Statement for Public Teleconference for the SAB review of "Draft Toxicological Review of Libby Amphibole Asbestos" (EPA/635/r/002a)

Anatomical Considerations of Localized Pleural Thickenings (Pleural Plaques)

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ILO (2000) Definitions Incorrectly Used

- EPA's draft Toxicological Review (August 2011) states that either of two conditions are recognized as LPT:

"Pleural thickening: The pleural lining around the lungs (visceral pleura) and along the chest wall and diaphragm (parietal pleura) may thicken due to fibrosis and collagen deposits. Pleural thickening (all sites) is reported as either localized pleural thickening (LPT) or diffuse pleural thickening (DPT). DPT of the chest wall may be reported as in-profile or face on, and is recorded on the lateral chest wall "only in the presence of and in continuity with, an obliterated costophrenic angle" (ILO, 2000). Localized pleural thickening may also be viewed in-profile or face-on and is generally a pleural plaque (parietal). Calcification is noted where present (ILO, 2000)." (p. 5-15)

"Localized pleural thickening (LPT) viewed on a standard radiograph may include both pleural plaques and pleural thickening that does not involve blunting of the costophrenic angle (ILO, 2000). Thus, both parietal plaques and localized thickening of the visceral pleura may be designated as LPT." (p. 5-17)

"In summary, the radiographic classification of localized pleural thickening (LPT) under current ILO guidelines may include both parietal plaques (in the pleura lining the interior of the ribcage) and diffuse visceral thickening (without CPA obliteration) (ILO, 2000)." (p. 5-21)

ILO (2000) Definitions Incorrectly Used (Cont.)

- ILO (2000) classifies as LPT **only** as pleural plaques located in parietal pleura

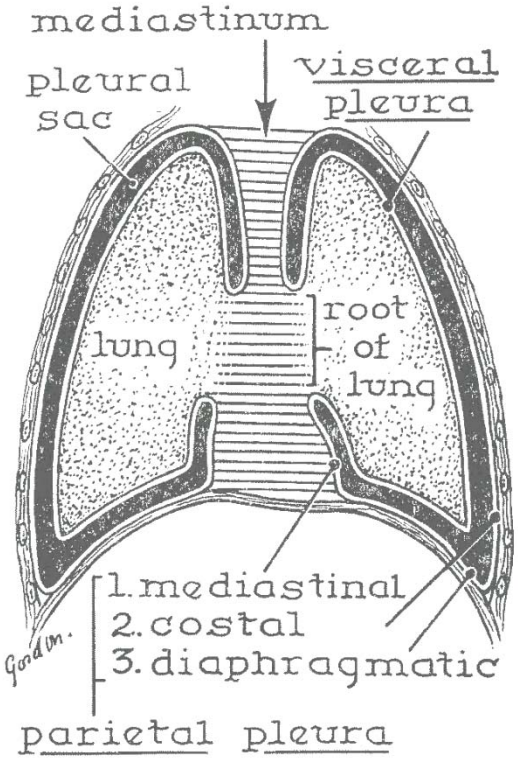
- ILO states that the category of diffuse pleural thickening requires 2 conditions:
  - (visceral) pleural thickening and costophrenic angle blunting.

"For the purpose of the ILO (2000) Classification, diffuse pleura thickening extending up the lateral chest wall is recorded *only* in the presence of, and in continuity with, an obliterated costophrenic angle." from ILO (2000)

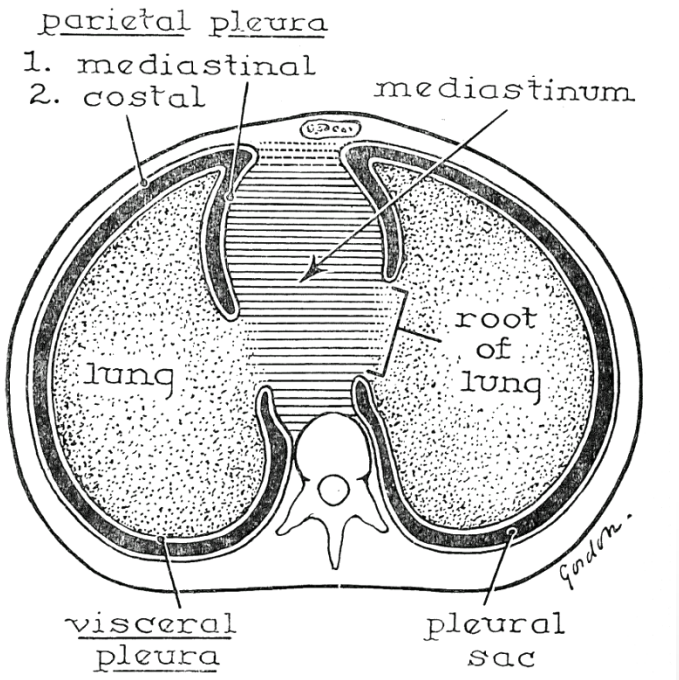
ILO (2000) does not have a category of observations for diffuse pleural thickening without CPA obliteration.

Pleural Plaques (LPT) Do Not Displace Lung Tissue

- Pleural plaques (LPT) occur in the parietal pleura
- Parietal pleura does not touch lung tissue
- Pleural plaques (LPT) have small volumes



Anterior



Posterior

Pleural Plaques (LPT) Are Not a Critical Effect of Asbestos Exposure

- EPA defines Critical Effect as:
  - The first adverse effect, or its known precursor, that occurs as the dose rate of an agent increases (http://www.epa.gov/iris/help_gloss.htm#c viewed 4/17/12)
- Disease endpoints of greatest concern due to asbestos exposure occur on/within lung tissue (not in parietal pleura):
  - Mesothelioma
  - Carcinoma of the lung
  - Asbestosis

Pleural Plaques (LPT) are Not an Intermediate Stage in Progression to Neoplastic Disease

Pleural Plaques (LPT)

- Well-organized histologically
- Connective tissue covered by epithelium
- Oligocellular
- Nonconfluent cells
- Minimal rate of mitosis
- Normal nuclei
- Extensive extracellular matrix
- Abundant collagen
- Essentially avascular

Tumors

- Lack of organization: chaotic
- Composed of *either* epithelium (carcinomas) *or* connective tissues (sarcomas)
- High cellularity
- Contiguous mass of cells
- High rate of mitosis
- Dysplastic or anaplastic nuclei
- Small amount of extracellular material
- Scarce collagen
- Vascularity increased beyond typical amount for the tissue