science summary

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Calculation of Molecular Dimensions Related to Indicators for Low Bioaccumulation Potential

Science Summary

Researchers at the Building Research Establishment and Liverpool John Moores University have carried out a study in which they compare several computer software products that can calculate the size and shape of a wide range of molecules. The aim was to investigate which methods might be used to indicate whether a chemical could be expected to have a low potential for bioaccumulation in the environment. The findings will help to inform future revisions of the guidance documentation for the REACH Regulation.

The authors report and compare the performance of several molecular modelling software packages (OASIS, MOE, TSAR, Mol2Mol and SPARTAN) using a set of 69 compounds that represent a broad range of sizes and shapes. They discuss how the output from different packages should be interpreted and their relevance to bioaccumulation potential.

The authors found that some molecular dimension descriptors correlate well across the packages, but generally there is considerable variation between methods. They point out that there is no practical means to identify which of these methods is “correct” because the actual dimensions of the molecules are not known. The study also highlights the importance of molecular conformation (shape) and flexibility in the calculation of molecular dimensions. There are no particular reasons to select any specific molecular conformation for analysis. Instead, the authors suggest that the minimum value from a range of conformations should be chosen, within acceptable limits (i.e., excluding high energy conformers). They acknowledge that an average value may prove more realistic.

The authors conclude that molecular dimensions are a good indicator of a chemical’s potential for bioaccumulation. Amongst a list of recommendations, they state that better standardisation and cross-referencing between models is essential to ensure that decisions are based on comparable results. However, they recommend the descriptors ‘maximum diameter’ and ‘maximum cross-sectional diameter’ as currently the most useful, and these can be readily calculated by the OASIS software.

The authors consider that ‘maximum molecular length’ is a potentially useful indicator, because it is a simple and fundamental molecular property. However, they recommend that the current criteria should be revised using a broad group of test compounds. The current indicator does not appear to have been calculated from a computational or molecular modelling approach. Consequently, it is not possible to directly relate this indicator to any of the outputs from the modelling tools and this makes it difficult to use.

This summary relates to information reported in detail in the following output(s):

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