dogs or cats is 0.0003%, with a 95% confidence interval of 0.0001-0.001%. From Group 3 countries (Germany, Austria, Slovenia, Czech Republic), the probability of introducing rabies when importing 1000 vaccinated and tested dogs or cats is 0.001%, with a 95% confidence interval of 0.0003-0.003%.

Considering all importations, the probability of introducing rabies remains below 0.6% per year as long as less than 1000 vaccinated dogs and cats are imported from Group 4 countries (with 95% confidence). In a ten-year period, the probability remains below 6%.

Assuming full compliance, i.e. all imported dogs and cats are vaccinated and have a valid serology test, the yearly probability of importing rabies when importing 1000 dog or cats from Group 4 countries is 0.01%, with a 95% confidence interval of 0.001-0.07%. For a ten-year period, the probability is 0.1%, with a 95% confidence interval of 0.01-0.7%. The expected number of years between the importations of rabies cases is 29550 years, with a 95% confidence interval of 1428-86137.

## Question 4. What is the probability of the introduction of rabies to Norway occurring through wild animals that freely cross the border?

Due to the geographical separation of Norway from areas where non-bat wildlife rabies is enzootic, the probability and the risk of introducing rabies to Norway by long-distance dispersal of wild carnivore species, i.e. Arctic fox, red fox, raccoon dog and wolf, infected with rabies, is considered very low. Although the Arctic fox, red fox and wolves can be long-distance wanderers, the potential for rabid animals coming to Norway from the southeast, will be reduced by Finland acting as a buffer zone. The lack of occurrence of rabies in Finland, despite being close to the Baltic countries, which have a relatively high prevalence of rabies, indicates that such long-distance transport is not a common occurrence.

The Arctic fox avoids crossing forest areas and forestation in the Russian, Finish and Norwegian border areas could be a barrier for migration.

The probability of introducing rabies via bats may be higher, since bats may migrate over long distances. The prevalence of rabies in bats is uncertain, because most insectivorous bat species in Europe are protected. However, there is little natural contact between insectivorous bats and domestic animals or humans.

#### **REFERENCES**

Amengual, B., Whitby, J.E., King, A., Cobo, J.S. and Bourhy, H. (1997) Evolution of European bat lyssaviruses. J. Gen. Virol. 78 (Pt 9), 2319-2328.

Anonymous (1991) Rabies. Surveillance 18 Special Issue, 20-22.

Bahloul, C., Badrane, H., Sacramento, D., Fayaz, A., Loza-Rubio, E., Aguilar-Setien, A., Bachir, K., Bourhy, H. and Tordo, N. (2000) [Genetic diversity of Lyssavirus]. *Bulletin de la Societe de Pathologie Exotique* **93**, 181.

Bourhy, H., Kissi, B., Audry, L., Smreczak, M., Sadkowska-Todys, M., Kulonen, K., Tordo, N., Zmudzinski, J.F. and Holmes, E.C. (1999) Ecology and evolution of rabies virus in Europe. *J. Gen. Virol.* **80** (Pt 10), 2545-2557.

Bourhy, H., Kissi, B., Lafon, M., Sacramento, D. and Tordo, N. (1992) Antigenic and molecular characterization of bat rabies virus in Europe. J. Clin. Microbiol. 30, 2419-2426.

Bourhy, H., Kissi, B. and Tordo, N. (1993) Molecular diversity of the Lyssavirus genus. *Virology* **194**, 70-81.

Brass, D. A. (1994) Rabies in bats: Natural history and public health implications. Livia Press.

Briggs, D.J., Smith, J.S., Mueller, F.L., Schwenke, J., Davis, R.D., Gordon, C.R., Schweitzer, K., Orciari, L.A., Yager, P.A. and Rupprecht, C.E. (1998) A comparison of two serological methods for detecting the immune response after rabies vaccination in dogs and cats being exported to rabiesfree areas. *Biologicals* 26, 347-355.

Brochier, B., Dechamps, P., Costy, F., Hallet, L., Leuris, J., Villers, M., Peharpre, D., Mosselmans, F., Beier, R., Lecomte, L., Mullier, P., Roland, H., Bauduin, B., Kervyn, T., Renders, C., Escutenaire, S.& Pastoret, P.P. (2001) Elimination of sylvatic rabies in Belgium by oral vaccination of the Red fox (*Vulpes vulpes*). *Annales de Medecine Veterinaire* **145**, 293-305.

Brookes, S.M., Aegerter, J.N., Smith, G.C., Healy, D.M., Jolliffe, T.A., Swift, S.M., Mackie, I.J., Pritchard, J.S., Racey, P.A., Moore, N.P. and Fooks, A.R. (2005) European bat lyssavirus in Scottish bats. *Emerg. Infect. Dis.* 11, 572-578.

Brown, F., Bishop, D.H., Crick, J., Francki, R.I., Holland, J.J., Hull, R., Johnson, K., Martelli, G., Murphy, F.A., Obijeski, J.F., Peters, D., Pringle, C.R., Reichmann, M.E., Schneider, L.G., Shope, R.E., Simpson, D.I., Summers, D.F. and Wagner, R.R. (1979) Rhabdoviridae. Report of the Rhabdovirus Study Group, International Committee on Taxonomy of Viruses. *Intervirology* 12, 1-7.

Cherkasskiy, B.L. (1988) Roles of the wolf and the raccoon dog in the ecology and epidemiology of rabies in the USSR. *Rev. Infect. Dis.* **10 Suppl 4**, S634-S636.

Cliquet, F., Aubert, M. and Sagne, L. (1998) Development of a fluorescent antibody virus neutralisation test (FAVN test) for the quantitation of rabies-neutralising antibody. *J. Immunol. Methods* **212**, 79-87.

Cliquet, F. and Picard-Meyer, E. (2004) Rabies and rabies-related viruses: a modern perspective on an ancient disease. *Revue Scientifique et Technique* 23, 625-642.

Cliquet, F., Verdier, Y., Sagne, L., Aubert, M., Schereffer, J.L., Selve, M., Wasniewski, M. and Servat, A. (2003) Neutralising antibody titration in 25,000 sera of dogs and cats vaccinated against rabies in

France, in the framework of the new regulations that offer an alternative to quarantine. *Rev. Sci. Tech.* 22, 857-866.

Cox, J.H. (1982) The structural proteins of rabies virus. *Comp. Immunol. Microbiol. Infect. Dis.* **5**, 21-25.

Dreesen, D.W. (1997) A global review of rabies vaccines for human use. Vaccine 15 Suppl, S2-S6.

Fooks, A.R., Brookes, S.M., Johnson, N., McElhinney, L.M. and Hutson, A.M. (2003) European bat lyssaviruses: an emerging zoonosis. *Epidemiol. Infect.* **131**, 1029-1039.

Gould, A.R., Hyatt, A.D., Lunt, R., Kattenbelt, J.A., Hengstberger, S. and Blacksell, S.D. (1998) Characterisation of a novel lyssavirus isolated from Pteropid bats in Australia. *Virus Res.* **54**, 165-187.

Hattwick, M. (1974) Human rabies. Public Health Rev. 3, 229-274.

Hemachudha, T., Laothamatas, J. and Rupprecht, C.E. (2002) Human rabies: a disease of complex neuropathogenetic mechanisms and diagnostic challenges. *Lancet Neurol.* 1, 101-109.

Herzog, M., Fritzell, C., Lafage, M., Montano Hirose, J.A., Scott-Algara, D. and Lafon, M. (1991) T and B cell human responses to European bat lyssavirus after post-exposure rabies vaccination. *Clin. Exp. Immunol.* **85**, 224-230.

Johnson, D. H. and Fong, D. W. Epidemiology of Arctic fox rabies. Wildlife rabies control. Proceedings of the international WHO symposium on Wildlife Rabies Control. Geneva 1990 and report of the WHO Seminar on Wildlife Rabies Control. Geneva 1990. 45-49. 1992. Wells Medical Corp.

Ref Type: Conference Proceeding

Johnson, N., Black, C., Smith, J., Un, H., McElhinney, L.M., Aylan, O. and Fooks, A.R. (2003) Rabies emergence among foxes in Turkey. J. Wildl. Dis. 39, 262-270.

Kaplan, C., Turner, G. S. and Warrell, D. A. (1986) *Rabies; The Facts*. Oxford: Oxford University Press.

Kuzmin,I.V. (1999) An Arctic fox rabies virus strain as the cause of human rabies in Russian Siberia. *Arch. Virol.* **144**, 627-629.

Kuzmin,I.V., Hughes,G.J., Botvinkin,A.D., Orciari,L.A. and Rupprecht,C.E. (2005) Phylogenetic relationships of Irkut and West Caucasian bat viruses within the Lyssavirus genus and suggested quantitative criteria based on the N gene sequence for lyssavirus genotype definition. *Virus Res.* 111, 28-43.

Linnell J.D.C.and Bjerke T. Frykten for ulven. En tverrfaglig utredning. Norwegian Institute for Nature Research (NINA). 2002.

Ref Type: Report

Lodmell, D.L., Smith, J.S., Esposito, J.J. and Ewalt, L.C. (1995) Cross-protection of mice against a global spectrum of rabies virus variants. *J. Virol.* **69**, 4957-4962.

McColl, K.A., Tordo, N. and Aguilar Setien, A.A. (2000) Bat lyssavirus infections. *Revue Scientifique et Technique* 19, 177-196.

Mørk, T. and Prestrud, P. (2004) Arctic rabies-a review. Acta Vet. Scand. 45, 1-9.

Mørk, T. and Presterud, P. (2001) Rabies i arktiske områder. Aktualitet for Norge. *Nor. Vet. tidsskr.* **113**, 361-336. (In Norwegian).

Muller, W.W., Cox, J.H. and Hohnsbeen, K.P. (1998) Summary of rabies in Europe. *Rabies Bull. Eur.* **22**, 3-15.

Nyberg, M., Kulonen, K., Neuvonen, E., Ek-Kommonen, C., Nuorgam, M. and Westerling, B. (1992) An epidemic of sylvatic rabies in Finland--descriptive epidemiology and results of oral vaccination. *Acta Vet. Scand.* **33**, 43-57.

Perrin, P., Joffret, M.L., Zanetti, C., Bourhy, H., Gontier, C., Fritzell, C., Leclerc, C. and Sureau, P. (1991) Rabies-specific production of interleukin-2 by peripheral blood lymphocytes from human rabies vaccinees. *Vaccine* **9**, 549-558.

Selhorst, T., Muller, T., Schwermer, H., Ziller, M., Schluter, H., Breitenmoser, U., Muller, U., Brochier, B., Pastoret, P.P. and Mutinelli, F. (2005) Use of an area index to retrospectively analyze the elimination of fox rabies in European countries. *Environmental Management* 35, 292-302.

Selimov, M.A., Botvinkin, A.D., Khozinskii, V.V. and Gribanova, L.I. (1994) [New data on the spread of P-41-positive strains of the rabies virus in Arctic and extra-Arctic regions]. *Zhurnal Mikrobiologii*, *Epidemiologii i Immunobiologii* 53-56.

Smith, J.S., Yager, P.A. and Baer, G.M. (1973) A rapid reproducible test for determining rabies neutralizing antibody. *Bull. World Health Organ* **48**, 535-541.

Steel, J. H., Fernandez and P.J. (1991) History of rabies and global aspects. In *The natural history of rabies* ed. Beynon, P.H. and Edney, A.T.B. pp. 76-79. London: British Small Animal Veterinary association.

Tuffereau, C., Desmezieres, E., Benejean, J., Jallet, C., Flamand, A., Tordo, N. and Perrin, P. (2001) Interaction of lyssaviruses with the low-affinity nerve-growth factor receptor p75NTR. *J. Gen. Virol.* 82, 2861-2867.

Wacharapluesadee, S. and Hemachudha, T. (2001) Nucleic-acid sequence based amplification in the rapid diagnosis of rabies. *Lancet* **358**, 892-893.

Wacharapluesadee, S. and Hemachudha, T. (2002) Urine samples for rabies RNA detection in the diagnosis of rabies in humans. *Clin. Infect. Dis.* 34, 874-875.

Warrell, M.J. and Warrell, D.A. (2004) Rabies and other lyssavirus diseases. Lancet 363, 959-969.

Webster, W.A., Casey, G.A. and Charlton, K.M. (1986) Major antigenic groups of rabies virus in Canada determined by anti-nucleocapsid monoclonal antibodies. *Comp. Immunol. Microbiol. Infect. Dis* **9**, 59-69.

WHO Expert Committee on Rabies. WHO Technical Report Series 824. Eight Report. 1992. Geneva, Switzerland, WHO.

Ref Type: Report

Willa Hansen, T. Rabies, en oversikt, utbredelse og vurdering av introduksjon av sylvatisk rabies til Norge. 2005. Norsk Institute for Naturforskning.

Ref Type: Thesis/Dissertation

Wunner, W.H., Larson, J.K., Dietzschold, B. and Smith, C.L. (1988) The molecular biology of rabies viruses. *Rev. Infect. Dis* **10 Suppl 4**, S771-S784.

Zalan, E., Wilson, C. and Pukitis, D. (1979) A microtest for the quantitation of rabies virus neutralizing antibodies. *J. Biol. Stand.* 7, 213-220.

#### **SCIENTIFIC PANEL MEMBERS**

#### Panel on Biological Hazards

Hilde Kruse (chair), Georg Kapperud, Jørgen Lassen, Bjørn Tore Lunestad, Truls Nesbakken, Espen Rimstad, Lucy Robertson, Eystein Skjerve, Yngvild Wasteson.

#### **ACKNOWLEDGMENTS**

This project benefited from information from many individuals. We would like to thank the following individuals for providing scientific input:

Dr. Carsten J Potzsch, WHO-collaborating centre for rabies surveillance and research Arild Pettersen, Norwegian Food Safety Authority (Mattilsynet)
Astrid Indrebø, Norwegian Kennel Club (Norsk Kennelklubb).

The Chair and members of the Working Group on this risk assessment are acknowledged for their valuable contributions to this mandate. The members of the Working Group have been: Espen Rimstad (chair), Eystein Skjerve, and Helga Høgåsen.

Scientific coordinator from the Secretariat; Siamak Yazdankhah.

Appendix A - List of third countries from which the importation to Norway of dogs, cats and ferrets is allowed without quarantine.

Vedlegg II del B avsnitt 2 og del C til forordning (EF) nr. 998/2003 - tredjeland som hund, katt og ilder kan innføres fra til Norge uten karantene.

ISO-kode	es fra til Norge uten karantene.  Land	Merknader
DEL B avsnitt 2	Lunu	17267 Kittuter
	Andorra	
AD	Sveits	
CH	Island	
IS		
LI	Liechtenstein	
MC	Monaco	
SM	San Marino	
VA	Vatikanstaten	
DEL C		
AC	Ascension	
AG	Antigua og Barbuda	
AN	De nederlandske Antillene	
AU	Australia	
$A\overline{W}$	Aruba	
BB	Barbados	
ВН	Bahrain	
BM	Bermuda	
CA	Canada	
FJ	Fiji	
FK	Falklandsøyene	
HR	Kroatia	
JM	Jamaica	
JP	Japan	
KN	Saint Christopher og Nevis	
KY	Caymanøyene	
MS	Moniserrai	
MU	Mauritius	
NC	Ny Cale donia	
NZ	New Zealand	
PF	Fransk Polynesia	
PM	Saint Pierre og Miquelon	
SG	Singapore	
SH	Sankt Helena	
US	USA	
VC	Sankt Vincent og Grenadinene	
VU	Vanuatu	
WF	Wallis- og Fulunaøyene	
YT	Mayotte	

Appendix B. Country summaries of reported rabies cases in Europe in 2003 and 2004

Country				Domestic animals Wildlife																					
Name	Code	EEA	gob	cat	cattle	ednine	goat sheep	pig	stray dog	other	subtotal	fox	racoon dog	racoon	wolf	badger	marten	other mustelides	other camivores	wild boar	roe deer	red deer	fallow deer	other	subtotal
ALBANIA	ALB	0	0	0	2	0	0	0	0	0	2	2	0	0	1	0	0	0	0	0	0	0	0	0	3
AUSTRIA	AUT	1	0	0	0	1	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	1
BELARUS	BLR	0	160	147	75	8	1	0	0	1	392	733	116	0	11	19	8	0	0	0	0	0	0	9	896
BELGIUM	BEL	1	٠ 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
BOSNIA A HERCEGOVINA	BIH	0	11	8	10	0	2	0	0	0	31	97	0	0	0	0	0	0	0	0	0	0	0	0	97
BULGARIA	BGR	0	2	2	2	1	4	0	0	0	11	17	0	0	2	0	0	0	0	0	0	0	0	0	19
CROATIA	HRV	0	34	29	3	2	5	0	0	3	76	1045	0	0	0	7	0	3	0	0	0	0	0	6	1061
CYPRUS	CYP	1	٠ 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
CZECH REPUBLIC	CZH	1	* 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
DENMARK	DNK	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ESTONIA	EST	1	58	48	66	1	2	0	0	2	177	408	512	0	0	15	0	8	3	0	0	0	0	5	951
FINLAND	FIN	1	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
FRANCE	FRA	1	3	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0
GERMANY	DEU	1	1	0	0	0	0	0	0	0	1	48	0	0	0	4	1	0	0	0	4	0	0	0	57
GREECE	GRC	1	* 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
HUNGARY	HUN	1	11	23	21	1	0	1	0	0	57	239	0	0	0	0	0	0	0	0	0	1	0	0	240
ICELAND	ISL	1	* 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
IRELAND	IRE	1	٠ 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ITALY	ITA	1	* 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
LATVIA	LVA	1	95	87	46	0	0	0	0	0	228	656	423	0	0	43	17	16	5	0	7	6	0	5	1178
LITHUANIA	LTU	1	95	115	217	17	2	0	11	0	457	575	460	2	1	12	109	29	5	1	3	0	0	7	1204
LUXEMBOURG	LUX	1	۰ 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
MACEDONIA	MKD	0	* 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
MOLDOVA	MDA	0	4	7	13	0	1	0	0	0	25	15	0	0	0	0	0	0	0	0	0	0	0	0	15
NETHERLANDS	NED	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
NORWAY	NOR	1	٠ 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
POLAND	POL	1	23	37	34	0	1	0	0	0	95	316	67	0	4	5	14	2	0	0	4	0	0	1	413
PORTUGAL	PRT	1	٠ 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
ROMANIA	ROU	0	36	23	26	3	7	0	0	1	96	172	0	0	0	4	0	1	0	0	2	0	0	7	186
RUSSIAN FEDERATION	RUS	0	985	629	705	24	57	31	42	2	2475	1748	77	0	27	11	12	16	15	1	1	1	0	14	1923
SERBIA A MONTENEGRO	SCG	0	25	48	7	4	5	1	7	0	97	370	0	0	1	0	2	0	1	0	0	0	0	0	374
SLOVAK REPUBLIC	SVK	1	19	24	1	1	1	0	1	0	47	321	0	0	0	1	9	1	3	1	0	0	0	0	336
SLOVENIA	SVN	1	0	0	0	0	0	0	0	0	0	10	0	0	0	0	0	0	0	0	0	0	0	0	10
SPAIN	ESP	1	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SWEDEN	SWE	1	* 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SWITZERLAND + LIEC.	CHE	1 :	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
TURKEY	TUR	0	110	11	92	6	23	0	0	0	242	20	0	0	1	0	1	1	0	2	0	0	0	0	25
UNITED KINGDOM	UNK	1	* 0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
UKRAINE	UKR	0	501	663	370	13	33	5	0	0	1585	1190	8	39	18	9	47	16	1	2	3	0	0	16	1349
TOTAL			2175	1901	1690	83	144	38	61	9	6101	7983	1663	41	66	130	220	93	33	7	24	8	0	70	10338
PER CENT			13.2%	11.5%	10.2%	0.5%	0.9%	0.2%	0.4%	0.1%	36.9%	48.3%	10.1%	0.2%	0.4%	0.8%	1.3%	0.6%	0.2%	0.0%	0.1%	0.0%	0.0%	0.4%	62.5%
* NO CASES			* NO	CASES		MPOR	TED CA		OM NO		AFRIC/		IMPO		CASE										