



(Name and address of the main and co-applicant, project title and an executive summary (in English) are provided through the on-line electronic submission system and will be automatically inserted at the front of the application)

Is this application part of a *coordinating project proposal*? O Yes If the above question is answered with "yes", please fill in the title of the coordinating project proposal. Title coordinating project proposal: BIRDHEALTH Health of Arctic and Antarctic bird populations

Related international IPY 'Full proposal'

(submitted to ICSU-WMO Joint Committee for IPY) Title: BIRDHEALTH Health of Arctic and Antarctic bird populations Lead contact (name, organisation, country): Dr. Maarten J.J.E. Loonen, Arctic Centre, University of Groningen, The Netherlands ID No: 172 Website URL for more information: www.birdhealth.nl

Geographic area of interest for this (IPY•NL) application

X Arctic

1a. Further details of the applicant(s)

Main applicant

| Gender: | Male |
|------------------|---|
| Tenure Position: | Yes |
| Research School: | Functional Ecology |
| Website URL: | http://www.nioo.knaw.nl/ppages/mklaassen/ |

Co-applicant

| Gender: | Male |
|------------------|--|
| Tenure Position: | Yes |
| Research School: | Molecular Medicine |
| Website URL: | www.molecularmedicine.nl www.virology.nl |

1b. Alternative contact

| Name: | Dr. Ron A. M. Fouchier |
|----------|-------------------------|
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1c. Does the local authority support your application? Yes

(did you inform your superior and accepts your institute/university the conditions for support by NWO)

1d.Renewed application?

No (in case of renewed application please summarize main changes under item 4) Dossier nr:

1e. Applying for: PhD student

(for PhD student please underline promotor in question 1f, composition of research group)





3b. Other relevant publications (max 1 page for publications, min 10 pts)

By the applying research group:

NIOO

- Clausen, P., Nolet, B.A., Fox, A.D. & Klaassen, M. 2002. Long-distance endozoochorous dispersal of submerged macrophyte seeds by migratory waterbirds in northern Europe - a critical review of possibilities and limitations. *Acta Oecologica* 23: 191-203.
- Klaassen, M., Bauer, S., Madsen, J. & Tombre, I. 2005. Modelling behavioural and fitness consequences of disturbance for geese along their spring flyway. *Journal of Applied Ecology (in press/available on line)*.
- Madsen, J., Klaassen, M. 2005. Assessing body condition and energy budget components by scoring abdominal profiles in free-ranging geese. *Journal of Avian Biology (in press)*
- Nolet, B.A., Bevan, R.M., Klaassen, M., Langevoord, O. & Van der Heijden, Y.G.J.T. 2002. Habitat switching by Bewick's swans: maximisation of average long-term energy gain? *Journal of Animal Ecology* 71: 979-993.
- Nolet, B.A., Klaassen, R.H.G. & Mooij, W.M. 2005. The use of a flexible patch leaving rule under exploitative competition: a field test with swans. *Oikos (in press)*

EMC

- **Fouchier, R.A.M.**, Olsen, B, Bestebroer, T.M., Herfst, S.,van der Kemp, L., Rimmelzwaan, G.F. & Osterhaus A.D.M.E. 2003. Influenza A virus surveillance in wild birds in Northern Europe in 1999 and 2000. *Avian Diseases* 47: 857-860.
- **Fouchier, R.A.M.**, Schneeberger, P.M., Rozendaal, F.W., Broekman, J.M., Kemink, S.A.G., **Munster, V.**, Kuiken T., Rimmelzwaan, G.F., Schutten, M., van Doornum, G.J.J., Koch, G., Bosman, A., Koopmans, M & Osterhaus, A.D.M.E. 2004. Avian influenza A (H7N7) virus associated with human conjunctivitis and a fatal case of acute respiratory distress syndrome. *Proceedings of the National Academy of Sciences, USA* 101:1356-1361.
- Fouchier, R.A.M., Munster, V., Wallensten, A., Bestebroer, T.M., Herfst, S., Smith, D., Rimmelzwaan, G.F., Olsen, B., & Osterhaus, A.D.M.E. 2005a. Characterization of a novel influenza A virus hemagglutinin subtype (H16) obtained from black-headed gulls. *Journal of Virology* 79:2814-2822.
- Munster, V.J. Wallensten, A. Baas, C. Rimmelzwaan, G.F. Schutten, M. Olsen, B. Osterhaus, A.D.M.E. & Fouchier, R.A.M. 2005. Mallards and highly pathogenic avian influenza ancestral viruses, Northern Europe. *Emerging Infectious Diseases* 11:1545-51.

FVM

- Stegeman A, Bouma, A., Elbers, A.R., de Jong, M.C., Nodelijk, G., de Klerk, F., Koch, G., van Boven, M. (2004): Avian influenza A virus (H7N7) epidemic in The Netherlands in 2003: course of the epidemic and effectiveness of control measures. *Journal of Infectious Diseases.*,190:2088-95
- Roberts, M.G. & Heesterbeek, J.A.P. 2003. A new method to estimate the effort required to control an infectious disease. *Proceedings of the Royal Society London, Series B*, 270, 1359-1364
 Neutel, A.M., Heesterbeek, J.A.P. & De Ruiter, P.C. 2002. Weak links in long loops enhance
- stability in real food webs. Science, 296, 1120-1123.
- Hudson, P.J., Rizzolli, A., Grenfell B.T., **Heesterbeek**, J.A.P. & Dobson, A.P. 2002. *The Ecology of Wildlife Diseases*. Oxford University Press, Oxford.

RUG

- Cope, D.R., Loonen, M.J.J.E., Rowcliffe, J.M. & Pettifor, R.A.. 2005. Larger barnacle geese (Branta leucopsis) are more efficient feeders: a possible mechanism for observed body size- fitness relationships. *Journal of Zoology: Proc. Zool. Soc. London* 265: 37-42.
- Loonen, M.J.J.E., Bruinzeel, L.W., Black, J.M. & Drent, R.H. 1999. The benefit of large broods in Barnacle geese: a study using natural and experimental manipulations. *Journal of Animal Ecology* 68: 753-768.
- Loonen, M.J.J.E., K. Oosterbeek & R.H. Drent 1997. Density dependent effects on growth of young and final adult size in Barnacle Geese Branta leucopsis. *Ardea* 85: 177-192.

Other references with respect to the application:

Krauss, S., Walker, D., Pryor, S.P., Niles, L., Chenghong, L., Hinshaw, V.S., Webster, R.G. 2004. Influenza A viruses of migrating wild aquatic birds in North America. *Vector-Borne and Zoonotic Diseases* 4: 177-189.





4. Detailed description of research area and research plan

(max 4 pages, min 10 pts, including figures)

(Objectives, innovative aspects, history/background, scientific approach and research methodology)

Introduction

With the outbreaks of highly pathogenic avian influenza (HPAI or "fowl plague") in the Netherlands (2003), and South-East Asia (1997-2005), we received a major reminder of the threats of HPAI in animals and humans. Although it will be impossible to totally prevent such outbreaks, a fundamental understanding of the origin and spread of influenza viruses (IV) through animal and human populations may play a key role in designing strategies to recognize the threats early and to minimize the risk of outbreaks. As will be pointed out below, various data indicate that Arctic breeding migratory waterfowl, notably geese and swans, may play a key role as reservoirs for avian IV, warranting detailed investigations on the interplay of the ecology of birds and avian IV.

It is generally accepted that in the influenza A pandemics in the last century, interspecies transmission of avian IV has played a crucial role. Notably waterfowl have been recognized as natural gene reservoirs of IV and some of the avian subtypes have circulated in humans (Fouchier et al. 2000, 2003,2004). Avian IVs preferentially infect cells lining the intestinal tract of birds and are excreted in high concentrations in their faeces. In North-western Europe a screening of wild birds proved the presence of avian IV in up to 60% of the birds, depending on the bird species, location and season (Fouchier et al. 2003). The transmission of IV between birds is thought to occur primarily via a faecal-oral route. Many species of birds are known to be potential carriers of Avian IV. However, possibly because of their highly social behaviour during the non-breeding season and their association with water—an ideal medium for the survival and distribution of excreted viruses (e.g. Krauss et al. 2004)—waterfowl are considered the prime host and vector for IV among birds.

Most waterfowl are highly migratory and large numbers are breeding in the Arctic while wintering at temperate latitudes. For these species the yearly peak in avian influenza occurs in late summer and early winter, coinciding with the waterfowl's southward migration. The Arctic thus seems to be an important area for the exchange of avian IV and it may even function as a reservoir for avian IV. Indeed there are a number of factors that put the Arctic into the limelight as an area playing a prime role in the perpetuation of avian IV:

- It is an important breeding and moulting area for many waterfowl, notably geese and swans.
- The juveniles from these species may be particularly susceptible to infection with avian IV.
- Breeding and moulting put high demands on the body stores and condition of adult birds also making them susceptible to infection.
- During the moulting period, when birds become flightless, the birds concentrate on lakes and ponds forming ideal conditions for IV exchange and survival.
- Soon after moult winter sets in and IV might survive the winter in these moulting ponds which often freeze up completely down to the bottom.

While this is an appealing scenario for the perpetuation of IV in wild birds, preliminary data collected by EMC and collaborators also leaves room for alternative hypotheses, at least for European birds. In recent studies in Sweden it was found that the prevalence of IV in ducks during spring migration was sufficiently high (>5% of birds infected) to ensure perpetuation of IV without the need for other (Arctic breeding) species as vectors. Yet, although the ecology and perpetuation of IV in wild birds in Europe and elsewhere might be complex, it is very likely that paramount processes take place in waterfowl in the Arctic.

Currently there is much fear that the highly pathogenic avian IV subtype H5N1 might be introduced into Western Europe by migratory birds. Although this fear is justified it should be born to mind that also less virulent IV subtypes constitute a potential health risk to man. For the introduction of novel IV subtypes to humans, various organisms such as pigs and men, may act as mixing vessels when simultaneously infected with human and avian IV. In the Netherlands, the human (16 million/41500 km²), pig (20 million) and poultry (95 million) densities are among the highest on earth and the number of free-ranging animals in The Netherlands is increasing rapidly, due to public demand. On the other hand, because of its many lakes and waterways, its location just south of the 0 °C January isotherm and its intensive agricultural production, The Netherlands forms the most waterfowl dense area in Europe (e.g. 1.5 million wintering geese). Additionally, both in autumn and





spring, the Netherlands is also a major staging site for waterfowl species that travel between their high latitude breeding areas and wintering areas in western Africa (notably Niger and Senegal deltas). Waterfowl have been recognized as important vehicles for dispersal of various kinds of organisms (Clausen et al. 2002, Klaassen & Santamaría 2002) and IV appears to be no exception finding its way to The Netherlands on board of waterfowl. Thus, all ingredients for HPAI outbreaks in animals and potential emergence of pandemic influenza are present in The Netherlands. Although many other places on our globe can be identified as high-risk areas for a pandemic influenza outbreak, the Netherlands is in an ideal position to study the role of Arctic breeding waterfowl as vectors for avian IV dispersal.

Again, eliminating the risk of large epidemics is impossible. Yet, there is considerable potential for quantifying, analysing and thereby possibly reducing the risk of outbreaks and for improving the management of outbreaks once they occur. Momentarily, worldwide networks monitor outbreaks of influenza in humans and poultry (WHO, OIE, FAO). The call for more intensive influenza surveillance of wild animals and integration of human and animal health research has been made (Fouchier et al. 2005b). More light needs to be shed on the interactions between birds and IV, their origin, temporal and spatial variation in circulating IV, and the epidemiology, ecology and evolution of IV.

Objectives

The general aim of this project is to establish a link between the ecology of IV and long-distance migratory Arctic-breeding waterfowl, notably geese and swans. We set ourselves the following tasks:

- 1. establish which species of arctic breeding waterfowl act as carriers of avian IV, the extent of this and correlates with species' distributions and ecology.
- 2. establish detailed knowledge on the spatial and temporal variation in prevalence of IV among Arctic-breeding waterfowl
- 3. study the prevalence of IV in individual birds in relation to their social status, condition, habitat choice and aggregation intensity with conspecifics and other species of birds, as well as any potential fitness effects of IV infection (e.g. can feverish birds fly?)
- 4. establish whether Arctic moulting ponds and lakes function as avian IV reservoirs.

Using a novel modelling approach as described in a sister application, these data will serve to parameterise these new models.

Methodology

To target these research challenges outlined above we envisage a multidisciplinary research team encompassing the disciplines of waterfowl ecology and virology.

IV screening in Arctic breeding geese and swans

The research will focus on Arctic breeding geese and swans. To identify the role of various species of Arctic breeding waterfowl as potential vectors for avian IV we will rely on our national and international BIRDHEALTH partners for circumpolar sampling of blood serum for the assessment of avian IV antibodies. NIOO and RUG have extensive knowledge and research projects on migratory waterfowl with many international contacts. This part of the study will identify what species act as carriers of avian IV and to what extend. Furthermore this screening will allow to study whether the presence of antibodies is correlated with the specific ecology and distribution of the species and populations studied.

The blood sampling requires the catching of waterfowl. Various goose and swan projects catch large numbers of their focal species on the Arctic breeding grounds during the moulting period, since the birds are flightless during this time of year. In many of these projects also canon-netting takes place on the wintering grounds. NIOO has ample experience in blood sampling under field conditions (e.g. an instruction video for wader biologists was produced by the main applicant) including separation and conservation of blood sera under the most primitive conditions.

The antibody screening will also allow identifying the potential candidates for more in depth research as to the spatial and temporal variation in IV among Arctic-breeding waterfowl. For Bewick's Swan, a sub-species of Tundra Swan, pilot investigations by EMC and NIOO have already indicated that this species is an important vector for avian IV dispersal. Initiatives to conduct antibody screening on other species and populations are ongoing. Thus, besides Tundra Swan we also hope to embark on in depth research on other species of Arctic breeding waterfowl from the very start of the project.





For these selected species we will try and boost the number of catches on the wintering and breeding grounds. For all birds caught we will collect cloacal swabs but also fresh droppings to assess IV prevalence with a high spatial and temporal resolution. For instance for three goose and swan species currently under study by NIOO and RUG a network of collaborators and annual expeditions to the breeding grounds allow the collection of fresh faeces at all major staging sites and throughout the complete annual cycle.

We aim to focus on at least three different species (one population per species). Yet screening for IV in additional species along various flyways is quite feasible within the BIRDHEALTH framework.

Importantly, in many species of waterfowl (and also those under study by RUG and NIOO) large numbers of birds are individually colour banded, allowing recognition of individual birds from large distances. Using a total system range finder (cf. Nolet et al. 2005) droppings of individual birds can potentially be retrieved through much of the annual cycle. Thus, the potential to derive at a detailed description of the intertwining ecology of IV and birds within the context of this research project is considerable.

Besides screening birds we will also take water samples from moulting ponds at least three times during the breeding season. Also these water samples will be tested for IV prevalence.

Fitness consequences of IV infection

Avian IVs are generally considered to be mostly non-pathogenic in their natural hosts. As we have learned from the H5N1 outbreak among bar-headed geese in western China this is certainly not always the case. Moreover, if not lethal there may still be other fitness consequences associated for the host that may be more subtle. It has been suggested that in a laboratory setting, wild birds do not suffer significantly from experimental IV infection. However, EMC recently obtained evidence that experimentally infected black-headed gulls became lethargic, lost their appetite, and displayed disinterest in bathing. In-vivo, such relatively mild effects can be investigated by e.g. comparing infected and non-infected birds in terms of their resighting probability. Preliminary data from EMC on migrating ducks in Sweden indicated that indeed, *in-vivo* infected ducks did return to foraging-sites less frequently than non-infected ducks. Also the pilot study on Bewick's Swans in The Netherlands provides an indication for lethargy among avian IV infected individuals.

At the breeding grounds the link between IV prevalence and fecundity will be investigated by collecting fresh droppings at the nest of both parents and relating these to clutch size and hatching success.

In the here proposed project all birds caught will be individually colour marked in a fashion that allows recognition even at large distances (using telescopes). Thus, fecundity, phenology and other aspects of behaviour can be assessed and this information be compared with IV data upon capture and marking. Notably for geese and swans this is a very feasible aspect of our project. The offspring of these species stay with the parents for almost a year, thus allowing to also link (previous) IV infection to fecundity. In addition, condition estimates can be assessed in these species without catching through abdominal profile scoring (e.g. Madsen & Klaassen 2006), also allowing for a long-term assessment of the consequences of IV infection.

Thus at the migratory staging and wintering grounds marked individuals with a known historic IV status will receive special attention. Resighting probability (i.e. timing of migrations but also mortality), body condition (i.e., abdominal profile scores) and fecundity (i.e. number of young) will be compared to historic data on IV status to study the potential impact of IV infection on the fitness of the birds or vice versa (cf. Cope et al. 2005).

Virological research

The dept. of Virology has developed high-throughput screening assays for the detection of avian IV (Fouchier et al. 2000). This methodology will form the backbone in the study on the ecology of avian IV. Cloacal swabs will be taken from caught birds. Droppings will be collected from groups of birds, breeding pairs on the breeding grounds, and (marked) individual birds (using the total station range finder). Notably in the first year, in addition to cloacal swabs, blood sera will also be sampled in all birds caught allowing for the screening of IV anti-bodies, since this will provide important information for the selection of the best model species. IV isolates will be characterised using serological tests and genomic sequencing. EMC is currently building a genetic database by full-





genome sequencing of virus isolates collected between 1998 and 2005. Genetic data will be generated for virus isolates collected in the context of this programme, to potentially determine evolutionary patterns within and between host species. Genetic data will be compared with data collected from avian IV isolated in Asia and the Americas as well as viruses responsible for HPAI outbreaks in Europe. Biological properties (host range, pathogenicity) will be studied for representative virus isolates.

Besides acquiring information on the current (through IV analyses in faeces and cloacal swabs) and past (through analysis of blood serum) avian IV infections of individual birds crucial to the success of the here described project, this aspect of the study will also allow to differentiate among various IV strains with respect to their fitness consequences, spread and persistence.

Mathematical epidemiological research

The ecological, epidemiological, immunological and evolutionary processes that govern the spread of IV among populations of birds are highly complex and involve non-linear interactions (e.g. due to build-up of immunity) and stochastic effects (e.g. mutation and selection). The models developed will quantify the relations between IV genetic variation, IV population dynamics and host population dynamics, and transmission within (and possibly between) species. For the latter aspect we will use behaviour-based models (e.g. stochastic dynamic models specially designed for migratory geese and swans [Klaassen et al. 2005]). This link between epidemiological and behaviour-based models will be conducted in a separate project. Our project will importantly contribute to the parameterisation and validation of the models to be developed.

Innovative aspects

The tremendous biocomplexity of disease problems implies that a multidisciplinary approach is our best hope of smart combat strategies. Despite the obvious need for an integrative approach in these matters (Fouchier et al., 2005b), there are currently few research efforts in the world that tackles the risk assessment for influenza outbreaks in our proposed multidisciplinary fashion.

The research project cannot be conducted by any of the research partners in isolation. For the collection of samples, the virologists rely on the waterfowl ecologists. For tuning their program towards the right areas, times of the year, and species, the waterfowl ecologists need to rely on the IV screening by the virologists, but can only do so after consulting epidemiologists with their experience in population dynamics in viruses. Ultimately, the ecological data from waterfowl and data on IV prevalence and genetics will feed into the epidemiological models.

At NIOO and RUG various projects are conducted on the population dynamics, migratory behaviour (Klaassen et al. 2005) and habitat use (Klaassen et al. 2005; Nolet et al. 2002) of waterfowl, among others in relation to global and regional change. NIOO has experience in retrieving droppings of individual birds using a total station range finder (cf. Nolet et al. 2005).

The dept. of Virology-EMC has developed screening assays for the detection of avian IV (e.g. Fouchier et al. 2000). Preliminary, cross-sectional studies on ~25000 samples collected from ~225 bird species were used to validate and streamline these tests and provided insight on species of interest, sample collection, transport, etc. (Fouchier et al. 2003). Genetic analyses have already identified several viruses of specific interest (e.g. Fouchier et al. 2004, 2005a), and the gene database that is present at EMC will be useful for the studies proposed here.

Epidemiologists at the Faculty of Veterinary Medicine-UU have several ongoing PhD projects on Avian Influenza, funded by the EU (1) and Thailand (2). At the moment the outbreaks of H7N7 (Netherlands and Thailand) and H5N1 (Thailand) are studied in detail (Stegeman et al. 2004). A large group of researchers is involved in the population dynamics and modelling of infectious diseases (Diekmann & Heesterbeek 2000), both for farmed and wild animals (e.g. Hudson et al. 2002), and for humans. This combined expertise will play a role in guiding the field work in this proposal and in guaranteeing an optimal integration of the findings in the new epidemiological models to be developed by the sister modelling project.

Thus, each of the four research groups is well established in their respective fields and has ongoing international collaborations in their specific area of expertise. Through this proposed collaboration, each of the groups will get access to the networks of the others, thereby strengthening their positions for the future, even beyond this 4-year project.





| 5. Timetable of the project and working pro | ogramm | e: | | | | | | | | | | | | | |
|---|---------|------|-----|-----|-----|------|-----|-----|-----|------|-----|-----|-----|------|-----|
| | 2006 | 2007 | | | | 2008 | 3 | | | 2009 | | | | 2010 |) |
| | Sum Aut | Win | Spr | Sum | Aut | Win | Spr | Sum | Aut | Win | Spr | Sum | Aut | Win | Spr |
| Wader & Waterfowl ecology | | | | | | | | | | | | | | | |
| dropping + serum sampling | | | | | | | | | | | | | | | |
| setting up sampling scheme and logistic organisations | | | | | | | | | | | | | | | |
| broad species sampling & data anlyses | | | | | | | | | | | | | | | |
| target species sampling & data anlyses | | | | | | | | | | | | | | | |
| Virology | | | | | | | | | | | | | | | |
| virus surveillance | | | | | | | | | | | | | | | |
| sample testing | | | | | | | | | | | | | | | |
| characterisation | | | | | | | | | | | | | | | |
| serological characterisation | | | | | | | | | | | | | | | |
| genomic sequencing | | | | | | | | | | | | | | | |
| phenotype studies | 1 | | | | | | | | | | | | | | |
| Finalising PhD | 1 | | | | | | | | | | | | | | |

The work will translate in the following chapters that will be included in the PhD thesis:

- 1. Arctic breeding waterfowl as vectors for avian IV as assessed from IV antibodies in blood serum from a large range of Arctic breeding waterfowl.
- 2. Temporal and spatial variation in the prevalence of Influenza A viruses among some Arctic breeding long-distance migratory waterfowl.
- 3. Social and condition dependent prevalence of Influenza A viruses among Arctic breeding longdistance migratory waterfowl.
- 4. Fitness consequences of Influenza A infection among Arctic breeding long-distance migratory waterfowl.
- 5. Temporal, spatial and host variation among influenza virus subtypes along the flyways of longdistance migratory Arctic breeding waterfowl.
- 6. The intertwined ecology of avian influenza viruses and their long-distance migratory hosts.

6. Affiliation with (inter)national research programmes

(This should include an explicit description of existing and planned cooperation)

For the screening of waterfowl for IV prevalence a network of researchers is required. BIRDHEALTH will be an important platform where these researchers will meet, greatly facilitating this effort. Furthermore, both RUG and NIOO can rely on an extensive network of collaboration on these groups of birds. For instance NIOO has (inter)national co-operations running on a number of potential target species including Bewick's Swans (with Dutch partners T. Haitjema and J. H. Beekman, and the British Wildfowl and Wetland Trust [Dr. E. Rees]), Pink-footed Goose (Danish National Environmental Research Institute [Dr. J. Madsen]) and Barnacle Goose (British Wildfowl and Wetland Trust [Dr. E. Rees]). Currently NIOO and RUG are co-operating with WWT and NERI in the framework of the 6th framework EU project "fragility of Arctic goose habitat: impacts of land use, conservation and elevated temperatures (FRAGILE)". Within this project NIOO models the long-distance migratory behaviour and population dynamics of Pink-footed Goose and Barnacle Goose, while RUG studies their impact on tundra vegetation.

With WWT and the two Dutch initiators of Bewick's Swan ringing schemes NIOO has recently embarked on a KNAW funded Avian Spatial Ecology co-operation which focuses on describing and modelling small scale spatial dynamics of Bewick's Swans. Additionally, NIOO co-operates with NERI on the breeding grounds of Pink-footed Goose (Spitsbergen). In the past NIOO has organised expeditions to the Russian breeding grounds of Bewick's Swans. An enterprise that we are intending to pick up in co-operation with WWT, which has continued to go there over the past years.

Besides these projects covering the complete flyways of the three species mentioned, NIOO and RUG have numerous other waterfowl contacts that will be especially of relevance for the initial broad scale surveillance.





The dept. Virology at EMC houses the Dutch WHO national influenza centre. EMC is coordinator of the EU framework 5 programme "NovaFlu", in which novel vaccine candidates for pandemic IVs are designed and tested. One of Dr. Fouchier's activities in this programme is the generation of an avian IV database. In this programme, avian samples are collected through a large international network of ornithologists. IVs collected within the context of this application will be added to the existing databases. After 2005, the database FP5 project will be continued in the NWO/WOTRO programme "Nivarec". As a fellow of the Royal Dutch Academy of Arts and Sciences from 2000-2005, Dr. Fouchier developed new methods to study determinants of IV zoonosis and pathogenesis, which will be invaluable for the current proposal. Fouchier is also one of 19 partners in the framework 6 programme coordinated action RiViGene (Risk Virus Gene database), for which Dr. Fouchier will generate and maintain genetic data on avian IVs. The genetic data from IV isolates in the current proposal will be compared with available datasets, and correlated with biological properties of the IVs. Virus isolates of subtypes H5 and H7 will be sent to the Central Institute for Animal Disease Control (CIDC; Dr. G. Koch), to test for pathogenicity in chickens, according to EU laws. Virus characteristics (genetic of phenotypic) will be implemented in the epidemiological models.

At the moment the group of theoretical and infectious disease epidemiologists of the Faculty of Veterinary Medicine at UU participates in several FP 6 EU projects (with two PhD students and two postdocs) relevant to the present proposal. One involves Avian Influenza (a thorough analysis of the Dutch outbreak of H7N7), the other two are from the theoretical side and involve emerging infections: i) EDEN (Emerging Infections in a changing European environment), this is a IP with more than 30 partners, where J.A.P.H. is in the Steering Committee and FVM is the partner coordinating the modeling work in the project as a whole; ii) SARSTRANS, this is a small project with only three European partners, led by the group of R.M. Anderson at Imperial College, London, and partners in the Far East, where FVM takes the lead in methods to estimate control effort needed and the usefulness of contact tracing. J.A.P. H. was awarded a VICI grant by ZonMw/NWO at the end of 2004, titled: Population dynamics and control of infectious diseases: modeling interaction at different scales. The IPY proposal fits well into that research activity, as it deals with both local (breeding grounds/winter habitat) and global (migration) scales and their mutual interaction.

7. Societal significance

Motivation of the relevant policy aspects, such as:.

- Political / societal significance in a national and international context
- Urgency for international and/or national policy
- (These are important for the evaluation of the proposal, because of the funding by several ministries.)

Influenza outbreaks pose a major threat to human health and economy. Waterfowl is thought to be among the most important reservoirs and vectors of transport for influenza viruses. With its dense human population, extensive pig and chicken farming, its many shallow water bodies, which attract migratory waterfowl in unparalleled numbers, The Netherlands form a hot spot for the development of new pandemic influenza outbreaks. The rapidly increasing numbers of outdoor ranging poultry and pigs further increase the risks in The Netherlands. For risk reduction, early recognition and management of outbreaks now and in the future, the proposed multidisciplinary research initiative will provide critical knowledge on the prevalence of influenza viruses in waterfowl and their potential to evolve to virulent viruses for humans. Our results will be invaluable for the discussions on the risk-management of avian IVs with respect to transmission to poultry, animals and humans in Europe.

8. Legal requirements

For fieldwork to Antarctica additional information is needed for an initial assessment whether or not the applicant will have to apply for a permit under the 'Wet bescherming Antarctica'.

Do you plan to visit Antarctica, South of 60°S? O No If the above question is answered with "yes" please fill in the separate 'WBA-IPY' form for details





Has been complied with the law and legal requirements with respect to the proposed Research, such as 'Wet op Dierproeven' and 'DNA-recombinant legislation? $$_{\rm O}$$ Yes

9a. Requested budget from ALW

| | 2006 | 2007 | 2008 | 2009 | 2010 |
|---------------------|----------|------|------|------|----------|
| Personnel (mm) | 6 | 12 | 12 | 12 | 6 |
| Research costs (k€) | | | | | |
| Equipment | 1.5 | | | | |
| Consumables | 20 | 40 | 40 | 40 | 20 |
| Fieldwork | 18 | 18 | 18 | 18 | |
| Education, | 15.5 | 0.5 | 0.5 | 0.5 | 0.5 |
| Outreach & | | | | | |
| Communication | | | | | |
| Coordination* | | | | | |
| Shiptime NIOZ-MRF | XXXXXXXX | | | | XXXXXXXX |
| (in days) | | | | | |

* Costs for coordination can only be requested if main applicant is lead contact of the related IPY "Full proposal". If this is a subproject of a coordinating project proposal, the coordination costs can only be requested in the application form of the coordinating project.

9b. Explanation and/or remarks to the proposed budget:

(Personell, equipment, consumables, fieldwork, EOC, coordination and Shiptime NIOZ-MRF) (Education, Outreach & Communication (EOC) plan must be included here)

a. Proposed personnel (please note that, unless your preliminary proposal deals with a multidisciplinary project involving at least 2 of the 3 research themes within this programme, you may not request more than 1 full person equivalent, f.t.e.)

PhD researchers (max. 4 years): 1 Dutch researcher

Post-doc researchers: None

b. Estimated research costs (durables+consumables+travel) (\in): All necessary equipment to conduct this research is available with the various partners. Only a portable PC needs to be acquired (\in 1500).

Consumables will be mainly required for the AI screening and antibody analyses which are extremely costly. For an estimated 2000 samples per year with an average analysis cost of \notin 20 per sample the annual costs amount to \notin 40000!

However, we will seek other sources to cover (part of) these expenses (see below)

For the Arctic fieldwork and the fieldwork in the staging and wintering quarters the annual budget for 2 people consists of travel (€7500), housing and food (€9000), consumables (€1500), totalling €18000 per year.

We think that this subject would be highly suitable for a scientific documentary. For Education, Outreach & Communication, we have therefore budgeted a €15000 to produce a scenario and film plans as well as seed money allowing further acquisition. This cost estimate origins from Musch & Tinbergen film productions. A small additional sum of money has been brought under the EOC banner allowing to travel for lectures, distribution of press releases and establishment and updating of a project web site.





c. Estimated costs of joint activities (€): 3000

For logistics and travel to meetings with project and national and international BIRDHEALTH partners.

d. If applicable, indicate the approximate amount and source of additional funding to be sought:

Notably for the antibody and IV analyses external funding will be sought. Currently all analyses on Dutch samples are covered by funding from the Dutch Ministry of Agriculture (LNV). If this would be continued in the future this would be a considerable alleviation of the project's budget. Additionally we will apply for EU and NIH funding to conduct the analyses.

10. Financial assistance from (an)other source(s)

Currently all analyses on Dutch samples are covered by funding from the Dutch Ministry of Agriculture (LNV). If this would be continued in the future this would be a considerable alleviation of the project's budget. In the current budget (see 9a) such support is not accounted for.

11. Relation research program university, large institutions, research schools, etc.

This research will be conducted within the framework of the research programme of the Research School for Functional Ecology.

(No signatures required for electronic submission)