STATUS OF BITUMENS UNDER THE REACH REGULATION.

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ABSTRACT

The REACH legislation requires that chemicals manufactured in, or imported into the EU in quantities of more than one tonne per year are registered. From a regulatory perspective, bitumens are - like other petroleum substances - chemicals and therefore subject to REACH. Bitumens are complex substances which are manufactured by different processes.Similar to other petroleum products, bitumens are recognized by REACH as substances of “Unknown or Variable composition, Complex reaction products or Biological materials” (UVCBs). Assessing the intrinsic hazards and, where applicable, the risks associated with UVCBs is highly challenging. Under its comprehensive risk assessment programme on petroleum substances, CONCAWE performed comprehensive human health and environmental hazard assessments of bitumen. Additional hazard data have become available since the registration in December 2010. This paper aims to explain the potential impact of the new data and also ECHA and CONCAWE REACH processes as far as they pertain to bitumen.

Keywords: Bitumen, REACH, regulation, IARC, hazard, risk, CONCAWE

1. INTRODUCTION

In the past few years, three events with a potential impact on the use of bitumen have occurred. The first is REACH, the new EU chemicals legislation, that was developed between 2002 and 2006 and came into force in 2007 (EC, 2006). The second is the publication of skin-painting studies in the USA, and the third the re-evaluation of the carcinogenicity of bitumen and its emissions by IARC (International Agency for Research on Cancer) in 2011 (Lauby-Secretan, 2011). All these events have the potential for significant impact on the regulatory status of bitumen and its use and are discussed in this review.

1.1 The REACH regulation

Legislation on Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) was accepted in the European Union in December 2006 (EC, 2006). This legislation, which entered into force in June 2007, applies to all chemicals manufactured in, or imported into the European Union in amounts greater than 1 tonne/year. High tonnage substances, defined as chemicals placed on the European Union market in quantities greater than 1000 tonnes/annum, had to be registered by December 2010. From a regulatory perspective, bitumen is considered to be a chemical and is therefore subject to REACH and needed to be registered by end of 2010. Like most petroleum substances, bitumen is recognised by REACH as a substance of "Unknown or Variable composition, Complex reaction product or Biological material" ("UVCB"). Since CONCAWE realized that the risk assessment of UVCBs in general and petroleum products in particular would be challenging, it started a comprehensive Risk Assessment Programme on Petroleum Substances in 2001 with the aim of developing methodologies to facilitate and improve the quality of such assessments.
For each substance, REACH calls for a Chemical Safety Report (CSR). A CSR requires provision of relatively straight-forward data on production volume, intended uses and physico-chemical properties, but also extensive data on environmental hazards, human health hazards, and hazards to man through indirect exposure via the environment. If substances are classified as hazardous according to the Dangerous Substances Directive, REACH requires that a health risk assessment be undertaken and a Chemical Safety Assessment (CSA) is submitted. If risks are identified, the registrant must characterize them and identify risk reduction measures to mitigate them. This makes the REACH evaluation basically a risk-driven process.

1.2 The IARC Evaluation

The International Agency on Research of Cancer (IARC) is an institution from the World Health Organisation. Its mission is to coordinate and conduct research on the causes of human cancer, the mechanisms of carcinogenesis, and to develop scientific strategies for cancer prevention and control. A particular task of IARC is the 'Monographs programme' which aims at identification of environmental factors that may increase the risk of human cancer. Factors considered include chemicals, complex mixtures, occupational exposures, physical agents, biological agents, and lifestyle factors. Interdisciplinary working groups of expert scientists review the available scientific literature and evaluate the weight of the evidence that an agent may increase the risk of cancer. This process leads to classification of substances based on their carcinogenic hazard potential. Although IARC classification has no formal legal status, national health agencies can use this information as scientific support for their actions to prevent exposure to potential carcinogens. It should be emphasised that the IARC evaluation itself is a hazard-driven process as it does not take into account the degree or severity of exposure.

2. CONCAWE APPROACH

2.1 REACH preparations

In 2001, the European Commission published the "Chemicals White Paper". In general, a "white paper" forms the basis of new envisioned EU legislation and this paper sketched the structure and ramifications of the REACH regulation. CONCAWE realized that assessment of the intrinsic hazard properties and, where applicable, associated risks for petroleum UVCBs, including bitumen, would be required under the new chemicals legislation. CONCAWE also realized that there would be no or only very scarce guidance generated on how to conduct hazard and risk assessments for complex substances such as petroleum products and decide to start a voluntary comprehensive Risk Assessment Programme on Petroleum Substances according to Technical Guidance available under the Existing Substances Regulation (EC, 1993). The intention was to conduct such a risk assessment, develop novel approaches that would be applicable to petroleum substances and discuss these with the European authorities, i.e. the European Chemicals Bureau in Ispra, Italy, during the quarterly meetings of the Technical Committee on New and Existing Substances. Since there are about 650 petroleum substances with a unique CAS registry number listed on the European Inventory of New and Existing Chemical Substances (EINECS) assessment of individual substances is not feasible. A science-based, pragmatic approach was needed to evaluate all these substances. Therefore, one of the methodologies employed was grouping of individual petroleum substances into a distinct number of categories, based on similarities in their manufacturing processes (distillation, cracking, hydrotreatment etc.), physical/chemical properties, likely composition (based on understanding of the manufacturing process) and tested or modelled environmental and human health hazard properties. Examples of such categories include for instance 'low boiling point naphthas (gasolines)', 'kerosines', and 'bitumen'. A risk assessment for gasoline was prepared applying several novel approaches, such as the hydrocarbon block methodology for environmental risk assessment (EMBSI, 2004). Finland volunteered to act as the leading member state and the approaches were discussed with the authorities. During the subsequent years, hazard and risk assessments were conducted for the other categories of petroleum substances in preparation for the REACH registration in 2010.

2.2 The bitumen hazard assessment and the DNEL (Derived No-Effect Level)

Under the CONCAWE comprehensive Risk Assessment Programme on Petroleum Substances also a hazard assessment for the bitumen category, comprising 9 CAS registry numbers, was prepared in 2007. Since, based on the available data, bitumens were not classified as hazardous according to the Dangerous Substances Directive, a full risk assessment was not required. Since a hazard assessment alone would satisfy the registration requirements there was no urgent need to develop additional exposure data. The hazard assessment was revised and updated in 2009 (Boogaard, 2009) and again bitumens were not deemed classifiable for human health or environmental hazards.

For any substance subject to registration which is manufactured or imported in quantities of 10 tonnes/year or higher, the REACH legislation requires the derivation and documentation of an appropriate Derived No Effect Level (DNEL) value to the extent that this is appropriate based on assessment of the available data. DNELs are a new concept under REACH representing 'the level of exposure above which humans should not be exposed' (Annex 1, Chapter 1 "Human health hazard assessment", article 1.0.1(EC, 2006)). DNELs play a crucial role in safety evaluation processes serving as benchmark value against which safe use can be determined by comparison of measured or modelled exposure data for each of the identified uses and Exposure Scenarios for the substance against the DNEL. The outcome of this process may then prompt development of appropriate information on safe use (e.g. necessary risk management measures, supporting operational conditions). The ratio of exposure to DNEL yields a risk quotient, the Risk Characterisation Ratio (RCR). A RCR value less than 1 indicates acceptable risk under REACH. Although DNALs have the same units as occupational exposure limits and seem to serve a similar purpose, they are not identical and serve different purposes. This difference, however, is beyond the scope of this overview.

Although bitumens were not classified as hazardous, chronic exposure to fumes from bitumen caused slight respiratory irritation not sufficient to trigger classification. In repeated-dose studies in rats exposed to bitumen fumes by nose-only inhalation, histopathological investigations showed some irritation of the respiratory airways. In a 2-year, nose-only inhalation study in which rats were exposed to 0, 6.8, 34.4 and 173 mg/m^3 of bitumen fumes (as total hydrocarbons, THC) during 6 hours/day and 5 days/week, clear signs of respiratory irritation were seen in the highest dose group, but only very minimal irritation of the upper respiratory tract was found in the 34.4 mg/m^3 exposure group. This value was taken as the LOAEL (lowest observed adverse effect level). Considering that in a similar 90-day repeated dose study in rats exposed to 0, 6.6, 33.4 and 177 mg/m^3 of bitumen fumes (as THC) during 6 hours/day and 5 days/week, no respiratory tract effects were seen at 33.4 mg/m^3, it was assumed that the actual NOAEL (no observed adverse effect level) would be slightly lower, but very close to the value of 34.4 mg/m^3. This LOAEL value was therefore divided by a factor 2 to provide a conservative estimate of the actual NOAEL for respiratory tract irritation due to chronic exposure to bitumen fume. The value of 17.2 mg/m^3 (as THC) was used as the point of departure for deriving a DNEL. The value was corrected for differences in exposure duration (workers being exposed to 8 h/day instead of 6 h/day) and for increased breathing volume of workers (10 m^3 per 8 h instead of 6.7 m3 per 8 h for resting individuals) yielding a corrected point of departure of 8.64 mg/m^3 (= 17.2 × (6/8) × (6.7/10)). To this value an assessment factor of 3 was applied to correct for interspecies differences yielding a DNEL of 2.9 mg/m^3 (as THC) for local effects due to chronic exposure, based on average exposure for an 8-h work shift (Boogaard et al., 2012).

2.3 The dossier: testing proposal

The bitumen hazard assessment formed the basis for the CSR that was prepared for the registration under REACH in 2010. As part of the dossier preparation, a data-gap analysis was performed to see whether there were any legal requirements that could not be met with the available data. With regard to physicochemical properties there were no certain data-gaps, but a possible data-gap for melting point. However, since melting point is not a relevant parameter for bitumens and a more relevant parameter, softening point, is available this was not considered essential. For ecotoxicological endpoints there were theoretically a large number of data gaps, but there were valid arguments as to why it would be inappropriate/unnecessary to undertake additional studies to fill these possible data gaps. These are related to the physical nature of bitumens, in particular the low water solubility of constituent hydrocarbons and the effect of the matrix in further limiting the solubility and availability of constituents of potential concern such as polyaromatic hydrocarbons. Finally, with regard to toxicological endpoints it was concluded that the vast majority of endpoints had adequate data available. The only notable exceptions concerned the reproductive (developmental and fertility) toxicology endpoints. Although a negative screening study for reproductive/developmental toxicity became available, it was deemed potentially insufficient to meet the legal requirement for reproduction toxicity as this was explicitly stated in an amendment of the REACH regulation (EC, 2009). As a consequence a testing proposal to conduct a two-generation reproductive toxicity study according to the OECD 416 guidelines was drafted and submitted to ECHA as part of the registration process.

2.4 Splitting the category

In the course of 2010, after the CSR for bitumen was prepared to meet the REACH registration requirements, new data on the skin carcinogenic potential of bitumen fume condensates became available. In the USA, a series of studies were conducted on fume condensates. For these studies, fumes were collected for paving asphalt (straight-run bitumen) and from roofing asphalt (oxidized asphalt, BURA Type III) from the head-space of storage tanks. A third sample of oxidised asphalt was collected under laboratory conditions (at higher temperature). The condensates of these fumes were subsequently tested in a two-year dermal carcinogenicity study in mice (mouse skin-painting assay) (Clark et al., 2011). The condensates from paving asphalt did not show carcinogenic properties in the assay, but the fume condensates from roofing asphalt caused a weak tumourigenic response in the mice. The fume condensates were further investigated in an initiation-promotion assay which allows to assess the nature of the carcinogenic response. The results of this assay were indicative of a genotoxic rather than a non-genotoxic mode of action (Freeman et al., 2011). Although the final reports were not available, the data generated suggested a difference in biological activity between condensates from straight-run paving bitumen and oxidised roofing asphalt. As a result, it was considered necessary to split the category into oxidised asphalt (CAS RN: 64742-93-4) and a bitumen category comprising the eight CAS RNs: 8052-42-4, 64741-56-6, 64742-85-4, 91995-23-2, 92062-05-0, 94114-22-4, 100684-39-7, and 100684-40-0. Hence, two separate dossiers but with very similar content, one for bitumen and another for oxidised asphalt were submitted to ECHA in 2010. In the course of 2011, the dossiers have been updated with technical information that became available more recently. The dossier for oxidised asphalt now contains the data from the skin painting studies (Clark et al., 2011) and the mechanistic studies (Freeman et al., 2011) indicating that oxidised asphalt with a PI > 2 may pose a hazard under certain conditions. Although still not classified as hazardous, it was decided to gather exposure information for certain uses and develop exposure scenarios. The dossier for the bitumen category also contains the data from the skin painting studies which essentially confirm the material is non-hazardous, so that further exposure data and exposure scenarios are not necessary. Both dossiers were also updated with new information relating to the testing proposals for reproductive toxicity. In addition, the available information was reviewed and re-arranged in both dossiers in response to the outcome of the IARC review in 2011.

3. IARC REVIEW

3.1 The process

Basically, IARC invites a number of independent experts to review all relevant published data on a substance during a 8-day period, at the end of which a decision is taken on its carcinogenic hazard potential. Four groups of experts look in detail at (1) the epidemiology, (2) animal data, (3) mechanistic data, and (4) exposure. With exception of the last group (exposure), each group prepares a proposal for classification and at the end of the review process, in a plenary meeting of all groups, a classification is reached through a voting process if consensus is not reached.
IARC classifies substances (and occasionally processes) into 5 groups: Group 1 –carcinogenic to humans, Group 2A – probably carcinogenic to humans, Group 2B – possibly carcinogenic to humans, Group 3 – not classifiable as to its carcinogenicity to humans, Group 4 – not a human carcinogen (Group 4 is not applied in practice and has only be assigned to a single substance in the past). Classification into Group 3 can either indicate that there are sufficient data, but that these data do not provide sufficient evidence that a substance is carcinogenic, or that there are insufficient data on which to base a classification. Substances are classified into Group 1 if there is sufficient epidemiological evidence that they pose a carcinogenic risk to humans. Since sufficient epidemiological data are often lacking and since the power of epidemiological studies is highly dependent on group size and specificity of the type of cancer, relatively few substances end up in this group. As a consequence, carcinogenicity studies in animals play a major role. When substances test positive in animal studies, they usually end up in Group 2. Substances are classified into Group 2B when there is limited animal evidence for carcinogenicity in humans and less than sufficient evidence of carcinogenicity in animals (e.g. only studies available with inadequate design or only carcinogenic in one species but not another species) or in Group 2A if there is limited evidence in humans and sufficient evidence for carcinogenicity from animal studies (e.g. substances found positive in more than one species or various positive studies). Mechanistic toxicological information is important as a substance can be moved up or down one level if that is supported by strong mechanistic evidence (Cogliano et al., 2008).

3.2 The outcome

The IARC working group evaluating bitumen and its emissions concluded that (a) occupational exposures to oxidised bitumens and their emissions during roofing are ‘probably carcinogenic to humans’ (Group 2A), (b) that occupational exposures to hard bitumens and their emissions during mastic asphalt work are ‘possibly carcinogenic to humans’ (Group 2B), and (c) that occupational exposures to straight-run bitumens and their emissions during road paving are ‘possibly carcinogenic to humans’ (Group 2B). As a result of this recent evaluatuion, all previous IARC classifications relating to bitumens and their emissions were withdrawn (Lauby-Secretan, 2011).

Considering the results of the recent mouse skin-painting studies (Clark et al., 2011) and the subsequent studies indicating that a genotoxic mechanism is likely to play a role in the development of skin tumours in mice painted with fume condensates of oxidised asphalt (Freeman et al., 2011), the outcome of the IARC review that emissions from oxidised asphalt during roofing operations should be considered as probably carcinogenic to humans (2A), is not unexpected as a hazard evaluation. The two other conclusions, i.e. that occupational exposures to both hard and straight-run bitumens and their emissions during mastic asphalt work and paving, respectively, are considered possibly carcinogenic to humans, was surprising. Based on a series of recent studies, CONCAWE had reached the conclusion that exposure to straight-run bitumens can be considered as non-hazardous under normal use conditions. These recent studies included the IARC nested-case control studies in European paving workers, which concluded that there was no consistent evidence of an association between inhalation or dermal exposure to bitumen and lung cancer risk (Olsson et al., 2010). These studies resolved the issues raised earlier by large epidemiological investigations in European bitumen workers performed by IARC (Boffetta and Burstyn, 2003; Boffetta et al., 2003). Moreover, they confirmed the general conclusions of a wide variety of epidemiological studies in bitumen workers. In addition, several animal studies, including the two-year nose-only inhalation study with an air-rectified bitumen in rats, also indicate that exposure to bitumen fume up to 173 mg/m^3, 6 h/day, 5 days/week (expressed as total hydrocarbons) does not pose a carcinogenic hazard. Moreover, extended histopathology did not show any effects apart from mild respiratory tract irritation (Fuhst, 2007). These studies were extended with a range of mechanistic investigations, including toxicogenomic analyses of lungs and nasal epithelium, a range of biomarkers, and the determination a variety of genotoxicity parameters. No indications of genotoxicity or of any significant gene dysregulation was found (Halter, 2007). Exactly the same parameters were also investigated in a range of studies in German mastic asphalt workers (Raulf-Heimsoth et al., 2011b). The data very nicely matched the animal studies, indicating clear exposure without any significant signs of genotoxicity but with some indications of mild respiratory tract irritation (Marczynski et al., 2011; Pesch et al., 2011; Raulf-Heimsoth et al., 2011a; Welge et al., 2011).

Based on the summary information available, it would appear that the IARC sub-groups reviewing the human and animal data agree with these conclusions for exposure to emissions during paving, which would have led to a classification into Group 3 (not classifiable as to carcinogenicity). However, in its overall evaluation, the working group decided to elevate exposure to paving bitumen emissions to Group 2B based on ‘strong *mechanistic* evidence in humans’ that a carcinogenic mechanism might be operational based on the presence of PAH in bitumen and its emissions (Lauby-Secretan, 2011). Mechanistic data can be used to classify a substance in a different category from that which would be warranted based on the epidemiological and animal data alone (Cogliano et al., 2008). IARC has done this for PAH on several occasions (Straif et al., 2005). IARC developed a weight-of-evidence approach to evaluate the available data for a mutagenic mechanism for tumourigenic PAH for which 4 criteria were deemed relevant: (1) the metabolic pathway to reactive intermediate(s) is well defined in a step-by-step manner in the tissue of interest, (2) DNA adduct formation has been shown in the tissue of interest, (3) mutagenicity of activated metabolites has been demonstrated, and (4) mutation in oncogene/tumour suppressor gene has been detected in the tissue of interest. If all 4 criteria are met, the evidence is considered strong; if only the first 3 criteria are met, the evidence is considered moderate. The evidence is weak if some mechanistic data are available to suggest a mechanism but significant data are missing to characterise it. When CONCAWE reviewed the mechanistic data, it came to the conclusion that the available data, particularly from exposed paving workers did not provide sufficient justification to be considered ‘strong evidence’. The limited information provided in the preliminary IARC publication does not seem sufficient basis either for moving paving bitumen from Category 3 to 2B (Lauby-Secretan, 2011). However, a more extensive explanation and data are expected to be included in the full monograph which will be reviewed by CONCAWE when it is published.

4. PROSPECTS

The situation with regard to bitumen has become more complex with the recent developments. We are still waiting for the publication of the full report to form a complete opinion but it seems that IARC considers occupational exposure to emissions from both bitumen bitumen and oxidised asphalt as a potential carcinogenic hazard based on the presence of PAH in the material. For proper health risk assessment and risk management, several issues have to be taken into account. Firstly, not all PAH are carcinogenic. Some PAH with 4 to 7 fused rings and specific molecular structures are carcinogenic and the mechanism for their carcinogenicity is well understood. Since these PAH are relatively volatile, their concentrations in bitumen and oxidised asphalt and their emissions are low, as would be expected based on the manufacturing process. Secondly, whether these small amounts of PAH pose an actual health risk depends on their bioavailability. In service the

PAH are trapped in the matrix and therefore are not bioavailable. However, through dilution with solvents or heating PAHs may be released from the material. In straight-run bitumens, the amounts of PAH are so low, that even in the highly sensitive mouse-skin painting studies with fume condensates (Clark et al., 2011) and numerous studies with solvent-diluted bitumen (Boogaard, 2009) no carcinogenic potential was observed. As a consequence, based on the available data, as presented in the CONCAWE review (Boogaard, 2009)and the IARC communication (Lauby-Secretan, 2011), bitumen is not classified as hazardous for intended uses and under normal working conditions. Very viscous bitumens, such as severely oxidised asphalt, require higher handling temperatures and their fumes may contain detectable levels of carcinogenic PAH. This is a possible explanation for the reason that the BURA Type III asphalt fume condensate was found to be a weakly genotoxic carcinogenic material (Freeman et al., 2011). Consequently, for oxidised asphalt more stringent precautionary measures are advised on safety data sheets (1) that exposure to fume condensate representative of fumes from a severely oxidised asphalt that would be found at field conditions above 230°C was weakly carcinogenic in animals, and (2) that exposure to fumes should be reduced by keeping operating temperatures as low as possible taking into account occupational exposure limits, safe handling temperatures, sufficient ventilation and local exhaust ventilation were possible.
It should be realised that a single CAS RN (64742-93-4) is used to describe both severely oxidised asphalt and air-rectified bitumen. Since for the latter high quality data are available indicating that it is not carcinogenic (Boffetta and Burstyn, 2003; Fuhst, 2007; Olsson et al., 2010), it is essential to make a distinction between these two materials in the REACH dossier for oxidised asphalt. This is done using a so-called Oil Industry Note (OIN) based on the penetration index (PI) with severely oxidised asphalts being defined by a PI > 2 and air-rectified bitumens by a PI ≤ 2. This physico-chemical difference is reflected in the different application temperatures that are used for the two types of material. This differentiation is also fully in line with the long-standing recommendation by Eurobitume to minimise temperature of use wherever possible and to observe a temperature limit of 200 ºC for bitumen and of 230 ºC for oxidised asphalt (PI > 2). The bitumen manufacturers will continue to work with the bitumen users to find pragmatic solutions to control exposures to bitumen fumes in order to manage any potential human health risks that may arise.

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