# Biocidal Products Committee (BPC)

Opinion on the application for approval of the active substance:

**Sulfur dioxide released from sodium metabisulfite**

**Product type: 9**

ECHA/BPC/355/2022

Adopted

26 September 2022

# Opinion of the Biocidal Products Committee

**on the application for approval of the active substance sulfur dioxide released from sodium metabisulfite for product type 9**

In accordance with Article 8(4) 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 9 of the following active substance:

| | |
|---|---|
| **Common name:** | **sulfur dioxide released from sodium metabisulfite** |
| **Chemical name of releaser:** | **disodium disulphite** |
| **EC No. of releaser:** | **231-673-0** |
| **CAS No. of releaser**: | **7681-57-4** |

**Existing active substance submitted under Article 7 of the BPR**

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 Micro-Pak Europe BV on 2 December 2013, the evaluating Competent Authority Germany submitted an assessment report and the conclusions of its evaluation to ECHA on 22 January 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 released from sodium metabisulfite in product type 9 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 released from sodium metabisulfite in product type 9 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 released from sodium metabisulfite in product type 9. Specifications for the reference source are established.

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

Validated analytical methods are available for the active substance as manufactured. Validated analytical methods are required and available for the relevant matrices (air).

Sulfur dioxide is regulated under Regulation (EC) No. 606/2009[1] as well as under Regulation (EC) No. 607/2009[2]. Sulfur dioxide as well as the releaser sodium metabisulfite are authorised under Regulation EC 1333/2008[3] as food additives named E 220 and E 223, respectively. In 2016, they have been re-evaluated by EFSA[4].

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 released from sodium metabisulfite in order to discuss potential divergences of opinions between the respective evaluations of sulfur dioxide, but EFSA did not have a formal role in this assessment.

A harmonised classification is available for the active substance sulfur dioxide as well as for the releaser sodium metabisulfite.

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[6] with the following classification and labelling of sulfur dioxide:

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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] 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.

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

| **Classification for sodium metabisulfite according to the CLP Regulation** | |
|---|---|
| Hazard Class and Category Codes | Acute Tox. 4*, H302<br>Eye Dam. 1, H318<br>EUH031 |
| **Labelling** | |
| Pictogram codes | GHS07<br>GHS05 |
| Signal Word | Danger |
| Hazard Statement Codes | H302 - Harmful if swallowed<br>H318 - Causes serious eye damage<br>EUH031 - Contact with acids liberates toxic gas |
| | |
| **Specific Concentration limits, M-Factors** | - |

**b) Intended use, target species and effectiveness**

Biocidal products releasing the active substance “sulfur dioxide released from sodium metabisulfite” are intended to control odour causing bacteria, mold and mildew on footwear and other leather, rubber, paper as well as textile goods enclosed in packaging during storage and transport.

The assessed representative biocidal product is a sticker containing the releaser sodium metabisulfite. This ready-to-use product is applied to shoe boxes by professional users prior to storage and/ or transport of leather shoes. During storage and transport, the sticker

releases sulfur dioxide, which inhibits microbial growth by e.g. binding to key metabolites / key metabolic enzymes.

The data on the representative biocidal product have demonstrated a basic efficacy against mold and mildew and two bacteria. A growth reduction of 50 % for mold and mildew was shown for a timeframe of 30 days when one sticker was applied per shoe box (volume 0.0039 $m^3$). Growth of *Staphylococcus aureus* and *Bacillus subtilis* was completely inhibited. No sufficient efficacy against *Pseudomonas aeruginosa* and *Candida albicans* was shown.

Depending on the claim, further data (e.g. against odour causing bacteria) needs to be provided at the stage of product authorisation.

Specific resistance mechanisms of yeast against sulfur dioxide are known from the literature and might also be valid for fungi and bacteria.

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

**Human health**

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. Sodium metabisulfite is harmful after oral exposure and damaging to eyes.

Occurrence of skin sensitisation in humans following exposure to sulphites was not considered sufficient for harmonised classification of sulfur dioxide gas by RAC. Sulfur dioxide and sodium metabisulfite are not sensitising to the respiratory tract

Bronchoconstriction is the predominant effect observed in humans following sulfur dioxide exposure whereas 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 mostly reported in animal studies following oral exposure of sodium metabisulfite. 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.

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 concluded on a 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. No data are available on immunotoxicity apart from allergic response.

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 and sodium metabisulfite are 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, there was a concern identified with the EAS-mediated parameters including interference in spermatogenesis. However, it is concluded that neither sulfur dioxide nor sodium metabisulfite are endocrine disruptors with regard to human health based on the available data and that further testing is not justified.

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** |
| Packaging of shoeboxes | Primary inhalation exposure to released sulfur dioxide (a.s.) and dermal exposure to sodium metabisulfite (MBS) during placing of stickers (with incorporated releaser MBS) into shoe boxes.<br><br>PPE and RMM: protective gloves and use of a dispenser box for the sticker | Professional user | Acceptable with PPE and RMM |
| Opening and unloading of a transport container | Secondary inhalation exposure to released sulfur dioxide during unloading of transport boxes from a shipping container containing shoe boxes treated with stickers. | Professional user | Acceptable |
| Unpacking of shoe boxes in retail businesses | Secondary inhalation exposure to released sulfur dioxide. Exposure occurring to employees in retail businesses during checking and preparing a new delivery of shoe boxes. | Professional user | Acceptable |
| Dermal contact with sticker (post-application) | Secondary exposure to the releaser $Na_2S_2O_5$ –dermal contact with a sticker by a consumer who opens a shoe box | General public - Adult | Acceptable |

| **Summary table: human health scenarios** | | | |
|---|---|---|---|
| Dermal contact with sticker and oral ingestions of sticker (post-application) | Secondary exposure to the releaser $Na_2S_2O_5$ –dermal contact with a sticker and oral ingestions of a sticker by a toddler who plays with a shoe box<br><br>RMM: Labelling products with ““Keep out of reach of children”. | General public - Toddler | Acceptable with RMM |
| Inhalation after opening of shoe box (post-application) | Secondary exposure to the active substance $SO_2$ – local inhalation exposure after opening a shoe box at home | General public | Acceptable |
| Inhalation after entry of sales room (post-application) | Secondary exposure to the active substance $SO_2$ – local inhalation exposure after entry of a sales room (opening of shoe boxes by professionals) | General public | Acceptable |

**Professional user**

The occupational risk assessment for the released active substance sulfur dioxide and the releaser sodium metabisulfite 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 approach and AEC approach. For local effects caused by dermal exposure a qualitative risk assessment according to the Guidance for Human Health Risk Assessment, Volume III – Part B is carried out.

For the risk characterisation the scenarios handling of stickers with releaser during packaging of shoeboxes (primary exposure), opening and unloading of a transport container with treated shoeboxes (secondary exposure) and unpacking of treated shoeboxes (secondary exposure) in retail businesses are assessed for the professional user.

No concern from systemic effects was identified for professional users in any of the assessed scenarios. For handling of the stickers during packaging of shoeboxes the use of protective gloves is necessary due to the resulting hand exposure and local effects (classification with Skin Sens 1, H317). In addition, the use of a product specific dispenser box was taken into account in the provided workplace measurements which is assessed as a technical risk mitigation measure reducing the inhalation exposure to the active substance.

**Non-professional user and general public**

Non-professional use is not foreseen.

For the general public, relevant worst-case secondary (indirect) exposure scenarios have been addressed (dermal contact (adult) and dermal contact and oral ingestion (toddler) after opening a shoe box as well as inhalation exposure of the general public).

For systemic exposure of adults, no risk has been identified. For toddlers a risk is considered possible (by ingestion) when handling the sticker, therefore risk mitigation measures are

necessary: Labelling like “Keep out of reach of children” is considered suitable to ensure the prevention of possible oral exposure of toddlers.

For local exposure to sulfur dioxide, no unacceptable risk for the general public is identified.

For local risk assessment concerning the classification of the biocidal product, identified risk is considered negligible. Nevertheless, a risk mitigation measure like labelling the product with “Do not touch” may be considered for national or Union authorisation to exclude possible contact with the biocidal product. In general, contribution of sulfur dioxide as a result of use to the background level seems to be very low.

Residues in food or feed from the intended use of sulfur dioxide in PT 9 biocidal products are not expected.

**Environment**

For the environmental risk assessment, the emission of sulfur dioxide to the atmosphere due to opening and unloading of ten transport containers containing shoe boxes preserved with the biocidal product, has been assessed. Due to the fact that this scenario describes a relative strong point source, it covers potential emissions from professional application as well as wide-dispersive emissions from the service life of shoe boxes containing preserved shoes (e.g. handling, storage, opening and disposal by general public).

As sulfur dioxide is an inorganic, ubiquitous gas which is a combustion product and has a variety of applications beside the biocidal use, a generic approach was chosen in order to assess the contribution of the biocidal use for the total atmospheric sulfur dioxide levels.

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 neither sulfur dioxide nor sodium metabisulfite are endocrine disruptors 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** |
| Opening and unloading of 10 transport containers at a logistic centre | Direct exposure of air; indirect exposure of freshwater and soil due to wet and dry deposition | Acceptable |

The predicted risks posed by the biocidal product to the only directly exposed environmental compartment atmosphere is considered as acceptable as no significant increase of atmospheric sulfur dioxide above the background level is predicted. Consequently, the risks for the environmental compartments surface water and soil, which might be exposed indirectly via atmospheric transport, are also considered acceptable.

**Overall conclusion**

In summary, the risk for professional users and professional bystanders resulting from the use of the releaser sodium metabisulfite and the released active substance sulfur dioxide is acceptable.

The described risk mitigation measures have to be taken into account in order to ensure safe use of the biocidal product. It is essential to indicate that the conclusion only applies to the releaser in the biocidal product and to the released active substance (and not to other ingredients). The risk identified for toddlers can be mitigated by appropriate labelling of the biocidal product, if not refined otherwise during product authorisation. The environmental risk assessment does not indicate unacceptable risks.

## 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 released from sodium metabisulfite 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 released from sodium metabisulfite 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 released from sodium metabisulfite does not fulfil criterion (d) of Article 5(1) |

| Property | | Conclusions | |
|---|---|---|---|
| | Section B of Regulation (EU) 2017/2100: ED properties with respect to non-target organisms | No | and does not fulfil criterion (e) of Article 10(1) |
| | 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 for sulfur dioxide.<br><br>Sulfur dioxide released from sodium metabisulfite does not fulfil criterion (b) of Article 10(1) | | |
| Concerns linked to critical effects others than those related to endocrine disrupting properties | Sulfur dioxide released from sodium metabisulfite does not fulfil criterion (e) of Article 10(1) | | |
| Proportion of non-active isomers or impurities | Sulfur dioxide released from sodium metabisulfite does not fulfil criterion (f) of Article 10(1) | | |

Consequently, the following is concluded:

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

Sulfur dioxide released from sodium metabisulfite 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"[7], "Further guidance on the application of the substitution criteria set out under article 10(1) of the BPR"[8] and "Implementation of scientific criteria to determine the endocrine –disrupting

[7] 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).
[8] 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).

properties of active substances currently under assessment[9]" 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

As sulfur dioxide and sodium metabisulfite are inorganic substances they do not fulfil the criteria laid down in the Stockholm Convention on Persistent Organic Pollutants (POPs) from 2001.

## 2.3. BPC opinion on the application for approval of the active substance sulfur dioxide released from sodium metabisulfite in product type 9

In view of the conclusions of the evaluation, it is proposed that sulfur dioxide released from sodium metabisulfite 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 releaser evaluated: 95 % 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. toddlers.

The active substance sulfur dioxide released from sodium metabisulfite 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 proposed 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.

[9] 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).

b. If an unacceptable risk for toddlers is identified following secondary dermal exposure to the releaser, labels, and where provided, safety data sheets, should indicate that products should be kept out of the reach of children.

c. As a result of the local risk assessment, a risk mitigation measure like labelling the product with “Do not touch” may be considered for national or Union authorisation to exclude possible contact of the general public with the biocidal product.

### 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 released from sodium metabisulfite.

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