Reference	Species (strain); n; Sex; Lifestage/Age (mean ± SD)	Exposure Details (concentration; duration)	Endpoints Examined
Animal Toxicolog			
<u>Halinen et al.</u> (2000b)	Guinea pig (Duncan- Hartley); n = 7-12/group; M; mechanically ventilated	1,000, 2,500, and 5,000 ppb SO <sub>2</sub> in cold dry air; 15 min pre-exposure to warm humid air, 10 min to cold dry air and each SO <sub>2</sub> concentration or just cold dry air, 15 min recovery to warm humid air; intra-tracheal with hyperventilation $(V_T = 11 \text{ mL/kg at}$ 80 breaths/min) during cold exposures	Intra-carotid (right) pressure transducer measurements before, during, and after exposure: Blood pressure Heart rate
<u>Halinen et al.</u> (2000a)	Guinea pig (Duncan- Hartley); n = 8/group; M; mechanically ventilated	1,000 ppb SO <sub>2</sub> in cold dry air; 60 min; intra-tracheal with hyperventilation $(V_T = 11 \text{ mL/kg at}$ 80 breaths/min)	Intra-carotid (right) pressure transducer measurements before, during, and after exposure: Blood pressure Heart rate
<u>Nadziejko et al.</u> (2004)	Rat (F344); n = 20/group; M; 18 mo old	1,200 ppb SO <sub>2</sub> ; 4 h; nose-only inhalation	Electrocardiogram 24 h before, during, and 24 h after exposure: • Heart rate • Arrhythmia frequency
Baskurt (1988)	Rat (Swiss albino); n = 51; male; adult; age NR	0.87 ppm whole body exposure 24 h	Hematocrit, sulfhemoglobin, and osmotic fragility; Whole blood and packed cell viscosity

## Table 5S-6Study-specific details of experimental studies of SO2 and<br/>cardiovascular effects.

## **Controlled Human Exposure Studies**

Tunnicliffe et al. (2001)	Human; n = 2 healthy adults (age 22-49), 12 adults with physician diagnosed mild asthma (age 20-54); M/F	200 ppb SO <sub>2</sub> ; 1 h at rest	Electroc exposur •	cardiogram 30 min before and during re: Heart rate (maximum, minimum) Heart rate variability (total power, HF power, LF power)
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## Table 5S-6 (Continued): Study-specific details of experimental studies of SO<sub>2</sub> and cardiovascular effects.

Reference	Species (strain); n; Sex; Lifestage/Age (mean ± SD)	Exposure Details (concentration; duration)	Endpoints Examined
Routledge et al. (2006)	Human; n = 20 healthy older adults (age 56-75), 20 older adults with stable angina, coronary artery disease (age 56-75); M/F	200 ppb SO <sub>2</sub> and ultra-fine carbon particles (50 μg/m <sup>3</sup> ), separately and in combination; 1 h at rest	<ul> <li>Electrocardiogram immediately before, immediately after, and 4 h after exposure: <ul> <li>Heart rate</li> <li>Heart rate variability (SDNN, rMSSD, PNN50, LF power, HF power, α-HF index, α-LF index)</li> </ul> </li> <li>Blood pressure (mean arterial pressure)</li> <li>Blood drawn 15 min before, immediately after, 4 h after, and 24 h after exposure: <ul> <li>Serum CRP, fibrinogen, D-dimer</li> <li>Hemoglobin, platelet count, platelet aggregation, differential white cell count</li> </ul> </li> </ul>

 $SO_2$  = sulfur dioxide; *n* = sample size; SD = standard deviation; M = male; ppb = parts per billion; min = minute; V<sub>T</sub> = tital volume; mo = month; h = hour; NR = not reported; F = female; HF = high frequency; LF = low frequency; m = meter; g = gram; SDNN = standard deviation of all normal-to-normal intervals; rMSSD = root mean square of successive differences; PNN50 = Proportion of pairs of successive normal simus intervals exceeds 50 milliseconds divided by the total number of successive pairs of normal simus intervals; CRP = C-reactive protein; D = distance in kilometers.