

# Master Development of drugs and health products

## TU N°10 – Environment

Exam 10 May 2023

### Question 1: Analytical chemistry

- 1-1-For what purposes is analytical chemistry applied in environmental health? (Answer the question in 5-6 lines).
- 1-2- Propose a method of sample preparation and quantitative analysis for the determination of traces of pharmaceuticals in river water (Specify the outline of a protocol without going into details).

### Question 2: Environmental Risk Assessment

The table 1 represents ERA data for angiotensin II receptor blockers (ARBs – antihypertensive drug) analyzed in the Tejo estuary in Portugal (Publication: Environmental risk assessment and bioaccumulation of pharmaceuticals in a large urbanized estuary, Vanessa F. Fonseca et al., Science of Total Environment 783 (2021) 147021).

Table 1:

Table 3

Risk assessment of pharmaceutical residues detected in the Tejo estuary water, determined for different taxa (algae, crustacea and fish), therapeutic group ( $\Sigma$ Therapeutic group) and the whole mixture ( $\Sigma$ All). Risk quotients (RQ) for individual compounds were calculated as the ratio between Measured Environmental Concentrations (MEC, ng/L) and Predicted No-Effect-Concentrations (PNEC, ng/L), as in Eq. (1). RQ for each therapeutic group and the whole mixture were calculated as the sum of toxic units (STU), as in Eq. (2) ( $RQ_{STU}$ ). Ecotoxicological data (Tox. Data) referring to acute LC50, EC50 or NOEC endpoints, in mg/L from the literature, was used to calculate PNEC, for freshwater (FW) or brackish-marine (BM) environments (Env). In toxicity estimates made via ECOSAR, brackish-marine (BM) environment criteria were applied.

Therapeutic group	Pharmaceutical residues	Taxa	Biota	Env	Tox. Data	Conc. (mg/L)	Toxicity	Endpoint	Reference	PNEC (ng/L)	MEC (ng/L)	RQ
Angiotensin II receptor blockers (ARBs)	Irbesartan	Algae	Green algae	BM	EC50	0.13	Acute (96 h)		ECOSAR	13	72.0	5.54
		Crustacea	Daphnid	BM	LC50	0.19	Acute (48 h)	Mortality	ECOSAR	19	72.0	3.79
		Fish	Fish	BM	LC50	0.32	Acute (96 h)	Mortality	ECOSAR	32	72.0	2.25
	Losartan	Algae	Green algae	BM	EC50	0.24	Acute (96 h)		ECOSAR	24	68.4	2.85
		Crustacea	Daphnid	BM	LC50	1.69	Acute (48 h)	Mortality	ECOSAR	169	68.4	0.40
		Fish	Fish	BM	LC50	0.23	Acute (96 h)	Mortality	ECOSAR	23	68.4	2.97
	RQ <sub>STU</sub> Σ ARBs		Most sensitive taxa	FW/BM								8.39

- 2-1- Define the PNEC. In estimating this parameter, a safety factor is used to account for the uncertainty of the estimate. What value was used for the table data?
- 2-2- Check RQ calculation for irbesartan and algae.
- 2-3- From what RQ value is a risk to the environment proven?
- 2-4- Do the 2 pharmaceuticals presented in the table 1 present an environmental risk? Which species seems the most sensitive?
- 2-5- The authors calculate an RQ ( $RQ_{STU} \Sigma$  ARBs) for the therapeutic class by summing the RQ values for the most sensitive species. Check the calculation made for the ARBs.
- 2-6- We often talk about the cocktail effect in ERA studies. What does this term correspond to?

### Question 3: Health Risk Assessment

Table 2 represents the toxicological reference values (TRVs) selected by the French National Institute for the Industrial Environment and Risks (*Institut National de l'Environnement Industriel et des Risques* - INERIS) concerning the effects of cadmium (Cd) for the general population.

3-1) Comment on the data in Table 1A by answering the following points:

3.1.a) Using the example of a threshold TRV in the table, explain what it means.

3.1.b) Explain how these threshold TRVs are constructed.

3.1.c) Which threshold TRV would you choose if you had to carry out a risk assessment for Cd exposure by inhalation? Justify your answer.

3-2) Comment on the data in Table 1B by answering the following points:

3.2.a) Using the example of a non-threshold TRV in the table, explain what it means.

3.2.b) Explain how these non-threshold TRVs are constructed.

3.2.c) Which non-threshold TRV would you choose if you had to carry out a risk assessment of Cd exposure by inhalation? Justify your answer.

**Table 2 : Toxicological reference values (TRV) selected by INERIS concerning the effects of cadmium (Cd) for the general population.**

#### A- Inhalation TRV for threshold effects of Cd

Denomination of the TRV	Value of the reference TRV for Cd	Source
CAA	0.45 µg/m <sup>3</sup>	ANSES, 2012
CAA	0.30 µg/m <sup>3</sup>	ANSES, 2012
REL	0.02 µg/m <sup>3</sup>	OEHHA, 2001
MRL	0.01 µg/m <sup>3</sup>	ATSDR, 2012

#### B- Inhalation TRV for non-threshold effects of Cd

Denomination of the TRV	Value of the reference TRV for Cd	Source
IUR	0.0018 (µg/m <sup>3</sup> ) <sup>-1</sup>	US-EPA, 1987
IUR	0.0042 (µg/m <sup>3</sup> ) <sup>-1</sup>	OEHHA, 1987

*Abv. : CAA : Concentration Admissible dans l'Air (Acceptable Air Concentration) ; REL : Reference Exposure Level ; MRL : Minimum Risk Level ; IUR : Inhalation Unit Risk ; DJA : Dose Journalière Admissible (Acceptable Daily Intake) ; TDI : Tolerable Daily Intake ; RfD : Reference Dose ; ANSES : Agence Nationale de Sécurité Sanitaire de l'alimentation, de l'environnement et du travail ( French National Agency for Food, Environmental and Occupational Health Safety) ; OEHHA : california office of Environmental Health Hazard Assessment ; ATSDR : Agency for Toxic Substances and Disease Registry ; US-EPA : United States - Environmental protection Agency ;*