

## Modelling ethanol exposure of health workers from disinfectants

**Level:** Master (Bachelors can do part of this study; to be determined)  
**Duration:** 20 weeks  
**Start:** From March 2022 onwards  
**Project form:** Literature review, data analysis, model development, model application  
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In addition to disinfection by hand-washing, an ethanol-based hand rub (EBHR) is considered best practice to prevent infections during care for patients in hospitals as well as other healthcare facilities and ambulant settings. A single EBHR application is considered to involve a relatively low health risk for the applicant due to limited local dermal burden and negligible systemic exposure. However, in certain hospital practices, such as the care for neonates, the frequency and intensity of EBHR applications is very high, i.e. up to 40 times per day. The question is whether this frequent use of EBHR is still safe for the applicant, especially in cases where a compromised dermal barrier would lead to increased dermal uptake of ethanol.

So far, no studies have been performed to study low exposures that could contribute to a short-term increased risk of reproductive and developmental toxicity and/or a risk of long-term exposure such as cancer. As ethanol is classified as a confirmed risk factor for reproductive health and for cancer in humans, this assessment is useful for protection of worker's health.

Recently, RIVM published a risk assessment for the use of hand disinfection products in adults and children using the ConsExpo model (Hendriks et al., 2021). As a worst-case scenario for severe eczema or damaged skin a complete (100%) absorption over a surface of 10% of the skin was assumed. This scenario increased uptake six-fold. It was estimated that a frequency of 25 EBHR applications would result in an exposure in compliance with the Dutch occupational exposure level (OEL). According to the risk calculations the extra risk of breast cancer would then be  $6.1 \times 10^{-4}$  for a working life period (40 y). Increasing the daily use frequency higher than 32 EBHR applications would lead to exceedance of the accepted attributable cancer risk of  $40 \times 10^{-4}$  for a working life exposure (action level of  $1.0 \times 10^{-4}$  per year of exposure). This could be problematic since the application frequency in some hospital units may be higher than 32 times a day.

With this background in mind, an experimental study will be performed to determine the contribution of skin absorption relative to inhalation as a route of uptake of ethanol following topical application of ethanol-based hand rubs (EBHR) in a controlled laboratory setting. The aim of the current MSc study is to support this study by developing and applying a physiologically-based kinetic (PBK) model for the uptake of ethanol through dermal uptake and inhalation. A PBK model describes the uptake and fate of chemical contaminants in the human body. The PBK model will be based on a previously developed human PBK model developed specifically for isopropyl alcohol (Huizer et al., 2012). The existing model must be extended with a dermal uptake module and be implemented in the software language R. The dermal pathway will be modelled using state-of-the-art knowledge on dermal uptake extracted from the scientific literature. Once the model has been extended with a dermal route, the model will be applied to simulate the exposure conditions of the experimental laboratory setting. Based on the results, the model will be further optimized and calibrated. The calibrated model will be used to answer the ultimate research question, i.e. whether the frequent application of EBHRs in a hospital setting is likely to result in unacceptable health risks for hospital workers.

Candidates for this topic must have affinity with systematic literature review, data analysis, and computer modelling in R. There is an option to assist in the practical work, i.e. a study during which 12 volunteers will be exposed to ethanol through EBHRs.

## Literature

- Huizer, D., Oldenkamp, R., **Ragas, A.M.J.**, Van Rooij, J.G.M., Huijbregts, M.A.J., 2012. Separating uncertainty and physiological variability in human PBPK modelling: The example of 2-propanol and its metabolite acetone. *Toxicology Letters* **214**: 154– 165.
- Hendriks, H.S., Woutersen, M., ter Burg, W., Bos, P.M.J., Schuur, A.G., 2021. Beoordeling van gezondheidsrisico's bij gebruik van ethanol bevattende handgel, National Institute for Public Health and the Environment, Bilthoven, RIVM Report no. 2021-0026, DOI 10.21945.