ISES Europe Training Series

DoE 3: Exposure Modelling

Module 1: Introduction, Context & Regulation, Concepts for Exposure Modelling

Hello everybody. Welcome to this domain of expertise 3 exposure modelling course.
It's part of the ISES Europe training series and presenters will be Natalie von Goetz, which is myself and Wouter Fransman. First some disclaimers and an overview of all training videos so that you know where we are. The domain of expertise 3, exposure modelling, contains 5 modules, two of which will be held by Wouter Franzmann and three by myself. We will start with module one, introduction, context and regulation concepts for exposure modelling.

I am Natalie von Goetz.
I currently work at the Swiss Federal Office of Public Health as a project leader, and I'm also still working as a lecturer at the Federal Institute of Technology, ETH Zurich, where I've previously worked as a group leader in human exposure modelling. My background is chemistry. I have a PhD in natural sciences, where I already did exposure modelling.

Again, some disclaimers and your learning objectives just for your files. And now we start with the lesson “Introduction, definitions, regulation”, which will be our first chapter in this module.

I would like to start with placing exposure assessment in the context of risk assessment. You have probably already listened to the domain of expertise two, where also hazard identification and dose response assessment were mentioned. And in the introductory course, which is domain of expertise one, you have already heard about the risk paradigm.
So, hazard on the one hand and exposure on the other hand, these are the determinants of the risk, which then feed into risk assessment. And since this is a course mainly designed to teach you more about exposure assessment, we have 3 domains of expertise, 3, 4, and 7, which deal with exposure assessment.

And why do we think exposure modelling is worth a whole domain of expertise? When exposure scientists of Europe, who are organized in the International Society of Exposure Science, came together in 2018 to discuss how we should move on in Europe about exposure science, we identified exposure modelling as one of the key areas. And we also founded the ISES Europe Exposure Modelling Working Group, which set some goals, some far and near-term goals. One of them was a training course on exposure modelling. Therefore, we have now included this domain of expertise in our whole series on exposure science.

Now some definitions: definitions are sometimes a bit boring, but they are very important because nomenclature is the basis for a scientific discipline and allows people to understand each other. So, exposure is defined by a contact between an agent and a target and measured by the concentration or amount of an agent. And then exposure assessment is the process of estimating or measuring exposure by measuring the frequency, duration, and so on. There already, you see, is mentioned estimation, which is modelling, what this whole course is about, and then measuring, which is monitoring, which is the subject of domain of expertise four.

A very important part of the exposure assessment is the definition of the exposure scenario. The scenario is the combination of facts, assumptions, and so on that define a discrete situation where potential exposures may occur. And this is so important because all these situations are very diverse, so that for the exposure assessment, one has to think of a suitable situation that can be representative for many other situations. I just have to note, the regulation REACH uses a slightly different definition, but this definition of exposure scenario is the one that is globally agreed.

Then some few words about European regulation. You will hear about this more in detail in the domain of expertise 7, which is all about legislation. For exposure science, legislation is very important because
large parts of the exposure science are driven also by legislation, by legislation on chemicals that requires risk assessment. Like for example, the REACH regulation in Europe, regulation on classification, labelling and packaging, regulation for pesticides. And these legislations require exposure assessments for three different domains, worker exposure, general population and environment. Some of them are specific for the specific targets, some of them require exposure assessments for all of them.

Now, when we come to measurement versus modelling, we have to think about the receptors or the targets in risk assessment for which we are doing the risk assessment and, hence, the exposure assessment. These can be human beings on the one hand, and then animals, plants, ecosystem on the other hand. And the effect that we are comparing the exposure to is defined in different scientific fields, like for the human being, toxicology, epidemiology, and for animals, plants, ecosystem, it is ecotoxicology. And these are distinct fields because we have a very profound difference between human beings and the rest, which is that normally we don't like really that chemical substances are being tested on human beings. We are doing this for medicine, but not for contaminants. Therefore, we are not doing the effect assessment directly on the target, but we are using for example, animal studies as a surrogate, like in toxicology, or we are using statistics on large population groups of human beings to look whether there is an effect, which correlates with a chemical exposure. But this is very different from ecotoxicology, where one can study directly the effect on the target. And then we have to divide further also the human being because we have the workers and we have the general population. These are divided because workers are often more exposed to chemicals, specifically in the past where there was not so much knowledge about chemicals and workers had to handle chemicals in a quite unsafe way. Whereas the general population is mainly exposed via food or via the environment, which contain much smaller concentrations of chemicals normally.

But this is not the only difference. Another difference is that the worker normally works in a more defined environment, or at least the working process is more defined than all the different things that the general population is doing in their daily life. And also for the worker, there is more history

in the establishment of threshold limit values. There is also more interest by the companies themselves. So, they put quite some effort into knowing what the exposure is and for worker exposure measurement is a more dominant method, than modelling. This is the other way around for the general population, because we have so diverse exposure scenarios. Therefore, for the general population modelling is much more important. This is more similar then to the environmental modelling, so we have large similarities also between the general population modelling and the environment modelling.
When we look closer into where exposure monitoring and modelling is introduced into the risk assessment process, we can look at this very nice figure of Kandlikar et al., where they have pictured the process of data generation and where this ends up in the risk assessment.

I would like to start from the right. Here we have the risk theorem. We have the exposure quantification on the one hand and the effect quantification on the other. And when we compare this, this is our risk assessment. For a quantification, we need data. We need calculations and we need to know about the path that a substance takes from the source to the receptor. It starts from the top with the pollutant emissions. For example, a pollutant is emitted by a factory into the air, and then this leads to environmental concentrations, and is finally translated by the food or by the air that we breathe into human exposure, and then is inside the body to the biologically relevant dose, interaction with macromolecules, and then finally to an adverse health effect. But where do we get the data from to know what is happening at the different steps? For example, for pollutant emissions, we have the emission factors. There are people who have developed emission scenarios, who have looked at the tonnage that is emitted by certain factories, for example, and these can be looked up and used for calculations. Then for environmental concentrations, we have environmental media monitoring. Most of the different countries in Europe have a systematic environmental media monitoring, be it air or soil or water. And then we have human exposure monitoring. This is newer, it is biomonitoring. Often you are looking into the substances in blood or urine, and then you know what the humans are exposed to. Altogether, these are the measurements.

And then on the other hand, you can have modelling that contributes to the knowledge about the source to receptor pathway. You can have environmental monitoring for the environmental concentrations, exposure modelling for human exposure, and pharmacokinetic modelling when it comes to the processes inside the human body. And then on the other hand, we have the data that contributes to the knowledge about adverse health effects. These are, on the one hand, epidemiological studies, which are a kind of monitoring studies. And on the other hand, the animal toxicity studies, in vitro toxicity studies, and QSARs, and these, are more on the modelling side. I put also animal toxicity on the modelling side because we need models to translate from the animal to the human. So here with this scheme, you know a little bit where and which data come in into the process on different scales.

And now I am coming to specific comparisons between exposure measurement and exposure modelling, also to know when to use what. The exposure measurements are usually very specific, you do this for a very specific situation. You can also then do some extrapolation. But this is only possible if you have a larger number of measuring points. On the other hand, exposure modelling is mostly generic. Often, you are starting with upper bound parameters, worst case parameters. This is more generic, and an extrapolation is quite easy to do if you are in the model application domain. The costs are also quite low for exposure modelling, rather high for exposure measurement. You

have to do the sampling and also the analytics, whereas for the modelling, you only need the hardware and some software, hence suitable exposure models, and then you can do it.
Hence, one of the important resources needed for exposure modelling are the model tools. Here you can obviously do some modelling yourself. You can think of the equations that you need, but there are also some ready-made models available and tools. An overview of these models and tools in the different domains has also been provided by the Exposure Modelling Group from ISES Europe. There's also another very important resource that is from the OECD. They have recently finalized a report on the survey of exposure models used in a regulatory context and have established a related database that is still under development. I would like to conclude here the measurement versus modelling part and come to the concepts for exposure modelling.

We will go more into the details of these concepts. I only want to touch very briefly on the basic principles. In exposure modelling, I already mentioned that source to dose modelling is very important, where you are looking into the whole pathway, the whole way that the substance takes from the source to the receptor. You're looking into the transport possibilities. For example, when a substance is originally in a carpet and then goes into the air and there it can be breathed in by a receptor, this would then be such a source to dose transition. If we think of other examples, for example, for the worker, the air at the workplace is very important; then also resources and devices used at work. As well, for the worker, we have a large focus on the skin, the dermal exposure, and on the inhalation exposure. For the consumer, the most important exposure source is food, then also consumer products and obviously the environment. For the environment, we have to think of the emissions coming from industry or also domestic emissions and from agriculture. So this would then be the source monitoring as a method. And on the other hand, we can then check the receptor concentrations and look how much ends up in the receptor by taking urine, blood, exhaled air, or mother milk from human beings or measuring the environment directly, which is human biomonitoring. For the environmental receptors environmental monitoring can be used directly.

The general idea of human exposure modelling is this: You have a source containing a substance, and then you have different intake routes, which are for example oral uptake, inhalation, dermal uptake, and then the substance ends up in the consumer. You can calculate then just by multiplying the concentration in a source by the uptake of the source, which is Q, divided by the body weight and some uptake fraction, and then you arrive at the dose for a specific source and a specific intake mode. But we have to keep in mind that exposure settings are highly diverse. To handle this, exposure assessment follows a tiered approach. So, in the first tier, normally you're using conservative upper bound assumptions, maximal intakes, use amounts together with maximal concentrations. These would be the input into your model. Then in the second tier, you are using refined upper bound assumptions. You are thinking about which data you could use to achieve a more refined assessment. And with the third tier, which would be of highest complexity and which needs more parameters and more resources, you will end up with a more realistic case. You will hear more about the different methods used for the different tiers in the following modules of this domain of expertise.

So as a summary for this introduction, I would like to stress that exposure modelling is needed because measurements cannot cover all possible exposure scenarios. Then second, differences and ranges in exposure settings can be modelled by parameter variation. And then the third take-home message is that it is important to use a tiered approach in exposure modelling as also in exposure

assessment, because otherwise we start with a lot of resources and a lot of complexity and will not get a very good picture.
The next module will be Human Exposure Modelling, General Concepts and Occupational, which will be held by Wouter Franzmann. And with this, I would like to thank you and hope that you stay tuned for the next module of our exposure modelling domain of expertise.