Institution: University of Sussex

Unit of Assessment: UoA 08 Chemistry

Title of case study: Detecting sex-changing chemicals in the environment

1. Summary of the impact

The contamination of water sources is a serious threat to the environment and to human health. Endocrine-disrupting chemicals (EDCs) cause sexual dysfunction in fish, potentially affecting the health of fish populations in the UK and abroad. Prof. Hill's research has used bioassays combined with chemical fractionation and mass-spectrometry profiling techniques to identify endocrine-disrupting chemicals present in wastewater effluents that are discharged into the environment and that can bio-accumulate in fish. This has enabled international and governmental organisations to assess the risk of chemical discharges to the environment, to develop tests to monitor the toxicity of these newly-discovered EDCs, and to inform policy decisions on environmental protection and conservation.

2. Underpinning research

Prof. Hill's work was the first to discover that endocrine-disrupting chemicals can bio-concentrate in the bile of fish many thousand-fold, allowing the identification and bio-monitoring of trace amounts of contaminants in surface waters [see Section 3, R1]. This has enabled the identification of hormone replacement chemicals as environmental oestrogens [R2].

Prof. Hill's group has also used bioassay-directed fractionation and mass-spectrometry analytical techniques to identify the structures of novel anti-androgenic contaminants present in wastewater effluents [R3, R4]. These contaminants, such as triclosan and chlorophenes, are present in household disinfectant agents and have not previously been recognised to contain anti-androgen activity.

In additional work, the use of bioassay-directed fractionation and identification techniques has led to the discovery of environmental oestrogens accumulating in river sediments at sites below wastewater discharges, raising concerns over the persistence in the environment and impacts on organisms in the water system [R5].

This research on the identification of new contaminants with endocrine-disrupting activity has raised concerns that aquatic animals are exposed to complex mixtures of chemicals that target their reproductive health and fertility. This work has been supported in the UK by the Environment Agency and government research councils (NERC), and in Europe under the EU Interreg programme.

Professor E.M. Hill held the positions of Senior Lecturer, Reader and, laterly, Professor at the University of Sussex, during the period of this work, and – as group leader – initiated and supervised this work, heading a team of postdoctoral researchers (Peck, Gibson and Rostkowski), PhD students (Evans, Smith and Oladapo) and a technician (Horwood).

3. References to the research

R1 Smith, M.D. and Hill, E.M. (2004) 'Uptake and metabolism of technical nonylphenol and its brominated analogues in the roach (Rutilus rutilus)', *Aquatic Toxicology*, 69(4): 359–70.

R2 Gibson, R., Smith, M.D., Spary, C.J., Tyler, C.R. and Hill, E.M. (2005) 'Mixtures of estrogenic contaminants in bile of fish exposed to sewage treatment effluents', *Environmental Science*

and Technology, 39(8): 2461–71.

R3 Hill, E.M., Evans, K.L., Horwood, J., Rostkowski, P., Oladapo, F.O., Gibson, R., Shears, J.A. and Tyler, C.R. (2010) 'Profiles and some initial identifications of (anti)androgenic compounds in fish exposed to wastewater treatment works effluents', *Environmental Science and Technology*, 44(3): 1137–43.

R4 Rostkowski, P.; Horwood, J.; Shears, J. A.; Lange, A.; Oladapo, F. O.; Besselink, H. T.; Tyler, C. R.; Hill, E. M. (2011) 'Bioassay-Directed Identification of Novel Antiandrogenic Compounds in Bile of Fish Exposed to Wastewater Effluents'. Environmental Science and Technology. 45, (24), 10660-10667.

R5 Peck, M., Gibson, R.W., Kortenkamp, A. and Hill, E.M. (2004) 'Sediments are major sinks of steroidal estrogens in two United Kingdom rivers', *Environmental Toxicology and Chemistry*, 23(4): 945–52.

Outputs R1, R2 and R3 best indicate the quality of the underpinning research.

Outputs can be supplied by the University on request.

Relevant grants

- February 2008–February 2010: NERC, £296,727.
  The Significance of Antiandrogens in Disrupting Sexual Function in Wild Fish in UK Rivers.

- February 2009–July 2013: EU Interreg, £619,159.
  DIESE: Determination of Pertinent Indicators for Environmental Monitoring: A Strategy for Europe.

- June 2005–June 2008: Environment Agency, £35,163.
  Analyses of Fish Bile Samples.

- October 2007–March 2009: Environment Agency, £6,000.
  Analysis of Archived Fish Samples – A Scoping Study.

4. Details of the impact

- **Impact on the EU regulation of endocrine-disrupting chemicals**

  The contamination of water sources is a serious threat to the environment and to human health. Our finding that fish can accumulate œstrogenic and anti-androgenic contaminants that can impact on their fertility and health, and that many of these compounds persist in the environment, has been cited in a European Environment Agency Technical report [see Section 5, C1, which cites Hill's publications R2, R3 and R5 above]. This EEA report has provided evidence that has underpinned EU policy on endocrine-disrupting chemicals and their regulation – specifically the proposal by the European Commission to regulate levels of œstrogens in surface waters under recent revisions to the Water Framework Directive (2000/60/EC) [C2]. Some of our work cited in the report was presented in informal meetings with the UK Environment Agency.

  A further report by the Institute of Environment and Sustainability, of the Joint Research Centre of the European Commission, cited work by Hill's group on the identification of anti-androgenic structures in wastewater effluents (see C3 which cites Hill's publication R4 listed above). The report collated information on chemical analytical methods for the new proposed Priority Substances under revisions of the European Water Framework Directive legislation [C2].

- **Impact on the development of *in vivo* fish-screening assays by the EU**

  Hill's identification of anti-androgenic contaminants in UK effluent has also been cited by the Environment Directorate Chemicals Committee as evidence for the need for *in vivo* fish-screening assays which, as a consequence, have now been developed by the EU [C4, which cites Hill's publication R3].

- **Impact on the regulation of Nonylphenol in California**

  Finally, our work on the toxicokinetics of the endocrine-disrupting chemical, nonylphenol, in fish has informed the risk assessment of this compound, which has influenced state policy and regulation in California [see C5 which cites Hill's publication R1].

  The beneficiaries of this impact are thus governmental organisations responsible for environmental policy, the environment and human health and, through them, populations living under their regulations.

5. Sources to corroborate the impact

C1 *The Impacts of Endocrine Disrupters on Wildlife, People and their Environments: The Weybridge+15 (1996–2011) Report*. European Environment Agency Technical Report No. 2/2012, ISSN 1725-2237, 10 May 2012.

C2 Proposal for a Directive of the European Parliament and of the Council amending Water Framework Directives 2000/60/EC and 2008/105/EC as regards priority substances in the field of water policy. Brussels, 31 January 2012. COM(2011) 876 final 2011/0429 (COD).

C3 Analytical Methods for the new proposed Priority Substances of the European Water Framework Directive (WFD). Revision of the Priority Substance List (2012). JRC Technical Report. Ed. Robert Loos. European Commission - DG Joint Research Centre, Institute for Environment and Sustainability © European Union, 2012.

C4 *Peer Review Report of the Validation of the 21-Day Androgenised Female Stickleback Screening Assay. Series of Testing and Assessment, No 127*. Environment Directorate Chemicals Committee and Working Party on Chemicals, Pesticides and Biotechnology. ENV/JM/MONO (2010)18. Revised August 2011.

C5 *Toxicological Profile for Nonylphenol*. Integrated Risk Assessment Branch, Office of Environmental Health Hazard Assessment, California Environmental Protection Agency. September 2009.