PROJECT SUMMARY

Chronic wasting disease (CWD) is an emergent disease first identified the late 1960s, which has since spread rapidly among wild and captive cervids (deer, elk, moose) across the USA and Canada, with devastating consequences for populations in some areas. CWD is a prion disease, similar to scrapie in sheep and bovine spongiform encephalopathy (BSE, or “mad cow disease”) in cattle. BSE transmitted to humans and has resulted in >200 deaths from variant Creutzfeldt-Jakob disease, thus the zoonotic potential of any emerging animal prion disease must be investigated to prevent similar incidents. Although there is no epidemiological evidence to date suggesting spread of CWD to humans, recent reports of experimental oral transmission to non-human primates give cause for concern.

Europe was considered to be free of CWD until 2016, when a novel prion disease was identified in a wild reindeer population in Norway. Subsequently small numbers of cases have been identified in moose in Norway, Finland and Sweden, and a single red deer in Norway. Analysis of biochemical properties of disease-associated prion protein (PrP^{Sc}) from Norwegian CWD cases, and transmission experiments in rodent models, have provided evidence for a number of distinct prion strains, which differ markedly from the predominant strains identified in North America.

The threats posed by the emergence of CWD in Europe depend critically on how rapidly the disease can spread through wild cervid populations, and how likely it is that infection can transmit from wildlife to farmed deer, other livestock species and man. Differences in European CWD strains and deer species/populations mean that risk assessments and control strategies cannot not be solely based on evidence from CWD in North America, and further research specific to the European context is urgently required.

This project will integrate research on the epidemiology and population dynamics of the disease in affected countries, with experimental approaches to study host/pathogen interactions relevant to disease transmission in wildlife, livestock and people. Using mathematical and statistical models, information on CWD cases in Norway and Sweden and population data will be used to evaluate surveillance strategies, to predict if and how CWD may spread in affected populations, and indicate potential for transmission through contacts with semi-domesticated reindeer and other livestock. Analysis of genetic susceptibility to CWD in the most numerous, widespread and economically important species of wild and farmed cervids in Europe will be assessed by *PRNP* gene sequencing and testing the effect of novel variants on prion replication using *in vitro* assays. The outcomes of this analysis will have an impact on the modelling of CWD spread, and may also identify *PRNP* alleles associated with disease resistance that could be used in selective breeding programmes for disease control. The risks of transmission of European CWD isolates to sheep, cattle, pigs and humans will be assessed using the *in vitro* protein misfolding amplification assay (PMCA) and *in vivo* models (transgenic mice expressing PrP from the target species). Understanding which CWD strains are most likely to cross species barriers, and which species are most at risk, will allow better targeting of surveillance and control measures.

The consortium brings together expertise, resources, models and data from leading European research groups working on animal prion diseases. Building on existing collaborations, this proposal will provide increased research capacity and coordination of activities, while avoiding unnecessary duplication of effort. The outcomes of the project will provide vital evidence to support detailed risk assessments of the potential impacts of CWD on animal/human health in Europe, and lead to improved and cost-effective surveillance and control strategies.