Models and human cells instead of lab animals

Traditionally, the safe limit for humans of toxic substances is determined by conducting trials with animals. But toxicologist Tessa van Tongeren discovered such risk assessments can also be done with the aid of a computer and human cells.

From a scientific perspective we might be able to replace some animal tests by methods that don't require lab animals. 'But it's also a social issue. As a society, we need to get used to not doing animal tests.' ◆ Photo Shutterstock

'We expose lab animals to varying doses of a substance. Then we investigate the effect of each dose on an organ, for example. Ultimately, we want to determine the maximum dose without a harmful effect,' explains Van Tongeren. 'In addition, we want to know how much of the substance actually ends up in the blood or in an organ.' This data is then used to calculate the safe exposure limit for humans.

'A computer model lets us determine the safe dose'

The results with lab animals can't always be assumed to apply equally to humans. And some forms of illness in humans are difficult to determine in animals. Then there are the ethical, economic and legal considerations pushing scientists to reduce animal testing or find substitutes. Van Tongeren, who received a PhD in Toxicology in early September, studied how to determine the toxicity — and consequently the safe limit — of a substance without using an animal's body. She did this for hormone-disrupting substances suspected of having androgenic and/or oestrogenic effects.

'What are termed bioactivity tests can be used to identify possible harmful effects. In these tests, we use human cells that have been modified to give them an androgen or oestrogen receptor. We also gave these cells properties that meant they emit a light signal if a substance binds to these receptors. Then we measure the intensity of the light signal: the more light there is, the more harmful the effect.'

Computer model

The exposure can be determined with the aid of computer models, says Van Tongeren. 'These days, it is possible to simulate a human body on a computer. You input the sex, age and illnesses, for instance, and then you get a prediction for a very specific population of the concentration of the substance in the blood if someone gets a certain dose of the substance.'
It works the other way round too.

'If the bioactivity tests tell us what concentration of a substance causes a harmful effect, we can translate that dose into concentrations in the blood. The computer model then lets us predict what exposure dosage is required to get that concentration in the blood. That lets you determine the maximum dose before you get this effect — the safe limit.'
According to Van Tongeren, that means that from a scientific perspective some animal tests can be replaced by methods that don't require lab animals. 'But it's also a social issue,' she says. 'As a society, we need to get used to not doing animal tests. And the legislation needs to change.' DV