ISES Europe Training Series

DoE 3: Exposure Modelling

Module 2: Human Exposure Modelling: General Concepts and Worker

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Hello and welcome to this ISES Europe Training Series, which I provide together with Natalie von Goetz. My name is Wouter Fransman, and you are now in Domain of Expertise #3 on exposure modelling.
Before I proceed, I need to provide this legal notice on fair use and also on copyright. This is an overview of all the training videos in the ISES Europe training series, and you can find all of them on the ISES website.
As I mentioned, we're now going to talk about exposure modelling, and this exposure modelling training consists of five different modules. Hopefully you've already watched Module 1 and will continue with the other modules as well. Currently, you're in Module #2 on human exposure modelling—the general concepts—as well as worker exposure modelling.
My name is Wouter Fransman. I work as a principal scientist at the Netherlands Organisation for Applied Scientific Research, in short TNO. In this lecture, Natalie and I are going to provide an introductory framework, so we cannot dive into all details and complexities. This is a simplified version for ease of understanding.
The learning objectives of this full series of modules in this exposure modelling lecture series include: What are exposure models? How do they relate to exposure measurements? What are the purposes of exposure models in different research areas such as environmental exposure, occupational exposure, and consumer exposure? We also aim to provide knowledge of scientific and technological principles of exposure modelling, how these models fit into a wider exposure assessment approach, the different types of exposure models that are available, and an introduction to a tiered approach. We cover exposure models for various routes— inhalation, dermal, and ingestion exposure—general advantages and limitations of using exposure models, and general considerations when applying exposure models. We will also provide further reading materials where you can find additional information.
The content of this Module 2 consists of five parts. I start with the source-to-dose modelling framework, then I will dive further into occupational exposure modelling. I will then provide information on exposure modelling in general, followed by dermal exposure modelling and oral

exposure modelling more specifically, and also aggregate exposure modelling. Finally, I will round off with a summary of the learning objectives of this module.

To start off, it is important to emphasize that on the left-hand side, there are various sources of external exposure. Many different chemicals are used in food products, toys, and cosmetics, but chemicals are also emitted from industries, cars, and various other sources that pollute the air. These emissions can cause external exposure when they come into contact with an entrance barrier. This could be the mouth when we talk about food exposure or oral exposure, the mouth and nose when we talk about inhalation exposure, and the skin when we talk about dermal exposure.
These three routes are the main entrance barriers, and the process of crossing them is what we call intake. When this intake moves further inside the body and the absorption barrier is passed, we call it uptake. The resulting internal exposure levels—the dose—represent the internal exposure or internal dose. These are usually identified within the GI tract for oral exposure, the lungs for inhalation exposure, and the skin for dermal exposure. Once the substance or chemical enters the body, the final step is the biologically effective dose, which is the dose at the specific target tissue. When the substance reaches this target tissue, an effect can occur in the populations, individuals, or children represented on the right-hand side of the diagram.
As mentioned, there are roughly three different intake routes: inhalation through the nose and mouth, ingestion through the mouth and GI tract, and dermal uptake throughout the entire surface of the skin on the body.
Inhalation exposure can occur to multiple contaminants through the air—such as aerosols, vapours, gases, and dusts. Ingestion can come from intake of food, drugs, and medication. Dust and cosmetics can also enter the GI tract through swallowing. Dermal uptake can come from cosmetics, personal care products, textiles, and other products that come into direct contact with the skin, and this can be modified by using protective equipment such as gloves or protective clothing.
Starting with oral uptake: once a substance has been swallowed, eaten, or otherwise enters the mouth, it goes into the stomach and subsequently into the GI tract further down into the intestines. The intestine of an average adult is roughly eight meters long—a long tubular system in which food is processed. Inside the intestine there are structures called villi, through which there is exchange between the intestinal surface and the blood. The total surface area of all these villi is between 400 and 500 square metres, which is an incredibly large surface if you think about it. A thin mucous membrane facilitates the exchange between the intestine and the blood.
Regarding the lungs: when you inhale air, you inhale not only air but also contaminants, aerosols, and dust present in the air. These enter your body through the nose and mouth, then go into the larynx. The larynx splits into the bronchi, and the bronchi branch further into alveoli. At the alveolar level, exchange between air and blood takes place. There are more than 300 million alveoli in our lungs, and the total surface area of all alveoli together is about 100 square meters. This provides a very large surface area for exchange to occur. The diffusion rate is about six litres per minute, meaning that on average we breathe around six litres of air per minute. The size of particles determines where they settle in the respiratory system: large particles deposit in the mouth and nose, medium-sized particles enter the bronchi, and very small particles may reach the alveoli.

Looking at the skin: from top to bottom we see the external skin surface, where hairs and hair follicles extend outward. The first protective layer beneath the surface is the epidermis. Beneath that lies the dermis, which is the layer where exchange of chemicals or contaminants between the skin surface and the bloodstream occurs. Beneath the dermis is the hypodermis or subcutaneous layer. Twelve to fifteen percent of an adult's body weight consists of skin. It is the largest organ of the body, with a surface area of between one and two square metres and a thickness ranging from 0.5 to 2 millimetres across the epidermis, dermis, and subcutaneous layers.

When we consider assumptions about uptake rates, these vary significantly across the three routes of exposure. For ingestion and inhalation, we often assume the uptake to be near 100%. For most organic chemicals, dermal uptake is much lower than 100%. Therefore, assumptions and experimental studies are needed to estimate dermal uptake. Experimentation has been performed with human dermis, human epidermis, or pig skin (which is similar to human skin), applying chemicals on one side of the skin and measuring their penetration into receptor fluids on the other side. This allows quantification of chemical penetration through the skin.

Once a chemical has entered the body through one of the three exposure routes—inhalation into the lungs, dermal uptake through the skin, or oral uptake into the intestines—it is exchanged with the blood. From the bloodstream, there is continuous distribution to different target tissues. Depending on the chemical, distribution occurs to specific organs or tissues. There is also excretion, either through feces via the intestines or urine via the kidneys. This entire system is what we call toxicokinetics or PBPK modelling (physiologically-based pharmacokinetic modelling), in which we simulate the movement and mass flow of chemicals through the body.

I will now proceed to the second part of this module, which focuses on worker exposure modelling, also called occupational exposure modelling.

First of all, as Natalie also emphasized in Module 1, we are talking about a single human being. Workers are exposed occupationally, but the same individuals are exposed in their daily life as well. People do not replace their lungs or skin or GI tract when they go home after work. It is important to keep this in mind, and I will come back to this when discussing aggregate exposure from multiple sources.

Effect assessments can be performed in two different ways: toxicologically (experimental studies) and epidemiologically (studying groups of people exposed to a certain chemical). When we compare worker and consumer exposure, workers generally operate in conditions that are relatively well-defined and known. By contrast, consumer exposure conditions in a home environment are highly variable and often unknown. For occupational exposure, the dominant methods for exposure assessment are workplace measurements and modelling, which I will discuss shortly. For consumer exposure, the assessment relies heavily on assumptions and modelling, as it is difficult to perform detailed exposure measurements in people's homes. Additionally, there are different legislative frameworks. For consumers, there is food legislation and REACH legislation for non-food products. For workers, occupational exposure is regulated under REACH and under long-established occupational limit values to which exposure must be compared.

Exposure models for workers often follow the source-receptor approach. As the name suggests, this consists of a source on the left-hand side—such as a chemical in a can or container—and a receptor on the right-hand side, which is the worker who inhales the airborne exposure. The model assumes that emission from the source is determined by the product's physicochemical properties and the activity performed with the product. Once emitted, the contaminant travels through the workroom air—this is called transmission. Transmission is influenced by local controls, ventilation, and structural elements such as walls or enclosures. Finally, the receptor—the worker—is exposed within the same workspace. Exposure can be reduced by using enclosures or personal protective equipment (PPE).

For each parameter in the source-receptor model, input values are defined. For example, dustiness for powders determines emission, volatility influences vapour generation, concentration affects emission potential, and local control efficiency affects transmission. All these parameters are assigned multipliers, and multiplying them together determines the estimated exposure level. This is the essence of the source-receptor approach. It is critical to remember that exposure modelling is always a simplification of reality. You must be aware of uncertainties and limitations when using models.

Now I will discuss tiered exposure modelling. When the REACH regulation was introduced in 2007, the number of required exposure assessments was overwhelming. It was impossible to conduct detailed exposure measurements for every single company and chemical. Therefore, a tiered approach was introduced to reduce complexity while still providing adequate and protective assessments. Different models existed at the time: ConsExpo for consumer exposure, Stoffenmanager for worker exposure, ECETOC TRA for consumer and worker exposure, the German BAuA EMKG-Expo tool, and others. These were often considered Tier 1 models because they used simplified approaches such as risk banding. Higher tier models, such as the Advanced REACH Tool (ART), provided more precision and complexity. The highest tier, Tier 3, consists of actual exposure measurements.

The purpose of the tiered approach is to reduce the required effort while maintaining protection. If a Tier 1 assessment produces an exposure value well below the limit value, the exposure can be considered acceptable. If not, you must implement risk management measures and reassess, or move to a higher-tier assessment with more precision. This iterative loop enables efficient and effective exposure assessment.

Here are some examples of tools. This is an introductory course, so I cannot explain each tool in detail, but their specific websites provide training resources. ECETOC TRA, the Targeted Risk Assessment tool, is Excel-based and calculates exposure for workers, consumers, and the environment. It is recognized by ECHA under REACH as a preferred approach for consumer and worker health risk assessment. You can download it from the website shown.

When using TRA, you must enter information about the substance, its physicochemical properties, the reference value (such as an OEL), and details of the worker exposure scenario. The tool then provides an exposure estimate.

The Advanced REACH Tool (ART) is an online tool that combines mechanistic modelling with exposure measurement data. Version 1.5 includes an integrated measurement database. ART follows the source-receptor approach described earlier. The model contains a set of exposure parameters, each assigned multipliers depending on scenario inputs. Background reading materials are available for those interested in details.

Assigning these multipliers results in a model score. Each parameter is given a value, and all parameter values multiplied together (along with a background contamination factor) yield a task score. This is a dimensionless score—it represents relative exposure and does not yet reflect concentration in mg/m³. These scores can be used to prioritize risk, for example by assigning them to exposure bands. Higher exposure scores correspond to higher priority for control.

This approach—known as risk banding or control banding—helps identify which chemicals and tasks pose the highest risk. For ART, efforts have been made to relate dimensionless model scores to measured concentrations to derive quantitative exposure in mg/m³. By plotting model scores against measured concentrations for many scenarios, relationships can be identified and translated into linear exposure models. This helps quantify the uncertainty of mechanistic models and allows more accurate exposure predictions.

It is important to distinguish between variability and uncertainty. Variability represents differences in exposure among workers performing the same task. For example, among 100 workers, each will have slightly different exposure. You can select a percentile (e.g., the 75th percentile) to define a protective exposure limit for the majority of workers. But modelled values also contain uncertainty—because of incomplete knowledge and uncertainty about model inputs. Each percentile therefore has its own uncertainty distribution. Both variability and uncertainty must be considered.

Now some details about dermal exposure modelling. Most modelling so far has focused on inhalation exposure, which is generally considered the dominant route for workers. However, workers are also exposed via the skin. Because dermal exposure assessment is complex, the Dermal Exposure Network was established in the 1990s to bring together experts and define standard terminology and conceptual models for dermal exposure assessment. This resulted in a conceptual model (published in the referenced paper), which describes contaminant mass transport processes and interactions among compartments in dermal exposure.

The conceptual model includes six compartments: the source; the air compartment (via emission); the skin surface contamination layer (via deposition); contaminated surfaces (via transfer); clothing contamination layers (outer and inner), and the skin contamination layer. Transport routes include direct deposition from air, direct emission from the source, and transfer from contaminated surfaces such as floors, tools, or machinery.

The conceptual model distinguishes between potential exposure (contamination on clothing or outer surfaces) and actual exposure (contamination that reaches the skin). This model does not account for absorption through the skin—that is, uptake is not part of this conceptual framework. It focuses on external contamination only.

Next is aggregate exposure modelling, which can be done in two ways. One way is by combining exposure through inhalation, dermal, and oral routes, because internal dose is the result of exposure through all routes. Workers can be exposed to contaminants through multiple pathways simultaneously. Models exist that combine inhalation and dermal exposure, and some efforts—such as those by the Institute of Occupational Medicine in Scotland—have focused on inadvertent oral exposure in workers.

A second form of aggregate exposure is combining exposures from multiple sources: occupational exposure plus exposure during daily life. This can be done from the occupational perspective or the general population perspective. Starting from the job perspective, you identify jobs in which occupational exposure is dominant—for example farmers or military personnel—model the occupational exposure through inhalation, dermal, or oral pathways, then assess non-occupational exposures from consumer products or the environment, and aggregate them.

From the general population approach, you start with exposures in daily life (food, environment, consumer products) and then identify which subset of the population holds specific jobs with additional occupational exposure. Based on the proportion of such workers in the population, job exposures are assigned and added to the general exposure. This yields an aggregated exposure estimate for the total population.

To summarise: it is important to identify all relevant routes of exposure. Do not assume exposure occurs only via inhalation; dermal and oral exposure may also be important. In exposure assessment modelling, always consider all potential routes and combine them if necessary to calculate aggregate exposure, especially when assessments involve multiple legislative frameworks. A tiered approach can help balance the required level of detail with available data. It is important to validate models by comparing predictions to measured concentrations, which remain the gold standard for exposure assessment.

This is the end of Module 2. There are three more modules in this series, so please consult those if you are interested in human biomonitoring, exposure of the general population, and validation and evaluation of exposure modelling. As mentioned at the beginning, other training series are also available as ISES Europe specialized training videos. Please consult the ISES website if you want to learn more. Thank you very much for joining Module 2. We appreciate your participation and attention and encourage you to explore the other training videos on the website.

If you want more information, please consult the further reading materials provided, where you can find more background information for additional study. Thank you very much.