Human drug trials are compromised by poor reporting of animal research

April 5 2018

Poor animal study design and reporting thwarts the ethical review of proposed human drug trials. Credit: nosheep, Pixabay

Poor animal study design and reporting thwarts the ethical review of proposed human drug trials, according to a study led by researchers at Hannover Medical School, Germany, in cooperation with researchers from McGill University, Canada. The study, publishing 5 April in the open access journal *PLOS Biology*, analyzed the descriptions of animal studies found in "investigator brochures" - the documents used by regulatory authorities and ethics committees to assess the potential efficacy of drugs that are being tested in patients for the first time.

Independent assessments of animal evidence are key to ensuring that patients are not exposed to undue risk when volunteering in trials. Based on documents obtained from three prominent German medical research centers, the study authors recommend that regulators need to develop standards to ensure the rigorous design and reporting of preclinical animal studies when trials of new drugs are launched.

Strikingly, less than one-fifth of investigator brochures referenced animal studies that had been through a peer-reviewed publication process. Less than 20% of animal studies that tested the efficacy of the new drug described the use of simple techniques, like randomization blinding or sample size calculation, that can reduce the effects of bias. And worryingly, of the more than 700 animal studies that the authors found in the investigator brochures, only 4% did not show positive effects of treatment.

"Our analysis shows that the vast majority of these documents lack the information needed to systematically appraise the strength of evidence supporting trials," said Dr Daniel Strech, professor for bioethics at Hannover Medical School and senior author of the study.

"We were also struck by the rarity of 'negative' animal studies in investigator brochures", said Jonathan Kimmelman, professor for bioethics at McGill University and co-author. "With a median group size

of 8 animals, these studies had limited ability to measure treatment effects precisely. Chance alone should have resulted in more studies being negative- the imbalance strongly suggests publication bias" said Susanne Wieschowski, a postdoctoral fellow in Strech's team.

"Why do regulatory agencies and other bodies involved in risk-benefit assessment for early human research accept the current situation?" asks Daniel Strech. "Why do they not complain about the lack of information needed to critically appraise the rigor of the preclinical efficacy studies and about the concerning lack of efficacy studies demonstrating no effects?"

More information: Wieschowski S, Chin WWL, Federico C, Sievers S, Kimmelman J, Strech D (2018) Preclinical efficacy studies in investigator brochures: Do they enable risk-benefit assessment? *PLoS Biol* 16(4): e2004879. doi.org/10.1371/journal.pbio.2004879

Provided by Public Library of Science