Biocidal Products Committee (BPC)

Opinion on the application for approval of the active substance:

Sulfur dioxide generated from sulfur by combustion

Product type: 4

ECHA/BPC/354/2022

Adopted

26 September 2022

Opinion of the Biocidal Products Committee

on the application for approval of the active substance sulfur dioxide generated from sulfur by combustion for product type 4

In accordance with Article 89(1) of Regulation (EU) No 528/2012 of the European Parliament and of the Council 22 May 2012 concerning the making available on the market and use of biocidal products (BPR), the Biocidal Products Committee (BPC) has adopted this opinion on the approval in product type 4 of the following active substance:

Common name:	**sulfur dioxide generated from sulfur by combustion**
Chemical name:	**precursor: sulfur**
	active substance: sulfur dioxide
EC No.:	**precursor: 231-722-6**
	active substance: 231-195-2
CAS No.:	**precursor: 7704-34-9**
	active substance: 7446-09-5

Existing active substance

This document presents the opinion adopted by the BPC, having regard to the conclusions of the evaluating Competent Authority. The assessment report, as a supporting document to the opinion, contains the detailed grounds for the opinion.

Process for the adoption of the BPC opinion

Following the submission of an application by Azufrera y Fertilizantes Pallarés S.A. on 29 November 2012, the evaluating Competent Authority Germany submitted an assessment report and the conclusions of its evaluation to ECHA on 06 March 2018. In order to review the assessment report and the conclusions of the evaluating Competent Authority, the Agency organised consultations via the BPC (BPC-44) and its Working Groups (WG V 2018, WG II 2019, WG IV 2020, WG I 2021; WG II 2022). Revisions agreed upon were presented and the assessment report and the conclusions were amended accordingly.

Adoption of the BPC opinion

Rapporteur: Germany

The BPC opinion on the application for approval of the active substance sulfur dioxide generated from sulfur by combustion in product type 4 was adopted on 26 September 2022.

The BPC opinion was adopted by consensus.

The opinion is published on the ECHA webpage at: http://echa.europa.eu/regulations/biocidal-products-regulation/approval-of-active-substances/bpc-opinions-on-active-substance-approval.

Detailed BPC opinion and background

1. Overall conclusion

The overall conclusion of the BPC is that sulfur dioxide generated from sulfur by combustion in product type 4 may be approved. The detailed grounds for the overall conclusion are described in the assessment report.

2. BPC Opinion

2.1. BPC Conclusions of the evaluation

a) Presentation of the active substance including the classification and labelling of the active substance

This evaluation covers the use of sulfur dioxide generated from sulfur by combustion in product type 4. Specifications for the reference source are established.

The physico-chemical properties of the active substance, the precursor and biocidal product have been evaluated and are deemed acceptable for the appropriate use, storage and transportation.

Validated residue analytical methods are available for determination of sulfur dioxide (determined as sulfate ion) in air and in drinking and surface water (determined as sulfite ion). For the analysis in wine, a reference method for sulfur dioxide determined as sulfuric acid or determined as sulfite is available. For the determination of residues of the active substance in soil, residue analytical methods are not required. For the determination of residues in body fluids and tissues, residue analytical methods are not feasible.

Sulfur dioxide is regulated under Regulation (EC) No. 606/2009[1] as well as under Regulation (EC) No. 607/2009[2]. Sulfur dioxide is authorised under Regulation EC 1333/2008[3] as food additives named E 220. In 2016, it has been re-evaluated by EFSA[4] as food additive.

EFSA's follow-up to its re-evaluation opinion of sulfur dioxide-sulfites (E 220-228)[5] addresses the data gaps previously identified and the recommendations issued at the time of the 2016 re-evaluation. EFSA participated in the discussion of sulfur dioxide generated from sulfur by combustion in order to discuss potential divergences of opinions between the respective evaluations of sulfur dioxide, but EFSA does not have a formal role in this assessment.

The precursor sulfur is approved as a pesticide under Regulation (EC) No 1107/2009[6].

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[1] COMMISSION REGULATION (EC) No 606/2009 of 10 July 2009 laying down certain detailed rules for implementing Council Regulation (EC) No 479/2008 as regards the categories of grapevine products, oenological practices and the applicable restrictions.

[2] COMMISSION REGULATION (EC) No 607/2009 of 14 July 2009 laying down certain detailed rules for the implementation of Council Regulation (EC) No 479/2008 as regards protected designations of origin and geographical indications, traditional terms, labelling and presentation of certain wine sector products.

[3] REGULATION (EC) No 1333/2008 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 December 2008 on food additives.

[4] 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; http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2016.4438/pdf.

[5] https://https://open.efsa.europa.eu/questions/EFSA-Q-2021-00110.

[6] REGULATION (EC) No 1107/2009 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC.

A harmonised classification is available for the precursor sulfur which has been confirmed by the RAC opinion adopted on 18 March 2022[7].

For the active substance sulfur dioxide, the eCA submitted a CLH dossier in June 2017 to change the existing harmonised classification. The RAC adopted its opinion on 26 November 2021[8] with the following proposal for classification and labelling of sulfur dioxide:

Classification for sulfur dioxide according to RAC opinion of 26 November 2021	
Hazard Class and Category Codes	Press. Gas Acute Tox. 3, H331 Skin Corr. 1B, H314 STOT SE 1, H370 (respiratory system, inhalation)
Labelling	
Pictogram codes	GHS04, GHS05, GHS06, GHS08
Signal Word	Danger
Hazard Statement Codes	H331 – Toxic if inhaled H314 – Causes severe skin burns and eye damage H370 – Causes damage to the respiratory system via inhalation
Specific Concentration limits, M-Factors	Inhalation: ATE=1000 ppmV (gases)

Classification for sulfur (precursor) according to RAC opinion of 18 March 2022	
Hazard Class and Category Codes	Skin Irrit. 2, H315
Labelling	
Pictogram codes	GHS07
Signal Word	Warning
Hazard Statement Codes	H315 – Causes skin irritation
Specific Concentration limits, M-Factors	-

b) Intended use, target species and effectiveness

Biocidal Products generating the active substance "sulfur dioxide generated from sulfur by combustion" are intended to be used by professional users in wooden wine barrels prior to dry conservation[9] of the wine barrels or prior to filling of the wine barrels with wine. The representative product is a sulfur tablet which is placed in a wooden wine barrel and subsequently releases sulfur dioxide after ignition.

Sulfur dioxide diffuses across the cell membrane and inhibits microbial growth by e.g. binding to key metabolites / key metabolic enzymes. Target organisms are the species of the microbial flora populating the inner surface of wooden wine barrels, i.e. bacteria (e.g. *Actinomyces*, *Streptomyces,* lactic acid bacteria of genus *Pediococcus* or *Lactobacillus*, acetic acid bacteria), spoilage yeast (e.g. *Brettanomyces* spp.) and fungi.

[7] RAC Opinion proposing harmonised classification and labelling at EU level of sulfur, adopted 18 March 2022; https://echa.europa.eu/documents/10162/0ee29de8-3fb7-7d84-5c84-afe6dab8df1b.
[8] RAC Opinion proposing harmonised classification and labelling at EU level of sulfur dioxide, adopted 26 November 2021; https://echa.europa.eu/documents/10162/5ea9c21b-8f7c-a6f0-6852-866fc7887902.
[9] Dry conservation means treatment of wooden wine barrels which are still moist (residual moisture in the wood). Wet conservation (the barrels are filled with water prior to addition of e.g. potassium metabisulfite or sulfur dioxide from gas cylinders) is not included in this application and has not been evaluated.

The studies provided are sufficient to demonstrate the innate efficacy of “sulfur dioxide generated from sulfur by combustion” against the yeast *Brettanomyces bruxellensis* in the framework of active substance approval.

Specific resistance mechanisms are known for yeast from the literature. Member States should be aware that there is a risk of development of resistance, as for many biocides when used at low (biostatic) concentration.

c) Overall conclusion of the evaluation including need for risk management measures

Human health

Sulfur dioxide

Sulfur dioxide was found to be acutely toxic when inhaled and corrosive to the skin and eyes. In the RAC opinion, the existing classification for acute toxicity as well as irritation/corrosion was concluded to be maintained. Various human studies showed bronchoconstriction and asthma as predominant symptoms. Cases of sulfite induced asthma (mild and life-threatening) are described in literature in the general population and in occupationally exposed workers. Severe life-threatening asthmatic, urticarial and anaphylaxis-like attacks have been documented after exposure to sulfiting agents.

Occurrence of skin sensitisation in humans following exposure to sulfites was not considered sufficient for harmonised classification of sulfur dioxide gas by RAC. Sulfur dioxide is not sensitising the respiratory tract in animal studies, but animals pre-treated with ovalbumin developed asthmatic reactions following sulfur dioxide exposure. Considering that sulfur dioxide is not an allergen itself and an existing allergy is a prerequisite for the observed asthma symptoms, classification with respiratory sensitisation does not apply. The available acute toxicity inhalation studies demonstrate clinical signs of airway hyperresponsiveness (AHR) such as bronchoconstriction induced by sulfur dioxide. RAC proposed classification as STOT SE 1 (H370 Causes damage to the respiratory system by inhalation).

There is some evidence for neurotoxic effects of sulfur dioxide. However, for these effects, no classification is considered necessary. In studies with sodium metabisulfite (which was used as part of a read-across concept), local effects such as histopathological changes in the epithelia of various organs and general toxic effects as reduction in food consumption and body weight were reported.

Results of in vitro and in vivo studies conducted with sulfur dioxide, sodium metabisulfite and other sulfite compounds indicated a clastogenic potential. A proposal for classification of sulfur dioxide as Muta 2 was submitted but RAC concluded that the evidence for in vivo mutagenicity was not strong enough to support classification, resulting in non-classification based on inconclusive data.

Sulfur dioxide is not classified for carcinogenicity, reproductive or developmental toxicity in accordance with Regulation (EC) No 1272/2008 and do not meet the criteria to be classified in relation to these hazards (properties) Regarding endocrine disrupting properties of sulfur dioxide, there was a concern identified with the EAS-mediated parameters including interference in spermatogenesis. However, it is concluded that sulfur dioxide is not an endocrine disruptor with regard to human health based on the available data and that further testing was not justified. No data are available on immunotoxicity apart from allergic response.

Sulfur

Sulfur has a harmonised classification for skin irritation based on erythema and oedema. No acute toxicity and no sensitisation were observed in the available studies. No adverse systemic effects were observed following oral application, but rats developed hyperkeratosis after dermal exposure. Sulfur showed no genotoxic effects *in vitro* and *in vivo*. For carcinogenicity and reproductive toxicity, no data are available. However, based on the available information from other endpoints, there is no indication that sulfur is carcinogenic or toxic to reproduction. There are also no sufficient data available on the neurotoxic and immunotoxic potential or on endocrine disrupting properties of sulfur.

The table below summarises the exposure scenarios assessed.

Summary table: human health scenarios			
Scenario	**Primary or secondary exposure and description of scenario**	**Exposed group**	**Conclusion**
Fumigation of wine barrels in wine cellars	Primary exposure during inserting a burning sulfur tablet in wine barrels and closing the barrel by seating a cork in the bung hole; the active substance sulfur dioxide is then released inside the barrel by combustion of sulfur; inhalation exposure of the operator to sulfur dioxide and dermal exposure to sulfur. Secondary inhalation exposure of professional bystander to sulfur dioxide.	Professional/ professional bystander	Acceptable with RPE
Entry during application	Secondary exposure – Entry of winemaking area (application area) during application by non-professional bystanders	General public	Not acceptable, access of general public has to be avoided
Re-entry (post-application):	Secondary exposure – Re-entry of winemaking area (application area) after application	General public	Acceptable with RMM (waiting period)

Professional user

The occupational risk assessment for the active substance sulfur dioxide in situ generated from sulfur by combustion and the biocidal product sulfur takes into account systemic effects as well as local effects. For systemic effects and local effects caused by inhalation the risk characterisation is carried out with the AEL and AEC approach. For local effects caused by dermal exposure a semi-quantitative risk assessment is carried out.

For the risk characterisation the scenario fumigation of wine barrels in wine cellars (primary exposure) and present occupational bystanders (secondary exposure) are assessed for the professional user.

No concern from systemic effects was identified for professional users/bystanders in the assessed scenario.

Concerning the dermal irritating properties of the biocidal precursor sulfur, the exposure is below the NOAEC for hyperkeratosis. The intended use does not lead to concern for professional users (no PPE required).

Due to the assessment of local effects after inhalation, it cannot be excluded that the high exposure levels of sulfur dioxide from the biocidal treatment of wine barrels will result in toxic effects for workers. If respiratory protective equipment (e.g. purifying respirator with helmet/hood/mask (TH2/TM2), or a full face mask with gas filter E1, yellow) is taken into account a risk for professional users and professional bystanders is acceptable.

General public

For secondary exposure excluding dietary exposure, entry during and re-entry after application by the general public is assessed. In addition to the systemic effect assessment, a local risk assessment concerning the classification of the biocidal product and the active substance is performed.

During application, personal protection equipment is necessary for professionals and professional bystanders. As the general public does not have access to personal protection equipment, a risk is identified. Entry of the application area by the general public has to be strictly avoided during application. Therefore, the biocidal product has to be labelled accordingly.

For re-entry of the general public, the concentration of sulfur dioxide in air should not exceed environmental background concentrations and should be as low as feasible. Thus, a waiting period of 24 hours is considered reasonable. The biocidal product has to be labelled accordingly.

Indirect exposure via food

The long-term intake of residues from the intended use is unlikely to present a human health concern. With regard to the short-term intake of residues, the health risk for consumers from sulfur dioxide residues in wine resulting from the intended uses is considered acceptable as maximal levels from authorised oenological practices[1] are about 10-fold higher than the estimated residues from the intended biocidal use. Additionally, specific provisions for the labelling of wine[2] containing sulfur dioxide and sulfites apply in order to avoid exposure of certain sensitive subpopulations.

Environment

The atmosphere is the only environmental compartment that is directly exposed due to the use of the biocidal product. Via wet and dry deposition, sulfur dioxide indirectly returns to the earth's surface and can affect ecosystem biogeochemistry, structure, and function. Although sulfur dioxide is naturally occurring in the atmosphere it contributes to acid deposition. Acid deposition reduces the pH of soils and surface waters leading to potential changes in soil and water quality. Regarding endocrine disrupting properties in relation to non-target organisms, there is insufficient information to conclude. However, it is concluded that further testing is technically not justified. Further tests with non-target organisms can be waived since the feasibility of testing is impaired *(*referring to second heading of Annex IV of the Regulation EU) No 528/2012) due to the physico-chemical properties of sulfur dioxide. Furthermore, testing does not appear scientifically necessary (first heading of Annex IV of the Regulation (EU) No 528/2012) since adverse effects of sulfur dioxide cannot clearly be assigned to an endocrine mode of action. Instead, sulfur dioxide induces oxidative

stress and cytotoxicity which can lead to secondary effects on the endocrine system of test organisms making it difficult to separate these indirect effects from adverse effects directly caused by an endocrine mode of action. Thus, additional testing would not provide any robust data capable to identify or exclude sulfur dioxide as an ED and should be avoided considering animal welfare reasons. On the other side, there are no indications for endocrine disruption in the available data set of sulfur dioxide. Consequently, it is concluded that sulfur dioxide is not an endocrine disruptor with regard to non-target organisms.

The table below summarises the exposure scenarios assessed.

Summary table: environment scenarios		
Scenario	**Description of scenario including environmental compartments**	**Conclusion**
Treatment of wine barrels - Emission of sulfur dioxide due to the combustion of sulfur tablets, wicks or candles (5 g sulfur)	Direct release of sulfur dioxide to the atmosphere. Indirectly exposed environmental compartments are soil and surface water.	Acceptable Emissions of sulfur dioxide to the atmosphere are negligible considering background levels of SO_2. Thus, no quantitative risk assessment has been carried out.

According to the intended use of the sulfur tablets, wicks or candles for the biocidal treatment of wine barrels direct release of the active substance sulfur dioxide to the environment will only occur to the compartment air. As the emission caused by the biocidal use does not significantly increase the atmospheric concentration above the background level, the risk to the atmosphere by the assessed biocidal use is considered acceptable.

Overall conclusion

In summary, the risk for professional users and professional bystanders resulting from the use of the precursor sulfur and the generated active substance sulfur dioxide is acceptable.

Risk reduction measures like RPE have to be taken into account in order to ensure safe use of the biocidal product. The risk for the general public is acceptable as long as access during application is avoided and a re-entry period of 24 hours is adhered to. It is essential to indicate, that the conclusion only applies to the precursor in the biocidal product and to the active substance (and not to other ingredients).

The risk posed by the biocidal use to the atmosphere as well as to the potentially subsequently exposed environmental compartments surface water and soil are considered acceptable.

2.2. Exclusion, substitution and POP criteria

2.2.1. Exclusion and substitution criteria

The table below summarises the relevant information with respect to the assessment of exclusion and substitution criteria:

Property		Conclusions	
CMR properties	Carcinogenicity (C)	No classification required	Sulfur dioxide does not fulfil criterion (a), (b) and (c) of Article 5(1)
	Mutagenicity (M)	No classification required	
	Toxic for reproduction (R)	No classification required	
PBT and vPvB properties	Persistent (P) or very Persistent (vP)	Not P or vP	Sulfur dioxide does not fulfil criterion (e) of Article 5(1) and does not fulfil criterion (d) of Article 10(1)]
	Bioaccumulative (B) or very Bioaccumulative (vB)	Not B or vB	
	Toxic (T)	Not T	
Endocrine disrupting properties	Section A of Regulation (EU) 2017/2100: ED properties with respect to humans	No	Sulfur dioxide does not fulfil criterion (d) of Article 5(1) and does not fulfil criterion (e) of Article 10(1)
	Section B of Regulation (EU) 2017/2100: ED properties with respect to non-target organisms	No	
	Article 57(f) and 59(1) of REACH	No	
	Intended mode of action that consists of controlling target organisms via their endocrine system(s).	No	
Respiratory sensitisation properties	No classification required. Reactive airway dysfunction syndrome (RADS) is reflected in classification conclusion by RAC for STOT SE 1 Sulfur dioxide does not fulfil criterion (b) of Article 10(1)		
Concerns linked to critical effects others than those related to endocrine disrupting properties	Sulfur dioxide does not fulfil criterion (e) of Article 10(1)		
Proportion of non-active isomers or impurities	Sulfur dioxide does not fulfil criterion (f) of Article 10(1)		

Consequently, the following is concluded:

Sulfur dioxide does not meet the exclusion criteria laid down in Article 5 of Regulation (EU) No 528/2012.

Sulfur dioxide does not meet the conditions laid down in Article 10 of Regulation (EU) No 528/2012 and is therefore not considered as a candidate for substitution. The exclusion and substitution criteria were assessed in line with the "Note on the principles for taking decisions on the approval of active substances under the BPR"[10],with "Further guidance on the application of the substitution criteria set out under article 10(1) of the BPR"[11] and with "Implementation of scientific criteria to determine the endocrine-disrupting properties of active substances currently under assessment"[12] agreed at the 54th, 58th and 77th meeting respectively, of the representatives of Member States Competent Authorities for the implementation of Regulation 528/2012 concerning the making available on the market and use of biocidal products. This implies that the assessment of the exclusion criteria is based on Article 5(1) and the assessment of substitution criteria is based on Article 10(1)(a, b, d, e and f).

2.2.2. POP criteria

The POP criteria do not apply to an inorganic compound like sulfur dioxide.

2.3. BPC opinion on the application for approval of the active substance sulfur dioxide generated from sulfur by combustion in product type 4

In view of the conclusions of the evaluation, it is proposed that sulfur dioxide generated from sulfur by combustion shall be approved and be included in the Union list of approved active substances, subject to the following specific conditions:

1. Specification: minimum purity of the precursor evaluated: ≥ 99.5 % w/w.
2. The authorisations of biocidal products are subject to the following condition(s):
    a. The product assessment shall pay particular attention to the exposures, the risks and the efficacy linked to any uses covered by an application for authorisation, but not addressed in the Union level risk assessment of the active substance.
    b. In view of the risks identified for the uses assessed, the product assessment shall pay particular attention to:
        i. professional users;
        ii. general public following secondary exposure.
3. For products that may lead to residues in food or feed, the need to set new or to amend existing maximum residue levels (MRLs) in accordance with Regulation (EC) No 470/2009 or Regulation (EC) No 396/2005 shall be verified, and any appropriate risk mitigation measures shall be taken to ensure that the applicable MRLs are not exceeded.

[10] See document: Note on the principles for taking decisions on the approval of active substances under the BPR (available from https://circabc.europa.eu/d/a/workspace/SpacesStore/c41b4ad4-356c-4852-9512-62e72cc919df/CA-March14-Doc.4.1%20-%20Final%20-%20Principles%20for%20substance%20approval.doc)

[11] See document: Further guidance on the application of the substitution criteria set out under article 10(1) of the BPR (available from https://circabc.europa.eu/d/a/workspace/SpacesStore/dbac71e3-cd70-4ed7-bd40-fc1cb92cfe1c/CA-Nov14-Doc.4.4%20-%20Final%20-%20Further%20guidance%20on%20Art10(1).doc)

The active substance does not fulfil the criteria according to Article 28(2) of the BPR to enable inclusion in Annex I of Regulation (EU) 528/2012. RAC proposes to classify sulfur dioxide as Acute Tox. 3 (H331), Skin Corr. 1B (H314) and STOT SE 1 (H370).

2.4. Elements to be taken into account when authorising products

1. The following recommendations and risk mitigation measures have been identified for the uses assessed. Authorities should consider these risk mitigation measures when authorising products, together with possible other risk mitigation measures, and decide whether these measures are applicable for the concerned product:

    a. If an unacceptable risk is identified for professional users, safe operational procedures and appropriate organizational measures shall be established. Products shall be used with appropriate personal protective equipment where exposure cannot be reduced to an acceptable level by other means.

    b. If an unacceptable risk is identified for the general public following secondary exposure, labels and, where provided, instructions for use shall indicate that access of the general public/uninvolved parties during application has to be avoided and that re-entry is only possible 24 hours after application.

2.5. Requirement for further information

Sufficient data have been provided to verify the conclusions on the active substance, permitting the proposal for the approval of sulfur dioxide generated from sulfur by combustion.

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[12] See document: Implementation of scientific criteria to determine the endocrine-disrupting properties of active substances currently under assessment (available from https://circabc.europa.eu/ui/group/e947a950-8032-4df9-a3f0-f61eefd3d81b/library/5ac61098-3765-48a7-800c-74ae41960ba0/details)