Table 19.6 Predicted Toxicological Profile of N-Acetylcysteine

	Multicase	
SAR Model	Probability (%)	Potency (units)
Structure alerts	0	0
Salmonella mutagenicity	0	0
SOS chromotest	0	0
umu/SOS repair	0	0
Carcinogenicity: rodents-NTP	0	0
Carcinogenicity: mice-NTP	0	0
Carcinogenicity: rats-NTP	0	0
Carcinogenicity: rodent-CPDB	0	0
Carcinogenicity: mice-CPDB	0	0
Carcinogenicity: rats-CPDB	0	0
Inhibition gap junction intercell comm	0	0
Binding to Ah receptor	0	0
Mutations in mouse lymphoma (NTP)	0	0
Mutations in mouse lymphoma (GenTox)	0	0
Sister chromatic exchanges in *vitro*	0	0
Chromosomal aberrations in vitro	0	0
Unscheduled DNA synthesis in vitro	0	0
Cell transformation	0	0
Drosophila somatic mutations	0	0
Sister chromatic exchanges in vivo	0	0
Induction of micronuclei in vivo	0	0
Yeast malsegregation	0	0
Inhibition of tubulin polymerization	0	0
Sensory irritation	89	72
Eye irritation	72	52
Respiratory hypersensitivity	0	0
Allergic contact dermatitis	95	44
Rat lethality (LD50)	0	0
Mouse MTD	0	0
Rat MTD	0	0
Cellular toxicity (3T3)	0	0
Cellular toxicity (HeLa)	0	0
Nephrotoxicity: male rats ($\alpha 2\mu$globulin)	0	0
Inhibition human cyt. P4502D	0	0
Developmental toxicity: hamster	0	0
Developmental toxicity: human	0	0
Aquatic toxicity (minnows)	0	0
Water solubility: 3.88	log P (Octanol: water): −1.79	
Electronegativity: 0.10		

NTP and CPDB refer to the U.S. National Toxicology Program carcinogenicity assays (45) and to the Carcinogenic Potency Data Bases (46), respectively.

Based on all of these considerations, the "human expert" would overrule the prediction of rodent carcinogenicity. Additionally, in overriding the computer-based prediction, cognisance was also taken of the understanding that the vast majority of recognized human carcinogens are genotoxicants, i.e., "genotoxic carcinogens" (41–44). Epitholone A, on the other hand, was not predicted to be genotoxic (i.e., a DNA-damaging agent), evidenced by its lack of potential to induce mutations in Salmonella, error-prone DNA repair, or unscheduled DNA synthesis in rat hepatocytes (Table 19.5). Thus, even if the potential for murine carcinogenicity were accepted, in view of the fact that the vast majority of rec-