Simulation is becoming the primary tool in predicting the performance, reliability, and safety of engineered systems. To many managers, decision makers, and policy makers, simulations can appear most convincing with their captivating graphical animations. Terminology such as “virtual prototyping,” “virtual testing,” and “full physics simulation” are extremely appealing when budgets and schedules are highly constrained, or when competitive pressures force project managers to move forward with little or no testing of systems. Many contend that higher fidelity physics modeling, combined with faster computers, is the path forward for improved simulation-informed decision making. I argue that improved predictive uncertainty is the most constructive path forward in many situations. Predictive uncertainty estimation is the emerging field attempting to capture all aspects of uncertainty in the simulation of a system. The tradition in uncertainty estimation is to focus on propagation of input uncertainties through a mathematical model to obtain uncertainty in the system response quantities of interest. In contrast, predictive uncertainty estimation attempts to bound all potential sources of uncertainty. These include numerical solution error, model form uncertainty, and uncertainty in the environments and scenarios to which the system could be exposed, either intentionally or unintentionally. This talk will briefly review traditional uncertainty quantification approaches, particularly Bayesian estimation. An important distinction is made between uncertainties that are random or stochastic (aleatory uncertainties) and those that are due to lack of knowledge (epistemic uncertainties). It is argued that Bayesian estimation and imprecise probability approaches serve different goals in simulation-informed decision-making.