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EPDLA comments concerning the proposed harmonized classification and labelling of 1,2-benzisothiazolin-3-one

The European Polymer Dispersion and Latex Association (EPDLA), a CEFIC sector group, welcomes the opportunity to comment on the proposed harmonized classification and labelling of 1,2-benzisothiazolin-3-one (BIT), and in particular with regards to the dermal sensitization hazard endpoint and the proposed Specific Concentration Limit (SCL).

Introduction

Polymer dispersions are used in a myriad of industrial and consumer applications including adhesives, paints, coatings, paper and board manufacture and many others. In our applications, the use of preservatives is vital to ensure product stability, prevent microbial contamination during storage, maintain product performance thereby reducing waste and have allowed for the substitution of solvent based formulations and thus enabled a move towards safer, more environmentally friendly technologies.

BIT is a highly effective and important preservative used in water-based formulations such as polymer dispersions. It is highly compatible with different matrices, stable across a range of pH, and demonstrates excellent efficacy against a wide range of microorganisms. Due to the current limited availability of suitable alternatives [1], [2] BIT is an increasingly important biocide in our and our customer's applications.

Since biocides are designed to target and interact with biological matrices, they are often associated with inherent but manageable toxicities. With isothiazolinones biocides the primary hazards of concern are local, point-of-contact toxicity, such as irritation/corrosion as well as sensitisation following dermal exposure.

Having reviewed the dossier submitted by the Spanish Competent Authority, the EPDLA would like to express its support for the current proposed classification of BIT as a dermal sensitizer and specifically the proposed maintenance of the current SCL for dermal sensitization of 500ppm. We would however like the Committee to take into consideration our comments listed below:

1) BIT should not be considered equivalent to other isothiazolinones

Under the BPR review programme, significant substance specific data has been submitted to support the evaluation of BIT. Substance specific data is the only reliable data to assess intrinsic hazard i.e. that with which CLP is concerned since effects can be directly attributed to the substance under study.

In the evaluation of Sodium Pyrithione, the evaluating Member State, (Sweden) noted that despite structural similarities with Zinc Pyrithione and Copper Pyrithione it was considered inappropriate to use

[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)).

[2] Dr. Christof Walter (VdL): Vermarktung und Verwendung von Farben und Lacken im Spannungsfeld zwischen CLP Einstufung, Biozid-Wirkstoffverfahren und Arbeitsschutz; BAuA Informations- und Dialogveranstaltung 25. Februar 2021.

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grouping or read-across due to its distinct physicochemical and toxicological properties, a position noted by the RAC in its subsequent CLH opinion.

When comparing, the information provided in the CLH dossiers for BIT and the other isothiazolinones, it is clear that BIT has distinct physicochemical properties, e.g. much lower vapour pressure compared to CMIT/MIT or MIT. The toxicological properties are somewhat distinct in that the irritant nature of BIT appears much less apparent compared to other isothiazolinones, which in turn translates into oral LD50 values an order of magnitude higher than CMIT/MIT or MIT and a lack of positive skin irritation responses in animal studies. Furthermore, skin penetration studies indicate BIT is much less bioavailable via this route (ca. 25% vs >70%) and positive responses in animal models for dermal sensitization are only achieved at much higher concentrations than for other isothioazolinones indicating it is of significantly lesser potency.

Taken together this information indicates that BIT should be assessed as a stand-alone substance and read across to other structurally similar molecules is not warranted and not necessary given the extensive data that exists.

2) The prevalence of contact allergy associated with BIT exposure is not significant

The clinical prevalence of contact allergy is not significant compared to other isothiazolinones, indeed whilst there are case reports of allergic contact dermatitis reported in the literature, these are significantly fewer than for other members of this biocide family. This indicates that the current use levels and labelling limits are protective of the vast majority of the population and there is no significant public health concern despite the widespread use of BIT in industrial and consumer applications.

Frequency of positive tested occupational dermatitis patients, 2007-2016 (own table, based on IVDK 2020)[3]:

Contact allergen	Percentage of OD patients from the occupational group of Painters, Varnishers and related workers with positive reaction to the allergen	Percentage of OD patients from all occupational groups with positive reaction to the allergen
Epoxy resins	10.2%	3.7%
Methylisothiazolinone (MIT)	7.0%	6.9%
Methylchloroisothiazolinone / Methylisothiazolinone (MCIT/MIT)	5.2%	5.8%
Benzisothiazolinone (BIT)	-	-
Octyl isothiazolione	-	1.3%
Propolis	1.2%	2.5%
Formaldehyde	0.9%	1.9%
Quaternium 15	-	1.0%

It should be noted that clinical monitoring data and case reports are not suitable for setting substance specific SCLs since it is not possible to accurately quantify the exposure of any individual which subsequently lead to the acquisition of allergic contact dermatitis. ECHA guidance on the application of the

[3] As indicated in Footnote #1 above: 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)).

CLP criteria states that SCLs should never be set on the basis of testing of a mixture and logic follows that individuals reporting to clinics will have been prior exposed to products containing BIT rather than BIT alone. In the context of CLP, the clinical data is therefore best used for hazard identification and category assignment (e.g. 1A, 1 or 1B).

Having noted the above however, the clinical data do give a real-world indication of the already protective effect of a labelling limit of 500ppm and setting lower limits would not necessarily result in greater protection for workers and consumers. It is worth noting this already applied limit is further reinforced by the elicitation labelling limit set at 1/10th the SCL, which allows for products to be clearly labelled as containing BIT and permits those few individuals who are susceptible to adverse responses to make informed choices to avoid such products.

To the best of the knowledge of the EPDLA member companies, the use of BIT in dispersions has never led to increasing cases of sensitizations.

3) Individuals sensitized to other isothiazolinones do not cross-react to BIT

In addition to point 2 noted above, there is also significant recent clinical information reported in the literature to indicate that cross-reactivity does not occur between BIT and the other isothiazolinones, that is to say that individuals with primary allergic contact dermatitis caused by other isothiazolinones e.g. CMIT/MIT or MIT will not have a re-emergence of their skin allergy following subsequent exposure to products containing BIT. This is significant for 2 reasons:

- It further demonstrates, in real-world use, a difference in hazard profile of BIT versus other isothiazolinones
- Setting a more restrictive labelling limit is not necessary to protect potentially sensitive subpopulations

It has been noted that a significant population exists which is already sensitized to MIT, primarily following its use in cosmetic applications. Whilst the prevalence of positive responses is declining for MIT, the lack of widespread reports of allergic contact dermatitis caused by subsequent BIT exposure indicates that this allergic subpopulation is not significantly at risk and therefore it doesn't warrant setting more restrictive labelling limits for BIT in order to protect these individuals.

Conclusion

For the reasons outlined above, the EPDLA supports the proposal of the dossier submitter to maintain the current SCL of 500ppm for BIT since further reductions in the labelling limit would not result in greater public protection but would place downstream users under significant regulatory burden when placing safe products on the market.

BIT should be evaluated distinctly from the other isothiazolinones, since considerable substance specific data exists which permits the Committee to do so. Whilst any report of allergic contact dermatitis is concerning, the societal benefits of the continued use of BIT are considerable and all available toxicological and clinical information indicates the current classification and labelling of BIT for the hazard of dermal sensitization are protective of the very vast majority of European population.

Disclaimer

- The present position paper has been developed by EPDLA members in good faith, to the best of its knowledge and following the latest scientific evidence.
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- EPDLA commits to update this document in view of any new relevant available information.

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About EPDLA

EPDLA (European Polymer Dispersion and Latex Association), a Cefic Sector Group founded in 1991, is dedicated to promote the safe manufacture, transportation, distribution, handling and use of waterborne polymer dispersions, in compliance with regulatory requirements and industry guidelines. EPDLA members are committed to Responsible Care® principles and have implemented risk management according to the precautionary principles.