Invasive Species Management and Control:

West Nile virus (WNV)

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1.0 INTEGRATED MANAGEMENT

Because of the large impact of WNV on human and animal health, it is critical to develop effective methods to limit WNV transmission and prevent and/or treat WN disease.

Currently, control measures to curtail WNV transmission include reducing mosquito vector populations and limiting exposure to mosquito bites with protective clothing and repellents. Vector control agencies often use a combination of approaches (mosquito population monitoring, mosquito source reduction, larvicide and adulticide application, and public education) to reduce mosquito populations.

In 2002, a program relying on surveillance and larvicide and adulticide applications was implemented in St. Tammany Parish, Louisiana, resulting in reductions in mosquito populations below the five-year average and a subsequent drop in new human WNV cases (Palmisano et al. 2005 in Kramer et al. 2008)

2.0 SURVEILLANCE AND PREDICTION

Since the virus life cycle is maintained by mosquitoes feeding on birds, mosquitoes with a preference for birds are considered the most competent enzootic vectors and amplifiers of the virus (Yaremych et al. 2004). Thus monitoring mosquito and vector populations is an effective way of predicting virus outbreaks. One of the most effective and useful surveillance techniques focuses on sampling the larval habitats of the mosquito (Irwin et al. 2008), although monitoring of adults is common and there are a wide range of techniques available (CDC 2003b).

Monitoring the effectiveness of mosquito control programs and targeting control efforts to high-risk areas and peak mosquito activity periods are critical to maximize benefits. Studies indicate that host-seeking and oviposition behaviours in Culex mosquitoes in the northeastern United States peaked approximately two hours after sunset. Thus timing applications of insecticide during this period is likely to improve control outcomes (Reddy et al. 2007 in Kramer et al. 2008).

Several GIS based spatial models of WNV transmission have been developed to predict outbreaks(Cooke et al. 2006; Ruiz et al. 2007; Tachiiri et al. 2006 in Kramer et al. 2008; Zhou et al. 2007). These models use a variety of predictor variables, including temperature, rainfall, vegetation, landscape, and geographic data, to predict locations of high WNV transmission risk. This type of information is useful for targeting mosquito control efforts, locating trapping sites for surveillance, and focusing prevention efforts (Kramer et al. 2008).
3.0 PREVENTATIVE MEASURES

3.1 PERSONAL PROTECTION

Individuals should reduce their contacts with mosquitoes by taking the following actions: 1) when outdoors, clothing should be worn that covers the skin, such as long sleeve shirts and pants, 2) effective insect repellent containing DEET (N,N-diethyl-meta-toluamide) or other effective chemical should be applied to clothing and exposed skin, and 3) outside activity should be curbed during the hours that mosquitoes are feeding, which often includes dawn and dusk. In addition, screens should be applied to doors and windows and regularly maintained to keep mosquitoes from entering buildings (CDC 2003a). The use of fans and mosquito traps may also reduce mosquito exposure (Trevejo et al. 2008).

A study in Ontario found that people who practiced at least two personal protective strategies (wearing repellent, wearing protective clothing, or avoiding outdoor exposure to mosquitoes) were about half as likely to have been infected with WNV than people who did not practice at least two protective strategies (Loeb et al. 2005 in Petersen and Hayes 2008) A study comparing two adjacent communities in Colorado found that the incidence of WNV disease was better correlated ecologically with the practice of personal protection strategies than with the level of local mosquito control efforts (Gujral et al. 2003 in Petersen and Hayes 2008).

3.2 CONTROL OF MOSQUITO VECTORS

According to the CDC (2003a), the most effective and economical way to control West Nile virus is to control mosquitoes by larval source reduction through locally funded abatement programs that monitor mosquito populations and initiate control before disease transmission occurs.

These measures include removal of any potential mosquito breeding habitat such as containers or old tires that collect standing water. “Depending on state regulations, ponds or water tanks can be stocked with mosquito fish (Gambusia affinis) that feed on mosquito larvae. Local mosquito-and vector-control agencies often provide the public with mosquito fish free of charge as well as consultation on mosquito-control issues” (Trevejo et al. 2008). A simple strategy for reduction of mosquito larvae is floating polystyrene beads on water surfaces which results in suffocation of larvae as they cannot penetrate the water surface to breathe (Curtis 2005 in Kramer et al. 2008). This would be useful for control of mosquitoes in enclosed spaces such as flooded basements or cess pits (Kramer et al. 2008).

Mosquito larvae and adults are also controlled through use of larvicides and pesticides (adulticides) respectively (Trevejo et al. 2008). Elnaiem et al. (2008) report effective control of mosquitoes in Sacramento, California using aerial applications of pyrethrin insecticide. Spraying
of pyrethrin significantly reduced mosquito abundance and number of infective bites received by
humans. However the authors point out the environmental and health hazards of pesticides, and
emphasise that “mosquito adulticiding should be used as part of a comprehensive intervention
program, when surveillance indicates an increased risk of infection to humans” (Elnaiem et al.
2008).

Due to increased resistance of mosquito populations to conventional control agents, research has
gone into developing biopesticides. These are based on recombinant bacterial strains expressing
toxins of *Bacillus thuringiensis* and *B. sphaericus* (Park et al. 2005 in Kramer et al. 2008),
mosquito baculoviruses such as *C. nigripalpus* nucleopolyhedrovirus (Becnel 2006 in Kramer et
al. 2008) or entomopathogenic fungi (Kanzok and Jacobs-Lorena 2006 in Kramer et al. 2008).

There have also been a number of new mosquito control strategies proposed in recent times.
Mass-trapping using mosquito traps with attractants (heat, carbon dioxide, octenol) have
demonstrated good levels of control (Kline 2006 in Kramer et al. 2008). As knowledge of
mosquito attractants improves mass trapping may become a more viable control option (Kramer
et al. 2008). A strategy currently being researched to control malaria and dengue is creation of
transgenic mosquitoes that are incapable of transmitting pathogens (Franz et al. 2006; Ito et al.
2002 in Kramer et al. 2008). However Kramer et al. (2008) suppose that this strategy may be
more difficult for control of WNV as the transmission cycle is more complex.

### 3.3 VACCINATION

There are several approaches for vaccination. The first is inoculation of multiple doses of
inactivated (killed) virus (Samina et al. 2005 in Kramer et al. 2008). “Killed vaccines are
considered relatively safe, because the virus cannot replicate and cause clinical disease.
However, they tend to have a reduced capability to induce and sustain an effective and balanced
immune response, thus requiring multiple and repeated doses to maintain protection” (Wolf et al.
2008).

“The second strategy involves expression of WNV viral proteins in a host to elicit an immune
response. Viral proteins can be inoculated directly into the host, as a recombinant subunit
vaccine (Chu et al. 2007; Ledizet et al. 2005; Lieberman et al. 2007), or they can be produced by
host cells following inoculation of DNA plasmids (Davis et al. 2001) or virus vectors that
express WNV genes (Karaca et al. 2005)” (Kramer et al. 2008).

The third strategy involves the use of chimeric viruses containing the PrM and E genes of WNV
within a heterologous attenuated flavivirus backbone. The yellow fever 17D vaccine strain,
which has been safely used for large-scale human immunisation for over 60 years, is an excellent
vector for delivering protective antigens of flaviviruses (Monath et al. 2006 in Kramer et al.}
2008). Yellow fever DEN2 PDK-53 (Hubalek and Halouzka 1999 in Kramer et al. 2008) and DEN4–3delta30 (Pletnev et al. 2002) have also been used as backbones.

The final vaccination strategy is based on attenuated (non-virulent) West Nile virus isolates, which provide protection against virulent strains. “Kunjin virus is a naturally attenuated West Nile virus subtype that could provide protective immunity in mice against the virulent New York West Nile virus strain (Hall et al. 2003). An attenuated non-epidemic West Nile virus strain (lineage II) was also shown to be an effective vaccine against virulent epidemic strain (lineage I) in mice (Yamshchikov et al. 2004)” (Kramer et al. 2007).

For other flaviruses attenuation has been based on mutations into nonstructural genes resulting in reduced virus replication (Hall et al. 2003; Yamshchikov et al. 2004 in Kramer et al. 2008), or by introducing mutations into the capsid gene, disabling the release of the virus from the cell (Mason et al. 2006; Seregin et al. 2006 in Kramer et al. 2008). These approaches could have potential to be used in development of West Nile virus vaccines (Kramer et al. 2007).

### 3.3.1 HUMAN VACCINES

At present there is no vaccine approved for use in humans, although there has been progress in development with four clinical trials underway. “The first is inoculation of multiple doses of inactivated (killed) virus (Samina et al. 2005). A second strategy involves expression of WNV viral proteins in a host to elicit an immune response. Viral proteins can be inoculated directly into the host, as a recombinant subunit vaccine (Chu et al. 2007; Ledizet et al. 2005; Lieberman et al. 2007), or they can be produced by host cells following inoculation of DNA plasmids (Davis et al. 2001) or virus vectors that express WNV genes (Karaca et al. 2005). The third strategy involves the use of chimeric viruses containing the PrM and E genes of WNV within a heterologous attenuated flavivirus backbone [Yellow fever 17D (Monath et al. 2006), DEN2 PDK-53 (Hubalek and Halouzka 1999) or DEN4–3delta30 (Pletnev et al. 2002)]. The final vaccination strategy is based on attenuated viruses. Several types of attenuated viruses have been created by introducing mutations into nonstructural genes (Hall et al. 2003, Yamshchikov et al. 2004), resulting in reduced virus replication, or by introducing mutations into the capsid gene (Mason et al. 2006, Seregin et al. 2006), disabling the release of virus from the cell” (Kramer et al. 2008).
3.3.2. HORSE VACCINES

“Given the potential severity of WNV infection in horses, the American Association of Equine Practitioners recommends vaccination of all horses in North America (AAEP 2005). There are several commercially available vaccines for equine use that contain either killed virus or modified-live recombinant virus. The initial administration of vaccine is followed by a booster in 3 to 6 weeks” (Trevejo et al. 2008)

“Foals can be vaccinated starting at 3 to 4 months of age, and even earlier in foals from non-vaccinated mares (AAEP 2005). Vaccination is recommended in advance of the mosquito season to allow sufficient time for development of neutralizing antibodies. Although vaccination may not fully prevent clinical disease, it does reduce the risk of severe disease and death associated with WNV infection, even when vaccination is not performed sufficiently in advance of mosquito-related WNV transmission activity (Ward et al. 2006; Salazar et al. 2004). There is no evidence of adverse effects resulting from vaccination of pregnant mares (Vest et al. 2004)” (Trevejo et al. 2008).

For further information see the American Association of Equine Practitioners West Nile virus vaccination guidelines.

Although approved only for horses, commercial WNV vaccine has been used for the purpose of protection of nondomestic species, including avian, equid, and rhinoceros species (Wolf et al. 2008).

Many zoological facilities have initiated WNV vaccinations to at-risk and endangered species (Sirpenski, pers. comm.; Vuolo, pers. comm. in Davis et al. 2008), although the safety and efficacy of vaccines in these species is generally unknown. There have been a number of WNV vaccine trials in various avian species, including penguins, flamingoes, chickens, hawks, crows and condors although results have been inconsistent (see Davis et al. 2008).

4.0 TREATMENT

No vaccine or specific treatment exists to prevent or combat the West Nile virus infection in humans. Treatment of severe illness includes hospitalization, use of intravenous fluids and nutrition, respiratory support, prevention of secondary infections, and good nursing care. Medical care should be sought as soon as possible for persons who have symptoms suggesting severe illness (CDC 2003a).
“Several antiviral compounds and therapies are being tested in clinical trials. Patients with WNV encephalitis have been successfully treated with intravenous immunoglobulin derived from donor plasma with high levels of WNV antibodies (Shimoni et al. 2001); the safety and efficacy of this treatment are being tested in phase I/II clinical trials” (Kramer et al. 2008).

Antibody therapy using humanized monoclonal antibodies directed against the WNV envelope protein is therapeutically effective in mice and hamsters. A single dose of these antibodies given to animals at 5 days post-infection (when neurons are infected with WNV) protected animals from WNV-induced mortality and resulted in decreased viral titers in the brain (Morrey et al. 2006; Oliphant et al. 2005 in Kramer et al. 2008).

“Interferon therapy effectively controlled WNV infection in vitro and in animal models (Anderson and Rahal 2002; Samuel and Diamond 2005). A clinical trial is currently underway to test the safety and efficacy of interferon therapy for West Nile meningocephalitis in humans” (Kramer et al. 2008).

“Oligomers with complementary sequence to portions of the WNV genome (antisense therapies) have shown significant antiviral activity in vitro (Deas et al. 2005; Torrence et al. 2006). The safety and efficacy of one antisense compound (AVI-4020) against WNV ND are being tested in a clinical trial” (Kramer et al. 2008).

High-throughput assays developed by two groups (Gu et al. 2005, Puig-Basagoiti et al. 2005 in Kramer et al. 2008) are being used to screen compounds for antiviral activity. One of these assays identified triaryl pyrazoline as an inhibitor of multiple flaviviruses in cell culture through inhibition of viral RNA replication. It has potential to be developed into treatment for flavivirus infection (Puig-Basagoiti et al. 2006).

Detailed information on West Nile virus management is available in the publication Epidemic/Epizootic West Nile Virus in the United States: Guidelines for Surveillance, Prevention and Control, produced by the Centers for Disease Control and Prevention.