Poorly conducted (or reported) animal tests put humans at risk

Sir — Animal clinical research paradigms are part of the mechanism for assessing the risks of new drugs to humans. To extrapolate the results to humans requires that animal experiments are designed adequately and conducted properly, with the methods fully reported. But these goals are often not met, either because collection of equivalent clinical parameters is held to be too difficult or time-consuming, or because of an effort to oversimplify complex biological systems in animals that are not identical or useful to the human paradigm[1–3]. This problem needs rectifying.

The sort of information that should be recorded and reported includes means and standard deviations for weight, electrolytes and glucose and the exact time of day of key treatments (including weekends). This would reveal whether such variables were kept constant throughout the experiment, and would show whether failures were due to failure of treatment or of support care.

Another area requiring more detailed reporting is that of pain detection and alleviation, which is not evident in publications of studies supported by the US Public Health Service (PHS). The PHS and the US Department of Agriculture require alleviation of pain in most animals, but this information isn't appearing in the methods sections of publications.

In order to provide information about the dynamic nature of the success or failure of treatment, clinical pathological data should be used, from tests such as complete blood count, clinical chemistries and organ profiles, carried out on living animals at specified times during a disease. Pathological data alone (from tests carried out after death, such as liver biopsies) are not adequate.

Omissions in reporting are prevalent. Take for example recent problems in human gene therapy[4]. Primate experiments clearly suggested risk. But in the animal work, the nature of the morbidity in one paper[5] was described only in terms of pathological data. The reader is informed that appetite in the survivors was normal, but weight changes were not reported. It is not recorded whether the animals were housed in groups (usually required for primate social needs) or singly, leaving the knowledgeable reader wondering whether a cage-mate ate the food. Additionally, mortality was described only by pathological criteria based on liver biopsies, rather than including information from, for example, liver function tests, complete blood count information, haemodynamic criteria and subjective scores in both survivors and dead animals. This left the events occurring between life and death open to speculation.

In a slightly improved reporting scheme in canine research[6], when using pericardial adenoviral-mediated vascular endothelial growth factor (VEGF), investigators reported a severe dose-dependent physiological reaction after administration. Substantial information about morbidity and mortality was included, but key aspects about related events were omitted. For example, no information was given about intense electrolyte changes, nausea and occasional thrombocytopaenia — seen and treated by the veterinary staff — which could have contributed to the later drug and technical failures of VEGF and adenovirus in human patients[7].

Scientists and the public need access to correct information about clinical protocols in animals. We need more of the right kind of clinical study design, and more collaborative reporting from inside animal facilities.

Such partnerships between veterinarians and scientists are stuck — they require a change in thinking. Scientists need to stop viewing veterinary care as a burden and see it as a quality assurance for drugs that are destined for human use. As well as allowing a more accurate risk–benefit analysis for human drug trials, introduction of such reporting standards in non-human experiments could also reduce the amount of costly regulation required at the later stages of commercialization of drugs.

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1. Scientists Center for Animal Welfare: http://www.scaw.com/summary.htm
2. NIH Initiative to Reduce Regulatory Burden. http://grants.nih.gov/grants/policy/regulatoryburden/index.htm
3. Foundation for Biomedical Research. http://www.fbresearch.org/press-ardf.html
4. *Washington Post* 12 July (2000).
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Why don't creationists use private schools?

Sir — In his recent review of Niles Eldredge's *The Triumph of Evolution and the Failure of Creationism* (*Nature* **406,** 935; 2000), Robert W. Cahn speculates on why creationism has surfaced only among Christian fundamentalists in the United States. He says ultraorthodox Jews and fundamentalist Muslims are more concerned with daily ritual, dietary practice and appropriate observance of holy days, while fundamentalist Christians are wholly focused on belief — causing the current ground swell of activism to curb the teaching of evolution in US schools.

There is no reason to believe that ultraorthodox Jews and fundamentalist Muslims are any less fervent in their beliefs about creation by an all-powerful deity. However, most choose to educate their children in private religious schools where they can control the science curriculum without infringing on the rights of others to learn about evolutionary theory.

Apparently, Christian fundamentalists feel they are entitled to publicly sponsored and funded schools where the teaching conforms to their religious beliefs, even though this is prohibited by the US constitutional separation of church and state. Perhaps they should be encouraged to send their children to private schools, so that other children are no longer deprived of their right to be taught a current, well-validated scientific theory.

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Survival on the edge: the tube worm's strategy

Sir — In his otherwise excellent Millennium Essay[1], Roel Snieder proposes an analogy between scientific specialists and tube worms found at deep-sea hydrothermal vents. He advocates *Homo universalis*, an interdisciplinary 'team-player' who can communicate effectively with colleagues from other fields.

But although individual tube worms themselves don't move into new (vent) fields when conditions change, it is now becoming apparent that their notable symbioses with chemoautotrophic bacteria, their remarkable physiological adaptations and their impressive reproductive capabilities allow their species to deal quickly with changing conditions by colonizing new opportunities (vents) — and yes, even interbreeding among different colonies, in time[2].

And a good thing, too, because deep-sea vents at fast-spreading centres are, individually, some of the most unstable habitats on this planet. Perhaps tube worms would make good interdisciplinary scientists, after all.

John D. Rummel

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1. Snieder, R. *Nature* **406,** 939 (2000).
2. Van Dover, C. L. *The Ecology of Deep Sea Hydrothermal Vents* (Princeton Univ. Press, 2000).