

# Transformation of occupational hygiene into exposure science to meet practice demands in the 21st century

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## INTRODUCTION

Over our lifetimes we are exposed, daily, to agents that have the potential to affect our health – through the personal care products we use, our water intake, the food we eat, the soil and surfaces we touch, and the air we breathe. With this holistic view, described as the human ‘exposome’, exposure science addresses the intensity and duration of contact of humans or other organisms with those agents (defined as chemical, physical or biologic stressors) and their fate in living systems.<sup>1</sup> Recently, a number of reports have been published by the US National Academy of Sciences, which elaborate on exposure science and its role in risk assessment.<sup>2,3</sup> Exposure science is described by the National Research Council (NRC) as “the collection and analysis of quantitative and qualitative information needed to understand the nature of the contact between physical, chemical or biological stressors, and receptors”, e.g. residents, consumers, workers, etc.<sup>2</sup> Importantly, at the level of the receptor, this contact, defined as an ‘exposure event’<sup>4,5</sup> results in intake, uptake, dose and, possibly, an (adverse) health effect (Figure 1).

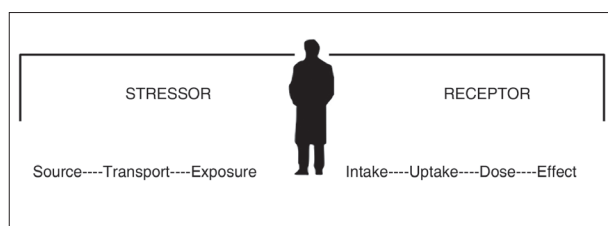
In order to harmonise exposure-related terms, the International Society for Exposure Analysis (now the International Society for Exposure Science) adopted an official glossary in 2005<sup>5</sup> (which was amended by Mattingly et al., 2012) to their Exposure Science Ontology framework.<sup>4</sup> In the amendment, the terms ‘agent’ and ‘target’ were replaced with ‘exposure stressor’ and ‘exposure receptor’, respectively (Table 1).

The concept of the exposome requires consideration of an individual’s exposure over the lifecourse rather than focusing on a specific exposure stressor in a specific domain, e.g. residential, consumer or occupational exposure, over a defined period.<sup>1,7-9</sup> The concept of an aggregate exposure pathway,<sup>10</sup> representing

multiple sources and transfer through single pathways to the target site exposure (TSE), single sources and transfer through multiple pathways to the TSE, or any combination thereof,<sup>11</sup> should raise awareness about the contribution of the exposure from various domains. Focusing on the contribution to the lifetime exposure of the working lifestage, a number of attributes of occupational exposure are relevant. First, exposure associated with, and emanating from, occupational sources will (most likely) occur during adulthood – the lifestage during which an individual is considered to be less susceptible than childhood, adolescence and late adulthood. Second, occupational exposure is temporally intermittent, i.e. periods of exposure are followed by periods of absence of exposure, e.g. before and after work, weekends, and vacation periods, which is pivotal to physiological recovery, i.e. clearance, metabolism, excretion, etc. Third, levels of occupational exposure can substantially exceed exposure levels in other domains.

Not surprisingly, there are some similarities between the descriptions of exposure science and occupational hygiene. The International Occupational Hygiene Association (IOHA) provides the following description: “Occupational hygiene is the discipline of anticipating, recognising, evaluating and controlling health hazards in the working environment with the objective of protecting worker health and well-being and safeguarding the community at large”.<sup>12</sup> Occupational hygiene has also been defined as the practice of identifying hazardous agents in the workplace (chemical, physical and biological) that could cause disease or discomfort, evaluating the extent of the risk due to exposure to these agents, and the control of the risks to prevent ill-health in the long or short term.<sup>12</sup>

Apart from including biomechanical and psychological stressors in occupational hygiene, another important difference with regard to the definition of exposure science by the NRC<sup>2</sup> is that, in the definition of occupational hygiene, the terms ‘control’ (of exposure and risk) and ‘prevention’ (from an adverse outcome) are explicitly used. This makes sense since, in contrast to other exposures, e.g. through ambient air, water or food, exposure in the work environment can be relatively easily controlled as the exposure source is, in most cases, in the worker’s (micro) environment, or even emanates from the activity of the worker himself or herself. It should be noted, however, that a number of scientists had already addressed the prevention issue in 2006, when they described exposure science as “the study of human contact with



**Figure 1. Pathways of the stressor from source to receptor, and the fate in the receptor, resulting in an (adverse) effect (figure inspired by US-EPA, 2016<sup>6</sup>)**

**Table 1. Definition of some terms used in exposure science**

Term	Definition	Reference
Absorption barrier	Any exposure surface that may retard the rate of penetration of an exposure stressor into an exposure receptor	Zarterian et al., 2005 <sup>5</sup> Mattingly et al., 2012 <sup>4</sup>
Dose	The amount of an exposure stressor that enters an exposure receptor after crossing an exposure surface. If the exposure surface is an absorption barrier, the dose is the absorbed/uptake dose; otherwise, it is an intake dose	Zarterian et al., 2005 <sup>5</sup> Mattingly et al., 2012 <sup>4</sup>
Exposure	Contact between a stressor and a receptor. Contact takes place at an exposure surface over an exposure period. A person's contact with the concentration of a material before and after it crosses a boundary (nose, skin or mouth) between the human and the environment, over an interval of time leading to a potential biological effective dose	Zarterian et al., 2005 <sup>5</sup> Mattingly et al., 2012 <sup>4</sup>  NRC, 2012 <sup>2</sup>
Exposure event	An interaction between an exposure stressor and exposure receptor	Mattingly et al., 2012 <sup>4</sup>
Exposure receptor	An entity that interacts with an exposure stressor during an exposure event	Mattingly et al., 2012 <sup>4</sup>
Exposure stressor	An agent, stimulus, activity or event that causes stress or tension on an organ and interacts with an exposure receptor during an exposure event	Mattingly et al., 2012 <sup>4</sup>
Exposure surface	A surface on an exposure receptor where an exposure stressor is present. Examples of outer exposure surfaces are the conceptual surface over the nose and open mouth, and the skin surface. Examples of inner exposure surfaces are the respiratory and gastro-intestinal tracts	Zarterian et al., 2005 <sup>5</sup> Mattingly et al., 2012 <sup>4</sup>
Intake	The process by which an exposure stressor crosses an outer exposure surface of an exposure receptor without passing an absorption barrier, e.g. through inhalation or ingestion. Inhalation intake = concentration (mg/m <sup>3</sup> ) x inhalation rate (l/min) x exposure duration (min)	Zarterian et al., 2005 <sup>5</sup> Mattingly et al., 2012 <sup>4</sup>
Uptake	The process by which an exposure stressor crosses an absorption barrier	Zarterian et al., 2005 <sup>5</sup> Mattingly et al., 2012 <sup>4</sup>

chemical, physical or biological agents in their environments, and advanced knowledge of the mechanisms and dynamics of events either causing or preventing adverse health outcomes".<sup>13</sup>

The application of exposure science in risk evaluations is expected to develop risk assessments of individuals rather than groups further, by improved exposure assessment of individuals through better characterisation of the various micro-environments, and detailed activity (residence) time patterns of individuals and the use of (relatively) low-cost sensors in combination with tracking systems.<sup>14</sup> In addition, computational exposure assessments (use of exposure models) and statistical techniques, e.g. Monte Carlo simulations and Bayesian statistics, in combination with appropriate high-throughput toxicological screening techniques, will enhance probabilistic risk assessments which take into account variances in the populations and stressor levels.<sup>3,15</sup> This will replace the often-used (in occupational hygiene) simplification of the risk assessment, i.e. the ratio between a time-weighted average (TWA8h) and an occupational exposure limit (OEL).

In this paper, we advocate transforming the discipline of occupational hygiene into a sub-specialism of exposure science.

## THE PRINCIPLES OF EXPOSURE SCIENCE

Exposure can be considered to be the result of a cascade of underlying processes which, in general terms, can be described by a source-receptor model with the key elements of release, emission, transmission and immission (Table 2). At the source, a chemical/biological agent or physical stressor is released by natural or anthropometric processes, e.g. volatilisation, evaporation, leaching, combustion, mechanical stress, etc. After release, the stressor is emitted to a compartment such as ambient or indoor/workplace air, surface water, soil, or the skin. The transmission process within the compartment is affected by numerous processes (ventilation, air currents, etc.) which, in the air compartment, govern agglomeration, deposition (of aerosols) and dilution; in some cases, resuspension of the deposited particles may occur. In other compartments, e.g. the skin, surface transmission is driven by diffusion at the molecular level (permeation). Immission is a generic term and alternative terms are used specifically for inhalation exposure: 1) the concentration and particle size distribution in the near field (referred to as a virtual cube 1 m around the nose and mouth of the receptor which may be the worker)<sup>16</sup> and, 2) the breathing zone concentration (usually within a 0.3 m (or 10 inch))

**Table 2. Key processes of a source-receptor model**

Term	Description
Release	The liberation of a stressor during a natural or technical process, which may be expressed without a specific metric, as a dispersion-specific fraction or percentage of the total release, or as a mass per unit of area or unit quantity of the matrix
Emission	The transfer process of a liberated stressor to a compartment, e.g. the workplace air; usually expressed as flow, e.g. quantity per unit time or unit of area
Transmission	The transfer of a liberated stressor to the receptor through the compartment, e.g. the workplace air. Efficacy is determined by interception or distraction (e.g. absorbent materials or baffles, in the case of noise), dilution by ventilation (in the case of chemical and biological stressors), and deposition and resuspension (in the case of particles)
Immission	The introduction of the stressor into the near field zone of the receptor; usually expressed as a concentration or an energy/ pressure level
Exposure (event)	The contact of the stressor at an exposure surface over an exposure period; usually expressed as concentration, or an energy/pressure level x exposure duration, or as a time weighted average (TWA) over the exposure period

radius of the nose and mouth).<sup>17</sup> The assumptions are that a contaminant in the near field zone is homogeneously distributed, and that its concentration is equivalent to the concentration inhaled by the receptor. It should be noted that in life cycle assessment (LCA) and residential and consumer exposure assessment, the term 'near field' is used for the indoor environment to distinguish from 'far field' pathways, such as ambient air, soil, drinking water and diet.<sup>18</sup>

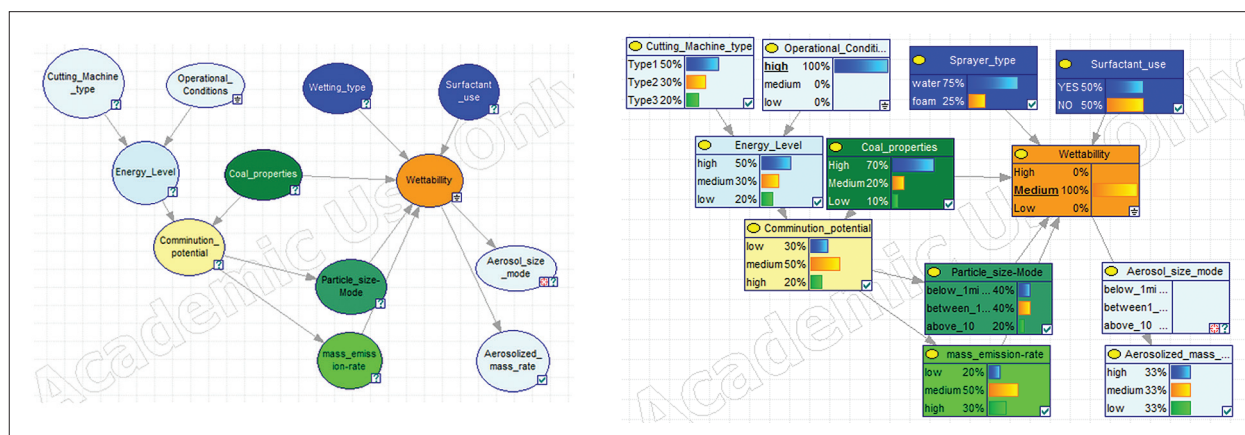
If no personal protective equipment (PPE) is used, e.g. respiratory, skin or ear protection, the near field concentration will be equal to the concentration at the exposure surface, i.e. the conceptual surface over the nose and mouth, skin, and ear, respectively (Table 1). If PPE is used, the exposure concentration will be the attenuated 'near field' concentration. Note that the transmission process can also be direct contact, e.g. direct contact of the skin with water while swimming, or with indoor surfaces.

**SCRUTINISING THE UNDERLYING PROCESSES**

The underlying processes that result in exposure might be complex as each process is governed by determinants and modifying factors. To illustrate the complexity, on one hand, and, on the other hand, to show how this complexity can be reduced by breaking it into sections, the following scenario is presented as an example:

extracting coal in an underground room and pillar type of mine, using a continuous miner (CM). In this scenario, the release of coal dust will be determined by 1) the CM-type and, 2) the conditions under which the CM is operating. In combination, these factors will determine the energy level of the fragmentation (the stress level) that will be employed. This stress level, in combination with the properties of the coal, e.g. type (rank – degree of metamorphism, and grade – range of impurities) will determine the ease of fragmenting. The level of comminution will determine which fraction of the released particles will emanate in debris (the actual product) and which fraction has the potential to become airborne (dust). The probability of becoming airborne, i.e. emitted into the stope air, will be modified by the wettability of the coal seam. The latter is the result of the use and the efficacy of surface wetting, e.g. the type of wetting system, the use of surfactants, and the surface physical properties of the coal. The resulting emission can be described by aerosolised mass-rate and size-distribution.

The relationship between the discrete influencing variables and their outcome can be captured in a graphical presentation, e.g. a Bayesian belief network (BBN) which shows Bayesian variables or nodes, subdividing 'parent' variables with their direct links (arrows) to their 'child' variable(s).<sup>19,20</sup> In Figure 2 (left panel) the example of dust formation during coal excavation, as described



**Figure 2. Graphical structure of the Bayesian belief network (BBN) model for emission of dust in an underground coal mine (left panel); the right panel shows the associated conditional probability tables**

above, is illustrated in a BBN. However, the quantitative relationship between the variables is often unknown. The advantage of a BBN is that limited knowledge can be used to build so-called conditional probability tables (CPTs). Each network variable contains a limited number of sets to which their realised value can belong. This can also be considered as a probability distribution. Looking more closely at the CPTs of the example in Figure 2 (right panel), the distributions of the probability of the two parent variables are shown: first, the probability that a specific type of CM (type 1, 2 or 3) is used and, second, the probability of the operational conditions (high, medium or low load). The probability of the value of the resulting 'child' variable, i.e. the energy level of the fractioning, is a function of the probability distribution of both 'parent' variables. Numerous software tools are currently available to support the development of BBNs.<sup>20</sup>

The model can be further extended by adding similar BBNs for the determinants affecting the transmission, e.g. dust suppression, dilution, air velocity, etc., to develop, in combination with an activity-time profile, a rudimentary scenario-specific exposure model.

If quantitative data are not available, the development of a BBN and, more specifically, the CPTs, relies heavily on the experience, expertise and intuition of experts. Structured inputs by experts can be achieved by expert elicitation protocols as demonstrated by Shandilya et al. (2018) in their development of a nanomaterial release model for waste shredding.<sup>21</sup>

## RELATIONSHIP BETWEEN OCCUPATIONAL HYGIENE AND EXPOSURE SCIENCE

### Anticipation and recognition

Both anticipation and recognition of potential risk due to exposure to harmful stressors require knowledge of the processes leading to release/emission, i.e. thorough knowledge of the materials and products to be used or produced, the associated processes, operations and tasks, and the operational conditions. Cross-reading of (similar) technical processes and exposure models are tools that can be used to understand whether a process or operation may pose a risk. Computational exposure assessment, or the use of exposure models, plays a pivotal role in anticipating potential for exposure, especially in the case of a future or envisioned scenario, e.g. the introduction of a new chemical agent or a different physical form of an existing agent in an existing process, change of operational conditions of an existing process, a totally new process, etc. Currently, a number of mechanistic, deterministic and empirical models (and combinations of these) exist and are accessible as web-based- or down-loadable standalone tools. With respect to inhalation exposure to chemical stressors, various mechanistic or deterministic models are captured in IH-Mod 2.0, e.g. well-mixed box room and various two-box models.<sup>22</sup> IH-Mod 2.0 is a mathematical modelling MS Excel spreadsheet used for estimating occupational exposures. Most of the models are described in a series of articles published in the *Journal of Environmental and Occupational Hygiene*.<sup>23-26</sup> Examples of exposure predictive tools that are a mixture of mechanistic and empirical models are Stoffenmanager®<sup>27</sup> and the Advanced Reach Tool (ART).<sup>28</sup>

The mechanistic part of Stoffenmanager® is a source-receptor model that is captured in an algorithm, whereas the empirical part calibrates the outcome scores of the algorithm, using exposure data.<sup>29-31</sup> ART is based on Stoffenmanager® and incorporates a mechanistic model of inhalation exposure and a statistical facility to update the estimates, with measurements selected from an in-built exposure database or from the user's own data.<sup>32-34</sup> In addition, a number of scenario-specific predictive models have been developed, e.g. for spray painting, pesticide application, etc. Generic models that predict dermal exposure are limited;<sup>35</sup> however, some empirical models have been published.<sup>36,37</sup> Recently, research has been conducted to develop a model for inadvertent ingestion exposure by hand-mouth contact.<sup>38</sup>

For biological stressors, the models for airborne transmission of pathogens are more complicated as they also consider the (conditions of) viability of the pathogens during transmission. Therefore, the transmission model component is often incorporated into a risk model.<sup>39-41</sup>

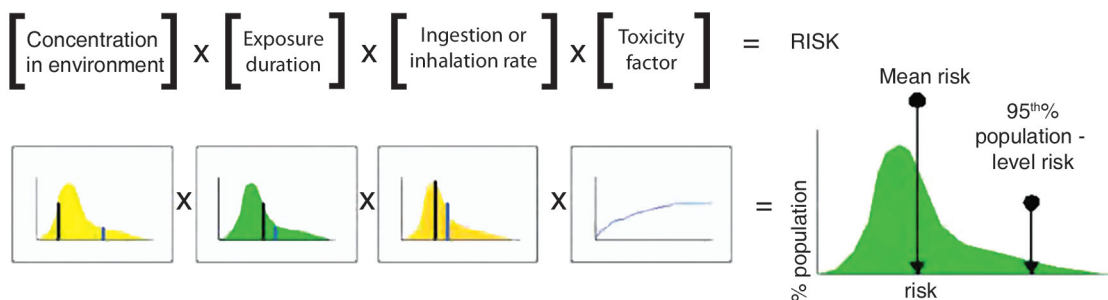
For physical stressors, the transmission from source to receptor is generally governed by the inverse-square law, which states that a specified physical quantity or intensity is inversely proportional to the square of the distance from the source of that physical quantity. The propagation of the energy can be affected, however, in case the free field is disturbed by (un)intentional obstacles, such as shields or baffles.

Anticipation can also be considered as an approach that encompasses the selection of safer materials, processes or technologies. The most stringent method of anticipation is 'designing the risk out'. This so-called prevention through design (PtD) has been promoted over the last decade, especially in the context of emerging technologies.<sup>42</sup> However, comparative risk assessment, addressing both hazard and exposure of potential alternatives, and 'life cycle thinking' should be taken into consideration to avoid similar risks, risk shifts, or risk trade-offs.<sup>43</sup>

### Evaluation and control

Biological monitoring is a key component in the exposome and exposure to exogenous and endogenous chemicals at the level of the receptor and the individual's characteristics, with regard to his or her specific toxicokinetics (absorption, distribution, metabolism and excretion). Such a top-down approach will provide very relevant information for risk assessment, and employs the collection and analysis of biological samples, which is feasible with rapidly-developing analytical techniques.<sup>3</sup> A drawback, however, is that the exposure cannot be directly linked to the sources and their pathways; thus, interventions to reduce exposure cannot be targeted. Therefore, a bottom-up approach, i.e. sampling of sources of exposure, will remain important from the perspectives of risk assessment, exposure analysis and control.

Unfortunately, the current practice of occupational hygiene measurements in South Africa focuses on demonstrating compliance with OELs set by regulatory bodies, such as the Departments of Mineral Resources and Labour. Measurements are important since workplaces need to comply with the relevant Acts and



**Figure 3. Illustration of a probabilistic risk assessment of exposure to a hazardous chemical agent in air (source: US-EPA<sup>47</sup>)**

Regulations and, since the results may have legal implications, quality assurance and control of the measurements are essential. However, compliance measurements are not a substitute for a risk assessment, nor do they automatically support the risk assessment itself. First, the regulatory OELs are not necessarily health-based values. For example, the descriptions of the OELs in both the current and proposed revisions of the Hazardous Chemical Substance/Agents<sup>†</sup> Regulations explicitly address OEL-recommended/restricted limits feasibility issues related to implementation and enforcement, in practice, and additional socio-economic impact issues related to OEL-control/maximum limits. Second, the format of the measurements is a time-weighted average (TWA) over a defined period (15 min (STEL) or 8 hr), which is not necessarily an accurate reflection of the duration of exposure. Third, OELs are generally defined as an (airborne) concentration of a hazardous (chemical) substance/agent and not necessarily as personal exposure. Fourth, if the OEL did represent a health-based value, the ratio of the OEL-value/ TWA8h-value could only be an indicator of the risk potential. This is because a full risk assessment takes into account the intake (see Table 1) as a proxy for the dose, rather than the external exposure (concentration, energy). In the widely-accepted method for risk assessment of residential and environmental exposure to a chemical agent,<sup>44</sup> the risk of non-carcinogenic effects is expressed by the hazard quotient (HQ) which is the (aggregated) daily intake divided by the reference concentration (or dose) of the agent (RfC and RfD, respectively). The RfC or RfD is the estimate of the chemical concentration or dose, respectively, that will not cause non-carcinogenic effects during a specified exposure period.<sup>45</sup> For carcinogenic effects, the cancer risk is expressed as the (aggregated) daily intake multiplied by the cancer slope factor (CSF), where the CSF is the slope of the curve representing the relationship between dose and cancer risk.<sup>46</sup> Note that, with substantial increases in computational power and advances in analytical and integrative methods, the current trend is to move from deterministic analyses towards probabilistic risk assessment (Figure 3). The probabilistic approach incorporates information regarding uncertainty and/or variability into analyses to provide insight regarding the degree of certainty of a risk estimate, and how the risk estimate varies among different members of an exposed population, including sensitive populations and lifestyles.<sup>47</sup> This contrasts with the outcome of the deterministic analyses which report risks as point

estimates, e.g. 'central tendency' (mean, median), or 90<sup>th</sup> percentile.

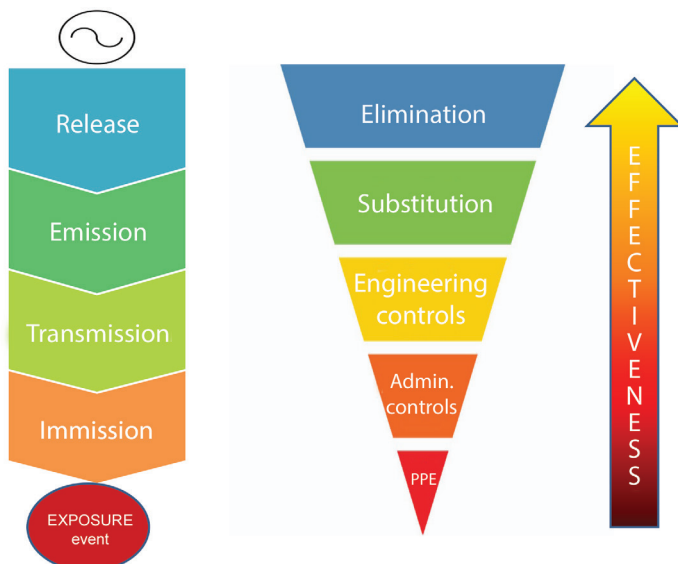
In addition to supporting risk assessment, occupational measurements can also support the analysis of the underlying processes of exposure. As outlined in Table 2, the starting point of any exposure is the release from a source followed by emission. Specific measurements will provide an estimate of the release or emission of materials and products during a process, task or handling, e.g. release of asbestos fibres from asbestos cement products by weathering,<sup>48</sup> or release of nanoparticles by mechanical treatments.<sup>21</sup> The use of direct reading instruments, e.g. those integrated in a task-based exposure assessment strategy, can already provide a first impression of the source strength.<sup>49,50</sup> Since release indicates the potential for exposure, release libraries can be helpful in mapping the exposure processes.<sup>51,52</sup>

As stated, a well-founded knowledge of the underlying processes resulting in exposure plays a pivotal role in developing an effective exposure control strategy. It provides information about which intervention option would achieve the highest efficacy. Therefore, exposure control should be more than a reference to the generic hierarchy of control, but should provide tailor-made intervention options. However, a successful intervention depends not only on the expected efficacy but also on the selection of the optimum control option that takes into account the (cost-related) efficiency, the acceptance of control options by the stakeholders, e.g. the workers, and other implementation issues.

Since exposure emanates from release at a source and consecutive emission in a compartment, followed by its transmission and, consequently, results in immission at a receptor, interventions can focus on the various stages of this exposure process. The types of interventions are captured in the so-called hierarchy of control,<sup>53</sup> which is strongly linked to the source receptor-based exposure process and therefore also represents the decline of effectiveness towards the lower levels of the hierarchy (Figure 4).

As already mentioned, especially with regard to the elimination by PTD, for the substitution option, it is key to select alternatives that do not pose similar risks, risk shifting or risk trade-offs. Formal frameworks, e.g. alternative assessment, have been developed to assist industry and academics to select chemical alternatives.<sup>54,55</sup> However, their extensive use by industrial experts is hampered by methodological challenges.<sup>43</sup>

<sup>†</sup>HCA2018: Draft Revision of Regulations for Hazardous Chemical Substances



**Figure 4. The relationship between the cascade of processes resulting in exposure (left section) and the hierarchy of control, demonstrating the increase of effectiveness of an intervention closer to the source**

Critical but often under-valued aspects of exposure control relate to the decision-making<sup>56</sup> or selection where, in addition to efficacy and costs, the above-mentioned aspects should be considered.<sup>57</sup> Moreover, the implementation stage and, more explicitly, the barriers and enablers perceived by the various stakeholders, should receive sufficient attention to enhance a successful implementation of a proposed exposure control.

## DISCUSSION AND RECOMMENDATIONS

To date, the relationship between exposure science and occupational hygiene has not been extensively described and both fields appear to exist in separate silos. Even within the International Society for Exposure Science, there is a strong focus on target groups such as consumers, residents, the general public, and environmental and indoor exposures, rather than workplace exposures, which does not correspond with the concept of the exposome. Integration of these fields from this holistic perspective should be encouraged since the two fields have much to offer each other. As illustrated, workplace exposures have the unique feature (compared with many other exposures) of frequently having the exposure source within the same domain or manageability area, i.e. the workplace. However, a pre-condition is that the exposure pathways from source to receptor should be identified and well understood. Occupational hygiene can keep pace with developments in other fields that are consolidated in the field of exposure science. In our view, higher education institutions that offer curricula in the field of environmental and occupational health and hygiene should evolve their programmes to train students to develop a broader view about environmental, residential and occupational exposures. In addition to the current occupational hygiene and environmental health curricula, students should be challenged with the fundamentals of comparative risk assessment, computational exposure assessment, implementation science, and decision-making and analysis, in order to understand and apply these concepts.

We acknowledge that it is impossible to cover all aspects of

exposure science extensively thus, inevitably, sub-specialisms will be needed for every individual exposure domain, target group, or exposure pathway, e.g. through food, drinking water, etc. Occupational hygiene should be one of these sub-specialisms. The process of transformation is imminent.

## REFERENCES

- Rappaport SM. Implications of the exposome for exposure science. *J Exposure Sci Environ Epidemiol* 2011; 21(1):5-9.
- National Research Council. *Exposure science in the 21st century: a vision and a strategy*. Washington, D.C.: NRC; 2012.
- National Academies of Science, Engineering and Medicine. *Using 21st century science to improve risk-related evaluations*. Washington, D.C.: National Academies Press; 2017.
- Mattingly CJ, McKone TE, Callahan MA, Blake JA, Hubal EA. Providing the missing link: the exposure science ontology ExO. *Environ Sci Technol*. 2012; 46(6): 3046-53.
- Zartarian V, Bahadori T, McKone T. Adoption of an official ISEA glossary. *J Exposure Anal Environ Epidemiol*. 2005; 15(1):1-5.
- United States. Environmental Protection Agency. *Guidelines for Human Exposure Assessment*. Washington, D.C.: EPA; 2016.
- Wild CP. The exposome: from concept to utility. *Int J Epidemiol*. 2012; 41(1):24-32.
- Lioy PJ, Rappaport SM. Exposure science and the exposome: an opportunity for coherence in the environmental health sciences. *Environ Health Perspect*. 2011; 119(11):A466-A467.
- Lioy PJ, Smith KR. A discussion of exposure science in the 21st century: a vision and a strategy. *Environ Health Perspect*. 2013; 121(4):405-509.
- Teeguarden JG, Tan YM, Edwards SW, Leonard JA, Anderson KA, Corley RA, et al. Completing the link between exposure science and toxicology for improved environmental health decision making: the aggregate exposure pathway framework. *Environ Sci Technol*. 2016; 50(9):4579-4586.
- Teeguarden JG, Tan YM, Edwards SW, Leonard JA, Anderson KA, Corley RA, et al. Expanding on successful concepts, models, and organization. *Environ Sci Technol*. 2016; 50(17):8921-8922.
- International Occupational Hygiene Association. *What is Occupational Hygiene?* Available from: <https://ioha.net/faq/> (accessed 5 Nov 2018).
- Barr DB. Human exposure science: a field of growing importance. *J Exposure Sci Environ Epidemiol*. 2006; 16:473.
- Guidotti TL. Exposure science comes of age. *Arch Environ Occup Health*. 2014; 69(3):127-128.
- Egeghy PP, Sheldon LS, Isaacs KK, Özkaynak H, Goldsmith MR., Wambaugh JF, et al. Computational exposure science: an emerging discipline to support 21st-century risk assessment. *Environ Health Perspect*. 2016; 124(6):697-702.
- Cherrie JW, Maccalman L, Fransman W, Tielemans E, Tischer M, Van Tongeren M. Revisiting the effect of room size and general ventilation on the relationship between near- and far-field air concentrations. *Ann Occup Hyg*. 2011; 55(9): 1006-1015.
- United States. Occupational Safety and Health Administration. *Standard Interpretations. Correct placement of air sampling cassettes on employees performing welding operations; 1999*. Available from: <https://www.osha.gov/laws-regs/standardinterpretations/1999-02-03> (accessed 4 Dec 2018).
- Fantke P, Aylward L, Bare J, Chiu WA, Dodson R, Dwyer R. Advancements in life cycle human exposure and toxicity characterization. *Environ Health Perspect*. 2018; 126(12):125001.

19. Uusitalo L. Advantages and challenges of Bayesian networks in environmental modelling. *Ecol Model.* 2007; 203(3):312-318.
20. Landuyt D, Broekx S, D'Hondt R, Engelen G, Aertsens J, Goethals PLM. A review of Bayesian belief networks in ecosystem service modelling. *Environ Model Softw.* 2013; 46: 1-11.
21. Shandilya N, Ligthart T, Van Voorde I, Stahlmecke B, Clavaguera S, Philippot C, et al. A nano material release model for waste shredding using a Bayesian belief network. *J Nanopart Res.* 2018; 20(2):33.
22. United States. American Industrial Hygiene Association-Exposure Assessment Strategy Committee. IH-Mod\_2\_0. AIHA-EASC; 2018. Available from: <https://www.aiha.org/get-involved/VolunteerGroups/Pages/Exposure-Assessment-Strategies-Committee.aspx> (accessed 4 Dec 2018).
23. Hewett P, Ganser GH. Models for nearly every occasion: Part I - One box models. *J Occup Environ Hyg.* 2017; 14(1):49-57.
24. Ganser GH, Hewett P. Models for nearly every occasion: Part II - Two box models. *J Occup Environ Hyg.* 2017; 14(1): 58-71.
25. Hewett P, Ganser GH. Models for nearly every occasion: Part III—One box decreasing emission models. *J Occup Environ Hyg.* 2017; 14(11):907-918.
26. Ganser GH, Hewett P. Models for nearly every occasion: Part IV—Two-box decreasing emission models. *J Occup Environ Hyg.* 2017; 14(11): 919-930.
27. Stoffenmanager®. Available from: <https://stoffenmanager.com/> (accessed 12 Dec 2018).
28. Advanced Reach Tool. Available from: <https://www.advancedreach-tool.com/> (accessed 12 Dec 2018).
29. Marquart H, Heussen H, Le Feber M, Noy D, Tielemans E, Schinkel J, et al. 'Stoffenmanager'®, a web-based control banding tool using an exposure process model. *Ann Occup Hyg.* 2008; 52(6):429-441.
30. Tielemans E, Noy D, Schinkel J, Heussen H, Van der Schaaf D, West J, et al. Stoffenmanager® exposure model: development of a quantitative algorithm. *Ann Occup Hyg.* 2008; 52(6):443-454.
31. Schinkel J, Fransman W, Heussen H, Kromhout H, Marquart H, Tielemans E. Cross-validation and refinement of the Stoffenmanager as a first tier exposure assessment tool for REACH. *Occup Environ Med.* 2010; 67(2):125-132.
32. Fransman W, Van Tongeren M, Cherrie JW, Tischer M, Schneider T, Schinkel J, et al. Advanced reach tool (ART): development of the mechanistic model. *Ann Occup Hyg.* 2011; 55(9): 957-979.
33. Schinkel J, Warren N, Fransman W, Van Tongeren M, McDonnell P, Voogd E, et al. Advanced REACH Tool (ART): calibration of the mechanistic model. *J Environ Monit.* 2011; 13(5): 1374-1382.
34. Schinkel J, Ritchie P, Goede H, Fransman W, Van Tongeren M, Cherrie J W, et al. The advanced REACH tool (ART): incorporation of an exposure measurement database. *Ann Occup Hyg.* 2013; 57(6):717-727.
35. Fabian CL, Binder CR. Dermal exposure assessment to pesticides in farming systems in developing countries: Comparison of models. *Int J Environ Res Pub Health.* 2015; 12(5):4670-4696.
36. Oppl R, Kalberlah F, Evans PG, van Hemmen JJ. A toolkit for dermal risk assessment and management: an overview. *Ann Occup Hyg.* 2003; 47(8):629-640.
37. Warren ND, Marquart H, Christopher Y, Laitinen J, Van Hemmen JJ. Task-based dermal exposure models for regulatory risk assessment. *Ann Occup Hyg.* 2006; 50(5): 491-503.
38. Gorman Ng M, Davis A, Van Tongeren M, Cowie H, Semple S. Inadvertent ingestion exposure: hand-and object-to-mouth behavior among workers. *J Exposure Sci Environ Epidemiol.* 2016; 26(1):9-16.
39. Liao CM, Chang CF, Liang HM. A probabilistic transmission dynamic model to assess indoor airborne infection risks. *Risk Anal.* 2005; 25(5):1097-1107.
40. Issarow CM, Mulder N, Wood R. Modelling the risk of airborne infectious disease using exhaled air. *J Theor Biol.* 2015; 372:100-106.
41. Noakes CJ, Sleigh PA. Mathematical models for assessing the role of airflow on the risk of airborne infection in hospital wards. *J R Soc Interface.* 2009; 6(Suppl 6):S791-S800.
42. Schulte PA, Rinehart R, Okun A, Geraci CL, Heidel DS. National prevention through design (PtD) initiative. *J Safety Res.* 2008; 39(2):115-121.
43. Tickner J, Jacobs M, Malloy T, Buck T, Stone A, Blake A, et al. Advancing alternatives assessment for safer chemical substitution: a research and practice agenda. *Integr Environ Assess Manag.* 2019. Available from: <https://doi.org/10.1002/ieam.4094> (accessed 29 Nov 2018).
44. United States. American Industrial Hygiene Association. Demonstrating the business value of industrial hygiene. Methods and findings from the value of the industrial hygiene profession study. Fairfax: AIHA; 2008. Available from: [https://www.aiha.org/votp\\_new/pdf/votp\\_report.pdf](https://www.aiha.org/votp_new/pdf/votp_report.pdf) (accessed 3 Jan 2019).
45. United States. Environmental Protection Agency. A review of the reference dose and reference concentration processes. Washington, D.C.: EPA; 2002.
46. United States. Environmental Protection Agency. Guidelines for carcinogen risk assessment: Washington, D.C.: EPA; 2005.
47. United States. Environmental Protection Agency. Probabilistic risk assessment methods and case studies. Washington, D.C.: EPA; 2014.
48. Oberata AF, Poye L, Compton SP. Releasability of asbestos fibers from weathered roof cement. *J Occup Environ Hyg.* 2018; 15(6):466-473.
49. Eastlake AC, Beaucham C, Martinez KF, Dahm MM, Sparks C, Hodson LL, et al. Refinement of the nanoparticle emission assessment technique into the nanomaterial exposure assessment technique (NEAT 2.0). *J Occup Environ Hyg.* 2016; 13(9):708-717.
50. Brouwer D, Van Duuren-Stuurman B, Berges M, Jankowska E, Bard D, Mark D. From workplace air measurement results toward estimates of exposure? Development of a strategy to assess exposure to manufactured nano-objects. *J Nanopart Res.* 2009; 11(8):1867-1881.
51. Koivisto AJ, Jensen ACØ, Kling KI, Nørgaard A, Brinch A, Christensen F, et al. Quantitative material releases from products and articles containing manufactured nanomaterials: towards a release library. *NanoImpact.* 2017; 5:119-132.
52. Levin M, Rojas E, Vanhala E, Vippola M, Liguori B, Kling KI, et al. Influence of relative humidity and physical load during storage on dustiness of inorganic nanomaterials: implications for testing and risk assessment. *J Nanopart Res.* 2015; 17:337.
53. Peterson J. Principles for controlling the occupational environment. The industrial environment – its evaluation and control. Washington, D.C.: NIOSH; 1973. pp 511-517.
54. United States. National Research Council. A framework to guide selection of chemical alternatives. Washington, D.C.: NRC; 2014. Available from: <https://www.nap.edu/catalog/18872/a-framework-to-guide-selection-of-chemical-alternatives> (accessed 10 Dec 2018).
55. Organization for Economic Cooperation and Development. OECD substitution and alternatives assessment toolbox; 2017. Available from: <http://www.oecdsaatoolbox.org/> (accessed 10 Dec 2018).
56. Malloy T, Zaunbrecher V, Beryt E, Judson R, Tice R, Allard P, et al. Advancing alternatives analysis: The role of predictive toxicology in selecting safer chemical products and processes. *Integ Environl Assess Manag.* 2017; 13(5):915-925.
57. Linkov I, Bates ME, Trump BD, Seager TP, Chappell MA, Keisler JM. For nanotechnology decisions, use decision analysis. *Nano Today.* 2013; 8(1):5-10.