

Proposition 65

Interpretive Guideline No. 2021-01
Consumption of Sulfur Dioxide in Soy
Sauce

April 2021



Office of Environmental Health Hazard Assessment
California Environmental Protection Agency

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Summary

Under Proposition 65¹, a warning for exposure to sulfur dioxide (SO₂) from consumption of soy sauce is not required. Exposure will be below the Maximum Allowable Dose Level (MADL) for the reasonably anticipated rate of intake by the average user of the product.

Scope of Interpretive Guideline

The Office of Environmental Health Hazard Assessment (OEHHA) may issue an Interpretive Guideline that interprets Proposition 65 and its implementing regulations, as applied to specific facts. The Interpretive Guideline reflects OEHHA's scientific interpretation of the available information as the lead agency for implementation of the Act².

SO₂ was listed as a chemical known to cause reproductive toxicity under Proposition 65, effective July 29, 2011. This interpretative guideline applies only to SO₂ in soy sauce. This guideline calculates estimates of average-user exposures to SO₂ based on worst-case estimates of SO₂ concentrations in soy sauce and compares them to the Maximum Allowable Dose Level (MADL) for the chemical. Exposures at or below a MADL are exempt from the warning requirements of Proposition 65.

Sulfur Dioxide Concentration in Soy Sauce

SO₂ is often used in food to preserve the color and flavor of many foods and to act as an antimicrobial agent.

The presence of water in foods allows SO₂ to dissolve into solution³. SO₂ is either bound or free and the combination is referred to as total sulfite(s), or sometimes as "total SO₂"⁴. Total sulfite includes sulfur compounds both reversibly and irreversibly bound to food components^{5,6}.

Free sulfite (sometimes referred to as "free SO₂") represents the total dissolved SO₂ which exists as an equilibrium among molecular SO₂ (which is a dissolved gas), bisulfite

¹ Safe Drinking Water and Toxics Enforcement Act of 1986, Health and Safety Code section 25821.C.2 *et seq.*

² Health and Safety Code section 25249.12

³ Brown, A. (2010). "Understanding Food: Principles and Preparation". Belmont, CA, Wadsworth.

⁴ DeMan, J. M., Ed. (1999). "Principles of food chemistry." Aspen Publishers.

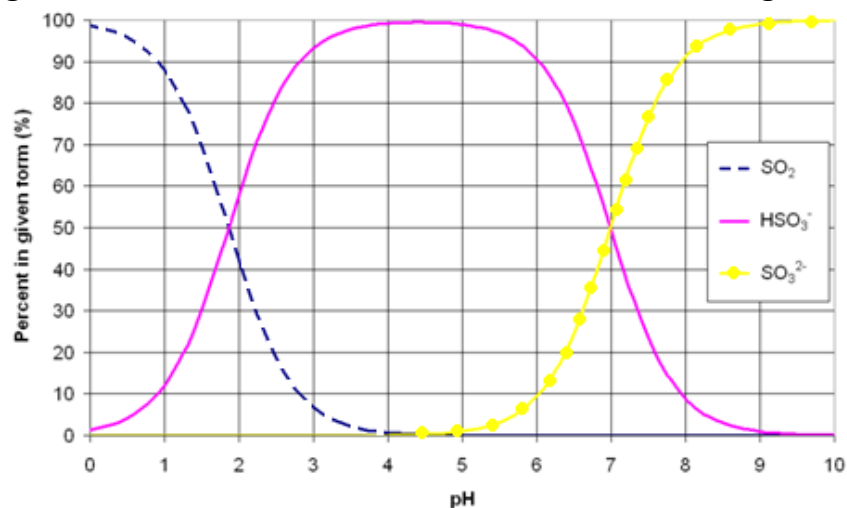
⁵ Wedzicha B.L. (1992). "Chemistry of sulfating agents in food". *Food Additives and Contaminants* 9(5):449-459.

⁶ Wedzicha, B. L., I. Bellion, and S.J. Goddard (1991). "Inhibition of browning by sulfites." In: *Nutritional and Toxicological Consequences of Food Processing* M. Friedman (Ed). Pub. Plenum Press.

ion (HSO_3^-), and sulfite ion (SO_3^{2-})⁷. **Only molecular SO_2 falls under the Proposition 65 listing of sulfur dioxide.** Free sulfite is used to calculate the amount of molecular SO_2 in soy sauce, as discussed below.

The equilibrium between molecular SO_2 and the ionic forms is dependent on pH. As shown in Figure 1⁸, since the pH of soy sauce is generally in the range of 4.4–5.4^{9,10}, the proportion of unbound SO_2 in soy sauce in the form of molecular SO_2 is expected to be very small, as shown below.

Figure 1. Percent of Free SO_2 forms in solution at a given pH



The amount of molecular SO_2 cannot be directly measured, but can be calculated by means of the equation¹¹:

$$\text{Molecular } \text{SO}_2 = \text{Free } \text{SO}_2 / (10^{(\text{pH} - 1.81)} + 1)$$

This equation indicates that at a pH of 4.4 the amount of molecular SO_2 will be less than 0.26% of free SO_2 , and at a pH of 5.4 it would be 0.027%.

⁷ Rotter, B. (Jan 2001). "Sulfur Dioxide", available at <http://www.brsquared.org/wine/>

⁸ Carswell, D.R. (1977). *The Determination of Sulfur Dioxide in Food – a Literature Review*. Scientific & Technical Surveys No. 103

⁹ https://www.engineeringtoolbox.com/food-ph-d_403.html

¹⁰ Diez-Simon C, Eichelsheim C, Mumm R, Hall RD. Chemical and Sensory Characteristics of Soy Sauce: A Review. *J Agric Food Chem*. 2020 Oct 21;68(42):11612-11630. doi: 10.1021/acs.jafc.0c04274. Epub 2020 Sep 17. PMID: 32880168.

¹¹ University of California at Davis, Cooperative Extension. *Enology Briefs Vol 1(1)*, 1982. Available at <http://www.moundtop.com/so2/EnologyBriefs-1-1.pdf>

In the US, ingested sulfur dioxide is “generally recognized as safe”¹². Estimates of concentrations of sulfites expressed as sulfur dioxide in soy and related sauces can be used to identify potential maximum values of free sulfur dioxide:

- 198.4 milligrams per kilogram (mg/kg) (as SO₂) was the reported maximal level measured in Indonesia for “Seasonings and condiments, vinegars, mixer for soups and broths, and other soybean sauces”; the maximal permitted level was 300 mg/kg¹³;
- 555 mg/kg was the maximal value observed by the European Food Safety Authority¹⁴ in 35 samples of savory sauces.

Thus an estimate of a worst case level of 600 mg/kg for sulfites as free sulfur dioxide appears reasonable. The level of molecular sulfur dioxide in soy sauce would be expected to be less than 1.54 mg/kg given the above equation.

Calculation of Level of Exposure to Sulfur Dioxide in Soy Sauce

Level of Exposure to Proposition 65 Chemicals Reproductive Toxicants

Proposition 65 regulations address how to calculate the exposure to chemicals listed as known to cause reproductive toxicity:

“For purposes of Section 25249.10(c) of the Act, the level of exposure to a chemical listed as causing reproductive toxicity shall be determined by multiplying the level in question (stated in terms of a concentration of a chemical in a given medium) times the reasonably anticipated rate of exposure for an individual to a given medium”¹⁵.

By this provision, the reasonably anticipated rate of exposure to a chemical for a given individual is used in exposure calculations. The regulations give further guidance for

¹² 21 CFR 182.3862, This substance is generally recognized as safe when used in accordance with good manufacturing practice, except that it is not used in meats; in food recognized as a source of vitamin B1; on fruits or vegetables intended to be served raw to consumers or sold raw to consumers, or to be presented to consumers as fresh. See https://www.ecfr.gov/cgi-bin/retrieveECFR?gp=&SID=024414b3790619e44e99952fd23e3cb0&mc=true&n=pt21.3.182&r=PART&t=y=HTML#se21.3.182_13862

¹³ Fanaïke R, Andarwulan N, Prangdimurti E, Indrotristanto N, Puspitasari R. Dietary exposure to sulfites in Indonesians. *Asia Pac J Clin Nutr.* 2019;28(1):122-130. doi: 10.6133/apjcn.201903_28(1).0017. PMID: 30896423.

¹⁴ EFSA Panel on Food additives and Nutrient Sources added to Food, Scientific Opinion on the re-evaluation of sulfur dioxide (E 220), sodium sulfite (E 221), sodium bisulfite (E 222), sodium metabisulfite (E 223), potassium metabisulfite (E 224), calcium sulfite (E 226), calcium bisulfite (E 227) and potassium bisulfite (E 228) as food additives, *EFSA Journal* 2016;14(4):4438

¹⁵ Title 27, Cal. Code of Regs., section 25821(b)

calculating the reasonably anticipated rate of exposure for chemical exposures from consumer products:

“For exposures to consumer products, the level of exposure shall be calculated using the reasonably anticipated rate of intake or exposure for average users of the consumer product, and not on a per capita basis for the general population. The rate of intake or exposure shall be based on data for use of a general category or categories of consumer products, such as the United States Department of Agriculture Home Economic Research Report, Foods Commonly Eaten by Individuals: Amount Per Day and Per Eating Occasion, where such data are available”¹⁶.

Level of Exposure to Sulfur Dioxide in Soy Sauce

The National Health and Nutrition Examination Survey (NHANES) provides data on consumption of particular types of foods by consumers of these foods. NHANES is a program of studies administered by the US Centers for Disease Control and Prevention (CDC) designed to assess the health and nutritional status of individuals throughout the United States. NHANES includes a dietary survey¹⁷, from which an average consumption of foods in their various forms specified can be calculated.

OEHHA calculated an average consumption by consumers of soy sauce using NHANES dietary survey data. Average daily consumption of soy sauce for users is calculated using NHANES 2007-2016 data, summarized in the chart below. OEHHA used NHANES dietary survey data for individuals reporting consumption of a particular food on either day of the two-day dietary survey for the years 2007-2016¹⁸. Published data on daily consumption from Asia and serving size are also included in the chart for comparison.

The average daily consumption for US soy sauce consumers is 16.6 grams/day, based on the NHANES 2007-2016 dietary survey. In this survey, 3.1% of the population used soy sauce. The median and maximum daily consumption are 12.1 and 148.8 grams/day, respectively. This analysis only includes pure “soy sauce” (regular or reduced sodium) and not other sauces that may contain soy sauce as an ingredient, such as teriyaki or hoisin sauces.

¹⁶ Title 27, Cal. Code of Regs., section 25821(c)(2)

¹⁷ CDC National Center for Health Statistics, NHANES Dietary Data. Available at <https://wwwn.cdc.gov/nchs/nhanes/search/datapage.aspx?Component=Dietary>

¹⁸ *Ibid.*

Daily consumption data for soy sauce

NHANES 2007-2016	
Nationwide Food Consumption Survey food code	41420300 (regular) 41420350 (reduced sodium)
Total persons consuming	3.1%
Average daily consumption for users (grams/day)	16.6
Median daily consumption for users (grams/day)	12.1
Maximum daily consumption for users (grams/day)	148.8
From literature¹⁹	
Daily consumption in milliliters/day	30
Daily consumption in grams/day*	28.8
Package label serving size	
milliliters/serving	15
grams/serving*	14.4

*Density estimated from the package label

The average daily consumption of sulfur dioxide is calculated by multiplying the soy sauce consumption rate (in kilograms per day) by the sulfur dioxide concentration (in milligrams per kilogram). The average daily consumption of 16.6 grams per day is 0.017 kilograms per day. Multiplying this by an estimated worst-case concentration of molecular SO₂ in soy sauce of 1.54 milligram per kilogram results in 0.026 milligrams per day, or 26 micrograms per day.

Comparison of Sulfur Dioxide Exposure from Soy Sauce to the MADL

OEHHA adopted in regulation a maximum allowable dose level for SO₂ of 10,000 micrograms per day²⁰. This MADL is based on inhalation data. All of the studies that formed the basis for listing SO₂ were of exposure to SO₂ as a gas. There are currently no available studies on exposure to SO₂ solely by the oral route. However, based on review of relevant information²¹, OEHHA has concluded that exposure to SO₂ by the

¹⁹ M Kobayashi, Nutritional Functions of Polysaccharides from Soy Sauce in the Gastrointestinal Tract, in: RR Watson and VR Preedy (Eds), Bioactive Food as Dietary Interventions for Liver and Gastrointestinal Disease, 2013.

²⁰ California Code of Regulations, Title 27, Section 25805(b).

²¹ Office of Environmental Health Hazard Assessment. Evidence on the Developmental and Reproductive Toxicity of Sulfur Dioxide, 2011. Available at <https://oehha.ca.gov/media/downloads/proposition-65/chemicals/so2hid022511.pdf>.

oral route²² is expected to pose no more risk, and may pose less risk, than exposure to the equivalent amount by the inhalation route.

The calculated worst case daily exposure of 26 micrograms from consumption of sulfur dioxide in soy sauce is far less than the MADL of 10,000 micrograms. Therefore, no warning would be required for these exposures.

The analysis in this Interpretive Guidance applies only to the specific compound SO₂, and does not apply to sulfites, bisulfites and metabisulfites. These chemicals are not listed under Proposition 65 and are therefore not subject to the law's warning requirement. As stated previously, only a small percentage of the total sulfite that is "free SO₂" in the soy sauce is molecular SO₂.

Conclusion

OEHHA concludes that consumption by the average consumer of soy sauce will not result in an exposure to SO₂ exceeding the MADL. Therefore, a warning is not required under Proposition 65 for exposure to SO₂ from consumption of soy sauce.

²² There may be some inhalation exposure because a small amount of sulfur dioxide can partition from the soy sauce into the air.