



Scientific validity of animal experiments in Switzerland

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Key words

Scientific validity, reproducibility, bias, authorization, multi-laboratory studies, online survey, meta-analysis

Aim of the study

This study aimed to assess the scientific validity of animal experiments conducted in Switzerland. To this end, we evaluated applications for animal experiments (Form A) and publications derived from these experiments for indicators of internal validity (measures to avoid risks of bias) and external validity (features of experimental design aimed to increase generalizability). In addition, we conducted a survey among animal researchers to assess how they design and conduct their experiments, and how they report this in publications, as a basis for interpreting the results assessed from applications and publications in terms of the true validity of the research. Furthermore, we assessed whether multi-laboratory designs improve the reproducibility of results.

Material and methods

A sample of 1277 applications (Form A) and 50 publications derived thereof were evaluated for the rate of reporting of the seven most relevant measures against risks of bias (including blinded outcome assessment, randomization, and sample size calculation) and how such reporting varied depending on study characteristics such as animal species, degree of severity, research institution, authorizing canton etc. To facilitate interpretation of these results, we further conducted an online survey among all registered active animal researchers in Switzerland ($n=1891$, of which 28% ($n=530$) returned partially completed and 16% ($n=302$) fully completed surveys) about their awareness of potential risks of bias, and their knowledge of measures against these risks. In addition, personal interviews were conducted with senior scientists to facilitate interpretation of the survey. The reproducibility of multi-laboratory vs. single laboratory designs was assessed using computer simulation based on real data from single laboratory studies on the effect of hypothermia on lesion volume in animal models of stroke.

Results and significance

Reporting of measures against risks of bias was low for all seven measures with a mean score of 0.104 ($<1/7$ measures reported) for applications, and 0.162 for publications. Reporting in applications was not significantly affected by any of the study characteristics. Furthermore, endorsement of the reporting guidelines ARRIVE by journals had no effect on reporting rates in publications, while the journal impact factor was negatively correlated with reporting rates in publications. However, results from the online survey and the interviews indicated that Swiss animal researchers apply measures against risks of bias to a much greater extent than they report in applications and publications. While this indicates that estimates of scientific validity based on measures against risks of bias as reported in applications or publications may underestimate the true scientific validity of animal experiments considerably, our data also revealed a considerable lack of awareness of risks of bias and of knowledge to avoid these among Swiss researchers. Furthermore, we could show that multi-laboratory designs including as few as 3-4 laboratories improve the external validity and reproducibility of results considerably.

Taken together, our data demonstrate that the authorization of animal experiments in Switzerland is based on trust rather than evidence of scientific validity, and that there is a need to improve awareness of risks of bias and knowledge of measures to avoid them by targeted education for researchers as well as members of the authorities about experimental design and conduct, and scientific integrity. In addition, we propose to revise Form A to provide a better basis for the final harm-benefit analysis. Furthermore, our simulation study indicates that the external

validity and reproducibility of results can be increased considerably through multi-laboratory designs or other means of heterogenizing study populations.

Publications, posters and presentations

- Würbel, H. Power failure: Larger sample sizes fail to solve the reproducibility problem in animal research. 10th World Congress on Alternatives and Animal Use in the Life Sciences, Seattle, USA, 20.-24. August 2017.
- Würbel, H. More than 3Rs - The 3Vs to improve the validity and reproducibility of animal research. 10th World Congress on Alternatives and Animal Use in the Life Sciences, Seattle, USA, 20.-24. August 2017.
- Würbel, H. Wissenschaftliche Qualität von Tierversuchen: Erkenntnisse und Massnahmen. 10. STS Tierversuchstagung, Olten, Schweiz, 9. Mai 2017.
- Würbel, H. Evaluation of the scientific validity of animal experiments in Switzerland. SGV Meeting, Basel, Schweiz, 13.-14. September 2016.
- Würbel H.; Reichlin, T.S.; Voelkl, B.; Vogt, L. More than Refinement – improving the validity and reproducibility of animal research. 50th ISAE Congress, Edinburgh, U.K., 12. - 16. July 2016.
- Vogt, L.; Reichlin, T.S.; Voelk, B.; Würbel, H. Effect of multi-laboratory designs on the reproducibility of animal experiments – a meta-analytic approach. 13th FELASA Congress, Brussels, Belgium, 13. - 16. June 2016.
- Vogt, L.; Reichlin, T.S.; Würbel, H. (2015) Evaluation of the scientific validity of animal experiments in Switzerland. 19th European Congress on Alternatives to Animal Testing and 16th Annual Congress of EUSAAT, Linz, Austria, 20. - 23. September 2015, Altex Proceedings, Vol 4, No 2, p. 245.
- Reichlin, T.S.; Vogt, L.; Würbel, H. (2014) Study on the scientific validity of animal experiments in Switzerland. 9th World Congress on Alternatives and Animal Use in the Life Sciences, Prague, Czech Republic, 24. - 28. August 2014, Altex Proceedings, Vol 3, No1, p. 175.
- Voelkl B.; Vogt, L.; Sena, E.; Würbel, H. (in prep.) Multi-laboratory designs improve reproducibility of preclinical animal experiments. Submitted to various high-impact journals without success, currently under revision for Current Biology.
- Würbel, H. 2017. More than 3Rs: the importance of scientific validity for harm-benefit analysis of animal research. Lab Animal, 46 (4), 164-166.
- Vogt, L.; Reichlin, T.S.; Nathues, C.; Würbel, H. 2016. Authorization of animal experiments in Switzerland is based on confidence rather than evidence of scientific rigor. PLOS Biology, 14 (12), e2000598.
- Reichlin, T.S.; Vogt, L.; Würbel, H. 2016. The researchers' view - Survey on the design, conduct, and reporting of in vivo research. PLOS ONE, 11 (12), e0165999.

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