Summary of Findings Regarding the Association between Specific Health Outcomes and Exposure to Herbicides Used in the Vietnam War

(Changes in *Update 2006* are italized)

Sufficient Evidence of Association

- Chloracne
- Cancers:
  - Chronic lymphocytic leukemia (CLL)
  - Non-Hodgkin's lymphoma
  - Hodgkin's disease
  - Soft-tissue sarcoma

Limited or Suggestive Evidence of Association

- Early-onset transient peripheral neuropathy
- *AL amyloidosis*
- *Hypertension*
- Porphyria cutanea tarda
- Type 2 diabetes (mellitus)
- Cancers:
  - Larynx
  - Lung, bronchus, or trachea
  - Multiple myeloma
  - Prostate
- In offspring of exposed individuals:
  - Spina bifida

Inadequate or Insufficient Evidence to Determine Association

- Neurobehavioral disorders (cognitive and neuropsychiatric)
- Movement disorders, including Parkinson's disease and amyotrophic lateral sclerosis
- Chronic peripheral nervous system disorders
- Respiratory disorders
- Gastrointestinal, metabolic, and digestive disorders (changes in liver enzymes, lipid abnormalities, ulcers)
- Immune system disorders (immune suppression, autoimmunity)
- * Ischemic heart disease
- Circulatory disorders (other than hypertension)
- Endometriosis
- Effects on thyroid homeostasis

Cancers:
- Oral cavity (including tongue), pharynx (including tonsils), or nasal cavity (including ears and sinuses)
- Pleura, mediastinum, and other unspecified sites within the respiratory system and intrathoracic organs
- *Esophagus*
- *Stomach*
- *Colorectal cancer (including small intestine and anus)*
- Hepatobiliary cancers (liver, gallbladder, and bile ducts)
- *Pancreas*
- Bone and joint
- * Melanoma
- Non-melanoma skin cancer (basal cell and squamous cell)
- * Breast
- Reproductive organs (cervix, uterus, ovary, testes, and penis; excluding prostate)
- Urinary bladder
- Kidney
- *Brain and nervous system (including eye)*
- Endocrine cancers (thyroid, thymus, and other endocrine)
- Leukemia (other than CLL)
- Other and unspecified sites

Abnormal sperm characteristics and infertility

Spontaneous abortion (other than for paternal exposure to TCDD)

In offspring of exposed individuals:
- Neonatal or infant death and stillbirth
- Low birth weight
- Birth defects (other than spina bifida)
- Childhood cancer (including acute myelogenous leukemia)

* The committee could not reach consensus as to whether the evidence for these health outcomes related to exposure to the chemicals of concern was "limited, suggestive" or "inadequate," so they were retained in the inadequate category.

Limited or Suggestive Evidence of *No* Association

(*the possibility of a very small increase in risk can never be excluded)*

Spontaneous abortion following paternal exposure to TCDD

Categories of Association

Sufficient Evidence of Association
Evidence is sufficient to conclude that there is a positive association. That is, a positive association has been observed between exposure to herbicides and the outcome in studies in which chance, bias, and confounding could be ruled out with reasonable confidence. For example, if several small studies that are free from bias and confounding show an association that is consistent in magnitude and direction, there could be sufficient evidence of an association.

Limited or Suggestive Evidence of Association
Evidence suggests an association between exposure to herbicides and the outcome, but a firm conclusion is limited because chance, bias, and confounding could not be ruled out with confidence. For example, a well-conducted study with strong findings in accord with less compelling results from studies of populations with similar exposures could constitute such evidence.

Inadequate or Insufficient Evidence to Determine Association
The available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of an association. For example, studies fail to control for confounding, have inadequate exposure assessment, or fail to address latency.

Limited or Suggestive Evidence of *No* Association
Several adequate studies, which cover the full range of human exposure, are consistent in not showing a positive association between any magnitude of exposure to the herbicides of interest and the outcome. A conclusion of "no association" is inevitably limited to the conditions, exposure, and length of observation covered by the available studies. *In addition, the possibility of a very small increase in risk at the exposure studied can never be excluded.*