

The issue of the lack of an excess of skin tumors observed in most studies of therapeutic coal tar use (Jones et al 1985; Muller and Kierland, 1964) was discussed by the SAB, and there appear to be two major components to the overall consideration: 1) psoriatic skin proliferates much more rapidly than normal skin, and appears resistant to skin cancer; 2) the clinical studies involving the use of coal tar are incomplete. First, the skin of psoriasis patients who receive these treatments is not normal skin, and therefore psoriasis patients are unlikely to be a relevant comparison population. Psoriasis patients are known to shed skin cells at greatly increased rates (Weinstein & McCullough, 1973). Desquamation can reduce penetration beyond the stratum corneum, so lipophilic compounds, including the PAHs, may not reach the metabolically-active layers of the skin (Reddy et al., 2000). The finding by Roelofzen et al. (2012) of reduced 1-hydroxypyrene in urine and reduced PAH-DNA adducts in biopsied skin of psoriasis patients, compared to healthy volunteers, following dosing with coal tar ointments is consistent with this logic. The second consideration is focused on the available clinical studies, and the committee agrees with the EPA that many of these studies suffer from small sample size, inadequate follow-up, undercounting of skin cancers in particular and a large potential for exposure misclassification. The limitations of these studies, and the nature of psoriatic skin, make the available studies largely uninformative with regard to the question of whether benzo[*a*]pyrene induces skin cancer in humans. The historic studies of an excess of scrotal cancers in chimney sweeps, and more recent studies demonstrating an excess risk in asphalt workers, are all consistent with benzo[*a*]pyrene being a risk factor for skin cancer.

Reddy MB, Guy RH, Bunge AL. Does epidermal turnover reduce percutaneous penetration? *Pharm Res.* 2000; 17(11):1414-9.

Roelofzen JH, van der Valk PG, Godschalk R, Dettbarn G, Seidel A, Golsteijn L, Anzion R, Aben KK, van Schooten FJ, Kiemeny LA, Scheepers PT. DNA adducts in skin biopsies and 1-hydroxypyrene in urine of psoriasis patients and healthy volunteers following treatment with coal tar. *Toxicol Lett.* 2012; 213(1):39-44

Weinstein GD, McCullough JL. Cytokinetics in diseases of epidermal hyperplasia. *Annu Rev Med.* 1973;24:345-52.