

Deleterious Gene Spread

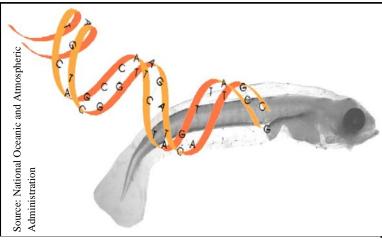
U.S. ARMY CORPS OF ENGINEERS

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ANS Control: Deleterious Gene Spread – Daughterless Gene and Trojan Y Chromosome Technologies

Targeted Species: This geneticallybased technology is an effective control for fish. Specific ANS identified as ANS of Concern – CAWS¹ that may be controlled with this technology include bighead carp *(Hypophthalmichthys nobilis)*, black carp *(Mylopharyngodon piceus)*, sea lamprey *(Petromyzon marinus)* and silver carp *(H. molitrix)*.

Selectivity: This experimental



DNA can be manipulated to produce only male offspring, leading to the eventual extinction of a species.

technology is under consideration for targeting bighead carp, black carp, sea lamprey and silver carp. (Teem et al. 2011).

Developer/Manufacturer/Researcher: All projects are presently in the research phase. Research organizations include the Commonwealth Scientific and Industrial Research Organisation (CSIRO) in Australia, U.S. Fish and Wildlife Service, and the US Geological Survey's Hammond Bay Biological Station, MI.

Brief Description: There are hundreds of genetically-based strategies that have been or are currently being experimentally tested to control a target population of a non-native species (Pimentel et al. 1989; Muir & Howard 2002; Kapuscinski et al. 2003; Thresher & Kuris 2004; Kapuscinski 2005; Snow et al. 2005; Bergstedt & Twohey 2007). This fact sheet addresses only those with the highest potential to manage ANS fish species in the CAWS. These techniques involve the production and release of genetically altered fish that bear a deleterious genetic construct (transgene) designed to disrupt a specific aspect of the organism's life cycle or biology. Genetic disruption is achieved by releasing fish that produce: offspring of a single sex; sterile offspring; or non-viable embryos (Kapuscinski 2005; Kapuscinski & Patronski 2005; Grewe et al. 2005). A variety of genes could be targeted to control aspects of development, survival, or gametogenesis in offspring. Two autocidal genetic biocontrol methods have been proposed as a means to eliminate invasive fish by changing the sex ratio of the population: the daughterless gene strategy and the Trojan Y.

<u>Daughterless Gene</u> – Daughterless gene technology is a form of sex ratio distortion, where a transgene disrupts a key step in sexual development (i.e., expression of aromatase enzyme) to produce all-male

¹ For a complete list of the 39 specific ANS of Concern – CAWS, please see Table 1 of the main report.

offspring (Werren et al. 1981; Thresher 2008; Thresher & Bax 2003, Kapuscinski & Patronski 2005; Thresher et al. 2002). The transgene is inheritable to future generations (Thresher & Bax 2003) and progressively skews the population sex ratio to the point where the population's reproductive output begins to decline leading to extinction (Grewe 1997; Burt 2003).

<u>*Trojan Y Chromosome*</u> – The Trojan Y chromosome strategy makes use of a genetically engineered female fish with multiple Y chromosomes. In this approach, a female fish with two Y chromosomes (Trojan Y) is added to a target population. Subsequent mating of the Trojan Y fish with males of the target population would result in the production of all male progeny, half of which are super males (males with two Y chromosomes, making them sterile) (Gutierrez & Teem 2006). Models indicate that for fish species that mature and reproduce once a year, the timeframe for extinction is about 70 years if the Trojan Y fish is stocked at 1.66% of the total population annually (Teem et al. 2011).

Prior Applications: The concept of daughterless gene technology has been around since the mid 1960s (Hamilton 1967). Models indicate that these technologies are feasible, at least under laboratory conditions, and they have been considered for experimental use in Australia, Florida, and the Great Lakes (Bergstedt & Twohey 2007). Thresher (2008) reported that the CSIRO would be ready to conduct a field test of daughterless carp technology in as little as 5 years (2013) in Australia. The Trojan Y chromosome strategy has not been attempted in wild populations.

General Effectiveness: Deleterious genes have not been field tested, but mathematical models have been developed to demonstrate their potential effect.

<u>Daughterless Gene</u> – Preliminary modeling done by Thresher & Bax (2003) showed that when 5% of wildtype carp recruits in a year were replaced with daughterless carriers, a common carp population would show a significant decrease in population levels by 2020 and near extinction by 2030 in Australia. Although the daughterless gene technology appears to have lab research that is the most developed of all transgenic biocontrol strategies, a vast majority of the research has been done outside of North America. Literature indicates that this technology is genetically feasible and has the potential to control aquatic nuisance species, but the potential efficacy of this technique will depend on site- and species- specific characteristics.

<u>*Trojan Y Chromosome*</u> – A model that compared daughterless gene and Trojan Y chromosome strategies showed that the Trojan Y chromosome strategy worked faster and required the introduction of fewer genetically engineered fish to the target population to achieve local extinction (Teem et al. 2011).

Operating Constraints: Manipulation of genes can manifest unforeseen and significant undesirable side effects and would require extensive research before being accepted as a Control (Liberman et al. 1996). Unintended consequences, such as the spread of genetic material to other species, should be understood before application of this Control. The ecological and economic costs of non-selective treatments will be important to weigh against the risk of spreading genetic material to other species. The subtle effects of even minor variability in some genetic parameters suggest that genetic techniques be applied in an active adaptive management framework (Bax & Thresher 2009). The Food and Drug Administration regulates genetically engineered animals through its New Animal Drug Application

process under the Federal Food, Drug, and Cosmetic Act, and would be the lead Federal agency for permitting the application of this technology in the United States.

Cost Considerations:

- *Implementation:* Implementation costs would include the cost of fish and staffing fish release activities. Planning and design activities in this phase may include research and development of this Control, modeling, site selection, site-specific regulatory approval, plans and specifications, and real estate acquisition. Design will also include analysis of this Control's impact to existing waterway uses including, but not limited to, flood risk management, natural resources, navigation, recreation, water users and dischargers, and required mitigation measures.
- *Operations and Maintenance:* Operations and maintenance costs would include effectiveness monitoring and continued release of fish.
- *Mitigation:* Design and cost for mitigation measures required to address impacts as a result of implementation of this Control cannot be determined at this time. Mitigation factors will be based on site-specific and project-specific requirements that will be addressed in subsequent, more detailed, evaluations.

Citations:

- Bax, N.J. & R.E. Thresher. 2009. Ecological, behavioral, and genetic factors influencing the recombinant control of invasive pests. *Ecological Applications*, vol. 19(4), pp. 873-888
- Bergstedt, R.A. & M.B. Twohey 2007. Research to support sterile-male-release and genetic alteration techniques for sea lamprey control. *Journal of Great Lakes Research*, vol. 33 (Special Issue 2), pp. 48–69
- Burt, A. 2003. Site-specific selfish genes as tools for the control and genetic engineering of natural populations. *Proceedings of the Royal Society of London*, vol. 270, pp. 921-928
- Grewe, P., N. Botwright, J. Beyer, J. Patil, & R. Thresher. 2005. Sex-Specific apoptosis for achieving Daughterless Fish. Proceeding of the 13th Australasian Vertebrate Pest Conference, Wellington, New Zealand
- Grewe, P. 1997. "Potential of Molecular Approaches for the Environmentally Benign Management of Carp." Pp 119-129 in *Controlling Carp: Exploring the Options for Australia.*, Jane Roberts & Richard Tilzey (eds). Commonwealth Scientific and Industrial Research Organisation & Murray–Darling Basin Commission, Canberra
- Gutierrez, J.B. & J.L. Teem. 2006. A model describing the effect of sex-reversed YY fish in an established wild population: the use of a Trojan Y chromosome to cause extinction of an introduced exotic species. *Journal of Theoretical Biology*, vol. 241(22), pp. 333-341
- Hamilton, W. D. 1967. Extraordinary sex ratios. Science, vol. 156, pp. 477-488

- Kapuscinski, A.R. 2005. Current scientific understanding of the environmental biosafety of transgenic fish and shellfish. *Revue Scientifique et Technique International Office of Epizootics*, vol. 24, pp. 309-322
- Kapuscinski, A.R., R.M. Goodman, S.D. Hann, L.R. Jacobs, E.E. Pullins, C.S. Johnson, J.D. Kinsey, R.L. Krall, A.G.M. La Viña, M.G. Mellon, & V.W. Ruttan. Making 'safety first' a reality for biotechnology products. *Nature Biotechnology*, vol. 23, pp. 599-601
- Kapuscinski, A.R. & T.J. Patronski. 2005. Genetic methods for biological control of non-native fish in the Gila River basin: Development and testing of methods, potential environmental risks, regulatory requirements, multi-stakeholder deliberation, and cost estimates. Contract report to the U.S. Fish and Wildlife Service (USFWS agreement number 201813N762). University of Minnesota, Institute for Social, Economic and Ecological Sustainability, St. Paul, Minnesota. Minnesota Sea Grant Publication F 20
- Liberman, D.F., L. Wolfe, R. Fink, & E. Gilman. 1996. "Biological Safety Considerations for Environmental Release of Transgenic Organisms and Plants." Pp. 41- 63. In *Engineered* Organisms in Environmental Settings: Biotechnological and Agricultural Applications, Levin, M.A. & E. Israeli, (Eds). CRC Press, Boca Raton, FL
- Muir, W.M. & R.D. Howard. 2002. Assessment of possible ecological risks and hazards of transgenic fish with implications for other sexually reproducing organisms. *Transgenic Research*, vol. 11, pp. 101-114
- Pimentel, D., M.S. Hunter, J.A. LaGro, R.A. Efroymson, J.C. Landers, F.T. Mervis, C.A. McCarthy, & A.E. Boyd. 1989. Benefits and risks of genetic engineering in agriculture. *BioScience*, vol. 39, pp. 606-614
- Snow, A.A., D.A. Androw, P. Gepts, E.M. Hallerman, A. Power, J.M. Tiedje, & L.L. Wolfenbarger. 2005. Genetically engineered organisms and the environment: current status and recommendations. *Ecological Applications*, vol. 15, pp. 377-404
- Teem, J.L., J.B. Guierrez, & R.D. Parshad. 2011. A comparison of the Trojan Y chromosome and daughterless carp eradication strategies. *Biological Invasions*. In Press
- Thresher, R. E. 2008. Autocidal technology for the control of invasive fish. *Fisheries*, vol. 33, pp. 14-121
- Thresher, R.E. & A.M. Kuris. 2004. Options for managing invasive marine species. *Biological Invasions*, vol. 6, pp. 295-300
- Thresher, R E., L. Hinds, P. Grewe, & J. Patil. 2002. Genetic control of sex ratio in animal populations. International Publication number WO 02/30183 A1. World International Property Organization

- Thresher, R.E. & N. Bax. 2003. "The Science of Producing Daughterless Technology; Possibilities for Population Control Using Daughterless Technology; Maximizing the Impact of Carp Control." Pp. 19-24 in *Proceedings of the National Carp Control Workshop*, 5-6 March, Canberra, Lapidge, K (ed.). Cooperative Research Centre for Pest Animal Control, Canberra
- Werren, J.H., S.W. Skinner, & E.L. Charnov. 1981. Paternal inheritance of a daughterless sex ratio factor. *Nature*, vol. 293, pp. 467-468