Mass or molar units? Australia’s drug problem persists

To the Editor,

Lack of standardisation of reporting units among laboratories increases the risk that results will be misinterpreted by clinicians. A major risk in the context of therapeutic drug reporting is failure to identify toxicity when different units are used for laboratory results and the clinical decision tools used to interpret them, such as nomograms for paracetamol. Delayed diagnosis of toxicity has been anecdotally reported due to clinician confusion over reporting units and the decision limits indicating toxicity.

Although the units used to report most biochemistry analytes by Australian laboratories are well standardised, the units used to report therapeutic drug concentrations have previously been found to be inconsistent. In 2007, it was reported that mass and molar units were both in frequent use within Australia for commonly requested drugs.

The variation in reporting units was recognised as an unnecessary source of clinical risk. In response, a recommendation was published in 2013 that, with only isolated exceptions, Australian and New Zealand laboratories should report therapeutic drug concentrations in mass units. The recommendation was endorsed by multiple professional bodies, including the Royal College of Pathologists of Australasia (RCPA).

This study used data from the RCPA Quality Assurance Programs (RCPAQAP) to examine whether laboratories have adopted the recommendation. The RCPAQAP General Serum Chemistry program allows participants to enter drug results in either mass or molar units. These units are likely to be the same as those used for patient results because reporting in the same units avoids unit conversion calculations and, moreover, participants are instructed to treat RCPAQAP samples in an identical manner to patient specimens.

The reporting units used by participants for a sample in Survey 10 of the program, CP-GC-22-19, were examined. To avoid data entry errors influencing findings, the units entered by each participant were compared to those used for a sample in Survey 1, CP-GC-22-01. If these units were not identical for any participant, then all submissions they made for the drug during 2022 were reviewed to determine the correct units.

Reporting units used by laboratories in Australia and New Zealand were assessed separately and compared to those used in 2007. The reporting units employed within each Australian state and territory were also evaluated. This was done because the risk of clinical error is likely to be highest in regions with the poorest local standardisation. A total of 1672 therapeutic drug results were submitted for sample CP-GC-22-19, comprised of 1457 (86.3%) results from Australian laboratories and 215 (12.7%) results from New Zealand laboratories. Thirty-nine (2.3%) results were excluded because they were submitted by laboratories located in other countries. Five data entry errors were identified and corrected.

The units being reported by Australian and New Zealand laboratories are shown in Table 1. Except for the antibiotics, gentamicin and vancomycin, there was significant inconsistency in the use of mass and molar units for drug reporting by Australian laboratories. In New Zealand, all laboratories used molar units for the non-antibiotic drugs. Mass units were used universally for gentamicin and vancomycin by all participating laboratories in both Australia and New Zealand.

The use of mass units has increased in Australia since the recommendations for therapeutic drug reporting were published. For a single sample in the 2007 General Serum Chemistry program, the RCPAQAP received 1116 result submissions for non-antibiotic drugs from Australian laboratories, of which 377 (33.8%) were in mass units.

In 2022, the RCPAQAP received 1013 such submissions, 648 (64.0%) of which were in mass units, a statistically significant increase ($p<0.01$). The proportion of results submitted in mass units for each drug in 2007 and 2022 are shown in Fig. 1. Also illustrated in this figure is the finding that gentamicin and vancomycin reporting improved from near-complete standardisation in mass units in 2007 (96.6% and 95.7%, respectively) to universal reporting in mass units (100.0% for both drugs) in 2022.

The reporting patterns within the Australian states and territories are summarised in Fig. 2, which reveals that the inconsistency in units can be attributed to both intrastate and interstate variation. Notably, both mass and molar units are used to report non-antibiotic drugs in Victoria, New South Wales and, to a lesser extent, the ACT. Molar units are used by all South Australian and Tasmania laboratories for non-antibiotic drugs, while mass units are used to report all drugs in the Northern Territory, Queensland and Western Australia.

While the 2013 recommendation regarding drug reporting units’ appears to have contributed to a general increase in the use of mass units by Australian laboratories, this study highlights that clinical risk from variation in reporting units persists. The inconsistency of reporting units in Victoria, New South Wales and ACT is of most concern. In these regions, standardisation would be improved by non-complying laboratories adopting the recommendation. Therefore, prompt action from these laboratories is encouraged. However, in doing so, it should also be acknowledged that a temporary period of heightened clinical risk occurs when individual laboratories change reporting units. Several steps can be considered to mitigate this risk. Well in advance of the change, education of all relevant stakeholders may commence regarding the nature of the change and its timing. Once implemented, report comments could highlight that the change has occurred and direct users to sources of further information. Additionally, clinicians need to be able to compare patient results reported prior to, and following, the change. This could be done by temporary dual reporting of units but might be better achieved by providing unit conversion factors on reports.

Laboratories in South Australia and Tasmania were found to be using molar units universally for the non-antibiotic drugs. While inconsistent with the 2013 recommendations,
this finding is associated with a lower clinical risk than the results from Victoria, New South Wales and ACT, due to state-wide standardisation. In these regions, individual laboratories adopting recommended units would worsen, rather than improve clinical risk. Instead, state-wide coordination would be necessary. Firstly, it would need to be decided, among representatives from both public and private laboratories and relevant clinical groups, whether there was a desire to proceed with adopting mass units. If so, state-wide coordination of risk mitigation steps and the timing of the change would be beneficial.

A limitation of the study was that it did not involve all drugs measured in laboratories in Australia and New Zealand for which the RCPAQAP receives results, such as those in the Anti-Fungals and Immunosuppressants programs. Nevertheless, laboratories are encouraged to review whether the units they use to report these drugs comply with recommendations. Further, the study does not examine unit reporting practices in other areas of laboratory medicine that may benefit from standardisation, such as trace elements.

In summary, some common therapeutic drugs are being reported in different units by laboratories in Australia. Clinical risk from this practice was highlighted and led to the publication of recommendations a decade ago, yet standardisation has not been reached. The use of both mass and molar units by laboratories in Victoria, New South Wales and ACT is of most concern. It is hoped that laboratories in these regions can act swiftly to adopt recommendations and reduce the risk of clinical errors.

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