Available online at www.sciencedirect.com
SCIENCE DIRECT®
Regulatory Toxicology and Pharmacology 44 (2006) 14–23
Regulatory Toxicology and Pharmacology
www.elsevier.com/locate/yrtph

Principles and practices of health risk assessment under current EU regulations

Christina Rudén *

Royal Institute of Technology, Department of Philosophy and the History of Technology, Teknikringen 78B, SE-100 44 Stockholm, Sweden

Received 29 September 2004
Available online 26 September 2005

Abstract

Risk assessments serve as the foundation of regulatory decision-making on whether to take actions to reduce (or otherwise manage) a toxicological or ecotoxicological risk or not. To understand the complex process that leads from the generation of scientific data, via risk assessment to risk management decision-making, close studies of the scientific basis and risk assessment methods must be undertaken. This paper consists of two main parts. In the first part the principles of the European Union process for risk assessments, as defined by legislations and official guidelines, are briefly outlined. In the second part the actual workings of this system are exemplified by the results from case studies of the risk assessment processes for trichloroethylene and for acrylamide. The analysis and comparison of these two cases illustrates: (1) that generation of a large amount of data does not ensure consensus among risk assessors, (2) that controversy can regard different levels of detail, (3) that controversy can arise at different organizational and theoretical levels, (4) that risk assessments may be subject to (public) criticism even if the experts agree, and (5) that "scientific" controversies have a significant policy component.
© 2005 Elsevier Inc. All rights reserved.

Keywords: Toxicological risk assessment; Risk management; Acrylamide; Trichloroethylene; Regulatory toxicology; Scientific controversy; Bias

1. Introduction

Risk assessments serve as the foundation of regulatory decision-making on whether to take actions to reduce (or otherwise manage) a toxicological or ecotoxicological risk, and in that case, to choose appropriate risk management measures. The basis of risk assessments constitutes: (1) the scientific data relevant to the assessment, and (2) the general principles and assumptions used to interpret the data and to overcome data gaps. Both the requirements for data generation, and the choice of principles and assumptions to be used in the risk assessment process, are determined by policy as incorporated in the legislation (Commission Directive, 93/67;Commission Regulation, 1488/94).

To understand the complex process that leads from the generation of scientific data, via risk assessment to risk management decision-making, close studies of the scientific basis, principles, and assumptions must be undertaken. A deeper understanding of the risk assessment process is particularly motivated since with the implementation of REACH the number of substances to be risk assessed will increase and so will the number of actors performing risk assessments.

This paper consists of two main parts. In the first part the principles of the European Union process for risk assessments, as defined by legislations and official guidelines, are briefly outlined. In the second part the actual workings of this system are exemplified by the results from case studies of the risk assessment processes for trichloroethylene and for acrylamide. Finally these results are discussed in the light of the proposed new European Union chemicals regulations, REACH.

2. Risk assessment

Health risk assessments may have different aims and scopes, but they always include an attempt to identify the

* Fax: +46 8 790 9517.
E-mail address: cr@infra.kth.se.

0273-2300/$ - see front matter © 2005 Elsevier Inc. All rights reserved.
doi:10.1016/j.yrtph.2005.04.009

potential adverse effects that a substance may cause in humans. This encompasses a description of the nature of these effects and some estimation of the likelihood that they will occur as well as of their extent or severity (European Commission, 2003a).

According to the general theoretical model, the process of risk assessment is usually divided into four steps. The first step consists of *hazard identification*. This part of the process aims at determining the inherent properties of a substance, i.e., its potential to cause harm in an experimental animal or in the human body. This part of the risk assessment does not take exposure into account and therefore it does not estimate the magnitude of the risk. The next step is the *dose–response assessment*. The purpose of the dose–response assessment is to describe the relationship between the administered dose and the response of the exposed population. The third step of the risk assessment process is the *exposure assessment*. The exposure assessment aims at determining the likelihood of human exposure, the magnitude, and duration of the doses that humans may receive, as well as the potential exposure routes. The exposure assessment have to be based on measured data and/or the use of theoretical exposure models. The final step is *risk characterization*, which involves comparing the quantitative or qualitative information on human exposure to the dose–response relationship for the critical effect, or when possible, a qualitative evaluation of the likelihood that an effect will occur at any given exposure (European Commission, 2003b).

2.1. Toxicity data

The first part of a health risk assessment, the hazard identification, must be based on scientific (toxicity) data. A major problem in regulatory toxicology is that toxicity data for most chemical substances are lacking. A report from the European Commission showed that 79% of the 2500 EU high production volume chemicals have less than base-set data (Allanou et al., 1999).[1] Comprehensive toxicological knowledge is only available for a handful of chemical substances and knowledge about adverse health effects from exposure to mixtures of chemicals is almost completely lacking.

The generation of toxicity data is partly driven by research in, e.g., toxicology and environmental and occupational medicine, and partly through legislative testing requirements. In Europe the requirements for the chemical industry to generate toxicity data for previously untested existing chemicals will increase according to the new proposed strategy for a future European chemicals policy, REACH (European Commission, 2003a). However, for the majority of substances regulated by REACH the data requirements as currently proposed are not sufficient to provide the information required for a basic hazard assessment (see Rudén and Hansson, this issue).

Toxicity data can be obtained either from experimental systems such as in vitro assays or in vivo animal experiments, or from epidemiological studies of exposed humans.

In experimental research the methods are designed to serve specific research purposes. In contrast, for toxicity testing as legally required, the use of standardized test methods is preferred since it facilitates comparisons of results for different substances, e.g., in risk assessment and for classification and labelling.

The procedures for designing, performing, and reporting standardized toxicity tests are laid down in official guidelines, such as the OECD testing guidelines. There are a large number of standardized animal bioassays. They differ, e.g., in the number of animals used, in the duration of exposure, and in which endpoints are studied.

In a full chronic toxicity study a total of at least 400 animals are required. The animals are dosed during the major part of their life span, which for rodents means between 1.5 and 2 years. This type of study is thus both time- and resource-consuming. The cost of performing a full scale chronic and carcinogenicity test is in the order of 600,000–1,500,000 € depending on the species and exposure route. Chronic toxicity data are only available for few substances, and risk assessments will consequently in most cases have to be based on toxicity data obtained from more limited studies, both in terms of the size of the study and the duration of exposure.

In epidemiology the effects on humans exposed to chemical substances (and other agents) are studied. Epidemiology is an observational and not an experimental science. Epidemiologists study exposures and disease occurrence in a real-life setting, and thus depend on a multitude of influences (a myriad of exposures, genetic aspects, human behaviour, life-style factors, etc.), many of which are interrelated and have strong confounding potential. The design of an epidemiological study has therefore to be determined depending on the prerequisites available. Due to the obstacles in designing these studies, we can expect conclusive epidemiological data to become available only for a limited number of substances.

The main advantage of using epidemiological data in risk assessment is that no species or dose extrapolation of the data is necessary since the exposed individuals, and the size and nature of exposure are directly relevant to the assessment of human risk.[2] Therefore, epidemiology provides important contributions to a health risk assessment and (high quality) epidemiological data are usually assigned significant weight in the risk assessment process. The main disadvantage is of course that these data become available only after humans have been exposed and poten-

[1] The most extensive toxicity tests included in the base-set is a 28-day study in rodents and short-term testing of fish, *Daphnia*, and algae.

[2] If occupational exposures are studied it must however be noted that the exposure of workers may differ from the exposure of the general population, and furthermore that the exposed workers may not be representative of the population at large (which includes all subpopulations, e.g., children, older people, and people with different kinds of diseases).

Download English Version:

https://daneshyari.com/en/article/2593174

Download Persian Version:

https://daneshyari.com/article/2593174

Daneshyari.com