SCIENCE DISCUSSION DOCUMENT ON

THE DEVELOPMENT OF AIR STANDARDS

FOR

SULPHUR DIOXIDE (SO_2)

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Standards Development Branch
Ministry of the Environment
and Climate Change

Executive Summary

This document describes the science the Ministry of the Environment and Climate Change has reviewed to inform the development of updated Ambient Air Quality Criteria (AAQCs) and air standards for sulphur dioxide (SO_2) (CAS # 7446-09-5). This contaminant was identified as a high priority for air standard update based on its release pattern in Ontario, identification as a priority by federal and national committees, and recent toxicological information that was published subsequent to the development of the existing standard in 1974, and retained in 2005.

The current Science Discussion Document is primarily based on the recent health risk assessment carried out by Health Canada (2016) during their work on developing Canadian Ambient Air Quality Standards (CAAQS) for SO_2, and also considers information from other agencies such as the United States Environmental Protection Agency (U.S. EPA) and the World Health Organization (WHO).

Sulphur dioxide is a colourless gas at room temperature and typical environmental conditions. As it is heavier than air, it may accumulate at ground level under some ambient conditions. SO_2 is released from natural sources (e.g., forest fires, wildfires), and from anthropogenic sources in quantities that may substantially affect local air quality. Major anthropogenic sources in Ontario include non-ferrous smelting and refining, petroleum refining, iron and steel industry, transportation sources (e.g., air and marine transportation), incinerators, and other industrial sources (e.g. cement plants, pulp and paper mills, chemical industry). The odour of SO_2 has been described as irritating and pungent (U.S. National Library of Medicine, 2016), with a consensus odour threshold value of 500 ppb (1300 $\mu g/m^3$) (Health Canada, 2016).

SO_2 can affect elements of ecosystems via direct impact on plants through soil uptake or direct adsorption of SO_2 from air, and indirectly through the deposition and retention in soils of other sulphur-containing compounds such as sulphuric acid and sulphate particles. Acute and chronic exposures to SO_2 have phytotoxic effects on vegetation which include foliar injury, decreased photosynthesis, and decreased growth. Lichens are among the first species affected by acidifying deposition and have been used as early warning indicators of air pollution, particularly acidifying sulphur pollutants.

In humans, inhaled SO_2 is rapidly solubilized in the upper respiratory tract and may be absorbed across nasal mucosa and the mucosal cells of the trachea (ATSDR, 1998; Arts et al., 2006). With increasing physical activity, the shift from nasal to oronasal breathing results in greater SO_2 penetration into the bronchial region of the respiratory tract. SO_2 is not likely to reach the lungs. Once absorbed across mucosal cells,

hydrated SO_2 transforms to sulphite/bisulphite at physiologic pH. However, sulphite levels in the body are predominately influenced by endogenous production and by ingestion of sulphites in food.

Inhaled SO_2 stimulates bronchial epithelial irritant receptors in the tracheobronchial tree. This initiates a reflexive contraction of smooth muscles in the bronchial airways associated with bronchial constriction. It is this bronchial constriction that is associated with respiratory morbidity. Using a weight of evidence approach, Health Canada and the United States Environmental Protection Agency (U.S. EPA, 2008; 2015; Health Canada, 2016) concluded that the strongest causal relationship exists between short-term SO_2 exposure and respiratory effects. These adverse effects include bronchoconstriction, changes in lung function, airway inflammation, airway hyper-responsiveness, and emergency room hospital visits. Respiratory morbidity can be considered the underlying critical effect for the formation of a SO_2 AAQC. However, exposure estimates are considered to be more accurate in human clinical studies under controlled conditions (i.e., chamber studies) compared to epidemiological data, and thus are typically relied upon for quantitative evaluation by various jurisdictions.

The U.S. EPA amassed data from a series of chamber studies and performed a meta-analysis, demonstrating dose response findings in respiratory function and percent of affected asthmatics These studies formed the basis of the consensus benchmarks in the development of the U.S. EPA National Ambient Air Quality Standards (NAAQS). Health effect consensus benchmark concentrations of 200 ppb and 400 ppb were used to perform a quantitative exposure and risk assessment on two proposed 1-hour values at 50 ppb and 100 ppb, in order to predict the frequency in days of 5 minute exceedences of the benchmark concentration. From this, the U.S. EPA inferred that at a 75 ppb 1-hour limit, there is potential for a few daily 5 minute exceedences of the health effects benchmark concentrations of 200 and 400 ppb over a year. Thus, the 75 ppb (200 $\mu g/m^3$) 1-hour average NAAQS for SO_2 was established to be protective of public health, with an adequate margin of safety.

Health Canada (2016) developed a SO_2 reference concentration (RfC) from the statistically significant lowest observed adverse effect concentration (LOAEC) of 400 ppb, resulting in lung function decrements from controlled human exposure studies of asthmatics exposed for 5-10-minutes at increased ventilation (WHO, 2005; U.S. EPA, 2008; Johns and Linn, 2011). To account for the uncertainties in the controlled human exposure dataset, and to consider the supporting evidence from epidemiology, a combined uncertainty factor (UF) of 6 was applied. This resulted in a 10-minute inhalation RfC of 67 ppb (180 $\mu g/m^3$), which was converted to a 1-hour limit of 40 ppb (100 $\mu g/m^3$) in consideration of the stability of the metric. The RfC of 67 ppb (180 $\mu g/m^3$) was used to inform the CAAQS management levels.

In attempting to identify a key study for AAQC development, the Ministry's will focus on data that will allow for protection to all individuals in the general population, including those who are likely to be susceptible to developing the critical effect. Specific life-stages or groups thought to be at risk for increased susceptibility to SO_2-mediated adverse health effects include asthmatics. Estimates of exposure are considered to be more accurate in chamber studies, and thus will be relied upon for quantitative evaluation. The Ministry proposes to utilize these studies as a group, to be representative of the 'key study' for AAQC and air standard development. In consideration of the U.S. EPA (2008) analysis of a number of chamber studies, consensus benchmarks concentrations of 200 ppb (525 $\mu g/m^3$) and 400 ppb (1050 $\mu g/m^3$) are noted, and as used by Health Canada (2016) in developing the 10-minute RfC of 67 ppb (180 $\mu g/m^3$).

A review of the mode of action and controlled human studies support intermittent spikes in the 5-10-minute range as being the most health-relevant. Thus, a short averaging time is appropriate. The selection of the appropriate averaging time, however, needs to be balanced with monitoring practicalities, modelling capabilities, jurisdictional consistency, and other implementation considerations.

In addition, a chronic AAQC and air standard aimed to protect vegetation from direct SO_2 effects will be considered by the Ministry, based on the WHO vegetation effects range of 4 ppb (10 $\mu g/m^3$) to 8 ppb (20 $\mu g/m^3$) on an annual basis.

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1.0 Introduction

The Ontario Ministry of Environment and Climate Change (the Ministry) has identified the need to develop and/or update air standards for priority contaminants. The Ministry's Standards Plan, which was released in October, 1996 and revised in November, 1999 (MOE 1996; MOE 1999), identified candidate substances for which current air standards will be reviewed or new standards developed. Sulphur dioxide (CAS # 7446-09-5) was identified as a high priority candidate for air standard development based on its release pattern in Ontario, identification as a priority by federal and national committees, and recent toxicological information that was published subsequent to the development of the existing standard in 1974, and retained in 2005.

The purpose of this Science Discussion Document is to summarise the science on the adverse effects of sulphur dioxide (SO_2) exposure in support of developing Ambient Air Quality Criteria (AAQCs) and air standards for SO_2. This document is primarily based on the recently released health risk assessment carried out by Health Canada (Health Canada, 2016), and also considers information from assessments performed by other agencies, such as the United States Environmental Protection Agency (U.S. EPA) and the World Health Organization (WHO).

2.0 Background

2.1 Overview of the AAQC/Standard Setting Process

AAQCs and air standards are set at concentrations that are protective against adverse effects. They are based solely on science, informed by information such as the substance's physical chemical properties and environmental fate (Section 3.0), its environmental effects (Section 4.0), its toxicology and human health effects (Section 5.0) and approaches taken by other jurisdictions in setting effects-based criteria, in particular, those of Health Canada and the U.S. EPA (Section 6.0).

The Ministry first develops an AAQC, which is used to evaluate regional air quality that results from all sources of a contaminant to air. Air standards are based on AAQCs and set under Ontario Regulation 419: Air Pollution – Local Air Quality (O. Reg. 419/05). Air standards may be numerically the same as an AAQC but are tools that contribute to the management of local air quality. Under the regulation, air standards are used to assess the contributions of a contaminant to air by a regulated facility.

The current process for setting AAQCs and air standards was established in 2008, through consultation with stakeholders. The first step is for the Ministry to prepare a Science Discussion Document and to invite interested stakeholders to discuss the science in a "pre-consultation" meeting. The Science Discussion Document (i.e., this document) summarizes the science that will inform the development of the AAQC and air standard; however, no regulatory limit is proposed. Science Discussion Documents are e-mailed to stakeholders interested in that substance, and are followed by pre-consultation meetings to enable stakeholders to discuss the science with the Ministry and each other before a regulatory standard is proposed. Written comments can also be submitted on the Science Discussion Document. This is referred to as the 'pre-consultation' step.

After giving consideration to outstanding issues which may arise from the pre-consultation phase, a regulatory proposal is made through a Rationale Document, which undergoes formal public consultation by posting on the Ontario Environmental Bill of Rights Environmental Registry. This is referred to as the 'consultation' step. The posting of the Rationale Document provides an opportunity for input from stakeholders regarding the proposed AAQCs and air standards. Meetings with stakeholders may also be held during this step. The Ministry considers comments received during the consultation to inform its decisions on the proposed AAQCs and air standards. A Decision Document is prepared, which includes key comments from stakeholders and the responses provided by the Ministry. The air standards are added to O. Reg. 419/05 and the final decisions are posted on the Environmental Registry.

2.2 Direct Toxicity vs. Indirect Toxicity

SO_2 is associated with both direct and indirect health and environmental effects. Briefly, direct inhalation of SO_2 may affect human health by altering respiratory function. SO_2 can adversely affect vegetation both directly and after formation acidifying compounds. Regional effects of continued acid deposition may include the acidification of ecosystems, with the ensuing stress harming the overall ecosystem health. Acidifying compounds are also corrosive and can damage materials such as metals, stone and bricks. Also indirectly, SO_2 is a precursor to fine particulate matter ($PM_{2.5}$) and contributes to the formation of ozone. Exposure to both $PM_{2.5}$ and ozone increases the risk of adverse human health effects contributing to respiratory and cardiovascular disease and premature death.

In general, the Ministry sets AAQCs and air standards based on the direct effects of the substance.

2.3 The SO_2 CAAQS Process

Through the Canadian Council of Ministers of the Environment (CCME), the Ministry participates with other provinces and territories and the federal government in developing Canadian Ambient Air Quality Standards (CAAQS) for selected air contaminants. The CAAQS are intended to drive air quality improvements through public reporting and air zone management. New CAAQS for $PM_{2.5}$ and ozone were established as objectives under the Canadian Environmental Protection Act 1999, in May 2013 and replaced the existing Canada-wide Standards for particulate matter and ozone.

Work began in 2014 on CAAQS for SO_2, which will be brought forward for approval by provincial and territorial Ministers at the 2016 fall meeting of the CCME. Once approved, each jurisdiction can work to achieve the CAAQS in a manner consistent with their own regulatory framework and policies. It should be emphasized that while CAAQS are based on considerations of both science and implementation, AAQCs are based on only science considerations.

2.4 U.S. EPA NAAQS Process

The Clean Air Act requires the US Environmental Protection Agency (U.S. EPA) to set National Ambient Air Quality Standards (NAAQS) for selected contaminants of concern to public health and the environment: carbon monoxide, lead, nitrogen dioxide, ozone,

particulate matter, and sulphur dioxide. NAAQS are established levels that reduce risk but do not necessarily reflect concentrations at which no effects are expected. The goal is to protect public health with an “adequate margin of safety”. The U.S. EPA does not consider the costs or other implementation issues in setting the NAAQS. The health assessment performed by the U.S. EPA during the development of the SO_2 NAAQS (U.S. EPA, 2008) significantly informed the development of the SO_2 CAAQS.

3.0 SO_2 as an Environmental Contaminant

3.1 Physical and Chemical Properties

Sulphur dioxide (CAS # 7446-09-5) is colourless gas at room temperature and typical environmental conditions. As it is heavier than air, it may accumulate at ground level under some ambient conditions. The following physical and chemical properties are derived from the U.S. National Library of Medicine Toxnet Toxicology data network (U.S. National Library of Medicine, 2016).

Molecular formula:	SO_2; O=S=O
Molecular weight:	64.064
Boiling point:	-10.05°C
Melting point:	-75.5°C
Corrosive:	Corrosive when hydrated (forming sulphuric acid)
Specific gravity:	2.619 g/L
Water solubility:	Soluble
Ethanol solubility:	Soluble
Index of refraction:	1.3396 at 25°C
Vapour density:	2.264 at 0°C
Vapour pressure (mmHg):	3000 at 25°C (estimate)
Henry's Law constant:	8.10×10^{-4} atm- m^3/mol at 25°C
Conversion ratio:	1 ppb = 2.66 µg/m^3 (at 20°C and 1 atm)

3.2 Sources

The information discussed below was primarily gleaned from the recent health risk assessment carried out by Health Canada (2016), unless noted.

3.2.1 Natural Sources

Volcanoes and landscape fires (forest fires, wildfires and controlled burns) are the largest natural sources of SO_2 emissions. While volcanic sources are not considered to be of great significance to Ontario, landscape fires result in SO_2 release when the sulphur bound in amino acids of vegetation gets oxidized during combustion. Reduced sulphur gases are also emitted by marine organisms, as well as by anaerobic bacteria in marshes and estuaries. Other sulphur species emitted by natural sources include dimethyl sulphate, hydrogen sulphide, sulphur oxide, and the general category of total

reduced sulphur. Sulphur dioxide remains the most important of the gas-phase sulphur oxides with regard to both atmospheric chemistry and human health effects.

The estimated total SO_2 emissions in 2011 from natural sources in Canada were approximately 100 tonnes; however, estimates were not available for other potential natural sources (e.g., marine organisms or anaerobic bacteria), likely due to difficulties in quantifying such releases. Additionally, year-to-year variability is to be expected from natural sources due to the nature of their release.

3.2.2 Anthropogenic Sources

While naturally occurring SO_2 is largely derived from the oxidation of sulphides emitted by low flux "area" sources, anthropogenic emissions of sulphur are primarily in the form of SO_2 emerging from "point" sources, and in quantities that may substantially affect local and regional air quality (U.S. EPA, 2015). While the largest SO_2-emitting sector within the U.S. remains coal-fired power plants, Ontario passed legislation in 2015 to permanently ban coal-fired electricity generation in the province (MOECC, 2015). Thus, major anthropogenic sources of SO_2 in Ontario include non-ferrous smelting and refining, petroleum refining, iron and steel industry, transportation sources (e.g. air and marine transportation), incinerators, and other industrial sources (e.g. cement plants, pulp and paper mills, chemical industry). Environment Canada estimated total SO_2 anthropogenic emissions of just over 1 million tonnes (without including open sources such as agriculture, waste, and prescribed burning), with approximately 25% of emissions attributed to Ontario (Environment Canada, 2014).

3.3 Environmental Levels and Environmental Fate

Local emission sources, local weather conditions and geological formations can significantly affect ambient concentrations of SO_2, making SO_2 monitor-to-monitor correlations weak unless they are in proximity to the same emission source. Using the National Air Pollution Surveillance (NAPS) monitoring results, Health Canada (2016) has described 2011 annual averages having a range from below the detection limit to 23 $\mu g/m^3$. In general, ambient air levels of SO_2 air have decreased by 96% in Canada since 1970 (Environment Canada, 2011), largely as a result of the use of low-sulphur fuels, and pollution controls and regulations that have limited SO_2 emissions (Chen et al., 2007). Similarly, U.S. emissions of SO_2 have declined by approximately 70% for all major sources since 1990 (U.S. EPA, 2015).

Ambient air concentrations of SO_2 are generally higher in urban areas compared to rural areas; however, some rural sites have exhibited higher SO_2 concentrations than some urban sites, likely due to significant anthropological point source emissions of SO_2

in the vicinity. For example, while the average daily 1-hour maximum SO_2 concentration reported during 2010−2012 in the U.S. was 24 µg/m^3, the 99th percentile can approach 200 µg/m^3 at some monitors located near large anthropogenic or natural sources (U.S. EPA, 2015). Similarly, 5-minute data demonstrate that on some occasions (99th percentile and above) concentrations can be greater than 530 µg/m^3 near anthropogenic sources. Similar findings were described in Canada, where monitoring stations with a nearby point source having higher annual average and 1-hour maximum concentrations of SO_2 in comparison to non-point-source monitoring sites (Health Canada, 2016). According to the most recently available Air Quality in Ontario Report (MOECC, 2013), Hamilton Downtown recorded the highest annual mean (13 µg/m^3) and 24-hour maximum concentrations (115 µg/m^3) during 2013, whereas Sudbury recorded the highest one-hour maximum concentration (527 µg/m^3).

Another key point about environmental SO_2 environmental concentrations is the significance the reported metric has on conveying exposure levels. For example, by looking at the 2003 to 2005 U.S. data reported by the U.S. EPA (2008), the mean, 99th percentile, and maximum readings recorded (all 1 hour averages) were 35 µg/m^3, 250 µg/m^3, and 1860 µg/m^3, respectfully. Here, the data suggests that the mean value, taken alone, may mask the peak exposure level, by up to 1-to-2 orders of magnitude.

SO_2 is highly soluble in water and is rapidly oxidized to sulphur trioxide (SO_3) and sulphuric acid (H_2SO_4) and its anion, sulphate (SO_4^{2-}), upon emission into the atmosphere. It is these sulphates that condense onto existing particles when particle loadings are high, or nucleate to form new particles under lower concentration conditions (Health Canada, 2016). As well, with the formation of H_2SO_4, SO_2 is considered the main cause of acid rain. For the purposes of this document, only gaseous SO_2 will be considered.

It should be noted that although SO_3 may also be directly emitted from some point sources, it reacts extremely rapidly with water in the stacks or immediately after release into the atmosphere to form H_2SO_4. Due to such rapid oxidation, only SO_2 is present in the tropospheric boundary layer at concentrations of concern for human exposures (U.S. EPA, 2015). Also due to rapid oxidation, there are significant spatial variations in SO_2 concentration related to the distance from the source of emissions.

3.4 Odour

The odour of SO_2 has been described as strong, irritating and pungent (U.S. National Library of Medicine, 2016). Odour detection thresholds have been reported ranging from approximately 300 to 3,800 ppb (van Gemert, 201; Health Canada, 2016). The

odour detection threshold of 500 ppb (≈1300 µg/m^3) was derived by independent studies (El-Dars et al., 2004; van Thriel et al., 2010), and is considered to be a reasonable consensus value. However, as noted by Health Canada, the odour detection threshold of 500 ppb is greater than the air quality criteria or standards regulated federally or provincially, as well as by international governments, and thus is not considered to be a driving force in the development of an updated SO_2 AAQC.

4.0 Environmental Effects of SO_2

4.1 Background

SO_2 is an acidifying substance and thus acts as a corrosive agent that can damage materials and structures, by causing or contributing to the aging of buildings, the corrosion of metals, the deterioration of brick and stone, and the cracking and fading of exterior painted surfaces. In humid air and under fog conditions, SO_2 dissolves in the water molecules leading to the formation of a sulphuric acid mist, which can bring about a significant increase in the potential of adverse effects on plants, and is identified as one of the major causes of acid deposition (WHO, 2000).

SO_2 can affect elements of ecosystems directly on plants and through soil uptake or directly through adsorption of SO_2 from air, and indirectly through the deposition and retention in soils of other sulphur-containing compounds such as sulphuric acid and sulphate particles. Acute and chronic exposures to SO_2 have phytotoxic effects on vegetation which include foliar injury, decreased photosynthesis, and decreased growth.

The direct effects of SO_2 on plants may be acute or chronic, depending on the duration and intensity of the exposure. SO_2 inhibits photosynthesis by disrupting the photosynthetic mechanism and the biosynthesis of lipids which works as a barrier to prevent water loss and protect against pathogens and other environmental stress (Ohlrogge and Browse, 1995). The opening of the stomata is promoted by SO_2, resulting in an excessive loss of water. The cumulative effect of sulphurous pollution is the reduction of the quantity and quality of plant yield. Generally, its impact is more severe when in combination with other pollutants such as oxides of nitrogen, fluorides, and ozone. At the ecosystem level, SO_2 affects species composition by eliminating more sensitive species. This reduces primary productivity and alters trophic relationships which may have far-reaching implications for the animal and microbial populations in the community. Another indirect effect results from the acid rain which leaches out nutrients from plant canopy and soil. The acidic run-off changes the pH of the receiving waters and adds large quantities of nutrients which disturb the equilibrium of aquatic communities. Plants vary widely in their tolerance to SO_2. Lichens and bryophytes (mosses and liverworts) are among the most sensitive and have been used as indicators of SO_2 pollution.

4.2 Uptake of Sulphur Dioxide by Plants

4.2.1 Direct Effects

SO_2 penetrates into leaves primarily in gaseous form through the stomata. The aperture of the stomata is controlled largely by the prevailing environmental conditions,

such as humidity, temperature and light intensity. Thus, these external factors influence the rate of uptake of SO_2, and therefore the degree of injury. When the stomata are closed, as occurs under dark or drought conditions, resistance to gas uptake is very high and the plant has a significantly low degree of susceptibility to injury. Unlike higher plants, mosses and lichens do not have a protective cuticle exposed to SO_2, which is the major reason for their extreme sensitivity to this compound.

Different plant or foliar injuries may occur depending on the exposure duration and concentration (WHO, 2000). Acute exposure (1 to 24-hours) to high SO_2 concentrations can produce visible injury in the form of foliar necrosis such as yellowed and brown leaves. Foliar injury may be caused by the effects of acidification of plant tissues following the formation of sulphite and sulphate within the plant from the up-taken SO_2 (Narendra et.al., 2012). Chronic exposure (months to years) to low SO_2 concentrations can result in reduced growth and yield with little visible sign of injuries (WHO, 2000). Specifically, the WHO (2000) observed that acute exposure may be of lesser concern than chronic exposure in that acute effects are far less important in the field than chronic injury, which results from long-term exposure to much lower concentrations of the gas and is essentially cumulative in nature, taking the form of reduced growth and yield and increased senescence. The U.S. EPA, however, asserts that acute exposure appears to be the more relevant concern since during the most recent review (U.S. EPA, 2012b) of their secondary SO_2 standard for the protection of vegetation they retained their 3-hour standard of 500 ppb (≈1300 $\mu g/m^3$), and did not adopt a long-term standard.

In fumigation experiments on sensitive clones of eastern white pine (*Pinus strobus*), acute adverse effects were observed at ambient concentrations as low as 25 ppb (≈66 $\mu g/m^3$) over a six hour exposure. In less sensitive white pines, which better represented the forest population, acute adverse effects were observed at 250 ppb (≈660 $\mu g/m^3$) at exposures of 1 to 2 hours. In the mid-1960s, field measurements near a nickel smelter in Sudbury, Ontario found visible injury on trees in natural forests at ambient concentrations of 250 ppb for an 8-hour exposure. Other field studies also in the Sudbury area in the mid-1950s and 1960s observed chronic effects during the growing season on eastern white pine trees at concentrations of 17 ppb (≈45 $\mu g/m^3$), and slight chronic effects at concentrations of 8 ppb (≈20 $\mu g/m^3$) (Linzon, 1985).

The WHO (2000) provides an update on the vegetation standards established in 1988 by the United Nations Environmental Commission for Europe (UNECE). Here, they mention studies which confirmed the UNECE 1988 annual standards, and provided information for a revision of the standards. These UNECE annual standards are 30 $\mu g/m^3$ (≈11 ppb) for the protection of major agricultural crops, and 20 $\mu g/m^3$ (≈8 ppb) for the protection of forests and natural vegetation. Of note is that the 20 $\mu g/m^3$ ppb

standard is consistent with the chronic effects observed at concentrations of 8 ppb in the Sudbury area in the 1960s.

4.2.2 Indirect Effects

The deposition of acidifying compounds can lead to increased acidification of ecosystems which can adversely impact the living organisms that inhabit them, from micro-organisms, and up the food chain to plants, trees, fish and mammals. For some organisms, changes in acidity levels, even for brief periods, can be harmful.

Common acidifying compounds include those resulting from SO_2 and oxides of nitrogen (NO_X). There are two broad types of deposition, commonly known as wet deposition and dry deposition. Wet deposition is the deposition of acidifying compounds through precipitation such as rain, snow, fog, etc. Dry deposition is the deposition of acidifying gases and particles through settling and interception.

The sensitivity of ecosystems to acid deposition is broadly quantified by the critical load of acidity of the ecosystem which is defined as: The maximum deposition of acidifying substances that will not cause chemical changes leading to long-term harmful effects on the ecosystem structure and function according to present knowledge (Nilsson and Grennfelt, 1988). When the annual acid deposition over an area exceeds the critical load of acidity value for that area, elements of ecosystems in the area are under stress or may have suffered harm (CCME, 2014).

4.2.3 Lichens

Typically, epiphytes (such as lichens) and bryophytes are among the first species affected by acidifying deposition in terrestrial ecosystems. Effects of SO_2 on lichens include reduced photosynthesis and respiration, damage to the algal component, leakage of electrolytes, inhibition of nitrogen fixation, reduced potassium absorption and structural changes. Acidifying deposition has an observable effect on lichen abundance and diversity within forest communities. In eastern North America and central Europe, areas that receive relatively high levels of acidifying deposition and high atmospheric concentrations of SO_2, nitrogen oxides, and reduced nitrogen have experienced noticeable reductions in cyanolichen abundance on both coniferous and deciduous trees (Richardson and Cameron, 2004). Effects on lichen species biodiversity are also likely (McCune, 1988; van Haluwyn and van Herk, 2002). In response to reductions after the 1970s in SO_2 exposure and acidifying deposition in London, lichen diversity increased dramatically (Hawksworth, 2002). However, the recovery of lichens in response to reduced sulphur and nitrogen inputs is inconsistent. For example, improvement for bryophytes has been reported to take both 1 year (Power et al., 2006) and 49 years (Strengbom et al., 2001). Additionally, it has been concluded that the

sulphur:nitrogen exposure ratio was as important as pH in causing toxic effects on lichens, based on experiments on *Cladina rangiferina* and *C. stellaris* (Scott,1989a; 1989b). Thus, it is not clear to what extent acidity may be the principal stressor under high levels of air pollution exposure. Nonetheless, the toxicity of SO_2 to several lichen species is greater under acidic conditions than under neutral conditions.

4.2.4 Lichens as Bioindicators of Air Quality and Climate Change

Due to their sensitivity, lichens serve as early warning indicators of air pollution, particularly acidifying or fertilizing sulphur and nitrogen-based pollutants, which has been documented in many scientific papers (McCune, 2000). Air quality monitoring studies have been done worldwide and permanent monitoring programs using lichens exist in the US and Europe. Lichens' sensitivity to air quality stems from their reliance on airborne nutrients and water, as well as lack of protective structures such as cuticles found in vascular plants. Trees and other vascular plants are affected by pollution but are much slower to show impacts than lichens (Muir and McCune, 1988).

More recently, lichens are being used in assessing climate in Europe and the US (McCune, 2000; van Herk, 2002). Distributions of certain species are a response to regional moisture and temperature gradients. Mapping distribution of climate sensitive species provides an indication of climatic conditions and monitoring over time reveals climate change effects.

Because ecosystems are complex, short-term studies are often unable to detect long-term trends such as climate change. It is more practical to answer these questions with a long-term monitoring program using ecological indicators. Indicators provide a practical way to monitor complex ecological conditions and to serve as early warning mechanisms. Thus indicators must be sensitive so that they indicate perturbation before significant impact occurs to the rest of the ecosystem. Further, indicators must be efficiently measurable. The role of lichens in ecosystem processes and biodiversity also makes them a useful group to monitor as they represent a significant proportion of biodiversity in many ecosystems (McCune, 2000). A study in boreal forests of Scandinavia showed increasing diversity of spiders with increasing lichen diversity (Pettersson, 1996). It has also been suggested that forest bird diversity may be associated with lichen diversity (Pettersson, 1996). Lichens also provide food for animals and habitat for invertebrates (Sharnoff, 1994; Stubbs, 1989). Many lichens are habitat specific and thus a diversity of lichens at a site indicates habitat heterogeneity (Cameron, 2002). Given the close relationship of lichens with other organisms, and their contribution to biodiversity, lichens provide an ideal group to monitor for changes in diversity in ecosystems. Lichens meet the criteria as useful indicators for assessing impacts of both air pollution and climate change.

5.0 Human Health Effects

5.1 Outline

Information in this section is primarily taken from the recent health risk assessment by Health Canada (2016), U.S. EPA (2008; 2015) and WHO (2005) unless noted. For comparison purposes, 1 ppb = 2.66 µg/m^3 (at 20°C and 1 atm).

5.2 Toxicokinetics

5.2.1 Absorption

The most relevant exposure pathway to humans is through inhalation, since SO_2 is a gas under standard conditions. Sulfur dioxide is very water soluble, and it is expected to be almost completely absorbed in nasal passages in humans, predominantly across nasal mucosa and the mucosal cells of the trachea (ATSDR, 1998; Arts et al., 2006). It is minimally absorbed by mucosa of the lower respiratory tract. However, with increasing physical activity, there is an increase in ventilatory rate and a shift from nasal to oronasal breathing, resulting in greater SO_2 penetration into the bronchial region. Similarly, due to their increased amount of oral breathing, children and individuals with asthma may be expected to have greater SO_2 penetration than healthy adults (U.S. EPA, 2015).

5.2.2 Distribution

Once absorbed across mucosal cells, hydrated SO_2 transforms to sulphites/bisulphites at physiologic pH. While inhalation-derived SO_2-products may distribute throughout the body, overall sulphite levels are predominately influenced by endogenous production and by ingestion of sulphite in food. Specifically, it has been estimated that endogenous sulphite production is two-or-more orders of magnitude higher than inhalation-derived sulphite levels for both children and adults, even for full day exposures to SO_2 at 200 µg/m^3 (which in itself is an order of magnitude higher than typical ambient SO_2 levels). While inhalation-derived SO_2 products accumulate in respiratory tract tissues, sulphite and other metabolites from ingestion or endogenous production do not (U.S., EPA, 2015). Thus, while this section of the document will focus on the human health effects of inhalation-derived SO_2 on the respiratory tract, it is worth briefly describing SO_2 metabolism and elimination.

5.2.3 Metabolism and Half-life

The following metabolic pathways for sulphite in the blood were reported by Health Canada (2016): 1) enzymatic oxidation to SO_4^{2-} by sulphite oxidase (SOX); 2) two-step enzymatic oxidation by peroxidases; 3) formation of disulphide bonds with proteins to form S-sulphonate; 4) reaction with amino acids; 5) transformation to thiosulphate; and 6) auto-oxidation to SO_4^{2-} in the presence of metals. It is was further noted that plasma levels of sulphonated proteins (R-S-sulphite) correlate positively with concentrations of SO_2 in the air in studies using humans exposed to SO_2 by inhalation (ATSDR, 1998). The metabolism of S-sulphonates is unknown, but it is hypothesized that they will be reduced by glutathione reductase and ultimately oxidized by SOX to SO_4^{2-}, with SOX being ubiquitous in human tissues.

Health Canada (2016) reported that the WHO was the only source for half-life data for derivatives of SO_2 in humans or animal models, which cited studies from the 1970s. An estimated SO_3^{2-} half-life in humans of 15 minutes and a plasma S-sulphonate half-life of 4 and 8 days in rat and monkey, respectively, were reported.

5.2.4 Elimination

The primary route of elimination has been identified as urinary excretion, primarily as sulphates (ATSDR, 2011), formed via SOX interaction. It remains unclear as to whether SO_2 is released from pulmonary capillaries during expiration (Health Canada, 2016).

5.3 Toxicodynamics

Briefly, one of the well-known principal effects of inhaled SO_2 is that it stimulates bronchial epithelial irritant receptors (i.e., chemosensitive receptors) in the tracheobronchial tree. This initiates a reflexive contraction of smooth muscles in the bronchial airways associated with bronchial constriction. It is this bronchial constriction that is associated with respiratory morbidity. Although other adverse health effects have been associated with SO_2 exposure (Table 5.2), this document focuses on respiratory effects (bronchoconstriction) as the critical health effect associated with exposure. For a fulsome description of SO_2 toxicodynamics, please see the recent health risk assessments by Health Canada (2016) or the U.S. EPA (2008; 2015).

Nonetheless, in lieu of a detailed discussion, a summary of the relevant SO_2 modes of action will be discussed in the sections describing the considerations in the development of AAQCs for SO_2 to protect human health (Section 7.0). A review of the epidemiologic, controlled human exposure, and toxicological studies on health effects of SO_2 is presented below.

5.4 Methodology: Weight of Evidence for Causal Determination

Data are available which characterize quantitative relationships between SO_2 inhalation exposure and adverse health effects. Specifically, these data have defined exposure metrics, consider the potential co-influence of other air pollutants correlated with SO_2, and examine potential at-risk populations and life-stages. Rather than generating a new review of these data, this document relies on the breadth and depth of recent SO_2 health assessments (US. EPA, 2008; 2015; Health Canada, 2016), which describe whether an association between SO_2 exposure and various adverse health effects are causal, likely to be causal, suggestive of a causal relationship, or inadequate to conclude that the relationship is causal. Both assessments examined the available scientific evidence using established considerations for assigning causal determination. These considerations, akin to Bradford Hill criteria, are succinctly summarized by Health Canada (2016), and include the following (italics in original):

> "the *strength* of the associations, including the magnitude and precision of the risk estimates and their statistical significance
>
> the *robustness* of the associations to model specifications and adjustment for potential confounders such as weather, temporal trends, and co-occurring pollutants
>
> the *consistency* of reported associations across studies and study designs conducted by different researchers in different locations and times
>
> the *biological plausibility* of the associations in light of what is known about the effects of this chemical, referencing data from experimental studies or other sources demonstrating plausible biological mechanisms
>
> the *coherence* of the relationship between exposure to the chemical and related endpoints within and across animal toxicology, controlled human exposure, and various types of epidemiological studies"

The definitions for the various degrees of causality utilized by both assessments had been established by the U.S. EPA (2008), and are presented in Table 5.1.

Table 5.1: **U.S. EPA weight of evidence for causal determination** (U.S. EPA, 2008)

Relationship	**Description**
Causal relationship	Evidence is sufficient to conclude that there is a causal relationship between relevant pollutant exposures and the health outcome. That is, a positive association has been observed between the pollutant and the outcome in studies in which chance, bias, and confounding could be ruled out with reasonable confidence. Evidence includes, for example, controlled human exposure studies; or observational studies that cannot be explained by plausible alternatives or are supported by other lines of evidence (e.g. animal studies or mechanism of action information). Evidence includes replicated and consistent high-quality studies by multiple investigators.
Likely to be a causal relationship	Evidence is sufficient to conclude that a causal relationship is likely to exist between relevant pollutant exposures and the health outcome but important uncertainties remain. That is, a positive association has been observed between the pollutant and the outcome in studies in which chance and bias can be ruled out with reasonable confidence but potential issues remain. For example: a) observational studies show positive associations but co-pollutant exposures are difficult to address and/or other lines of evidence (controlled human exposure, animal or mechanism of action information) are limited or inconsistent, or b) animal evidence from multiple studies, sex, or species is positive but limited or no human data are available. Evidence generally includes replicated and high-quality studies by multiple investigators.
Suggestive of a causal relationship	Evidence is suggestive of a causal relationship between relevant pollutant exposures and the health outcome, but is limited because chance, bias and confounding cannot be ruled out. For example, at least one high-quality study shows a positive association but the results of other studies are inconsistent.
Inadequate to infer a causal relationship	Evidence is inadequate to determine that a causal relationship exists between relevant pollutant exposures and the health outcome. The available studies are of insufficient quantity, quality, consistency or statistical power to permit a conclusion regarding the presence or absence of an association between relevant pollutant exposure and the outcome.
Suggestive of no causal relationship	Evidence is suggestive of no causal relationship between relevant pollutant exposures and the health outcome. Several adequate studies, covering the full range of levels of exposure that human beings are known to encounter and considering sensitive subpopulations, are mutually consistent in not showing a positive association between exposure and the outcome at any level of exposure. The possibility of a very small elevation in risk at the levels of exposure studied can never be excluded.

5.5 Summary of Human Health Effects Assessments

Table 5.2 is a summary of the human health effects assessments performed in the most recent SO_2 health assessments (U.S. EPA, 2015; Health Canada, 2016). The conclusions of an earlier U.S. EPA health assessment are also presented (U.S. EPA, 2008), as they provided the analytical foundation of the Health Canada assessment. Briefly the information from controlled human exposure, epidemiologic, and toxicological studies have been integrated by the agencies to form conclusions about the causal nature of relationships between SO_2 exposure and health effects. For details on the scientific evidence reviewed, the reader is encouraged to examine the relevant agency's human health assessments.

From the information in Table 5.2, it is clear that there is significant uncertainty regarding relationships between SO_2 exposure and adverse health effects outside of the respiratory system. The weight of evidence is, at best, suggestive of but not sufficient to infer a causal relationship with total mortality, reproductive and developmental effects, and cancer. While SO_2 itself is unlikely to enter the bloodstream, its reaction products, such as sulphite, may do so; however, endogenous sulphite levels from catabolism of endogenous sulphur-containing amino acids are expected to be 1-2 orders of magnitude higher than those resulting from SO_2 inhalation.

The strongest and most consistent findings across agencies and assessments within Table 5.2 indicate a causal relationship between short-term SO_2 exposure and respiratory effects. These adverse respiratory effects include respiratory symptoms (e.g., bronchoconstriction), changes in lung function, airway inflammation, airway hyper-responsiveness, and emergency department (ED) visits and/or hospitalizations. The respiratory morbidity epidemiological and controlled human chamber studies underlying this finding are discussed in the following sections.

Table 5.2: Summary of the human health effects assessment conclusions of recent SO_2 human health assessments. (Adapted from Health Canada, 2016)

Endpoint	Exposure duration	Effects	U.S. EPA (2008) conclusion	U.S. EPA (2015) conclusion	Health Canada (2016) conclusion
Respiratory morbidity	Short-term	Respiratory symptoms, lung function, airway inflammation, airway hyper-responsiveness, ED visits /hospitalizations	Causal relationship (No separate conclusion on subpopulation of children)	Causal relationship (No separate conclusion on subpopulation of children)	Causal relationship (adults) Suggestive of a causal relationship (children)
	Long-term	Respiratory symptoms and lung function	Inadequate to infer a causal relationship	Suggestive of a causal relationship	Inadequate to infer a causal relationship
Cardiovascular morbidity	Short-term	ED visits/hospitalizations	Inadequate to infer a causal relationship	Suggestive of a causal relationship	Inadequate to infer a causal relationship
	Long-term	Blood markers, arterial stiffness	No conclusion	Inadequate to infer a causal relationship	No conclusion
Mortality	Short-term	Non-accidental and cardiopulmonary	Suggestive of a causal relationship	Suggestive of a causal relationship	Suggestive of a causal relationship
	Long-term	Non-accidental and cardiopulmonary	Inadequate to infer a causal relationship	Suggestive of a causal relationship	Inadequate to infer a causal relationship
Carcinogenicity		DNA damage, carcinogenesis, tumour promotion, incidence of lung cancer	Inadequate to infer a causal relationship	Suggestive of a causal relationship	Inadequate to infer a causal relationship
Developmental		Congenital heart defects	No conclusion	No conclusion	Weakly Suggestive of a causal relationship
Reproductive/ Developmental		Preterm delivery	No conclusion	Suggestive of a causal relationship	Weakly Suggestive of a causal relationship
		IUGR, cleft lip/palate, neonatal hospitalization and infant mortality	No conclusion		Inadequate to infer a causal relationship
Prenatal and neonatal outcomes		Low birth weight	Inadequate to infer a causal relationship	No conclusion	Inadequate to infer a causal relationship

Abbreviations: ED, emergency department; IUGR, intrauterine growth restriction.

5.6 Respiratory Morbidity: Epidemiology

In their tabulation of key evidence underlying the causal determinations for SO_2, the U.S. EPA (2015) provided the following summary regarding the evidence from epidemiologic studies describing respiratory effects and short-term exposures:

> *"…Consistent evidence from multiple, high quality epidemiologic studies at relevant SO_2 concentrations shows an increase in asthma hospital admissions and emergency department visits in single- and multicity studies, in studies of all ages, children and older adults. These associations are generally unchanged in co-pollutant models involving PM and other criteria pollutants. Additionally there is some supporting epidemiologic evidence of associations with respiratory symptoms among children with asthma."*

The agency further states that the evidence from epidemiologic studies describing respiratory effects and long-term exposure "is generally supportive but not entirely consistent for increases in asthma incidence and prevalence related to SO_2 exposure" (U.S. EPA, 2015). Furthermore, the evidence from epidemiological studies is coherent with limited animal toxicological evidence of allergic sensitization, airway remodeling, and enhanced airway responsiveness, which are key events (or endpoints) in the mode of action for the development of asthma.

Despite such a strong causal relationship, key uncertainties and limitations remain in utilizing epidemiological data for the development of AAQCs for SO_2, and include the following:

- Exposure measurement error
  - Reliance on historical ambient air monitoring may lead to significant uncertainties in estimations of exposure. While not as significant in determining health effect causality, such uncertainties are critical when developing a toxicity reference value, such as an AAQC. These uncertainties present less accurate than those from human clinical exposure studies under controlled conditions (e.g., chamber studies)

- Co-pollutant confounding
  - SO_2 related health impacts are difficult to distinguish from other contaminants that have similar adverse health outcomes (e.g., PM and NO_x). Thus, the limitation of attributing an independent effect to SO_2 (i.e., due to the relationship of SO_2 levels to PM levels) remains a significant limitation in epidemiological studies

- Concurrent peak exposures

    - Although these epidemiological studies often report lower long-term (e.g. 24 hour or annual) SO_2 concentrations as being associated with adverse effects, it is generally understood that long-term ambient air concentration reflect concurrent peak concentrations that are the key determinates of initiation of an adverse effect

- Other etiological factors
    - Adverse effects classified as respiratory morbidity can also be associated with a variety of etiological factors, including underlying disease state, and life-stage.

In summary, although the numerous epidemiological studies are supportive of respiratory morbidity as the key adverse effect of SO_2 exposure on human health, uncertainty remains in quantifying the concentration-response relationship. Specifically, there are concerns regarding the accuracy of exposure estimates typical of epidemiologic studies, and their applicability in representing an individual's SO_2 exposure from ambient monitoring.

Thus, while there is consistency among evidence from epidemiologic, and toxicological studies, and biological plausibility for effects specifically related to respiratory morbidity, estimates of exposure are considered to be more accurate in human clinical studies under controlled conditions (e.g., chamber studies), and thus will be relied upon for quantitative evaluation.

5.7 Respiratory Morbidity: Controlled Human Studies

In contrast with epidemiological studies, controlled human clinical studies feature direct exposure to SO_2 at known levels for specific durations without the interference of other pollutants, and allow for sensitive measurements of lung function to be taken. Typically, volunteer subjects perform moderate levels of physical activity in controlled chambers such as exercising on a stationary bicycle.

With asthma sufferers prone to the health effects of bronchoconstriction, asthmatics are considered a susceptible population in studying the effects of SO_2. Typical subjects are asthmatic adults with mild-to-moderate controlled asthma not receiving medication; due to ethical reasons, children and those with severe or uncontrolled asthma are typically excluded.

Pulmonary resistance to airflow is the hallmark pathophysiology of bronchoconstriction, and can either be measured by an increase in specific airway resistance (sRaw) or a decrease in forced expiratory volume in 1 second (FEV_1). Specific airway resistance is

usually measured using a plethysmograph, and is adjusted for a specific lung volume, often measured as thoracic gas volumes. Forced expiratory volume in 1 second is the volume of air that can forcibly be blown out in one second, after full inspiration.

In their health assessment, the U.S. EPA (2008) noted that for individuals with lung disease (e.g. asthma), even moderate decrements in lung function (i.e., increase in sRaw ≥ 100% or decrease in FEV_1 ≥ 15%) would likely interfere with normal activities and result in additional and more frequent use of medication. The basis of the U.S. EPA position on what is considered an adverse effect, was formulated upon consideration of an American Thoracic Society (ATS) publication, *"What Constitutes an Adverse Health Effect of Air Pollution?"* (ATS, 2000). The U.S. EPA (2008) summarized their findings in the following statement:

> *"In their official statement, the ATS concluded that an air pollution-induced shift in a population distribution of a given health-related endpoint (e.g., lung function in asthmatic children) should be considered adverse, even if this shift does not result in the immediate occurrence of illness in any one individual in the population. The ATS also recommended that transient loss in lung function with accompanying respiratory symptoms attributable to air pollution should be considered adverse. However, it is important to note that symptom perception is highly variable among asthmatics even during severe episodes of asthmatic bronchoconstriction. An asymptomatic decrease in lung function may pose a significant health risk to asthmatic individuals as it is less likely that these individuals will seek treatment (Eckert et al., 2004; Fritz et al., 2007). Therefore, whereas the conclusions in the 1994 Supplement were based on SO_2 exposure concentrations which resulted in large decrements in lung function along with moderate to severe respiratory symptoms, the current review of data from human clinical studies focused on moderate to large SO_2-induced decrements in lung function along with respiratory symptoms ranging from mild (perceptible wheeze or chest tightness) to severe (breathing distress requiring the use of a bronchodilator)."*

In consideration of this position, the U.S. EPA amassed data from a sub-set of studies conducted by the same research group and performed under similar experimental conditions (Linn et al., 1987; 1988; 1990), and performed a meta-analysis. The results, presented in graphical form, highlight the dose response findings in both the magnitude of respiratory effect (i.e., FEV_1 and sRaw) and percent of asthmatics affected (Figure 5.1).

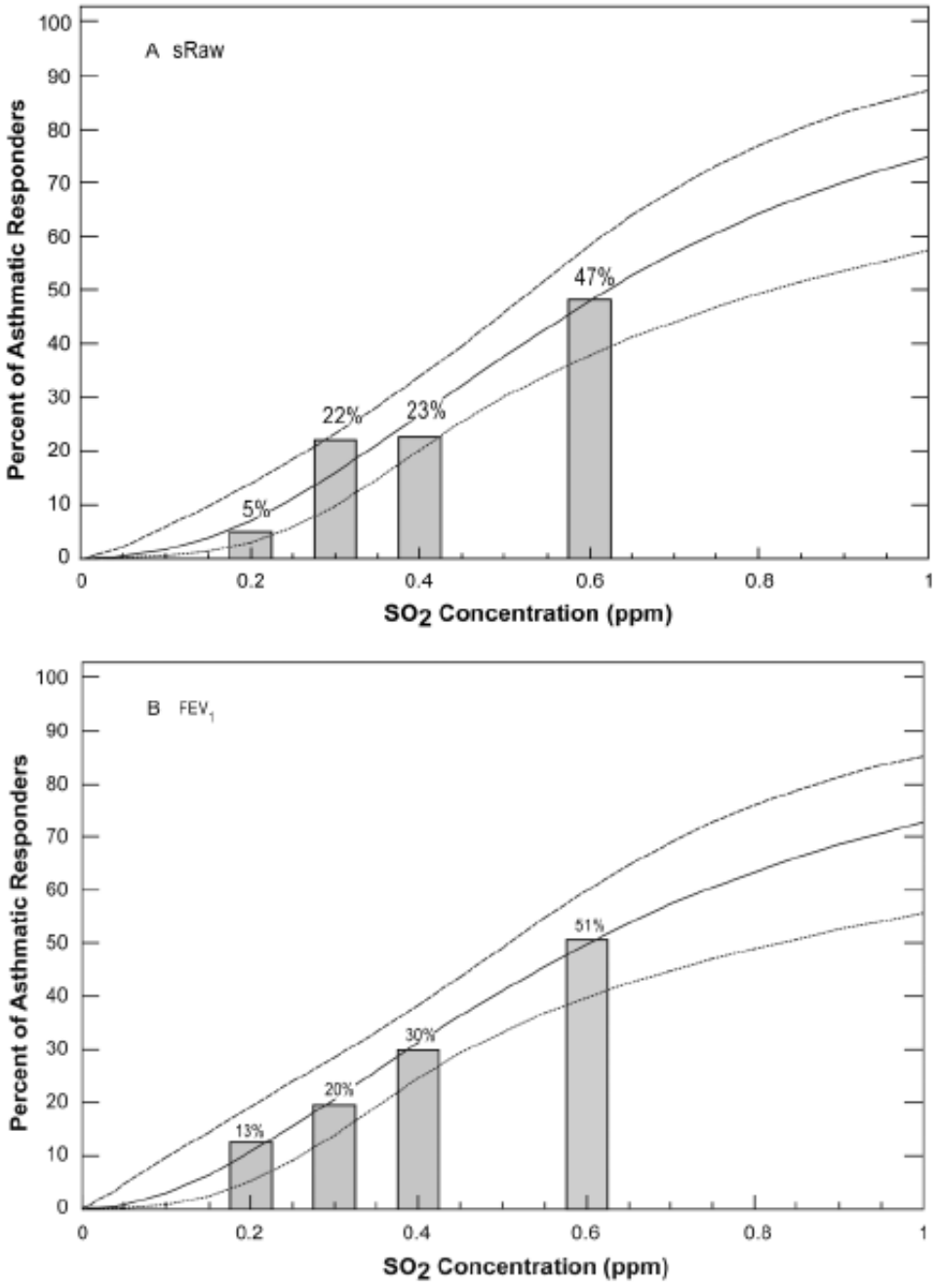

Figure 5.1. Dose-response of detriments in lung function in exercising asthmatics exposed to SO_2, using the Linn et al. subset of data (Linn et al. (1987; 1988; 1990). Percent of mild and moderate asthmatics experiencing an SO_2-induced increase in (a) sRaw of 100% or a decrease in (b) FEV_1 of 15%, adjusted for effects of moderate to heavy exercise in clean air. The data represents lung function measurements from 40, 41, 40, and 81 subjects at concentrations of 0.2, 0.3, 0.4, and 0.6 ppm, respectively (525, 800, 1050, 1600 µg/m^3). Lines represent a logistic model fitted to the data using Bayesian estimation with noninformative priors. For more details, see, U.S. EPA, 2008. (modified from U.S. EPA, 2008; Figure 4.1).

Briefly, asthmatics were grouped as minimal/mild (i.e., demonstrate airway hyper-reactivity to challenge, but had normal pulmonary function and did not require medication between episodes) or moderate/severe (i.e., required regular medication for clinical management, and some had persistent pulmonary function abnormalities). The grouped subjects were exposed for 10 minutes to SO_2 concentrations between 0 and 600 ppb during moderate to heavy exercise. In the first study, SO_2 was monitored in chambers to overall mean concentrations of 0 (clean air), 200, 400, and 600 ppb (0, 525, 1050, 1600 µg/m^3, respectively), within 1 ppb under 21^oC and 50% humidity (Linn et al., 1987). In the later studies, subjects were exposed to 0, 300, and 600 ppb SO_2 (Linn et al., 1988; 1990). Before each exposure, subjects were asked to withhold antihistamines for 48 hours, oral bronchodilators for 12 hours and inhaled bronchodilators for 8 hours to ensure that responses to SO_2 exposures were not influenced by medications. Exposures to SO_2 were considered quasi-double-blind; subjects and test technician would not know the test exposure concentration, though the high does may have been recognized by smell, taste or clinical responsiveness.

Usually subjects were first assessed by bicycle ergometer to determine individual workloads sufficient to increase ventilation to about 40 L/minute. This work load was deemed to be realistic of modelled voluntary outdoor activity or moderate to heavy exercise. This level of increased ventilation was likely attained by nearly all subjects and induces oronasal breathing (i.e., causing delivery of SO_2 to the bronchial region).

The percent of asthmatics experiencing moderate or greater SO_2-induced decrements in lung function (i.e., increase in sRaw ≥ 100% or decrease in FEV_1 ≥ 15%) is shown in a subset of studies highlighted in Figure 5.1, reproduced from U.S. EPA (2008). It should be noted that a dose-response relationship is evident; at 200 ppb, between 5 and 13% of subjects are affected, with this fraction increasing with increasing concentration, where approximately 50% of subjects experience respiratory effects at 600 ppb.

The studies utilized in the meta-analysis and others were used to develop the consensus benchmarks in the development of the U.S. EPA National Ambient Air Quality Standards (NAAQS) (see Section 6.2.7). The complete set of studies relied upon by the U.S. EPA health assessment (2008) are recreated in graphical form in Figure 5.2.

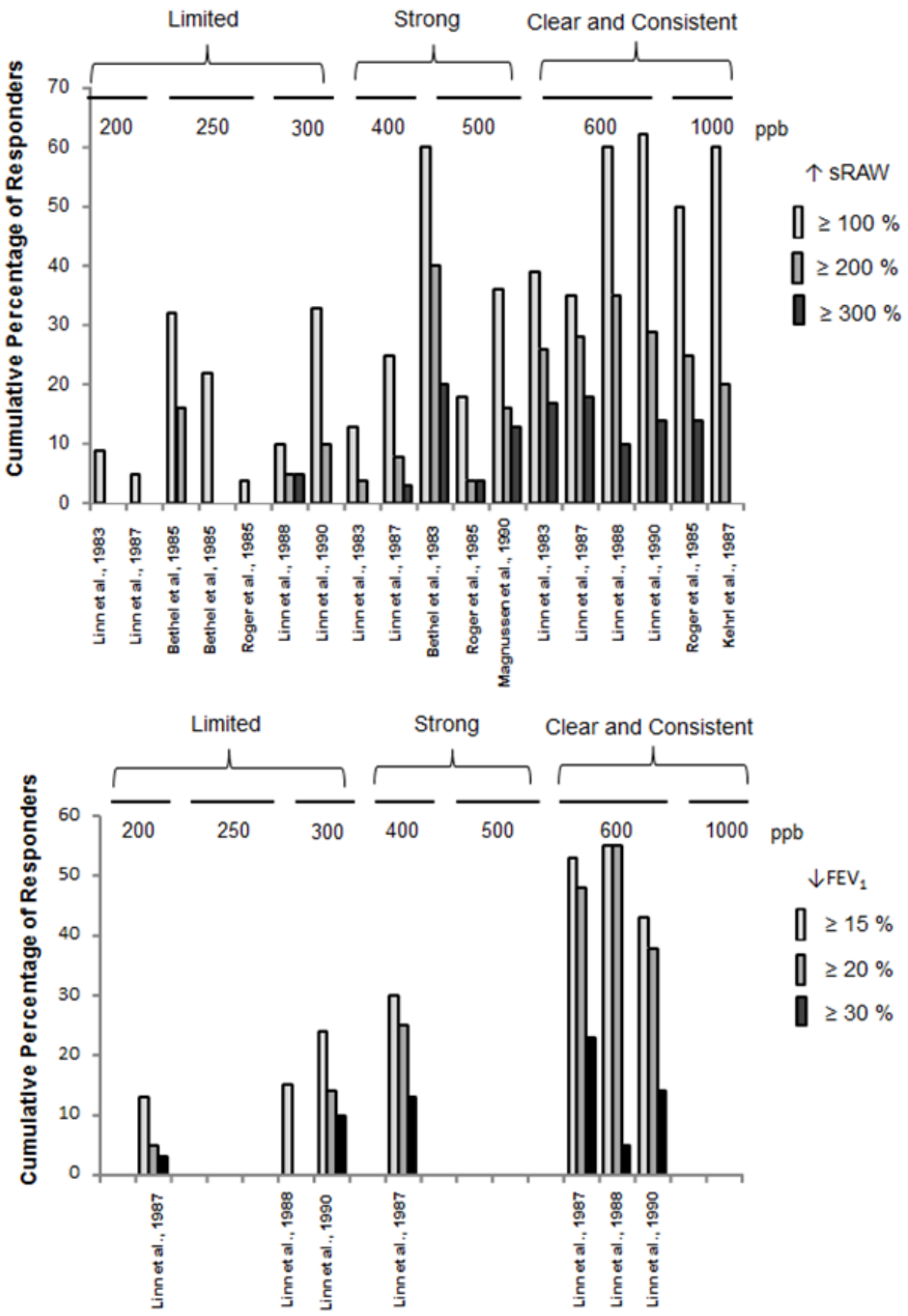

Figure 5.2. Percentage of asthmatic adults in controlled human exposures experiencing SO_2 induced decrements in lung function. Asthmatics in groups of 10 to 45, at ventilation rates ≥ 40 L/minute (equivalent to moderate to heavy exercise) and were exposed to doses of SO_2 for 5 to 10 minutes. Percentage of individuals who experienced (*top*) greater than or equal to a 100, 200, or 300% increase in specific sRaw, or (*bottom*), 15, 20, or 30% decrease in FEV_1. Lung function decrements are adjusted for effects of exercise in clean air (calculated as the difference between the percent change relative to baseline with exercise/SO_2 and the percent change relative to baseline with exercise/clean air) (Data taken from U.S. EPA, 2008; Table 3.1).

Taken together, the following categories were used by U.S. EPA (2008) to develop consensus benchmarks used in the development of the NAAQS, as referred to in Figure 5.2, which are summarized and described in Table 5.3.

Table 5.3. Summary of the strength of the supporting studies describing respiratory symptoms in human asthmatic adults in controlled human exposures experiencing SO_2- induced decrements in lung function.

U.S. EPA (2008) Descriptor	**Respiratory Symptoms and Supporting Studies**
Limited	Limited evidence of SO_2-induced increases in respiratory symptoms in some asthmatics: (Linn et al. 1990; Linn et al. 1988; Linn et al. 1987; Schachter et al. 1984; Linn et al. 1983)
Strong	Stronger evidence with some statistically significant increases in respiratory symptoms: (Balmes et al. 1987, Gong et al. 1995; Linn et al. 1987; Linn et al. 1983b Roger et al. 1985)
Clear and Consistent	Clear and consistent increases in SO_2-induced respiratory symptoms: (Linn et al. 1990; Linn et al. 1988; Linn et al. 1987; Linn et al. 1983b, Gong et al. 1995, Horstman et al. 1988)

In addition to the general conclusions of a quantitative assessment, the following summarizes some of the general features that emerge from the controlled human studies:

- Asthmatics represent a sensitive subpopulation and respiratory symptoms are unlikely to be reported in non-asthmatics. In general, changes in lung function in asthmatics may occur at concentrations an order of magnitude lower than in non-asthmatics (U.S. EPA, 2010). That is, what may present as symptomatic in an asthmatic, may present as asymptomatic in the non-asthmatic. Typical observations of decrements in lung function have generally not been demonstrated at concentrations ≤ 1000 ppb (≈2600 μg/m^3) in non-asthmatics (WHO, 2005; U.S. EPA, 2008).

- The greatest severity of SO_2 induced bronchoconstriction occurs during exercise. In exercise, the mode of breathing is an important determinant with the greatest responses occurring during oral breathing followed by oronasal breathing and the smallest responses observed during nasal breathing. For this reason, open chamber studies are preferred vs directly delivery of SO_2 from mouthpiece studies. Observations made in asthmatics that receive SO_2 directly mouthpiece studies (oral breathing) may respond at lower concentrations (100 ppb) (≈260 μg/m^3) (U.S. EPA, 2008). It is generally understood that SO_2 is highly soluble in water, and is expected to be almost completely absorbed in the nasal passages

under resting or normal breathing conditions. In nasal breathing up to 95% or greater SO_2 absorption occurs in the nasal passages, even under ventilation levels comparable to exercise.

- Response to inhaled SO_2 is observed to be immediate (Balmes et al., 1987), and normally resolves within minutes to hours, varying with the individual and the severity of the initial response (Hackney et al., 1984), highlighting the importance of the initial temporal aspects of exposure (i.e., first few minutes of peak exposure).

- Experimental clinical studies demonstrate that temperature and humidity within the range of ambient environmental conditions can affect the response. In general, cooler dry conditions have increase response (e.g., Ontario winters) vs hotter humid conditions (e.g., Ontario summers) (Sheppard et al., 1984, Linn et al., 1984, 1983).

- Asthma medications significantly reduce but not eliminate the respiratory effects of SO_2 including beta-adrenergic bronchodilators, cromolyn, theophylline, and leukotriene receptor antagonists (Koenig et al., 1987, 1988, 1992; Linn et al., 1988, 1990; Gong et al., 1996, 2001).

Although clear evidence for dose-dependent increase in bronchoconstriction occurs with increasing exposure to SO_2 in asthmatics, analysis of individual responses find that asthmatics responders at high concentrations (e.g., 600 ppb) are more likely to respond at lower concentrations (e.g., 200 ppb) (Johns et al., 2010). This is important to note, as the controlled chamber studies typically exclude more severe asthmatics, and that such individuals within the population may be more sensitive to respiratory effects of SO_2 at lower levels.

6.0 Jurisdictional Review

6.1 Overview

The current Ontario AAQCs and air standards for SO_2 are listed below (Table 6.1). In revising the SO_2 air standards for Ontario, the Ministry is considering assessments produced by environmental agencies world-wide. This document reviews the scientific basis for air quality criteria established by the WHO, the California Environmental Protection Agency (Cal/EPA), the U.S. EPA, Health Canada, and on the Canadian Council of Minister of the Environment (CCME) proposed Canadian Ambient Air Quality Standards (CAAQS).

Table 6.1: Current Ontario AAQCs and air standards for SO_2. Basis in parentheses.

AAQCs ($\mu g/m^3$)			**Air standards ($\mu g/m^3$)**		
1 hour	24 hour	annual	½ hour	1 hour	24 hour
690 (health & vegetation)	275 (health & vegetation)	55 (health & vegetation)	830 (health)	690 (health & vegetation)	275 (health & vegetation)

It is important to note that the SO_2 air quality criteria of the various jurisdictions have different stated mandates. For example, some criteria may represent maximum allowable ground level concentrations that are protective of adverse effects, while others may reflect targets for improvement for ambient air criteria with respect to current conditions. Other criteria may consider human health or ecological health, or may be simply an improvement target. Additionally, they may also be associated with multiple averaging times and require different means of demonstrating compliance. Therefore, direct comparison of different SO_2 criteria may not be straightforward.

6.2 Agency-specific Air Quality Criteria

6.2.1 Ontario (1974)

Ontario sets air standards via O. Reg. 419/05 to assess the contributions of contaminants to air by regulated facilities. The AAQCs and air standards for SO_2 (Table 6.1) were last updated in 1974 and retained in 2005.

Limited documentation was retrieved which outline the rationale for the original 1974 air quality values. According to a 1979 rationale document, the AAQCs for SO_2 were set based on consideration of health and vegetation effects, odour thresholds and comparisons with other jurisdictions. The 24-hour AAQC was established primarily to protect human health, based on relationships between SO_2 and particulate matter levels and increased respiratory-based admissions to hospital. It was also validated against Canada's maximum acceptable objective at the time, which was based on the same relationships.

The AAQCs for other averaging times (1-hour and annual) are equal to numerical values that would be calculated from the 24-hour AAQC using the Ministry's current conversion factors, which are based on empirical monitoring data, ratios of concentrations observed for different averaging times, and meteorological considerations. This suggests that the 1-hour and annual AAQCs were calculated based on the 24-hour AAQC, rather than being independently derived.

The 1979 rationale document provides some further information to explain why the 1-hour AAQC was set, stating it accounts for effects on vegetation as well as concerns regarding multiple sources of SO_2 emissions in an area, which may cause short-term peaks in exposures. No specific reference is made in the 1979 document to the annual AAQC but there is some discussion in the archived SO_2 AAQC records to suggest that this AAQC was set because of concerns about acid rain.

6.2.2 World Health Organization (2005)

For SO_2, the current World Health Organization (WHO, 2005) Air Quality Guideline (AQGs) are as follows:

500 $\mu g/m^3$ (≈190 ppb) – (10 minute average)

20 $\mu g/m^3$ (≈8 ppb) – (24-hour average)

Though WHO does not enforce their guidelines, they are provided as guidance for reducing the health impacts of air pollution world-wide, and have been widely adopted by other jurisdictions.

The WHO developed the 10 minute AQG based on controlled studies of exercising asthmatics. Here, a proportion of subjects experienced changes in pulmonary function and respiratory symptoms after exposure to SO_2 for periods as short as 10 minutes.

The WHO noted that a wide range of sensitivity has been demonstrated both among non-asthmatic and asthmatic individuals, and considers asthmatics to form the most sensitive group for pulmonary function changes. In developing this guideline, the WHO

considered the minimum concentrations associated with adverse effects in exercising asthmatics in chamber controlled studies.

Briefly, the overall conclusions of exposure-response relationship for exercising asthmatics after short-term (e.g., 10 minutes) exposures expressed as reductions in mean values of FEV_1 are:

- 200 ppb (≈525 µg/m^3) small changes of baseline FEV_1, (≈10%) not considered clinically significant (Linn et al., 1987)
- 400 ppb (≈1050 µg/m^3) small reductions of baseline FEV_1 (Linn et al., 1987)
- 500 ppb (≈1300 µg/m^3) reductions in baseline FEV_1 with moderate or severe but not light exercise (Bethel et al., 1983)
- 600 ppb (≈1600 µg/m^3) reductions in baseline FEV_1 with heavy exercise Linn et al., 1983; Linn et al., 1984)

The response was not greatly influenced by the severity of asthma. Based on this evidence, the WHO recommended that a value of 500 µg/m^3 (≈190 ppb) should not be exceeded over averaging periods of 10 minutes. As sharp peaks are dependent on the nature of local sources and on meteorological conditions, no longer term extrapolation was made.

It is worth noting for context that in 2000, the WHO earlier developed a 24-hour AQG of 125 µg/m^3 (WHO, 2000). It was based on day-to-day changes in mortality, morbidity or lung function related to daily average concentrations of SO_2 from epidemiological studies. These observations were made when people were exposed to a mixture of pollutants, with little basis for separating the contributions of each constituent, and was used to develop the guideline value of 125 µg/m^3. The WHO considered that within the epidemiological data there was considerable uncertainty as to whether SO_2 was the pollutant responsible for the observed adverse effects, or rather, a surrogate for ultrafine particles or other correlated substance.

The 24-hour AQG of 125 µg/m^3 was re-examined in the 2005 update (WHO, 2005), where the following was stated:

> *"In consideration of (a) the uncertainty of sulfur dioxide in causality, (b) the practical difficulty of reaching levels that are certain to be associated with no effects and (c) the need to provide greater degrees of protection than those provided by the guidelines published in 2000, and assuming that reduction in exposure to a causal and correlated substance is achieved by reducing sulfur dioxide concentrations, controlled studies of exercising asthmatics that indicated that a proportion experience changes in pulmonary function and respiratory*

symptoms after periods of there is a basis for revising the 24-hour guideline for sulfur dioxide downwards, adopting a prudent precautionary approach."

Thus, in 2005 a 24-hour AQG of 20 µg/m^3 was established, though a clear rationale for the derivation is not apparent. The WHO concluded that no obvious threshold level has been identified in the population-based studies.

Finally, an annual guideline was deemed not to be required, as compliance with the 24-hour level was thought to assure low levels for the annual average.

6.2.3 Office of Environmental Health Hazard Assessment (2008)

The Office of Environmental Health Hazard Assessment (OEHHA) of the California Environmental Protection Agency (CalEPA) has developed an acute (1 hour) reference exposure level (REL) for SO_2 (OEHHA, 2008):

≈660 µg/m^3 (250 ppb) – (1 hour average)

The acute REL is defined as an exposure that is not likely to cause adverse effects in a human population, including sensitive subgroups (such as infants and children), exposed to that concentration for one hour on an intermittent basis. The development of this REL stems from earlier work done by OEHHA (1994), which considered multiple studies and arrived at a consensus of 250 ppb (≈660 µg/m^3) as the value that would not result in discomforting respiratory effects (i.e., bronchoconstriction) in sensitive individuals (i.e., asthmatics with and without exercising) for a period of 1 hour.

Briefly, bronchoconstriction was the key adverse respiratory named, and NOAELs and LOAELs were identified from several studies identified:

LOAEL
- 400 ppb for 5 minutes (Linn et al., 1983)
- 400 ppb for 60 minutes (Linn et al., 1987)
- 500 ppb for 75 minutes (Roger et al., 1985)

NOAEL
- 250 ppb for 75 minutes (Roger et al., 1985)
- 200 ppb for 60 minutes (Linn et al., 1987)

Thus, OEHHA concluded that 250 ppb (≈660 µg/m^3) was comparable to a NOAEL in sensitive individuals. Predisposing conditions for SO_2 toxicity included underlying medical conditions (e.g., asthma) - especially when exercising or when in cold, dry air – and, in some individuals, Reactive Airways Disease Syndrome (RADS; acute, irritant-induced asthma). Similarly, it was stated that under co-exposure to other irritants (e.g., sulphuric acid, nitrogen dioxide, ozone), adverse effects may be potentiated.

6.2.4 Canada – National Ambient Air Quality Objectives (c.1970s)

The Canadian National Ambient Air Quality Objectives (NAAQOs) were established in the 1970s. NAAQO is a three-tiered system, defined as Maximum Tolerable, Maximum Acceptable and Maximum Desirable, and are described as follows (Table 6.2) (Environment Canada, 1990):.

- The maximum desirable objectives are long-term goals for air quality generally; they also provide a basis for an anti-degradation policy for the unpolluted parts of the country and for the continuing development of control technology.
- The maximum acceptable objectives are intended to provide adequate protection against adverse effects on humans, animals, vegetation, soil, water, materials, and visibility.
- The maximum tolerable objectives denote time-based concentrations of air contaminants beyond which, due to a diminishing margin of safety, appropriate action is required without delay to protect the health of the general population.

Table 6.2: **Canadian National Ambient Air Quality Objectives for SO_2**

SO_2 Concentration ($\mu g/m^3$)

	1 hour	24 hour	Annual	
NAAQO	450	150	30	Maximum Desirable
	900	300	60	Maximum Acceptable
		800		Maximum Tolerable

In general, most provincial and territorial SO_2 criteria have been adopted from the maximum desirable or maximum tolerable NAAQOs.

6.2.5 Health Canada (2016)

A Reference Concentration (RfC) for exposure to SO_2 by inhalation was derived based upon the conclusions of the *Health Risk Assessment of Sulphur Dioxide* prepared by Health Canada in 2016 (Health Canada, 2016):

≈180 $\mu g/m^3$ (67 ppb) – (10 minute average)

Health Canada defines an inhalation RfC as an estimate of the level of continuous inhalation exposure to the human population (including sensitive subgroups) that is likely to be without appreciable risk of adverse non-cancer health effects over a lifetime.

The RfC is derived from the statistically significant lowest observed adverse effect concentration (LOAEC) of 400 ppb SO_2, which resulted in lung function decrements from controlled human exposure studies of asthmatics exposed for 5-10 minutes at increased ventilation (WHO, 2006; U.S. EPA, 2008; Johns and Linn, 2011).

To account for the uncertainties in the controlled human exposure dataset, and considering the supporting evidence from the epidemiology, a combined uncertainty factor (UF) of 6 was applied resulting in an inhalation RfC of 67 ppb SO_2:

$$RfC = 400\ ppb \div 6 = 67\ ppb\ (\approx 180\ \mu g/m^3)$$

According to earlier draft information from Health Canada, the UF of 6 is comprised of a UF of 2 for the use of a LOAEC versus a NOAEC, as the sensitive asthmatic subset response at 200 ppb was statistically non-significant (despite being approximately half of the value observed in healthy asthmatics), and a UF of 3 for intra-species conversion, given that the study is already in a sensitive subpopulation of humans (pers. comm. to J. Gilmore, 2015)

The consideration of UFs was supported by the review of Johns and Linn (2011), and the accompanying critique by Johns et al. (2010) of controlled human exposure studies, wherein they considered 400 ppb as the LOAEL for asthmatic. This LOAEL was based upon consistent, coherent, statistically significant result from controlled human exposure studies, and took into account effects a concentrations of 200-300 ppb that introduced uncertainty related to intra-species sensitivity and that no NOAEL was established in the data set.

Additionally, the RfC also considers that:

- there is high certainty that respiratory morbidity following exposure to SO_2 will be observed in humans because the effect was observed in human controlled exposure studies
- biological plausibility for respiratory morbidity in adults has been demonstrated in both the epidemiology literature and controlled human exposure settings.
- even though susceptible subpopulation (i.e., asthmatics) were considered, further sensitivity was observed with some participants reacting at lower concentrations (i.e., as low as 200 ppb in chamber studies and 100 ppb in mouthpiece exposures (Johns and Linn, 2011))

- studies are usually conducted at room temperature, while some increase in response has been noted when sulphur dioxide is administered in cold dry air (WHO, 2005).

The studies generally have small sample sizes (i.e., 15 to 20 people) and participants are usually young adults who are otherwise healthy. Therefore it is expected that further susceptibility in the population due to genetic factors or other factors like age and disease status may result in a lower concentration associated with a response.

As part of the proposed Canadian Ambient Air Quality Standards (CAAQS) range, the 10 minute RfC at 67 ppb (≈180 µg/m^3) was converted to a 1 hour limit of 40 ppb (≈100 µg/m^3). The conversion was based on the average of linear regressed monitoring data from 29 reporting stations, which was used to estimate a 1 hour concentration corresponding to a 10-minute concentration of 67 ppb. This conversion was performed in consideration of a desire to establish a more stable metric for assessing compliance, and with regard to jurisdictional convention of regulating acute values with a 1 hour averaging time. The proposed CAAQS are considered further in Section 6.2.6.

6.2.6 CCME – Canadian Ambient Air Quality Standards (2016) – proposed

New Canadian Ambient Air Quality Standards (CAAQS) and management levels for SO_2 have been proposed and are scheduled to be brought before the Canadian Council of Minister of the Environment (CCME) Council of Ministers meeting in the fall of 2016. The CAAQS are health and environmental-based air quality objectives for pollutant concentrations in outdoor air, which act as benchmarks to support continuous improvement in air quality. CAAQS are not regulatory standards, and with the exception of Quebec, are implemented as part of air management practices to improve air quality within the framework of the federal Air Quality Management System (AQMS).

The scientific evidence for the direct health and environmental impacts of SO_2 form the foundation for the ranges of the concentration values that were considered by stakeholders to develop a consensus position on the recommended SO_2 CAAQS. Both a 1-hour standard that aims to protect both health and vegetation, and an annual standard aims to protect vegetation, have been developed.

For the 1-hour SO_2 CAAQS of 40 ppb to 70 ppb (≈100 to 190 µg/m^3), the range is within the observable health effects range:

- If the 1-hour CAAQS were set at 40 ppb, all members of the population, including sensitive subgroups such as individuals with asthma, would be expected to be protected if 40 ppb were not exceeded. The lower end of the range has been informed by the Health Canada RfC (2016).

- If the 1-hour CAAQS were set at 70 ppb, the general population would be expected to be protected but there would be times when sensitive subgroups such as individuals with asthma may not be protected, even if the 70 ppb were not exceeded.

For the annual SO_2 CAAQS, the range is within the observable vegetation effects range:

- If the annual CAAQS were set at 4 ppb (≈ 10 µg/m^3), all types of vegetation, including the most sensitive species such as lichens, would be protected if 4 ppb were not exceeded. Lichens are often used as biological indicators of long-term atmospheric pollution.

- If the annual CAAQS were set at 8 ppb (≈20 µg/m^3), most vegetation would be protected but there may be times when sensitive species such as lichens may not be, even if 8 ppb were not exceeded.

From this, the proposed SO_2 CAAQS considered the range of hourly and annual air concentration based on existing monitoring stations data, and on predicted 2025 modelled SO_2 levels, and are presented in Table 6.3.

Table 6.3 Proposed CAAQS for SO_2

Averaging Time	Lower Range (ppb)	Upper Range (ppb)	Statistical Form of the Standard
1-hour	40	70	The 3-year average of the annual 99th percentile of the SO_2 daily maximum 1-hour average concentrations.
1-calendar year (annual)	4	8	The arithmetic average over a single calendar year of all 1-hour average SO_2 concentrations.

6.2.7 U.S. EPA – National Ambient Air Quality Standards (2010)

The U.S. EPA establishes national ambient air quality standards (NAAQS) to assess regional air quality as part of the U.S. Clean Air Act. The NAAQS are required to protect public health with an adequate margin of safety. NAAQS are implemented at the state level by the designation of attainment and non-attainment areas. States must submit to the federal government state implementation plans (SIPs) for areas that do not attain the standard. The recently introduced NAAQS for SO_2 is as follows:

≈200 μg/m^3 (75 ppb) – (1 hour average)

(based on the 3-year average of the annual 99th percentile of 1-hour daily maximum concentrations)

This 1-hour limit replaced the two revoked NAAQS for SO_2 – for 24-hr and annual averaging times – as the latter two values were not seen to add additional public health protection, and the scientific literature suggested an importance of early acute peak exposures in the manifestation of adverse health effects.

The EPA rationale on the 2010 SO_2 NAAQS focused primarily on respiratory morbidity following short-term (5-minutes to 24-hour) exposure to SO_2, for which a causal relationship was determined. This assessment was based on a substantial amount of epidemiological research and a limited number of controlled human exposure studies. The guideline published by the American Thoracic Society (ATS) was used to define what constitutes an adverse effect of air pollution. The U.S. EPA noted that the 1-hour NAAQS is above levels measured in many U.S. locations where epidemiological studies have associated exposure to SO_2 with increased ED visits and/or hospitalizations.

It was deemed that the immediate effect of SO_2 on the respiratory system is bronchoconstriction, as measured by changes in lung function. Table 6.4 provides a brief description of the health effects benchmark concentrations – associated with 5 minutes exposures – utilized in the development of the SO_2 NAAQS.

Table 6.4 SO_2 Health Effects Summary. Notes: Lung Function - Bronchoconstriction and respiratory symptoms that are often followed by rapid shallow breathing. Symptoms include mild (perceptible wheeze or chest tightness) to severe (breathing distress requiring the use of a bronchodilator).

Health Effect Consensus Benchmark Concentrations (5 minute to 24 hour)	**≥ 200 ppb**	**≥ 400 ppb**
Lung Function	✓	✓✓
Group mean levels of statistically significant lung function changes	x	✓
Respiratory Symptoms	Asymptomatic	Symptomatic

Briefly, the U.S. EPA provides a summary overview of how the 1 hour limit of 75 ppb was derived (2010):

"At 200 ppb an appreciable percentage of exercising asthmatics exposed to SO_2 would be expected to have diminished reserve lung function and would be

expected to be at greater risk if affected by another respiratory agent for example, viral infection."

Specifically, with regard to the 200 ppb Health Effects Consensus Benchmark Concentrations*:*

- 200 - 300 ppb (≈525 - 800 μg/m^3) for 5-10 minutes represents the lowest concentration in free-breathing controlled human exposure studies where some individuals have moderate or greater decrement in lung function.
- approximately 5-30% exercising asthmatics experience moderate or greater decreases in lung function (i.e., ≥ 100% increase in specific airway resistance (sRaw), and/or a ≥ 15% decrease in FEV_1),
- group mean levels of lung function changes were not statistically different.

With regard to the 400 - 600 ppb Health Effects Consensus Benchmark Concentrations:

- 400 - 600 ppb (≈1050 - 1600 μg/m^3) for 5-10 minutes represents the lowest concentration in free-breathing controlled human exposure studies were moderate or greater decrements in lung function occurred and were frequently accompanied by respiratory symptoms.
- a greater percentage (20-60%) of exercising asthmatics experience moderate or greater decrease in lung function (i.e., ≥ 200% increase in specific airway resistance (sRaw), and/or a ≥ 20% decrease in FEV_1), and increasingly associated with respiratory symptoms (e.g., wheezing, chest tightness)
- at ≥ 400 ppb, group mean levels of lung function changes were statistically different.

Building upon this data, the U.S. EPA performed a quantitative exposure and risk assessment on two proposed 1-hour values at 50 ppb and 100 ppb including the form of the standard (based on the 3 year average of the annual 99^{th} percentile of the 1-hour daily maximum concentrations), in order to predict the frequency in days of 5 minute exceedances of the 200 ppb and 400 ppb Health Effects Benchmark Concentration. The assessments considered the likelihood that asthmatic children at moderate or greater exertions (i.e., while exercising) (Table 6.5).

Table 6.5 Quantitative exposure and risk assessment on two proposed 1-hour NAAQS values (50 ppb and 100 ppb). Note: * Percentage of asthmatic children protected refers to being protected from experiencing at least one- 5-minute exceedance of the health effects concentration during moderate or greater exertion.

Health Effect Benchmark Concentration (days)

Proposed 1-hour NAAQS **(for risk assessment purposes)**	≥200 ppb		≥400 ppb	
	Predicted # of days with 5-minute exceedances	Percentage of asthmatic children protected*	Predicted # of days with 5-minute exceedances	Percentage of asthmatic children protected*
50 ppb	2	>99%	0	>99%
100 ppb	13	>97%	2	>99%

The basis of the 75 ppb NAAQS primarily considered the air quality and exposure analyses that suggested that a 1 hour standard of either 50 or 100 ppb would result in minimal predicted exceedances of the health effect benchmark concentrations. The health effects benchmark concentrations of 200 and 400 ppb (5 minute) were reasonably judged important from a public health perspective. Thus, the level of 75 ppb was set at the average between 50 and 100 ppb. From this, the U.S. EPA inferred that at a 75 ppb 1 hour limit, and its form of implementation, there is potential for a few daily 5 minute exceedances of the health effects benchmark concentrations of 200 and 400 ppb over a year period of time.

Considered the findings from both epidemiological and controlled human exposure studies, as well as the results of air quality and exposure analyses, the U.S. EPA determined the 75 ppb (≈200 μg/m^3) 1 hour average NAAQS for SO_2 to be protective of public health, with an adequate margin of safety.

7.0 Considerations in the Development of a Short-term AAQC for SO_2

The Ministry considers the available toxicological and other relevant information to develop AAQCs and air standards that are protective of human health and the environment. Various considerations to be addressed in the development of a short-term AAQC and air standard for SO_2 are presented below.

7.1 Critical Effect

The strongest and most consistent findings across agencies and assessments indicate a causal relationship between short-term SO_2 exposure and respiratory morbidity (Table 5.2). These adverse respiratory effects include bronchoconstriction, changes in lung function, airway inflammation, airway hyper-responsiveness, and ED visits and/or hospitalizations. The respiratory morbidity epidemiological and controlled human chamber studies underlying this finding are relied upon by various jurisdictions in establishing limits. Thus, the Ministry concurs with other jurisdictions in identifying respiratory morbidity, as the underlying critical effect for the formation of a SO_2 AAQC.

7.2 Mode of Action

In defining the critical effect, the Ministry considers the potential for effects in both short-term and long-term exposures and evaluates the mode of action. Mode of action refers to the sequence of key events (as opposed to all events) on the path to the endpoint of interest. As discussed in this document, respiratory morbidity manifested as bronchoconstriction is the most commonly observed adverse effects following SO_2 inhalation exposure, found not only in the controlled human exposure literature, but also in the epidemiological literature. One of the key biological effects is the stimulation of bronchial epithelial irritant receptors (i.e., chemosensitive receptors) in the tracheobronchial tree. This initiates a reflexive contraction of smooth muscles in the bronchial airways, leading to bronchial constriction, which is associated with respiratory morbidity.

The bronchoconstrictive effect can be potentially explained by three modes of action: effects to vagus nerve receptors, neurogenic inflammation, and effects to other receptors involved with bronchoconstriction, all of which are discussed in depth by Health Canada (2016). None of the three modes of action, alone, account for the variation and degree of sensitivity to SO_2 exposure in the population. However, it is the effects to the vagus nerve receptors that are most well characterized, and is summarized by Health Canada (2016), as follows:

"Bronchoconstriction following acute SO_2 exposure results from chemosensitive receptors (vagus nerve afferents; i.e. rapidly activating receptors and sensory C-fibre receptors) in the tracheobronchial tree being activated. In animal models, activation of these receptors stimulates central nervous system reflexes, including bronchoconstriction from smooth muscle contraction, mucous secretion, mucosal vasodilation, cough, and apnea followed by rapid shallow breathing. There are also effects on the cardiovascular system, such as bradycardia and hypotension or hypertension. In some cases, C-fibre activation is theorized to cause secretion of neuropeptides, resulting in neurogenic inflammation, a situation important in animal models of airway inflammatory disease. The relevance of neurogenic inflammation to humans remains uncertain because of differences in respiratory tract innervation.

In humans, the mechanisms for SO_2-induced bronchoconstriction are less clear because of differences between asthmatic and non-asthmatic responses. Asthma is characterized by inflammation and airway hyperresponsiveness, which manifests as excessive bronchoconstriction to contractile stimuli (Barnes, 1996; Buels and Fryer, 2012)

….In non-asthmatics, bronchoconstriction occurs through cholinergic pathways and acetylcholine (Ach) release. In asthmatics, however, it appears that bronchoconstriction is the result of both parasympathetic (ACh-mediated) pathways and inflammatory or other pathways. Additionally, it has been reported that SO_2 triggers bronchospasm and also stimulates afferent receptors, leading to a reflex cholinergic bronchoconstriction (Barnes, 1996); consequently, therapeutic options differ between non-asthmatics and asthmatics experiencing bronchoconstriction following SO_2 exposure."

From these analyses, it can be inferred that the mode of action supports focusing on the high levels of intermittent short-term exposure as being relevant to the health effects observed.

7.3 Susceptible Populations

Sensitive sub-populations may be specifically considered in the identification of a critical effect, when data are available. The recent Health Canada (2016) health assessment document identified specific life-stages or groups in the population as being at risk for increased susceptibility to SO_2-mediated adverse health effects. These findings were made based on judgments of the consistency and coherence of evidence within and across disciplines (e.g., epidemiology, toxicodynamics), where "susceptibility" refers to

biological or intrinsic factors affecting the individual response to chemical exposure (e.g. life stage, sex, genetics, pre-existing disease/conditions) (U.S. EPA, 2012a). The identified populations are discussed below, with the information gleaned from the 2016 Health Canada health assessment, unless noted.

7.3.1 Asthmatics

There is significant evidence to demonstrate that people with asthma are at increased risk for SO_2-mediated health effects. It is estimated that asthma affects approximately 3 million Canadians, representing about 9% of the population, with 60% self-identified as not having control of their disease (ASC, 2016). According to the recent information provided by Statistics Canada (2014), Ontario asthma prevalence is 6.4% in males and 9.1% in females. Of particular note, there are higher prevalence rates in children between the ages of 4 and 11, and among certain ethnic or racial groups, including First Nations communities (Fenton et al., 2012; ASC, 2016).

The data show that respiratory effects experienced by asthmatics following SO_2 exposure appear to be more severe than among non-asthmatics, and appear to be mediated by a different mechanism than in non-asthmatics. Mechanistic analyses suggest that asthmatics experiencing adverse effects may not be able to control their symptoms using normal medications.

Some epidemiologic evidence suggests that children with asthma are more sensitive to exacerbation of their asthma symptoms following SO_2 exposure. For example, a trend toward increased hospital admissions of children for asthma symptoms related to SO_2 exposures, via acute air pollution exposure, is associated with time spent outdoors (Samoli et al., 2011).

7.3.2 *In utero* Exposure

Although the literature is not well established at this time, there is some evidence from epidemiology to indicate that there may be a correlation between SO_2 and various congenital anomalies to the heart and cleft lip incidence, with weeks 3-8 of gestation identified as the window of susceptibility. Additionally, there is some evidence to postulate a dose-response relationship with the risk of types of congenital heart defects, which increases with increased SO_2 exposure. While the data is still equivocal, there appears to be consistency in the risk of developing these congenital defects, and in some cases a dose-response relationship has been postulated (Health Canada, 2016).

7.3.3 Olfactory Impairments

It has been established that workers exposed to high levels of SO_2 sometimes experience impairment of olfactory function, and thus may not react behaviourally to the

smell of SO_2 in the same manner as those without such deficits. It is therefore reasonable to assume that individuals with an impaired or reduced sense of smell may still respond biologically to SO_2, despite being unable to detect the odour, and thus inadvertently be exposed with greater magnitude and frequency.

7.3.4 The Elderly

The ability to detect odour has been shown to decrease with age. Therefore, the elderly might not react to the smell of SO_2 in the same behavioural manner as those without olfactory deficiencies, and thus be exposed to greater amounts of SO_2. Additionally, the elderly have decreased SOX activity, which suggests they may be more susceptible to oxidative damage following exposure to SO_2 than the general population. Finally, while not exclusive to SO_2 exposure, epidemiology data indicate that the elderly may be more susceptible to death following exposure to air pollution than other age groups, due to underlying respiratory disease states, (e.g., COPD – chronic obstructive pulmonary disease).

7.3.5 Children

Due to the fact that the lung continues to develop well into adolescence, infants and children may be more susceptible to the respiratory-damaging effects of SO_2. Although not specific to SO_2, it is reasonable to assume that children may have increased exposures, due to greater time spent outdoors, being highly active, and having high minute ventilation. While there is some epidemiological data to suggest that ED visits or hospitalizations for respiratory causes or asthma may be higher in children than adults, the same cannot be said for adolescents (U.S. EPA, 2008). In addition, they may be exposed to higher levels than adults in the same location because of their short stature and the higher levels of sulfur dioxide found nearer to the ground, and because they are slow to leave the site of an exposure (ATSDR, 2011).

7.4 Vulnerability

Separate from susceptibility, Health Canada (2016) provides a discussion on populations vulnerable to SO_2 exposure. Here, vulnerability is defined as non-biological or extrinsic factors that influence a human being's response to chemical exposure. The identified populations include those likely to have higher exposures (e.g. live or work near emission sources; live in cold, dry environments; have high levels of outdoor physical activity) and those with lower socioeconomic status. As well, seasonal influences affect individual vulnerability to SO_2 exposures. Seasonal variation has been observed for ambient concentrations of SO_2, whereby the mean ambient concentrations

were higher in winter than in other seasons (Campbell et al., 2005; Wheeler et al., 2008; Brown et al., 2009), likely due to decreased rates of atmospheric oxidation.

7.5 Selection of Key Study

The selection of a key study describing respiratory morbidity is a product of the use of the most certain and predictive, rather than most conservative options. In attempting to identify such a key study, the Ministry's preference is to focus on a study that will allow for protection to all individuals in the general population, including those who are likely to be susceptible to developing the critical effect (e.g., children, pregnant women, elderly). However, it should be noted that the possibility remains of hypersensitive individuals who may exhibit idiosyncratic responses, which cannot be predicted from studying the health effects of a potentially toxic compound.

There remain concerns regarding the accuracy of exposure estimates from ambient measurements typical of epidemiologic studies, and their applicability in representing an individual's SO_2 exposure (spatially) and using average SO_2 estimates that may not represent peak exposures (temporally) that is understood to be the key determinant of acute effects. Thus, while there is consistency among evidence from epidemiologic and toxicological studies, and biological plausibility for effects specifically related to respiratory morbidity, estimates of exposure are considered to be more accurate in human clinical studies under controlled conditions (i.e., chamber studies), and thus will be relied upon for quantitative evaluation.

As described in Section 5.7, the U.S. EPA (2008) performed a meta-analysis on the evidence from multiple human clinical studies of exercising asthmatics, which demonstrated that moderate SO_2-induced decrements in lung function at the lowest levels tested (i.e., 200 to 300 ppb, 5 to 10 min exposures) in some individuals (approximately 5-30% of subjects). Here, statistically significant respiratory effects have been consistently observed at concentrations of 400-600 ppb, with 20-60% of asthmatics experiencing moderate to large decrements in lung function following 5-10 min exposures.

The Ministry proposes that these chamber studies, together, lend themselves to the quantitative dose-response effects seen with SO_2 exposure among asthmatics that exercise, and are, in fact, used by various jurisdictions in establishing their limits. Thus, the Ministry proposes to utilize these chamber studies as a group, to be representative of the 'key study' for AAQC development.

7.6 Point of Departure

In consideration of the U.S. EPA (2008) analysis of a number of chamber studies the following two consensus benchmarks concentrations were identified: 200 ppb (≈525 $\mu g/m^3$) and 400 ppb (≈1050 $\mu g/m^3$).

200 ppb Health Effects Consensus Benchmark Concentrations:

- 200 - 300 ppb (≈525 – 800 $\mu g/m^3$) for 5-10 minutes represents the lowest concentration in free-breathing controlled human exposure studies where some individuals have moderate or greater decrement in lung function
- approximately 5-30% exercising asthmatics experience moderate or greater decreases in lung function (i.e., ≥ 100% increase in specific airway resistance (sRaw), and/or a ≥ 15% decrease in FEV_1),
- group mean levels of lung function changes were not statistically different.

400 ppb Health Effects Consensus Benchmark Concentrations:

- 400 - 600 ppb (≈1050 – 1600 $\mu g/m^3$) for 5-10 minutes represents the lowest concentration in free-breathing controlled human exposure studies were moderate or greater decrements in lung function occurred and were frequently accompanied by respiratory symptoms.
- a greater percentage (20-60%) of exercising asthmatics experience moderate or greater decrease in lung function (i.e., ≥ 200% increase in specific airway resistance (sRaw), and/or a ≥ 20% decrease in FEV_1), and increasingly associated with respiratory symptoms (e.g., wheezing, chest tightness)
- at ≥ 400 ppb group mean levels of lung function changes were statistically different.

Both U.S. EPA (2010) and Health Canada (2016, supplemented with the analysis of WHO 2006, and a review by Johns and Linn, 2011) have differed in their approaches to the use of these benchmarks in their determinations of air limits. Both paths forward are presented here:

1) U.S. EPA (2010) used the short-term health effects consensus benchmarks in a quantitative exposure and risk assessment on two proposed 1-hour values at 50 ppb and 100 ppb, including the form of the standard (based on the 3-year average of the annual 99^{th} percentile of 1-hour daily maximum concentrations), in order to predict the frequency in days of 5 minute exceedances (Table 6.5). The 1 hour average of 75 ppb (100 ppb + 50 ppb / 2 = 75 ppb ≈200 $\mu g/m^3$) became the primary NAAQS, and was modelled to result in minimal predicted exceedances of the health effect benchmark concentrations. The health effects benchmark concentrations of 200 and 400 ppb (5 minute) were reasonably considered to be important from a public health perspective.

2) Health Canada (2016) developed an RfC in consideration of 400 ppb as the statistically significant lowest observed adverse effect concentration (LOAEC), which resulted in lung function decrements from controlled human exposure studies of asthmatics exposed for 5-10 minutes at increased ventilation. To account for the uncertainties in the controlled human exposure dataset, and considering the supporting evidence from the epidemiology, a combined uncertainty factor (UF) of 6 was applied resulting in an inhalation RfC of 67 ppb SO_2. Specifically, a UF of 2 was assigned for the use of a LOAEC vs NOAEC, as the sensitive asthmatic subset response at 200 ppb was statistically non-significant (despite being approximately half of the value observed in healthy asthmatics) and a UF of 3 was assigned for intra-species conversion, given that the study is already in a sensitive subpopulation of humans.

   The 10 minute RfC at 67 ppb (≈180 µg/m^3) was converted to a 1 hour limit of 40 ppb (≈100 µg/m^3) in consideration of the stability of the metric and used to inform the lower end of the proposed Canadian Ambient Air Quality Standards (CAAQS) range.

7.7 Consideration of Averaging Time

In general, averaging time selection is influenced by both the underlying toxicology of a substance, including exposure and effects (largely governed by science judgment), and implementation considerations, including modelling and monitoring (largely governed by science policy).

A review of the monitoring data suggests that typical exposures are likely to be in the form of short-term intermittent spikes. A review of the mode of action and controlled human studies support intermittent spikes in the 5-10 minute range as being the most health-relevant. Thus, short averaging time is appropriate. The selection of the appropriate averaging time, however, needs to be balanced with monitoring practicalities, modelling capabilities, jurisdictional consistency, and other policy consideration. Typically a 1-hour averaging time is often assigned in such cases.

7.8 Outstanding Issues

While developing revised air quality standards for sulphur dioxide in Ontario, and through the examination of the above listed possible paths forward, the Ministry is seeking scientific input on the following issues:

- Is there any relevant and critical information not addressed in the present document which may influence the development of a short-term air standard for sulphur dioxide? The Ministry encourages stakeholders to provide relevant and key scientific information supporting the presented paths forward, or describing and/or supporting reasonable alternative paths.
- Is there other recent scientific information available regarding sulphur dioxide in ambient air that the Ministry has not considered, as discussed above?

8.0 Considerations for a long-term AAQC for SO_2

In setting effects-based air standards, the Ministry considers the available toxicological and other information to determine the potential effects of exposure to a contaminant. Various considerations are presented below, which are to be addressed in the development of a long-term AAQC sulphur dioxide.

8.1 Critical effect

The Ministry notes that the Canadian Ambient Air Quality Standards (CAAQS) Development and Review Working Group (CDRWG) will select specific values for the annual SO_2 CAAQS for 2020 and 2025 and will recommend them to the Air Management Committee (AMC) of CCME for consideration. The annual standard aims to protect vegetation from direct SO_2 effects over the long-term.

Adverse effects on vegetation from SO_2 exposure can occur over both the short- (1 to 24- hours) and long-term (annual). As previously discussed (see Section 4.2), SO_2 can have direct effects on vegetation as plants uptake SO_2, and also indirect effects on vegetation, soils and lakes through the wet and dry deposition of sulphur containing compounds resulting from atmospheric SO_2. For the annual SO_2 CAAQS, the range proposed is within the vegetation effects range of 4 ppb (≈10 µg/m^3) to 8 ppb (≈20 µg/m^3). The lower bound of the range of concentration values was set at 4 ppb based on the WHO standard for the protection of lichens. However, the WHO mentions that their 4 ppb standard for lichens may have to be lowered as more detailed information becomes available (WHO, 2000). Lichens are likely the most widely used biological indicators of long-term atmospheric pollution (CCME, 2014).

For the 8 ppb upper bound of the range, consideration was given to the chronic effects observed at concentrations of 8 ppb in the Sudbury area as discussed earlier. This level is consistent with the EU 8 ppb standard for the protection of vegetation and which was also adopted by Alberta. If the WHO 11 ppb guideline for the protection of crops applies also to crops in Canada, the 8 ppb upper bound would also provide protection for crops (CCME, 2014).

8.2 Consideration of Averaging Time

In general, averaging time selection is influenced by both the underlying toxicology of a substance, including exposure and effects (largely governed by science judgment), and

implementation considerations, including modelling and monitoring (largely governed by science policy).

The Ministry will consider toxicological and implementation issues in assigning an averaging time for effects due to chronic exposure, as is the expected case for a standard designed to protect vegetation. In general, an annual averaging time is believed to be appropriate when addressing chronic effects (i.e., effects observed after long-term exposure), where intermittent peak exposures are not considered likely to significantly influence the effect.

8.3 Outstanding Issues

While developing revised air quality standards for sulphur dioxide in Ontario, and through the examination of the above listed possible paths forward, the Ministry is seeking scientific input on the following issues:

- Is there any relevant and critical information not addressed in the present document which may influence the development of a long-term air standard for sulphur dioxide? The Ministry encourages stakeholders to provide relevant and key scientific information supporting the presented paths forward, or describing and/or supporting reasonable alternative paths.
- Is there other recent scientific information available regarding sulphur dioxide in ambient air that the Ministry has not considered, as discussed above?

9.0 A Guide of Stakeholders Reviewing this Document

This Science Discussion Document will form the basis for the related science discussion meeting that follows shortly after the release of these discussion documents. The Ministry also welcomes written comments on this Science Discussion Document. Stakeholders are encouraged to provide comments which indicate whether they support or disagree with the scientific analysis. It is important that submissions include the rationale and reasoning supporting the stated positions so that the Ministry can make informed decisions on the proposed standard on the basis of clear, supportable arguments.

Comments on these and any other issues relevant to setting of air quality standards for sulphur dioxide can be sent to:

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11.0 Acronyms, Abbreviations, and Definitions

AAQC	ambient air quality criterion
Ach	acetylcholine
AQG	air quality guideline
AQMS	air quality management system
ATS	American Thoracic Society
ATSDR.	Agency for Toxic Substances and Disease Registry
CAAQS	Canadian Ambient Air Quality Standards
CalEPA	California Environmental Protection Agency
CAS	Chemical Abstracts Service
CCME	Canadian Council of Minister of the Environment
CDRWG	CAAQS Development and Review Working Group
COPD	chronic obstructive pulmonary disease
EC	Environment Canada
ED	emergency department
FEV_1	forced expiratory volume in 1 second
HC	Health Canada
IUGR	intrauterine growth restriction
LOAEC	lowest observed adverse effect concentration
LOAEL	lowest observed adverse effect level
NAAQO	National Ambient Air Quality Objectives
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NO_X	oxides of nitrogen
OEHHA	Office of Environmental Health Hazard Assessment

PIA	population improvement approach
PM	particulate matter
$PM_{2.5}$	fine particulate matter (≥ 2.5µm in diameter)
POI	point of impingement
RADS	reactive airways disease syndrome
REL	reference exposure level
RfC	reference concentration
SIP	state implementation plans
SO_2	sulphur dioxide
SO_3^2	sulphite
SOX	sulphite oxidase
sRaw	specific airway resistance
UF	uncertainty factor
UNECE	United Nations Environmental Commission for Europe
U.S. EPA	United States Environmental Protection Agency
WHO	World Health Organization

bw	body weight
ppm	parts per million
ppb	part per billion
g	a gram
mg	a milligram, one thousandth of a gram
µg	a microgram, one millionth of a gram
ng	a nanogram, one billionth of a gram