



Emergence of Animal Alternative Needs in Environmental Risk Assessment

Scott E. Belanger, Ph.D., Chair Michelle R. Embry, Ph.D.

Research Fellow

The Procter & Gamble Company

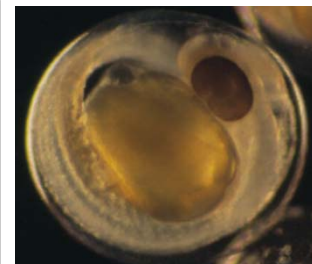
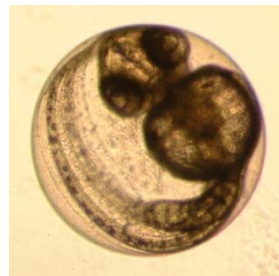
Cincinnati, Ohio USA

Senior Scientific Program Manager

ILSI Health and Environmental Sciences Institute

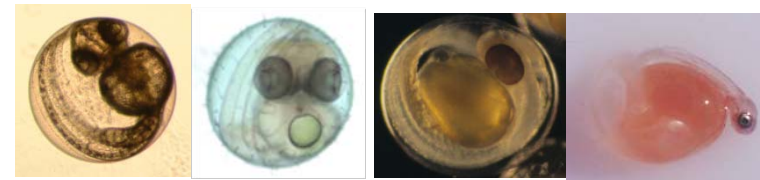
Washington, D.C. USA

*ILSI-HESI Annual Meeting
20 January 2009*



Sub-Committee History

- 2006 – Proposed and prioritized by EISC
- 2007 – Presented to HESI and added to HESI portfolio
- 2008 – Held the first workshop of the EI Subcommittee (report today)
- 2008/2009 – Petition for full project status, plan for on-going work



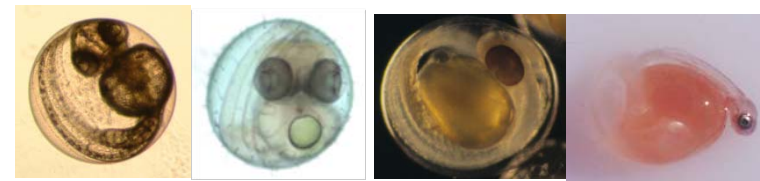
Animal Alternatives in ERA - Mission

- Develop the sound technical basis for embryonic fish tests as an alternative to standard fish toxicity test procedures around the globe.
- Provide a forum to coordinate the debates and best emerging practices of the fish alternatives and animal model development sciences to meet existing hazard assessment, effluent assessment, risk assessment, classification and labeling and regulatory needs.

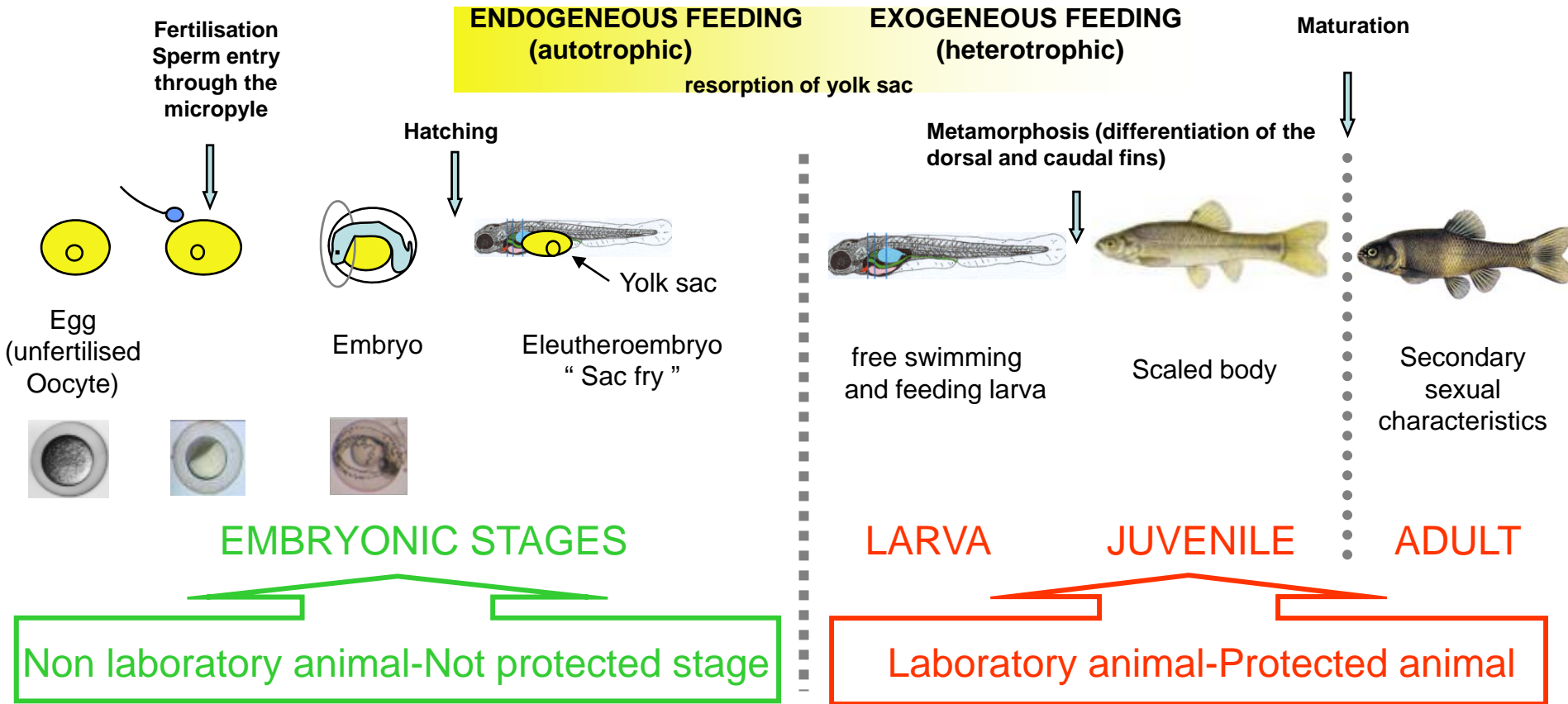
A Mission whose ideas are shared by other partners in this effort



ORGANISATION
FOR ECONOMIC
CO-OPERATION
AND DEVELOPMENT

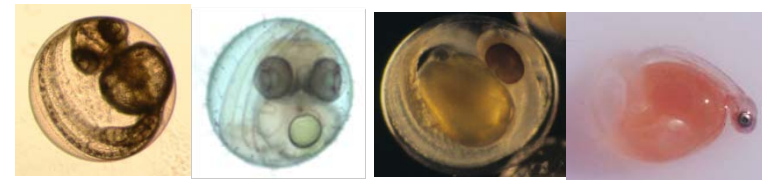


Fish Embryo and Eleutheroembryo Tests



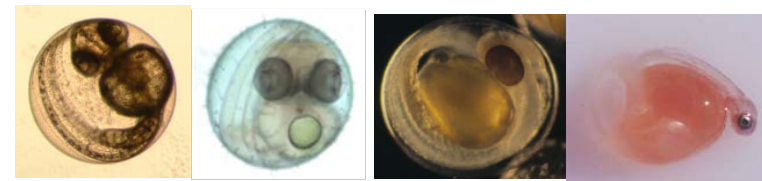
Acute lethality is endpoint of concern based on observations of:

- egg coagulation
- somite formation
- presence of heartbeat
- lack of tail detachment



HESI Environmental Animal Alternatives – Accomplishments (thus far)

- Held a major international workshop in March 2008 in Aulnay-sous-Bois, France on the Research Campus of L'Oréal (near Paris)
- Co-sponsored with ECETOC; additional funding by P&G, ECVAM (EC JRC), and L'Oréal
 - 41 scientists; 10 countries; 36 organizations; Europe, NA, Asia
 - Plenary/break-out format
- Focus on fish acute toxicity testing (low hanging fruit)
- Generate ideas, solutions, consensus (where possible) on a series of related topics



HESI Environmental Animal Alternatives

Steering Team

Scott Belanger (Chair)

Michelle Embry (Sr Sci. Program manager)

Thomas Braunbeck

Marlies Halder

David Hinton

Marc Léonard

Adam Lillicrap

Teresa Norberg-King

Graham Whale

Procter & Gamble

HESI

Heidelberg University

ECVAM

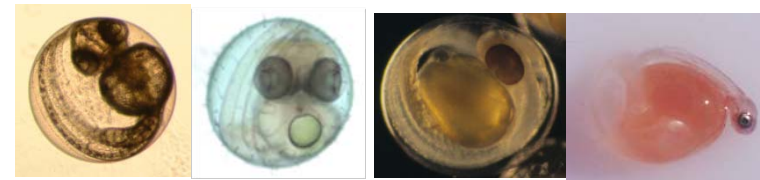
Duke University

L'Oréal

AstraZeneca

USEPA

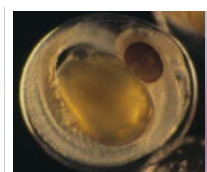
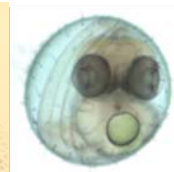
Shell UK



HESI Environmental Animal Alternatives

Workshop and Webconference Participation

- Aarhus University (Denmark)
- AstraZeneca (UK)
- BASF (Germany)
- Dow-Corning (US)
- Duke University (US)
- DuPont (US)
- EAWAG (Switzerland)
- ECETOC (Belgium)
- Ecogenomics (Japan)
- Environment Agency (UK)
- Environment Canada (Canada)
- ESPCI (France)
- European Commission/JRC/ECVAM (Italy)
- ExxonMobil (US)
- Federal Environment Agency (UBA) (Germany)
- Fraunhofer Institute (Germany)
- Griffith University (Australia)
- Home Office (UK)
- ILSI-HESI (US)
- Institute of Environmental Ecology (Japan)
- Institute of Natural Sciences (Japan)
- Kyoto University (Japan)
- L'Oréal (France)
- Monsanto (US)
- Miami University (US)
- Nalco (US)
- National Institute for Environmental Studies (Japan)
- Norwegian School of Veterinary Science (Norway)
- OECD (France)
- Procter & Gamble (US)
- Queen's University (Canada)
- RIFM (US)
- RIVM (Netherlands)
- Shell (UK)
- Shell (US)
- Syngenta (US)
- Technical University of Dresden (Germany)
- Unilever (UK)
- University of Guelph (Canada)
- University of Heidelberg (Germany)
- University of North Texas (US)
- UFZ Leipzig (Germany)
- USEPA (US)
- USGS (US)



Fish Alternatives Workshop Overview

Day One

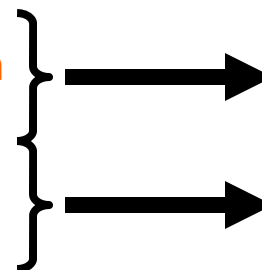
- Overviews of animal alternatives in environmental science
- Panel discussion on fish developmental biology, pain, and distress
- State of the science pertaining to fish embryo and eleutheroembryo tests



Break out groups with Session Chairs and Rapporteurs

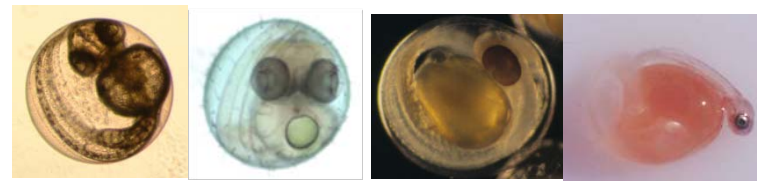
Day Two

- New science and applicability of embryonic fish tests
- Use of alternatives tests in environmental hazard and risk assessment



Day Three

- Assimilation of breakout group discussions
- Formation of additional groups/venues for progress



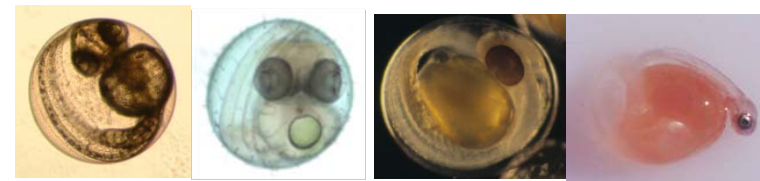
Fish Alternatives Workshop Products/Outcomes

Consensus Opinions

- Environmental safety/risk assessors need fish data
- Acute toxicity testing with fish embryos is a valid animal alternative (most reliably referred to as a “replacement” alternative)
- Extension of the test from beyond the egg interval to the eleutheroembryo interval is enormous “value-added” while remaining an alternative test
- Enormous opportunities exist to use fish embryos in environmental and human safety sciences

Not so Consensus

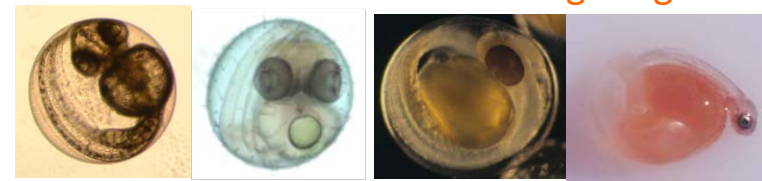
- Fish may or may not feel pain...there is a dearth of evidence (not unexpected)
- The Fish Embryo Test can be considered “validated” *sensu* OECD, ECVAM
- Many future needs, variety of constituencies



Fish Alternatives Workshop Products/Outcomes

Tangible Work Products

1. Publications (7 planned, 1 in press, 1 in review, 1 ready to submit)
 - Workshop summary: **The Fish Embryo Test as an Animal Alternative Method in Hazard and Risk Assessment and Scientific Research.** Embry, M.R., et al. Environmental Health Perspectives (to be submitted Jan 2009).
 - Plenary paper: **Nociception in Fish Embryos and Eleutheroembryos.** Calvino, B.. For submission to Pain.
 - Plenary paper: **Regulatory Aspects on the Use of Fish Embryos in Environmental Toxicology.** Halder, M.A., et al. For submission to Environmental Health Perspectives.
 - Plenary paper: **Natural Thresholds in the Early Ontogeny of Fishes Related to Definitions of Protected and Non-protected Life Intervals.** Belanger, S.E. et al. For Submission to Journal of Fish Biology.
 - Plenary paper: **Is the Fish Embryo Toxicity test (FET) with the zebrafish (*Danio rerio*) a potential alternative for the fish acute toxicity test?** Lammer, E. et al.. Comp. Physiol. Biochem. Part C (In Press).
 - Break-out session paper: **State of the Science and Future Prospects Using Fish Embryo Tests.** Hinton, D.A. et al. Submission TBD.
 - Break-out session paper: **Fish Embryo Tests in Hazard and Risk Assessment.** Norberg-King et al. Submission TBD.

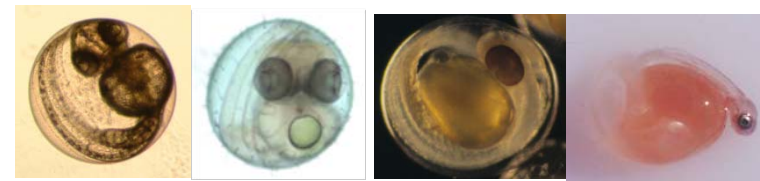


Fish Alternatives Workshop Products/Outcomes

Tangible Work Products

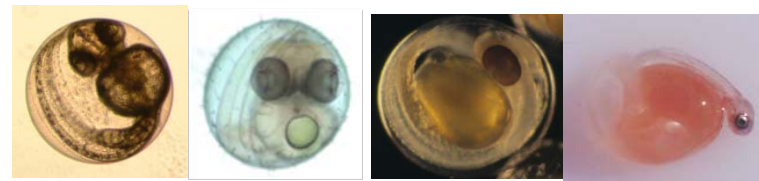
2. Organizational involvement/cross-talk

- HESI is invited as an independent observer and member of the OECD Fish Embryo Test Validation Management Group (led from ECVAM)
- SETAC (Society of Environmental Toxicology and Chemistry) has recognized this growing need and worked with HESI Fish Alternatives Committee members to establish a new SETAC Science Advisory Group on Animal Alternatives
 - New publications/editorial policies on adherence to animal welfare and encouragement of institutional oversight
 - Expanded view...birds, amphibians, field investigations, etc.
 - HESI workshop and results highlighted at 2 SETAC regional (EU, NA) and 1 World Congress
- Additional presentations:
 - EUROTOX (Dresden, 2009)
 - World Congress VII on Alternatives and Animal Use in the Life Sciences (Rome, 2009)



Fish Alternatives What Comes Next?

- The EI Steering Team assessed the potential to become a standing project team
 - Identified and secured interested industry contributors – broad cross section of sectors
 - AstraZeneca
 - Bayer HealthcarePharma
 - Dow Corning
 - DuPont
 - Exxon
 - L'Oreal
 - Procter & Gamble
 - RIFM
 - sanofi-aventis
 - Shell
 - Unilever
 - (3 additional industry members still in discussion)
- The EIC Steering Team held a webinar on 3 December 2008
 - Broaden the participation in the Steering Team
 - Identify next areas to work, additional leaders, participants (academic, government, industry, NGO)
 - Potential areas set out as thought starters, call participants voted on priority, interest level



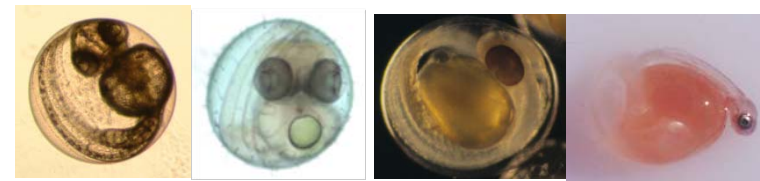
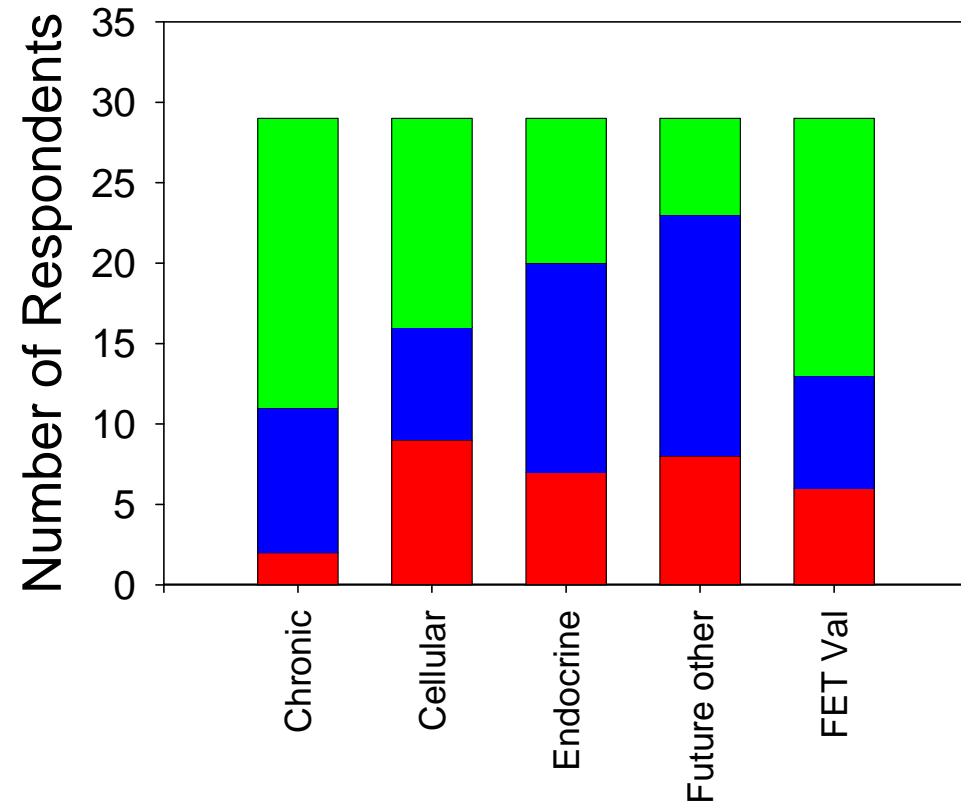
Fish Alternatives What Comes Next?

And the Survey Says!

1. Alternatives for chronic toxicity and validation of the FET are top priorities (esp. industry)
2. Development of cellular/sub-cellular methods is also a priority
3. Endocrine disruption alternatives was more important to regulators
4. All the areas had a constituency – all will find leaders and be progressed
5. Next steps are:
 - a. Sub-teams form and propose rational paths forward
 - b. Steering Team to be re-formed with new leaders to assist

Priority Ranking

- Low
- Medium
- High



Fish Alternatives in Environmental Risk Assessment: Conclusions

- Enormous progress since initiation in 2007
 - Highly successful workshop
 - 7 publications anticipated from subcommittee
 - Energized and focused debates, broad support across all stakeholders...already steered international activities
 - HESI seen as an essential collaborator; numerous organizational partners in addition to traditional academic, regulatory, and industry affiliates
- Charting a path forward for future environmental alternatives discussions is being actively worked
 - Areas of worked identified
 - Immediate past work will still receive effort (e.g., FET validation)
 - Workshops, white papers likely; funding of *de novo* research is dependent on breadth of industry involvement (opportunities for collaboration are great)
 - Call to broaden beyond fish is already being heard



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