Chemical regulation is challenged by the large number of chemicals requiring assessment for potential human health and environmental impacts. For example, the USEPA lists more than 85,000 chemicals on its inventory of substances that fall under the Toxic Substances Control Act (TSCA). Whereas developmental and reproductive toxicity (DART) testing is an important regulatory consideration, traditional animal-based test methods focusing on apical endpoints lack throughput and mechanistic support needed for chemicals management under TSCA reform. Hypothesis-driven Integrated Approaches to Testing and Assessment (IATA), in parallel with Adverse Outcome Pathways (AOPs) for DART can help focus resources by strategically targeting the most probable developmental hazards predicted by alternative in vitro assays and non-testing (in silico) platforms. This paradigm shifts regulatory emphasis to high-dimensional data streams drawing from extant knowledge of cellular and molecular embryology, a compendium of high-throughput screening and high-content screening (HTS/HCS) data, and web-based chemistry dashboards. For example, the ToxCast/Tox21 program has provided HTS/HCS data on thousands of chemicals and hundreds of in vitro assays that include biochemical assays, reporter cell lines, and zebrafish developmental toxicity. Newer assays derive from pluripotent stem cell platforms (mouse, human) in the near-term with microscale organotypic culture models and engineered microphysiological systems on the horizon. Vast collections of HTS/HCS data and chemistry information, in combination with AOPs, can flip the emphasis from descriptive end-points to mechanistic chemical-biological interactions. Translating local interactions into quantitative predictions of developmental toxicity is challenged by the complex cellular dynamics in an embryo (cell signaling, migration, proliferation, apoptosis, differential adhesion, matrix remodeling, ...). Mechanistic modeling through computational embryology can help navigate this complexity. Steady progress has been made with multicellular agent-based models (ABMs) that recapitulate morphogenetic drivers for somitogenesis, urethrogenesis, palatogenesis, and other events. Computational systems models such as these offer a novel heuristic approach to reconstruct tissue dynamics from the bottom-up, cell-by-cell and interaction-by-interaction. Individually, they simulate emergent phenotypes and can be used to predict adverse outcomes or cybemorphs that bring an AOP to life. Collectively, they form an integrative platform or ‘virtual embryo’ that represents the spatial and temporal diversity of morphological development for predictive DART. This abstract does not reflect US EPA policy.