A Pilot Study on the Refinement of Acute Inhalation Toxicity Studies: The Isolated Perfused Rat Lung as a Screening Tool for Surface-active Substances

Monika Fischer, Wolfgang Koch, Horst Windt and Clemens Dasenbrock

Fraunhofer Institute for Toxicology and Experimental Medicine, Hannover, Germany

Introduction

In the past, episodes of acute respiratory syndrome following exposure to waterproofing consumer sprays have been reported (1–3). Hazard characterisation and risk assessment of the acute toxic potential after inhalation of surface-active agents in waterproofing sprays are performed according to Organisation for Economic Co-operation and Development (OECD) Test Guidelines (TGs) 403, 433 or 436, which are regulated by OECD Guidance Document No. 39. For this study, only OECD TG 403 was considered, because the in vivo experiments that were used for comparison had been carried out by blind testing 12 surface-active substances. The results obtained compared well with data available from in vivo acute inhalation studies. Substances that triggered harmful effects, such as impaired lung compliance and atelectasis of the isolated perfused lung, were also found to cause changes in respiratory parameters, some of which would be severe enough to lead to death in in vivo tests with rats. The changes in respiratory parameters suggest that the mode-of-action is associated with impairment of the surfactant layer. Therefore, pre-testing in the isolated perfused rat lung allows the identification of surface-active substances with the potential for causing acute inhalation toxicity.

Materials and Methods

Animals and substances

Male (400g) and female (250g) Wistar WU rats (Crl:WI [WU]) were obtained from Charles River Laboratories, Sulzfeld, Germany. All the animals...