Table 1: Cancer-related biomarkers of tobacco smoke [Adapted from Hatsukami, 2006]

Biomarker	Measurement	*Relation to Tobacco use:* Difference: Users vs. Non-users	Change with Cessation	Dose Response with Use	Change with Reduced Use
1. Chemical Biomarkers					
NNAL and NNAL-Glucs in urine	Carcinogen (NNK) uptake	(Carmella et al., 1993) (S1)	(Hecht et al., 1999) (S2)	(Joseph et al., 2005) (S3)	(Hecht, Murphy et al., 2004) (S4)
3-Aminobiphenyl, 4 aminobiphenyl, and other aromatic amine-Hb adducts	Carcinogen (aromatic amines) uptake plus metabolic activation	(Castelao et al., 2001) (S5)	(Maclure et al., 1990; Skipper & Tannenbaum, 1990) (S6,S7)	(Castelao et al., 2001; Skipper & Tannenbaum, 1990) (S5, S7)	
1-Hydroxypyrene in urine	Carcinogen (PAH) uptake	(Hecht, 2002) (S8)	(Hatsukami et al., 2004) (S9)		(Hecht, Carmella et al., 2004) (S10)
Trans, *trans*-muconic acid in urine	Carcinogen (benzene) uptake	(Scherer et al., 1998) (S11)			
S-phenylmercapturic acid	Carcinogen (benzene) uptake	(Hecht, 2002; Lin et al., 2004; Maestri et al., 2005; Melikian et al., 2002; Tharnpoophasiam et al., 2004) (S8, S12, S13, S14, S15)			
Benzene and other volatile organic carcinogens (VOCs) in exhaled air	Volatile organic carcinogens	(IARC, 2004) (S16)		(IARC, 2004) (S16)	
Ethylene oxide-Hb adducts	Carcinogen (ethylene oxide) uptake	(Fennell et al., 2000) (S17)			
Other N-terminal valine adducts in Hb	Carcinogen uptake	(Carmella et al., 2002) (S18)			
Cadmium and other metals in blood and urine	Carcinogen uptake	In part[a] (IARC, 2004) (S16)			
Acetaldehyde-DNA and protein adducts	Carcinogen uptake				
F_2-isoprostanes and oxidized proteins	Oxidative damage, inflammation[c]	(J. D. Morrow et al., 1995; Pignatelli et al.,			

		2001) (S19, S20)			
8-OxoG or 8-oxo-dG in DNA or urine[b]	Oxidative damage, inflammation[c]	In part (Hecht, 2002; IARC, 2004) (S8, S16)			
Mercapturic acids of acrolein and related compounds in urine	Toxin uptake and metabolism	In part (Hecht, 2002) (S8)			
Benzo[*a*]pyrene diol epoxide-DNA and Hb adducts	Carcinogen (BaP) uptake and metabolic activation	In part (Boysen & Hecht, 2003) (S21)			
NNK and NNN-DNA and Hb adducts	Carcinogen (NNK/NNN) uptake and metabolic activation	In part (IARC, 2004) (S16)			
Apurinic sites in DNA ^{32}P-postlabelling of DNA	DNA damage Carcinogen uptake and metabolic activation	(IARC, 2004; Kriek et al., 1998; Phillips, 2002) (S16, S22, S23)	(IARC, 2004; Kriek et al., 1998; Phillips, 2002) (S16, S22, S23)		
Immunoassays for DNA damage	Carcinogen (mainly PAH) uptake and metabolic activation	(IARC, 2004; Kriek et al., 1998; Phillips, 2002) (S16, S22, S23)	(IARC, 2004; Kriek et al., 1998; Phillips, 2002) (S16, S22, S23)		
2. Cellular biomarkers Urine mutagenicity	Mutagen uptake	(IARC, 2004) (S16)	(IARC, 2004) (S16)	(IARC, 2004) (S16)	(Benowitz et al., 1986) (S24)
Sister chromatid exchange in peripheral lymphocytes	DNA damage	(IARC, 2004) (S16)	(IARC, 2004) (S16)	(Barale et al., 1998)(S25)	
Chromosomal aberrations and micronuclei frequency in lymphocytes	DNA damage	In part (IARC, 2004) (S16)			
HPRT mutant frequency in cultured lymphocytes	Gene mutations	In part (IARC, 2004) (S16)			
Bronchial metaplasia and dysplasia, sputum atypia	Preneoplastic changes	In part (Khuri et al., 2001; Lam et al., 1999; Lam et al., 2002; Prindiville et al., 2003) (S26, S27, S28, S29)	In part (Khuri et al., 2001; Lam et al., 1999; Lee et al., 1994; Prindiville et al., 2003) (S26, S27, S30, S29)		
Comet assay-DNA strand breaks	DNA damage	No consistent effect (Moller et al., 2000) (S31)			
3. Proteome differences	Effects on proteins				

Carcinoembryonic antigen	Inflammation[c]	In part (Ohwada et al., 1995; Stockley et al., 1986) (S32, S33)

Note. [a]"in part", some studies support change in biomarkers by smoking status. [b]Published values may be unreliable due to unrecognized artifact formation. [c]Uncertainty exists over whether the biomarker is a measurement of inflammation.

Supplemental Table 2: TP53 Association of environmental and occupational chemicals with possibly specific p53 mutations.

Carcinogen	**Cancer tissue**	**TP53 mutations**	**Reference**
Cigarette smoke Benzo(a)pyrene and other PAH- compounds	Lung	G:C to T:A in codons 157, 158, 247-249 and 273 Higher frequency	(S34) (S35) (S36) (S37) (S38)
Cigarette smoke	Colorectal	Higher frequency	(S39)
Cigarette smoke	Bladder	Higher frequency Double mutations A:T to G:C	(S40)
Cigarette smoke and alcohol	Head and neck	Codons 205, 245, 248	(S41)
Cigarette smoke and alcohol	Esophagus, head and neck	G:C to T:A	(S42)
UV-radiation	Skin	CC to TT	(S43) (S44) (S45) (S46)
Vinyl chloride	Liver	A:T to T:A	(S47, S48)
Mustard gas	Lung	Double G:C to A:T	(S49)
Chromate exposure Nickel exposure Metal industry	Lung	G:C to T:A on non-coding strand	(S36)
Petrochemical Industry	Lung	G:C to A:T at non- CpG sites	(S36)

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