Kinetic dietary exposure model (KDEM): Integration of half-life of Methyl Mercury in human for modeling the long term dietary exposure

Verger Ph[a]. Tressou J[a,b]. and Clémençon S[a,c].

a: INRA – Met@risk, INA P-G - Paris – France - b : Hong Kong University of Science and Technology - Hong Kong - c : Laboratoire MODALX –Paris X

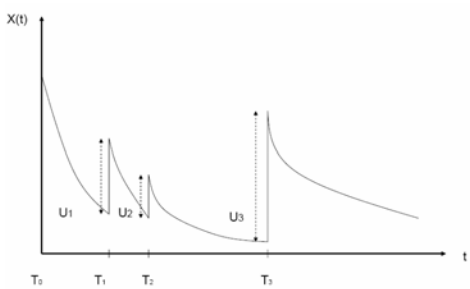
Background and objectives

The risk characterisation consists in the comparison of the dietary exposure with a health based guidance value established in a previous step. One of the identified weaknesses of this comparison is that the time is not considered in the description.
The aim of this paper is to describe, based on the example of Methylmercury in fish, the dietary exposure as a dynamic process determined by the accumulation phenomenon due to successive dietary intakes and by the pharmacokinetics ruling the elimination process in between intakes.

Materials and methods

The inputs of the *Kinetic Dietary Exposure Model* are the probability distributions governing intakes and inter-intake times, as well as the half-life of the contaminant in the human body. In this paper, an application to methyl mercury is considered, with exponential distributions for both the intakes and the inter-intake times, fitted from the French national consumption survey INCA, and a fixed half-life of 6 weeks for the elimination process.

Results

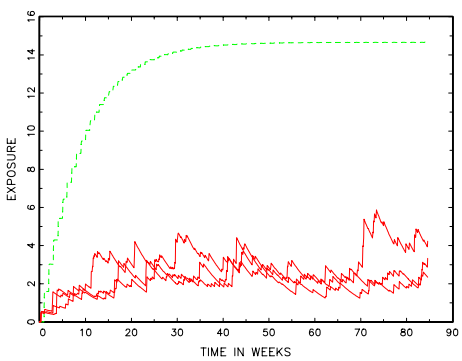


Representation of a typical trajectory of the dietary exposure process

- T_1, T_2, … are the eating occasions
- T_2-T_1, T_3-T_2… are the inter-intake times
- U_1, U_2, … are the intakes (product of the quantity consumed renormalized by the body weight and the contaminant concentration of the ingested food) at times T_1, T_2, …

According to its definition, the Provisional Tolerable Weekly Intake (PTWI) of 1.6 µg/kg bw is a level of MeHg to which consumers could be exposed all along their life without appreciable health risk. Therefore assuming a weekly dietary exposure of 1.6 µg/kg bw of MeHg allows to built a safe threshold or a “Kinetic Tolerable Intake” (KTI) for this contaminant integrating its kinetic of elimination. This reference process is plotted in Figure 4 (dashed/green curve) together with possible trajectories in the adult female population (solid/red curves). At the steady-state, the reference process stabilizes at a safe level (or safe body burden) for MeHg, that is 14.6 µg/kg bw. This level is simply obtained from the PTWI and the half-life expressed in weeks () by the formulae:

$$KTI = \lim_{n\to\infty} \sum_{i=0}^{n} PTWI \times \exp\left(-(n-i)\ln(2)/HL\right) = \frac{PTWI}{1-e^{-\ln(2)/HL}}$$



Reference exposure process and examples of trajectories in the French adult female population (Unit: µg/kg bw)

The solid/red curves are different trajectories with the same initial state $x_0=0$. The dashed/green curve is the reference exposure process which stabilizes in the long run at the *KTI* (14.6 µg/kg bw).

Conclusions and perspectives

On a toxicological point of view, we simply dealt with the probability for a consumer to exceed the safe threshold but other parameters could be estimated. Consumers can exceed the safe threshold for a period of time and then, because the inter-intake time is long, go below the threshold again: the total time above the threshold can therefore be estimated for pregnant women and young children. On a mathematical point of view, we deliberately present here a KDEM with exponential input distributions for both the intakes and the inter-intake times while other distributions could be more suitable. Moreover, for other chemical contaminants (like PCBs for example), the integration of more than one food source could be necessary. The validity framework elaborated by Bertail et al. (2007, available as a working paper on the Met@risk website) precisely allows for such extensions. However, under such assumptions, the steady-state behaviour of the process is a bit more complicated and the probability that a Kinetic Dietary Exposure oversteps the Kinetic Tolerable Intake, can only be estimated by simulation. For such a rare event, the naive Monte-Carlo simulation is not an efficient tool. Specific methods based on particle filtering are currently investigated for this application.