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Shouldn't enantiomeric purity be included in the 'minimum information about a bioactive entity? Response from the MIABE group

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We thank Professor Lentini for his comments on our article (Minimum information about a bioactive entity (MIABE). *Nature Rev. Drug Discov.* **10**, 661–669 (2011))[1] proposing guidelines for the minimum information about a bioactive entity (MIABE). In principle, the authors of the document agree that enantiomeric purity would be useful to include in the MIABE guidelines, and this could be added as an extension; it was always our intention that the MIABE document would be discussed and developed accordingly, rather than be a closed book. However, a few issues arose when enantiomeric purity was discussed during the preparation of the initial guidelines, and these have yet to be fully resolved, which led to its omission.

There are several general aspects of an impure compound (and we would regard an incompletely resolved compound as impure): first, we may not know precisely what is in the sample; second, there may be more than one potentially active compound in the sample; third, others repeating the experiment with different samples will probably have problems of reproducibility. However, it is more valuable for someone to acknowledge that their sample is known to be impure than to pretend it is pure, so a flag indicating this is important. Enantiomeric mixtures are one of the harder types of compound mixtures to separate, but they are not fundamentally different from other mixtures in terms of their representation. For a pure single enantiomer, the International Union of Pure and Applied Chemistry (IUPAC) International Chemical Identifier (InChI) string and/or other IUPAC names would be sufficient to describe the stereochemistry. For a compound that exists in two enantiomeric forms, the additional information on the relative amounts in a given sample for which biological data are being reported needs to be specified if it can be, and has been, measured. There are two well-defined entities that InChI can describe: a single enantiomer and a racemate. Both are pure compounds. However, a sample with an enantiomeric excess is impure and should be treated in the same way as, for example, a mixture of unseparated *cis-trans* isomers, a mixture of compounds with partial or variable substitution or a mixture of anomers.

In conclusion, we feel more work needs to be done on extending the controlled vocabulary to fully describe the various types of compound mixtures noted above. Enantiomeric purity could then be added to the next revision of the MIABE guidelines.

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doi:10.1038/nrd3503-c2

1. Orchard, S. *et al.* Minimum information about a bioactive entity (MIABE). *Nature Rev. Drug Discov.* **10**, 661–669 (2011).