ANIMAL WELFARE

Call to curb lab tests on dogs

Canine remains the default option in outdated pharmaceutical toxicology.

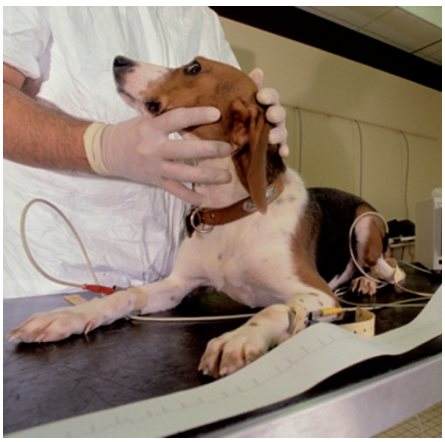
BY MARIAN TURNER

Man's best friend bears a heavy burden in the pharmaceutical industry. Every year, tens of thousands of dogs are subjects in drug-toxicity studies in Europe and the United States, even though many scientists think that they are poor predictors of drug effects in humans. Discussions on this sensitive issue have now been opened up by a hefty donation from Hildegard Doerenkamp, a Swiss philanthropist and passionate dog-lover, to the Zurich-based Doerenkamp–Zbinden Foundation, which supports work to reduce animal testing.

Toxicology researchers from academia and industry, and animal-welfare groups met in Budapest last week to develop an action plan and discuss how to spend Doerenkamp's donation of more than €1 million (US$1.4 million) to drive change. Scientists need to identify what information dog tests provide that tests *in vitro* or on rodent species cannot, they say. And regulatory authorities such as the US Food and Drug Administration (FDA) and the European Medicines Agency need to harmonize their requirements for dog testing so that pharmaceutical companies can minimize the number of animals they use.

Regulatory authorities usually require that drugs are tested for toxicity in both a rodent and a non-rodent species. The latter tends to be dogs, because they are readily available, easy to handle and in many ways physiologically similar to humans. Pharmaceutical testing accounts for around three-quarters of all dogs used in science.

But scientists inside and outside industry say that dogs are not always the best option for testing and could, in some cases, be replaced by *in vitro* tests. In spite of these reservations, and public disquiet over the use of dogs in testing, very little has been done to curb the practice, says Thomas Hartung, a molecular toxicologist and head of the Centre for Alternatives to Animal Testing (CAAT) at Johns Hopkins University in Baltimore, Maryland, which organized the meeting.



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Dogs make popular laboratory subjects, with uses including drug-toxicity testing, above.

Regulatory agencies are nervous of changing procedures. Any adverse reactions to a new drug, for example, could be blamed on new tests failing to spot dangers. Only if a battery of *in vitro* alternatives can match the level of toxicity prediction that dogs can provide will regulators agree to a change, says Hartung. So far only one such test — used to predict whether a compound could lead to cardiac arrhythmias — comes close, but it has not yet been internationally validated.

In its action plan, to be published in the next few months, CAAT will call for the setting up of a database of dog-test results to help to identify more targets for *in vitro* tests by highlighting physiological effects seen only in dogs. It will also call for a better definition of those tests for which dogs provide the best model, and those for which another species — such as the mini-pig — should be used instead. Toxicologist Georg Schmitt of Hoffmann La-Roche in Basel, Switzerland, says that pharmaceutical companies should not use dogs by default simply because facilities and test protocols exist. "Dogs can be oversensitive to some compounds, such as hormones, and their gastrointestinal system behaves differently to that of humans," says Schmitt. He says that studies in which dogs have proved to be poor models should be published.

The new effort takes inspiration from an initiative organized more than a decade ago by drug-testing expert David Smith, then employed by the London-based pharmaceutical giant AstraZeneca and now at the Laboratory Animal Science Association, based in Hull, UK. He brought together 12 pharmaceutical companies and welfare groups for secret discussions about dog testing. The group assessed the testing protocols for more than 100 compounds and developed standardized guidelines for dosage testing (D. Smith *Regul. Toxicol. Pharmacol.* **41,** 95–101; 2005). Smith says that this has resulted in up to 120 fewer dogs being used per company per year.

At the time, there was no formal mechanism for such collaborative efforts. CAAT is now providing an official framework. Before the Budapest meeting it formed an international committee of pharmaceutical companies to share best practices for dog care and experimentation.

CAAT's next step will be to do the same with regulatory authorities, says Hartung. Pharmaceutical companies will continue to perform tests if one major region requires them. For example, although the European Union scrapped the requirement for 12-month chronic-toxicity tests in dogs in 2006, the FDA still demands them.

Hartung hopes that this new focus on dogs will contribute to broader changes in animal testing. "It's not just about using fewer dogs, but about shaking up toxicology-testing standards that have been in place for over 40 years," he says. "These scientific improvements will better protect human health as well." ■

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