154 Development of an AOP describing effects of narcotics on membrane-bound mitochondrial processes in fish L. Vergauwen, University of Antwerp / Zebrafishlab Dept Veterinary Sciences SPHERE; E.D. Michiels, University of Antwerp / Zebrafishlab Dept Veterinary Sciences; E. Stinckens, University of Antwerp; S.N. Schmidt, P. Mayer, Technical University of Denmark / Department of Environmental Engineering; A. Covaci, University of Antwerp, Toxicological Center / Toxicological Center; G.T. Ankley, U.S. EPA / National Health and Environmental Effects Research Laboratory; R. Blust, University of Antwerp; D. Knapen, University of Antwerp / Zebrafishlab Dept Veterinary Sciences. Around 70% of industrial chemicals are hydrophobic compounds which are assumed to cause toxicity through narcosis by disrupting membrane integrity and function. The mechanistic details of how these chemicals cause toxic effects at the molecular and cellular level are largely unknown. Alternative tests including *in vitro* and zebrafish embryo tests could aid in classifying chemicals as narcotics and predicting toxicity complementary to quantitative structure activity relationships. In order to select the correct assays, we need more information on the mechanism of narcosis. We built an AOP network based on our hypothesis that the cell membrane is the first target of lipophilic compounds, which may then further partition into different organelle membranes where they can disrupt essential membrane-bound processes, such as the mitochondrial electron transport chain (ETC). We exposed zebrafish embryos to three narcotic compounds with increasing lipophilicities: 1,3,5-trichlorobenzene, phenanthrene, and pentachlorobenzene using a passive dosing method. To assess events along the hypothesized mitochondrially-related AOP, we measured electron transport chain activity, heart rate, swimming performance, growth and survival. The combined effects on ETC activity and other endpoints suggest that the initial increase of ETC activity at low exposure concentrations was due to a compensatory response. With increasing exposure concentration, ETC activity decreased coinciding with decreasing heart rate, increasing occurrence of malformations and severely decreased swimming activity indicative of a breakdown phase. Eventually ETC activity decreased below control levels at high exposure concentrations where we observed failure indicated by mortality and a 20% decreased heart rate. Additionally, we found that the maximum observed ETC compensation was log K_{ow} dependent. This relationship suggests that ETC compensation is an important characteristic of narcosis. Our data support the hypothesis that the electron transport chain is affected by narcotics. We also observed most of the adverse outcomes stipulated in the hypothesized AOP network, namely reduced survival, growth, heart rate and swimming activity. Currently, we are investigating whether narcotics directly affect electron transport chain complexes in *in vitro* tests, and whether the observed changes in cellular respiration result in changes in respiration at the organismal level.