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Regulatory risk assessment approaches for synthetic mineral fibres

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ABSTRACT

Exposure to synthetic mineral fibres (SMF) may occur in a number of workplace scenarios. To protect worker health, a number of different organisations worldwide have assessed the health risk of these materials and established workplace exposure limits. This paper outlines the basic principles of risk assessment and the scientific methods used to derive valid (justifiable) occupational exposure limits (OELs) and goes on to show how, for SMF, and particularly for refractory ceramic fibre (otherwise known as aluminosilicate wool, RCF/ASW), the methods used and the associated outcomes differ widely. It is argued that the resulting differences in established OELs prevent consistent and appropriate risk management of SMF worldwide, and that development of a transparent and harmonised approach to fibre risk assessment and limit-setting is required.

1. Introduction

Synthetic mineral fibres (SMF) – alternatively known as man-made mineral fibres (MMMF) – constitute a complex group of materials including synthetic vitreous fibres (SVF) and certain non-vitreous materials such as polycrystalline wools (PCW). SVFs include glass wool, rock/stone wool, slag wool, alkaline earth silicate (AES) wool and aluminosilicate wool (ASW) – also known as refractory ceramic fibre (RCF). The composition of these materials differs according to their intended use, though they typically include silicates and other mineral oxides. They may be manufactured from processed or un-processed mineral raw materials; fibres are normally produced by spinning or blowing the molten material, or by a sol–gel process. Most SMF are used for acoustic or thermal insulation, fire protection, reinforcement and filtering applications. ASW/RCF, along with AES wools and PCW, constitute a family of fibres known as High Temperature Insulation Wools (HTIW)[1] that are used in specialist industrial high temperature applications such as furnace linings. Worker exposure by inhalation to these fibres may occur during fibre production, product manufacture (processing) and assembly or installation operations, and during plant decommissioning or demolition. Exposure of the general public is generally low and for HTIW is negligible as these materials are not used in consumer products.

The toxicity of SMF is driven not by chemical constitution but – because of their fibrous nature – by their size, shape and biopersistence, as reflected in the so-called '3Ds' paradigm (Brown and Harrison, 2012; see Section 4.1). This makes the risk assessment and regulation of SMF rather more complex than for bulk

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[1] For definitions see: BS EN 1094–1:2008. Insulating refractory products. Terminology, classification and methods of test for high temperature insulation wool products.

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chemicals, for example. This article focuses on the way SMF are assessed and regulated in different jurisdictions, using ASW/RCF[2] as a case example.

The principal objective of this review is to describe and assess specifically the approaches that have been applied to SMF, and to ASW/RCF in particular. We also consider the need for harmonisation of the regulatory processes applied to SMF globally – including the derivation of OELs for ASW/RCF – to enable consistent and appropriate risk management. The first part of the paper briefly describes some general principles of risk assessment, followed by a description of the processes and procedures used to set occupational exposure limits. The next section looks at fibre-specific issues in risk assessment and leads into consideration of regulatory approaches to SMF in Europe and the USA. Finally, leading up to the discussion section, there is a detailed 'case study' reviewing regulatory approaches to ASW/RCF in different jurisdictions across the world.

2. Principles of risk assessment

Risk assessment traditionally constitutes three steps – *hazard identification*, *hazard characterisation* (or dose-response assessment), and *exposure assessment*. A fourth step, *risk characterisation*, is then applied to integrate the findings (Finer, 2006; NRC, 2009). Any attendant uncertainties relating to the first three steps are integrated into the risk characterisation step and it is this information that is drawn on for the related, but distinct, process of defining the necessary risk management measures (RMM) required to ensure safe use of the substance. Chemical risk assessment usually incorporates both qualitative and quantitative elements (Harrison and Holmes, 2006); these are briefly described below. The process is widely and comprehensively documented elsewhere by authoritative bodies (for example, EFSA, 2014; COC, 2012a; COC, 2012b; ECHA, 2012a; ECHA, 2012b; WHO, 2010; EFSA, 2009; EC, 2000a; US EPA, 2005).

Hazard identification is concerned with identifying the specific potential adverse effects of a chemical or mixture through consideration of its chemical and physical properties in conjunction with toxicological and toxicokinetic data. Hazard characterisation entails the evaluation of available data to develop a 'weight of evidence' (WoE) argument in support of a link between exposure to a chemical and the likelihood and severity of any adverse effect (the apical endpoint). Where a number of different endpoints are observed, the one that occurs at the lowest exposure level is usually selected as being 'critical' for risk assessment purposes. For the majority of chemicals it is possible, on the basis of mechanistic knowledge and available experimental data, to define a threshold dose/concentration – such as the 'no observed adverse effect level' (NOAEL) or benchmark dose (BMD) – that can be used as the point of departure (POD)[3] (also referred to as Reference Point) for risk extrapolation (discussed further in Section 2.2). If the dataset does not allow definition of an effective 'no effect' threshold then, provided understanding of the toxic mechanism is sufficient to support the theoretical existence of a threshold, it may be possible to define a dose at which only a minimal level of effect is apparent, termed the lowest observed adverse effect level (LOAEL). Due to the implicitly greater degree of uncertainty associated with a LOAEL, an additional assessment factor is incorporated into the risk assessment process (Section 2.2).

For a few types of toxic effect (e.g. cancer, mutation and sensitisation), the underlying mechanism may determine that it is theoretically not possible to establish a threshold below which no adverse effect will occur; in other words, any exposure to the chemical might elicit some degree of response (COC, 2012a). Such chemicals are treated differently from threshold chemicals in the risk assessment process (Section 2.1). It is to be noted, however, that the supposed absence of a threshold for genotoxic carcinogens is increasingly disputed (Greim and Albertini, 2015). Indeed, it can reasonably be argued that all substances (including genotoxic carcinogens) are likely to have some kind of threshold of effect – the problem is determining where this lies.

Human data for use in risk assessment can be sourced from case reports, epidemiology, and occupational and clinical studies. However, each of these sources has certain limitations (Devlin et al., 2005), and may not be available at all. For these reasons, data from studies on intact animals are often utilised; these have the advantage of being designed, controlled and conducted to address specific gaps in knowledge or use specific disease models to specific criteria and protocols (e.g. OECD guidelines for the testing of chemicals[4]). However, as responses of humans and animals to a given exposure may be substantially different (both physiologically and behaviourally), there are always inherent associated uncertainties when extrapolating from animals to humans. Further, animal studies have historically investigated dose-response relationships over a much higher concentration range than would be likely to occur for humans, necessitating extrapolation of the findings to lower dose levels, leading to further uncertainty. Importantly, animal studies can nonetheless provide valuable information on the Mode of Action (MoA) and Adverse Outcome Pathway (AOP) to complement the determination of a quantitative reference point for hazard characterisation (Devlin et al., 2005; EFSA, 2014). Supporting this aim, a number of *in vitro* models, *in silico* tools (e.g. ((Q)SARs and 'read-across' methodologies) and *'omics' technologies* (transcriptomics, proteomics, metabolomics) have been developed to investigate toxicokinetic and toxicodynamic processes at the organism, organ, cell and molecular levels (described more fully in EFSA, 2014; EC, 2011; Grant et al., 2010; EC, 2009; NRC, 2006; Devlin et al., 2005; Holme and Dybing, 2002).

2.1. Carcinogens and thresholds of effect

With potential carcinogens and mutagens (also sensitising agents), it is important to consider the MoA by which the chemical acts and the relationship between dose and adverse response so that the risk assessment process can allow for the presence or absence of a threshold. Conventionally, a distinction is made between *'genotoxic carcinogenicity'* and *'non-genotoxic carcinogenicity'* (COC, 2012a), and it is now further recognised that there is a difference between 'primary' and 'secondary' genotoxic carcinogenicity, where the latter has a measurable threshold. This is the case, for example, with certain fibres (see below) where the induction of reactive oxygen species (ROS) is responsible for a secondary genotoxic effect for which a threshold exists. There are a number of structured frameworks available for the assessment of the overall WoE for a postulated MoA (Cohen et al., 2003, 2004; Meek et al., 2003; Boobis et al., 2006).

For primary (DNA-reactive) genotoxic carcinogens considered

[2] ASW/RCF is categorized under the chemical abstracts service registry number (CAS Number) 142844-00-6 and EC List number 604-314-4. In Europe, under European Regulation 1907/2006 (REACH), ASW/RCF is defined as a type of UVCB (chemical substance of unknown or variable composition, complex reaction products and biological material).

[3] For most chemicals, POD is expressed as the dose (e.g. mass per kilogram bodyweight in a given period, e.g. mg/kg bodyweight/day) or as a concentration (e.g. mg/m^3 for atmospheric exposure) to which an organism is exposed.

[4] http://www.oecd.org/chemicalsafety/testing/oecdguidelinesforthetestingofchemicals.htm.