amc technical brief

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What should be done with results below the detection limit? Mentioning the unmentionable

What we should do when results of analytical measurements fall below the detection limit has long been a source of puzzlement. In fact the idea of a detection limit itself is puzzling: why else should we spend so much effort trying to define it once and for all, but never quite succeed! The common perception of detection limit as a kind of event horizon around a black hole, from which information cannot possibly emerge, is partly to blame for this difficulty.

Measuring zero

We tend to think that we should be working well above the detection limit if we are trying to make sensible measurements. That is a correct attitude in so far as it can be accomplished, but it simply ignores an obvious fact of life: many analytical scientists, unlike most other metrologists, are called on to measure concentrations that have a true value of zero. Let's consider an example: the concentration of a banned synthetic growth promoter in a sample of pig's liver. The true answer could be exactly zero, unless the pig has been given the substance illegally. Under these circumstances, and many others less extreme, we will encounter results that fall below the detection limit. Moreover, the problem of trying to measure zero will not go away with improved technology. How can we refine our ideas about reporting such results, and advise end-users of our data how to interpret them?

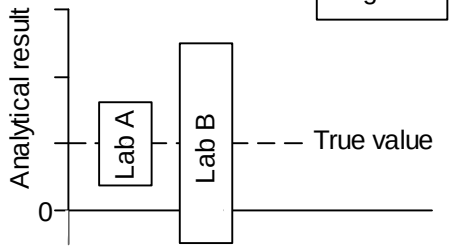
Reporting low concentrations

In the absence of a definitive answer, most of us have settled for reporting results below a detection limit c_L in one of the following possible ways.

- Not detected
- Less than c_L
- A value of zero
- An arbitrary fraction of c_L, e.g., $c_L/2$
- The result found, with a statement of its uncertainty.

Which of these is best? Clearly 'not detected' is the worst, as it contains hardly any information. A typical problem with 'not detected' is that of obtaining confirmatory results from a second laboratory. Suppose Laboratory A has the best available technology for the job in hand, with a detection limit of $c_{L,A}$, and detects a prohibited substance in the test material. Laboratory B, with older instrumentation and a higher detection limit $c_{L,B}$, tries to confirm the result but fails to detect the analyte. In Fig 1 the bars indicate the extended uncertainties around the two results.

Figure 1



In these circumstances, the result is not confirmed so no enforcement action can be taken. This is not theoretical nicety: it actually happens.

'Less than c_L' is next worst, for several reasons. First, it cannot be incorporated into a simple statistical appraisal, like calculating a mean. So it has to be left out of the calculations, which means that descriptive statistics are going to be biased by leaving out the very low values. 'Less than c_L' does slightly better on the Laboratory A/Laboratory B problem, because we could say that the unknown concentration *c* was probably bounded by $c_{L,A} < c < c_{L,B}$, although that does not help us in the confirmatory situation.

Setting the 'less than' values to a replacement value c_R, where $0 \le c_R < c_L$, is a better option than the above but not perfect because we simply have no idea which part of the range is correct. That may not matter if the 'less than' numbers are in a small minority, but if they are in a majority our choice may end up being misleading.

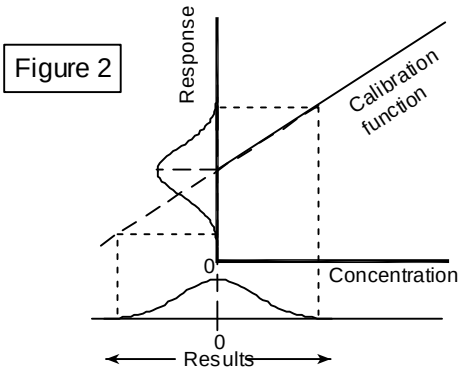
Reporting the value found, accompanied by its uncertainty, is clearly the best method of reporting because it provides the most information. Any of the other methods of reporting could be derived from such a result. (We have to bend slightly the ISO definition of uncertainty to do this, to allow the extended uncertainty to reach below zero. This does not detract from the main argument.)

Negative results

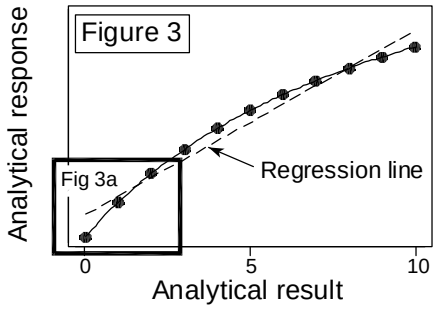
Some results are even more embarrassing than those simply falling below detection limit: they fall below

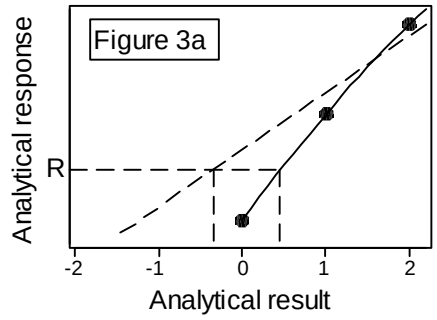
zero. Concentrations by definition can only be zero or greater, but we must remember that *analytical results are not concentrations but error-prone estimates of concentrations*.

Imagine a typical situation: we have a linear calibration and an unbounded analytical response, which is the usual case. In repeated measurements at zero concentration about half of the responses will be above the average and half below the average. Those below the average, when mapped onto the concentration axis, will give rise to negative results (Fig. 2). This effect is caused by random variations.



Systematic effects can also give rise to negative results. For example, over-correcting of interference effects is sometimes encountered in the determination of elements by atomic spectrometry and is one cause of the problem. Another common cause is lack of fit at the low end in a estimated calibration function (Fig. 3).





In this Figure, the solid line represents the true calibration function, while the broken line is the linear regression line. At a low concentration, which provides a response *R*, the fitted line provides a negative result.

What should we do when such negative results turn up? And they do turn up unless we censor them. If we convert negative values to zero, two things happen: we bias the mean result upwards, and we reduce the variance. Both of these effects could mislead us into thinking that analyte was present when it was not. From a scientific point of view, negative results should be left alone.

Reporting results - recommendations

The AMC recommends[1] that a distinction should be made between *recording* results and *reporting* results. From a strictly scientific point of view we should record results just as they come, including results below detection limit and negative results. We should also produce an estimate of the uncertainty, to put the results in context. We can then use such results for any statistical analyses that we are proposing to carry out, without any fear of introducing bias through our data recording practices. This is feasible in a context such as analytical quality control, where the results are internal to the laboratory producing them.

In contrast, it is hardly ever appropriate to report negative results to customers. The AMC recommends that the method of reporting should be a contractual matter between the analyst and the customer. However, the analyst should provide the customer with a statement of the method of editing negative values and results below the detection limit, along with the uncertainty of measurement. Further, the unedited results should also be retained in case they are needed for statistical analysis or an application not previously envisaged.

Reference

1. AMC, *Analyst*, 2001, **126**, 256-259.