





TOBACCO SPECIFIC NITROSAMINES

I History of Nitrosamines: Discovery, Carcinogenic Potential, Presence in Tobacco Products

- For well over thirty years researchers have known that nitrosamines are a class of powerful carcinogens that form readily from a variety of nitrogen compounds.
- Nitrosamines are present – generally in low amounts – in a range of foods and consumer products. The FDA has set maximum limits for nitrosamine levels in such things as foods, beer and even cosmetics.
- Tobacco contains nicotine and other alkaloids that are precursors of a particular group of nitrosamines commonly referred to as TSNAs, or tobacco specific nitrosamines.

II TSNAs: Chemical Structure, Formation, Metabolic Activation

- TSNAs are among the most abundant and potent carcinogens in tobacco and tobacco smoke.
- TSNAs form via nitrosation of nicotine and other tobacco alkaloids, primarily during the curing process. Green, uncured tobacco contains virtually no TSNAs.
- Four of the seven known TSNAs are pre-carcinogens; i.e., they require metabolic activation before they become carcinogenic in the body.

III TSNAs and The Carcinogenicity of Snuff

- Two of the TSNAs (NNN and NNK) and their metabolites are the only carcinogens in snuff known to cause oral tumors in rats.
- Long-term, heavy users of conventional snuff consume TSNAs in approximately the same dosage needed to induce tumors in lab animals.
- The incidence of cancer associated with oral tobacco use seems to be highest in Asia where TSNA levels are extremely high, and lowest in Sweden where the tobacco is processed specifically and carefully stored to prevent further increase in TSNAs during storage.
- Most of the known toxins (other than TSNAs) in smokeless tobacco, such as formaldehyde and Benzo(a)pyrene, appear to be present in levels at or below those found in air, drinking water, and/or food. According to a recent article, *American Chemical Society Symposium Series 553: Nitrosamines and Related N-Nitroso Compounds*, "To date, the nitrosamines derived from the tobacco alkaloids [TSNAs] are the only significant carcinogenic agents found in smokeless tobacco."
- Currently, though, there is no proof that reducing the TSNAs in Ariva™ will lead to a reduction in the health risk associated with its use.