

Additional Table 1. Biomarkers of exposure in the Total Exposure Study.

| Biomarker[2] | Component(s) | Matrix | Laboratory measurement technology | Related to which Harmful and Potentially Harmful Constituents of Tobacco Smoke [55, 56] |
|----------------------------|---|-------------|--|---|
| Particulate phase | | | | |
| Nicotine Equivalents (NE) | Nicotine, cotinine, trans-3'-hydroxycotinine and the corresponding glucuronides | 24 hr urine | Liquid chromatography-mass spectrometry/mass spectrometry (LC-MS/MS) | Nicotine or Nicotine (total) ³ |
| Serum cotinine | cotinine and trans-3'-hydroxycotinine [57] | Serum | Immunoassay | Nicotine or Nicotine (total) ³ |
| Total NNAL | Total 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol, and its glucuronide | 24 hr urine | LC-MS/MS | metabolite of NNK ⁴ |
| NNN ¹ | N-nitrosonornicotine | 24 hr urine | LC-MS/MS | N-nitrosonornicotine ⁵ |
| 4-ABP ² | 4-aminobiphenyl hemoglobin (Hb) adducts | Blood | Gas chromatography-mass spectrometry | 4-aminobiphenyl (CA) |
| Gas phase | | | | |
| 1-OHP ² | Total 1-hydroxypyrene | 24 hr urine | LC-MS/MS | polycyclic aromatic hydrocarbons ⁵ |
| 3-HPMA ² | 3-hydroxy-propylmercapturic acid | 24 hr urine | LC-MS/MS | metabolite of acreolein ⁶ |
| COHb ² | carboxyhemoglobin | Blood | Spectrophotometry | Carbon monoxide ⁷ (RDT) |
| MHBMA ² | Monohydroxyl-butenylmercapturic acid | 24 hr urine | LC-MS/MS | metabolite of 1,3 butadiene ⁵ |
| DHMBA ² | Dihydroxy-butyl-mercapturic acid | 24 hr urine | LC-MS/MS | metabolite of 1,3 butadiene ⁵ |
| S-PMA ^{1,2} | S-phenylmercapturic acid | 24 hr urine | LC-MS/MS | metabolite of benzene ⁸ |
| Naphthalene ^{1,2} | aka 2-aminonaphthalene | 24 hr urine | LC-MS/MS | 2-aminonaphthalene ⁵ |
| 3-OH-B[a]P ^{1,2} | 3-hydroxy-benzo[a]pyrene | 24 hr urine | LC-MS/MS | a metabolite of benzo[a]pyrene ⁵ |
| o-Toluidine ^{1,2} | 3,3'-dimethylbenzidine | 24 hr urine | LC-MS/MS | o-Toluidine ⁵ |

¹Not described by Roethig *et al* [2], but available in TES data. ²Biomarker is not tobacco specific. ³Reproductive or

developmental toxicant, RDT, and addictive, AD. ⁴ Metabolite of NNK, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone, a carcinogen, CA. ⁵CA. ⁶Respiratory toxicant, RT, and cardiovascular toxicant, CT. ⁷RDT. ⁸CA, CT, and RDT.