SHERWIN-WILLIAMS.

Sherwin Williams supports the proposed maintenance of the current Skin Sensitization 1B with concentration limit for dermal sensitisation of 500 ppm for 1,2- benzisothiazolin-3-one.

Founded in 1866, The Sherwin-Williams Company is a global leader in the manufacture, development, distribution, and sale of paints, coatings and related products to professional, industrial, commercial, and retail customers. In Europe our footprint includes over 20 production locations and employing approximately 3800 direct employees. We welcome the opportunity to comment on the proposed harmonized classification and labelling of 1,2- benzisothiazolin-3-one (BIT)

Water based paints and coatings require in-can preservatives for protection against microbial deterioration and the number of effective biocides that can be used to preserve water-based paints – and coatings is very limited. Without the use of biocides, water-based products have reduced stability and shelf-life resulting in increased spoilage, disposal and waste. The damage caused by micro-organisms on water-based products are varied: change of viscosity, change of pH, generation of bad smell, change of colour, destruction of the product ingredients with associated loss of product function/efficiency, generation of gas, visible surface growth and biofilm formation.

In the paint and-coatings industry, some manufacturers have compensated by increasing the pH of some products to approximately 11.3 to retard growth. This solution is restricted to formulas for indoor use and greatly limits the ability to tint paint. Manufacturers may also compensate by increasing the amount of solvents used in their formulas.

BIT is a highly effective preservative for low VOC water-based product formulations. It functions across a wide spectrum of pH and demonstrates excellent efficacy against a wide range of microorganisms. Due to limited availability of suitable alternatives[1], BIT is an increasingly important biocide in our and our customer's applications.

Available scientific evidence shows that BIT is a much less potent skin sensitiser in comparison with other isothiazolones for which other specific SCLs have been already identified. In light of this differences, and on the basis of the amount of significant BIT specific data, Sherwin Williams deems appropriate that the latter should be assessed as a stand-alone substance and grouping with other isothiazolones or read across to other structurally similar molecules should be avoided.

For these reasons, we support the retaining of the current **substance concentration limit (**SCL) for dermal sensitization of 500 ppm for BIT. This limit would guarantee an effective and safe use of the substance.

[1] 1 Survey on alternatives for in-can preservatives for varnishes, paints and adhesives (BAuA Report www.baua.de/dok/8841190; doi:10.21934/baua:report20200811 (online)); and
Dr. Christof Walter (VdL): Vermarktung und Verwendung von Farben und Lacken im Spannungsfeld zwischen CLP Einstufung, BiozidWirkstoffverfahren und Arbeitsschutz; BAuA Informations- und Dialogveranstaltung 25. February 2021

Any provision, requiring an inappropriate SCL for BIT under the CLP Regulation No (EC) 1272/2008 could lead to unintended conflicts with other regulations that are specifically drafted to govern the use of biocides. Where an excessively stringent SCL would preclude the use of BIT, this could trigger regrettable substitutions, and, as a worst-case scenario, drive formulations back to more hazardous solvent based paint alternatives. Creating roadblocks to the use of water-based paints will not support Europe's initiative to reduce solvents.

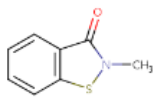
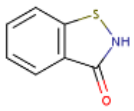
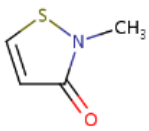
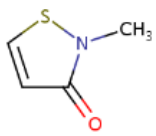
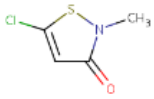
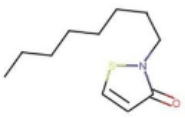
We have the following additions to support the proposed classification:

Skin sensitisation sub-categorisation

In addition to the data cited by the DS,[2]a number of independent studies or reviews have shown that BIT is a markedly weaker skin sensitizer than other isothiazolinones. This includes

- (Basketter et al. 1999)- paper compared the skin sensitisation potential of similar isothiazolones and concluded that BIT is a markedly weaker skin sensitizer than other isothiazolones.
- The RAC, in their review of octylisothiazolinone (OIT), published a comparison of the LLNA EC3's obtained on various isothiazolones (Table 1). The comparison showed BIT was the least potent of the isothiazolinones reviewed with all EC3 values greater than 2.[3]

Table 1 - Comparison of skin sensitising properties of several isothiazolinones (taken from RAC, 2018)

	MBIT (CAS 2527-66-4)	BIT (CAS 2634-33-5)	MIT (CAS 2682-20-4)	CMIT/MIT (3:1) (CAS 55965-84-9)	OIT (CAS 26530-20-1)
Chemical structure				 	
LLNA	EC3 = 1.04 % EC3 = 0.69 %	EC3 = 2.3 % EC3 = 32.4 % EC3 = 4.8 % EC3 = 10.4 %	EC3 = 0.86 %	EC3 = 0.003 % EC3 = 0.007 %	EC3 = 0.46 % EC3 = 0.66 % EC3 = 0.24 %
Classification	Skin Sens. 1A	Skin Sens. 1	Skin Sens. 1A	Skin Sens. 1A	Skin Sens. 1A (this opinion)
HRIPT	9/45 (20 %) volunteers showed dermal sensitization at 500 ppm	5/58 (9 %) at 725 ppm aq., 0/54 (0 %) at 360 ppm aq	1/116 (0.9 %) volunteers at 400 ppm and 1/210 (0.5 %) at 500 ppm	–	0/103 subjects at 50 ppm (0.005 %) 1/222 (0.45 %) subjects at 100 ppm (0.01 %)
SCL	0.0015 %	0.05 %	0.0015 %	0.0015 %	0.0015 % (this opinion)

[2] CLH Report on BIT- https://echa.europa.eu/documents/10162/580644f7-c28b-f232-c560-206c24323469

[3] https://echa.europa.eu/documents/10162/4f2ebbc7-d814-f967-12bb-223c17b9aeec

Based on a weight of evidence when considering the data available to the Dossier Submitter and additional information, we agree with the proposed sub-categorisation for BIT (Skin sensitisation Category 1B).

Skin sensitisation SCL
Sherwin Williams agrees with the proposals of the Dossier Submitter that the SCL should be maintained at ≥ 0.05%.

When considering ECHA Guidance on the Application of CLP Criteria (Version 5.0 – July 2017), a skin sensitiser in Category 1B is considered to have 'moderate' potency (Table 3.9). and would have a generic concentration limit of 1 % (w/v) (Basketter et al., 2005). SCLs are generally required when there is adequate and reliable documentation showing that the specific hazard is evident below the Generic Concentration Level (GCL) for classification. In the case of BIT, setting the SCL at 0.05% (i.e., 20x lower than the standard GCL set for a moderate skin sensitiser) is expected to be conservative and protective of both workers, professionals and consumers who may use products containing BIT.

The Dossier Submitter identified a study, conducted over 10 years ago, that considered the presence of BIT in disposable PVC gloves on the Finnish market (Aalto-Korte, 2007). Reported cases from two clinics in 2006 were reviewed for any evidence of contact sensitisation. The study concluded that 20 ppm (0.002%) BIT seemed sufficient for sensitisation but only in a small, specific cohort of the population (dental workers) with pre-existing dermatitis.

In general agreement with the Dossier Submitter, this study is not considered adequate to assess the skin sensitising potential of BIT under the CLP Regulation for the following reasons:

- Diagnostic patch testing only measures the concentration of a sensitizer needed to elicit a sensitisation, not the level of the original exposure which caused sensitisation to be induced. The induction of BIT sensitisation in the participants in this study may not be the result of exposure to BIT from the PVC gloves.
- Guidance on the CLP states that an SCL should not be based on a mixture containing the chemical substance.
- The dental professionals exposed to the BIT containing gloves had pre-existing dermatitis which may have compromised the integrity of the skin.
- The professionals responding to BIT were not assessed for atopy.
- Dermal exposure from gloves is a worst-case scenario combining occluded, prolonged (multiple hours per day) and repeated, daily workplace exposures.

A more recent study looked at concomitant reactivity to MIT, BIT and OIT recorded in the Information Network of Departments of Dermatology (IVDK) datasets between 2009 and 2013 (Geier et al. 2015). The data series contained cohorts from metal working fluid industries (where BIT, MIT and OIT is used), preservative industries (where BIT and MIT are used) and industrial biocides (where BIT and OIT are used). The patients would have been those with existing contact dermatitis.

Patch tests results for all three biocides) were summarised as per Table 2. The results showed 97% of the tests for BIT were negative, indicating that a low number of patients who potentially work

with BIT, were sensitized(the patch testing documents elicitation, which is an indicator of previous sensitisation).

Although this information itself is tenuous for deriving a SCL (which is primarily based on induction potential) the study documents a relatively low prevalence of contact sensitisation in a population including cohorts who are likely to come into contact with BIT. It also acts as a primary source of clinical information on the occurrence of skin sensitisation as mentioned in the ECHA Guidance on the Application of CLP Criteria.

The data also shows that MIT had a higher percentage of positive responses compared with BIT. OIT had a similar response rate to BIT but a much smaller cohort was available in comparison (less than half),and did not include preservative industry workers that may handle higher concentrations of biocide.

Table 2 - Patch test reactions to BIT (0.1% pet.), MIT (0.05% aq.) and OIT (0.025% pet.). (Adapted from Geier et al. 2015).

	BIT		MIT		OIT	
Response	n	%	n	%	N	%
Negative	8465	97.0	36664	94.6	4129	98.0
Doubtful (?)	91	1.0	239	0.6	28	0.7
+	112	1.3	956	2.5	26	0.
++	25	0.3	629	1.6	16	0.4
+++	4	0.0	186	0.5	0	0.0
Irritant reaction	31	0.4	88	0.2	14	0.3
Total	8728	100.0	38762	100.0	4213	100.0
Positive (+, ++, +++)	141	1.6	1771	4.6	42	1.0

Conclusion

Based on the available data on the skin sensitisation potential of BIT, the commenter agrees with the Dossier Submitter that the SCL should be retained at ≥ 0.05% and should be evaluated distinctly from the other isothiazolinones. Evidence of a causal relationship between BIT exposure and skin sensitisation at these concentrations is equivocal at best and does not support the kind of strict limitations that were implemented for other isothiazolones under the CLP and BPR. Creating roadblocks to the use of water-based paints will not support Europe's initiatives to reduce the use of solvents and volatile organic compounds.

References:

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