9) Model Building

a) Why mathematical modeling in risk assessment?
   i) Science-based risk is by definition a probability and therefore resolves quantitatively
   ii) Once a deliberative process has arrived at an agreed to problem formulation QRA allows for its translation into a risk finding
       (1) focuses on the problem to be assessed rather than on externalities
       (2) each input assumption is evident and can be challenged on the basis of its correctness
   iii) QRA “is similar to ‘what if’ scenarios in that it generates a number of possible scenarios” (or possible outcomes). “However, it goes one step further by effectively accounting for every possible value that each variable could take and weighing each possible scenario by the probability of its occurrence. QRA achieves this by modelling [representing] each variable within a model by a probability distribution.” [Vose D 2000 Risk Analysis: A Quantitative Guide, 2nd Ed., Wiley: New York.]

b) Spreadsheeting
   i) Translation of conceptual models into analysis models comprised of a liner system of equations
      (1) This is a general approach that broadly applies at some level to all nature of risk assessments
      (2) Does not address all levels of sophistication in QRA
          (a) Black box models (metamodels) used for screening level assessments
          (b) Transport models used for exposure characterization
      (3) Canned models used in specialized areas of RA
      (4) We will consider these additional tools as part of case studies throughout the course

c) Modeling approach taken in 570X
   i) Move from conceptual to deterministic mathematical to stochastic model
      (1) Conceptual model – in problem formulation, a written description and visual representation of predicted relationships between … entities [of concern] and the stressors to which they may be exposed.
         [www.epa.gov/watertrain/ecorisk/glossary.html](http://www.epa.gov/watertrain/ecorisk/glossary.html)
      (2) Deterministic model – mathematical models that are constructed for a condition of assumed certainty. The models assume there is only one possible result (which is known) for each alternative
course or action.

dssresources.com/glossary/dssglossary1999.html

(3) Stochastic model – a model involving or containing a random variable or variables; involving chance or probability.

www.investinginoptions.com/glossary_S.html

ii) Build the model

(1) Starting point:
(a) the conceptual model
   (i) ideally diagramed as a compartment model showing flow and interrelations of various data elements
(b) the formulation of risk – Risk = f(exposure, effect) – must be translated into mathematical form appropriate to the problem
(c) Examples of risk formulation starting points
   (i) Quotient methods: Q = [Exposure]/[Effect]
      1. Ecotoxicity [US]: RQ = EEC/[Toxicity Endpoint]
         a. RQ is the Risk Quotient
         b. EEC is the Estimated Environmental Concentration
            i. In some instances the EEC is replaced with an AEC (Actual environmental Concentration)
            ii. Worst Case should reflect highest actual/estimated instance
            iii. Typical Worst Case should reflect the HEEE (High End Exposure Estimate – the 90th percentile of actual/estimated instances
            iv. Typical case would represent the average of actual/estimated instances
            v. A partially stochastic case would use a distribution of EEC or AEC
         c. [Toxicity Endpoint] may be an LD_{50}, LC_{50}, EC_{50}, NOAEL etc.
            i. typically using a deterministic estimate of the 95% UB CI for the endpoint of interest
      2. Ecotoxicity [EU]: TER = LD_{50}/PEC
         a. TER is the Toxicity Exposure Ratio
         b. PEC is the Predicted Environmental Concentration
      3. Dietary Risk [Tier I pesticide – tolerance basis]: acute MOE = TMRC/PAD
         a. MOE is the Margin of Exposure
         b. TMRC = the Total Maximum Residue Concentration (tolerance level)
         c. PAD is the Population Adjusted Dose
i. \( \text{aRfD}/\text{UF}_{\text{FQPA}} \) (the acute reference dose divided by an uncertainty factor to account for sensitive subpopulations)

ii. \( \text{aRfD} = \text{NOEAL}/\text{UF}_1 \times \text{UF}_2 \) (\( \text{UF}_1 \) and \( \text{UF}_2 \) account for interspecies and intraspecies variation, respectively)

d. \( \therefore \) \( \text{MOE} = \text{TMRC}/\text{NOEAL} \times (\text{UF}_1 \times \text{UF}_2 \times \text{UF}_{\text{FQPA}}) \)

e. it is important to note that within this regulatory definition the toxicological endpoint (a no effect level) is replace with an endpoint of regulatory concern that incorporates uncertainty in the risk finding

(ii) joint probability formulation – this formulation is generally more flexible to account for fully stochastic assessments

1. \( R = P_e \times P_t \)
   a. Risk (a probability) equals the probability of exposure (\( P_e \)) times the probability of an effect (\( P_t \))
   b. \( P_e \) and \( P_t \)
      i. Can be deterministic thresholds – for instance the HEEE for \( P_e \) and the 95% UB CI for \( P_t \)
      ii. Or they may be distributions

(2) Expand the model to capture the necessary inputs to arrive at the risk estimate