

Welfare breach prompts *Nature* to update policy on publishing animal experiments

US-based team withdraws data and admits mouse tumours were allowed to grow too large.

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16 September 2015 | Clarified: [22 October 2015](#)

The journal *Nature* is publishing a correction to a study in which mouse tumours were allowed to grow too large — and says that in future it will require more information from scientists who report experiments on animals. But the scientist who first raised the problem says that the paper should be retracted.

In the paper¹, published in 2011, a team based at Massachusetts General Hospital and Harvard Medical School, and the Broad Institute in Massachusetts reported that a small molecule called piperlongumine could selectively kill cancer cells in mice.

According to the *Nature* correction², the experiments allowed tumours in some of the mice to grow to larger than an allowed maximum diameter of 1.5 centimetres — a stipulation that formed part of animal-welfare guidelines set for the work by the Institutional Animal Care and Use Committee (IACUC) of Massachusetts General Hospital.

That could have caused the mice to experience more suffering than allowed for, and represents a “breach of experimental protocol”, says a *Nature* Editorial on the issue³.

“As a result of this case, we are increasing the amount of information we request from authors. In experiments in which tumours are grown, we now require authors to include the maximal tumour size permitted by the institutional animal-use committee, and to state that this was not exceeded,” says the Editorial.

Correction argument

Some data in the paper that came from mice for which the rules were breached are being withdrawn, although the conclusions of the study remain valid, says the journal. (*Nature's* news team is editorially independent of its research editorial team.)

But David Vaux, who studies cell death at the Walter and Eliza Hall Institute of Medical Research in Melbourne, Australia, and raised concerns about the paper with *Nature*, says that the paper should be retracted. He says that by publishing the study and not retracting it, the journal is “giving tacit approval” to breaches of animal-welfare rules.

Vaux says that he was initially confused by some of the statistics in the paper. After he raised his concerns, a corrigendum was published in 2012 detailing errors in the reporting of tumour data and replacing a picture in the original paper with a new photograph of some of the mice used⁴. It was at this point, says Vaux, that he suspected the tumours were larger than should have been permitted.

“No animal ethics committee anywhere in the world would allow tumours the size of these ones,” Vaux says.

Standards on acceptable tumour sizes differ in institutions around the world. Guidelines from a UK group published in 2010 recommend mean diameters should not normally exceed 1.2 centimetres in mice — although this maximum increases to 1.5 centimetres for therapeutic trials⁵. US institutional guidelines often recommend 2 centimetres as a maximum size.

Vaux posted some of his concerns on the website PubPeer — as did Morten Oksvold, a cancer researcher at the Oslo University Hospital Institute for Cancer Research. Oksvold said in an e-mail to *Nature* that violation of welfare rules should lead to a retraction and an investigation by the institution concerned. The correction states that the IACUC has reviewed all the data now presented in the paper, and that “corrective measures have since been taken to avoid any irregularities happening again”.

Oksvold says that he has seen “many cases where mice suffer with all-too-large tumour sizes in scientific publications, many of them in high-impact journals”, and that he is surprised that such cases slip through the peer-reviewing system.

Asked to comment, *Nature* said: “We take all issues related to animal welfare and ethical animal research very seriously. If we become

aware of any breach of our editorial policies in any published *Nature* paper, we would look into it very carefully."

The research team was led by Anna Mandinova, Stuart Schreiber and Sam Lee, from whom *Nature's* news team has requested comment. In the correction, the researchers write: "Although the scientific conclusions of the original paper stand, we would like to apologize for the numerous inaccuracies in reporting our data, and for the breach of animal welfare guidelines in some of the original data."

Nature | doi:10.1038/nature.2015.18384

Clarifications

Clarified: The mean diameters for tumours of 1.2 cm given in the UK guidelines can be exceeded in therapeutic trials, where the maximum is recommended to be 1.5 cm. The text has been updated to make this clear.

References

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2. Raj, L. *et al. Nature* <http://dx.doi.org/10.1038/nature15370> (2015).
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4. Raj, L. *et al. Nature* **481**, 534 (2012).
5. Workman, P. *et al. Br. J. Cancer* **102**, 1555–1577 (2010).