Regional scale watershed management decisions must be informed by the science-based relationship between anthropogenic activities on the landscape and the change in ecosystem structure, function, and services that occur as a result. We applied process-based models that represent watershed loading, mercury processing, instream water quality, habitat suitability, and fish community dynamics, linked together in a feed-forward design to address these issues. Additional features of this approach are an automated method to retrieve data from national databases (Data for Environmental Modeling, D4EM), and a framework for assessing and communicating uncertainties that are relevant to the assessment, including natural variability, environmental data measurement error, analysis conceptualization, and model structure. We focused on the services of water quantity and quality, as well as fisheries habitat, productivity, and bioaccumulation. This approach has allowed us to examine the effects of alternative climate and land-use scenarios on services, and to statistically analyze results and extrapolate to the regional scale, with appropriate uncertainty characterization. We have found that for multimedia model development, specific problems drive technology development, and technology integration leads science integration.