

## Step 1: Problem Formulation and Protocol Development

## Step 2: Search for and Select Studies for Inclusion

## Step 3: Extract Data from Studies

## Step 4: Assess Quality of Individual Studies

## Step 5: Rate Confidence in the Body of Evidence

Initial Confidence by Key Features of Study Design	Factors Decreasing Confidence	Factors Increasing Confidence	Confidence in the Body of Evidence
<b>High (++++)</b> 4 Features	<ul style="list-style-type: none"> <li>• Risk of Bias</li> <li>• Unexplained Inconsistency</li> <li>• Indirectness</li> <li>• Imprecision</li> <li>• Publication Bias</li> </ul>	<ul style="list-style-type: none"> <li>• Large Magnitude of Effect</li> <li>• Dose Response</li> <li>• Residual Confounding                         <ul style="list-style-type: none"> <li>- Studies report an effect and residual confounding is toward null</li> <li>- Studies report no effect and residual confounding is away from null</li> </ul> </li> <li>• Consistency                         <ul style="list-style-type: none"> <li>- Across animal models or species</li> <li>- Across dissimilar populations</li> <li>- Across study design types</li> </ul> </li> <li>• Other                         <ul style="list-style-type: none"> <li>- e.g., particularly rare outcomes</li> </ul> </li> </ul>	High (++++)
<b>Moderate (+++)</b> 3 Features			Moderate (+++)
<b>Low (++)</b> 2 Features			Low (++)
<b>Very Low (+)</b> ≤1 Features			Very Low (+)

\* Note: if the only available body of evidence receives a "Very Low Confidence" rating, then conclusions for those outcomes will not move on to Step 6

## Step 6: Translate Confidence Ratings into Evidence of Health Effects

### Health Effect

### No Health Effect

Confidence in the Body of Evidence	Direction (effect or no effect)	Level of Evidence for Health Effect
(++++) High	Health effect	High
(+++ Moderate)	Health effect	Moderate
(++ Low)	Health effect	Low

Confidence in the Body of Evidence	Direction (effect or no effect)	Level of Evidence for Health Effect
(++++) High	No effect	Evidence of <b>no</b> health effect
(+++ Moderate)	No effect	Inadequate
(++ Low)	No effect	Inadequate

## Step 7: Integrate Evidence to Develop Hazard Identification Conclusions

### Possible Hazard Identification Conclusions for Health Effects

- **Known** to be a hazard to humans
- **Presumed** to be a hazard to humans
- **Suspected** to be a hazard to humans
- **Not classifiable** to be a hazard to humans

### Possible Hazard Identification Conclusions for No Health Effects

- **Not identified** to be a hazard to humans
- **Inadequate** to determine hazard to humans

Level of Evidence for Health Effects in Human Studies

