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Editorial

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Greener Writing: Higher-Quality Content and Fewer Wasted Words

Over the past 15 years or so I have come across a range of terms that are used commonly and, in my opinion, quite loosely. Terms such as amorphous, crystalline, purity, yield, precipitation, crystallisation, etc. All terms that are commonplace in the chemical literature and embedded within the technical reports we write for clients, regulators, or our employers. So what's the problem? For me the problem is the lack of consistency with which terms are used, failure to select and apply the correct term in association with the intended meaning, and consequent failure for a given document or part thereof to convey the true meaning to the reader without recourse to several readings of the passage or perhaps contacting the author.

Let us start with something simple, percentages and the items with which they are associated. First, there is yield. In general when we see a percentage yield written down, we assume this to be the percentage of theoretical yield based on the molar input and actual output as calculated against the maximum possible output if all starting material molecules were converted to product molecules and all product was recovered. This is fine. However, confusion starts to creep in when we see yields corrected for input purity or for output purity or for both input and output purity or for recovered starting material. All that is needed is for authors to be explicit. Next, there are weight/weight (or mass/mass) yields which are calculated on the basis of output product mass versus the input mass of a nominated starting material. This is a really useful number when calculating raw materials requirements; for instance for a manufacturing campaign it is especially helpful for scaling up or down and thus is often used by production managers or planners. I would ask that we all ensure that it is clear what is being reported, and again, has it been subject to correction for purities of input and/or output materials? In addition, be prepared to give occasional tutorials when asked by visitors how you managed to get over 100% yield when using mass/mass!

Now we have purities (and impurities). Are the numbers for normalised area purity from HPLC or GC, for instance, or for absolute assay purity? Perhaps solvents have been calculated from a proton NMR spectrum and are in fact molar percentages? Having established that, perhaps we are talking about weight/weight assay purity, we then need to dig more deeply and check if these data are 'as is' or have been corrected for water content, solvent content, etc.

The issues of yield and purities have often cropped up when I've been involved in technology transfer, whether between departments in the same organisation or when at a CRO and trying to transfer in a client's chemistry. The failure to apparently be able to repeat a piece of work can sometimes come down to a failure to report on the same basis—the song 'I say tomato, you say tomato' comes to mind!

Now, here are far trickier subjects: precipitation, crystallisation, crystalline, and amorphous—terms commonly (and often randomly!) applied which can have significant meaning, especially when reporting the final active pharmaceutical ingredient (API).

First, take precipitation and crystallisation. This is not as straightforward as it might at first appear. Tung, Paul, Midler, and McCauley[1] indicate that the process of reactive crystallisation is also known as precipitation but then go on to say that the term reactive crystallisation is generally applied only when the product is crystalline. If the product is amorphous or a mixture of amorphous and crystalline forms, then the term precipitation applies. Davey and Garside,[2] on the other hand, discuss particle size, commenting that crystals can be almost any size from a few nanometres to several millimetres; traditionally, when crystals are less than a few micrometres in size, the term precipitation is used. For most of us, I suspect that we think in terms of the speed with which a solid was formed and deposited from solution, with precipitation usually being 'fast'—but what is fast, and so it goes on.

I ask that chemists and engineers aim to be more precise in the terms applied and suggest that, unless it is obvious or the process is known to provide crystalline product, then the term precipitation is universally adopted for a reactive crystallisation such as salt formations that result in essentially immediate depositions of solids, and for all other cases simply state that solid was deposited, harvested, etc. Adopting this simple distinction can avoid the forward progression of what may have been a 'throw-away' comment in a laboratory book about the 'isolation of crystalline solid' into a legal battle in 15 years' time over solid state and patent validity!

So what about an amorphous solid versus a crystalline solid? Much as above, unless you know the solid product to be crystalline either by analysis or by virtue of the known process of isolation, avoid using either term—simply state 'solid product' was isolated etc. From a patent viewpoint, only factual data should be recorded; unless there is analytical data to confirm crystallinity, this is conjecture only, albeit educated conjecture.

To conclude, I am asking chemists to consider carefully what you record in your experimental notebooks (whether electronic or pen and paper); then you should think very carefully again when laboratory effort is converted into reports which will be used by others—the true legacy of your work. Next, I urge managers of these activities to be extremely diligent in their daily dealings with chemists to ensure that the rigor of communication is applied to the spoken word as well as the written word; therefore, exacting standards can be applied and used universally to ensure a scientific generation that clearly and accurately articulates experimental methods and outcomes for the benefit of others. This is a simple request made against the tide of diminishing communication skills as the world spirals downwards into 'tweets', 'texts', and e-mails devoid of any punctuation at all!

John Knight

Scientific Update, Maycroft Place, Stone Cross, Mayfield, East Sussex TN20 6EW, United Kingdom

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AUTHOR INFORMATION

Corresponding Author
john@scientificupdate.co.uk

Notes
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REFERENCES

(1) Tung, H.-H.; Paul, E. L.; Midler, M.; McCauley, J. A. *Crystallization of Organic Compounds: An Industrial Perspective*; John Wiley and Sons: Hoboken, NJ, 2009; Chapter 10, p 207.
(2) Davey, R.; Garside, J. *From Molecules to Crystallizers: An Introduction to Crystallization*; Oxford University Press: Oxford, 2000; Chapter 1, p 1.