



**HAL**  
open science

## Ecotoxicological impacts of cosmetic products preservatives in a zebrafish model

Christophe Morin, Adèle Bressy, Melissa Saichi, Clément Leroyer, Yaël  
Guttman, Régis Moilleron, Laure Garrigue-Antar

► **To cite this version:**

Christophe Morin, Adèle Bressy, Melissa Saichi, Clément Leroyer, Yaël Guttman, et al.. Ecotoxicological impacts of cosmetic products preservatives in a zebrafish model. 5th international symposium and workshop on Fish and amphibian embryos as alternative models in toxicology and teratology, Nov 2018, Aulnay-sous-Bois, France. hal-04284029

**HAL Id: hal-04284029**

**<https://enpc.hal.science/hal-04284029>**

Submitted on 14 Nov 2023

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

## Introduction

Parabens are ingredients of most personal care products (PCPs), as preservatives. From their massive use and their ubiquitous presence in the environment, these molecules have a potential negative effect on aquatic ecosystems as endocrine disruptors, thus representing a source of increasing concern. Parabens have been the subject of an alert following a 2004 publication, which reported a potential link between parabens and breast cancer. Growing consumer awareness led cosmetic industry to move away from parabens towards paraben-free or organic products and to use alternatives substances in their formulations, processes and packaging. Among the key unanswered questions, is the identification of the products used in the formulations that need to be substituted, and their replacement by other potentially harmful substances.

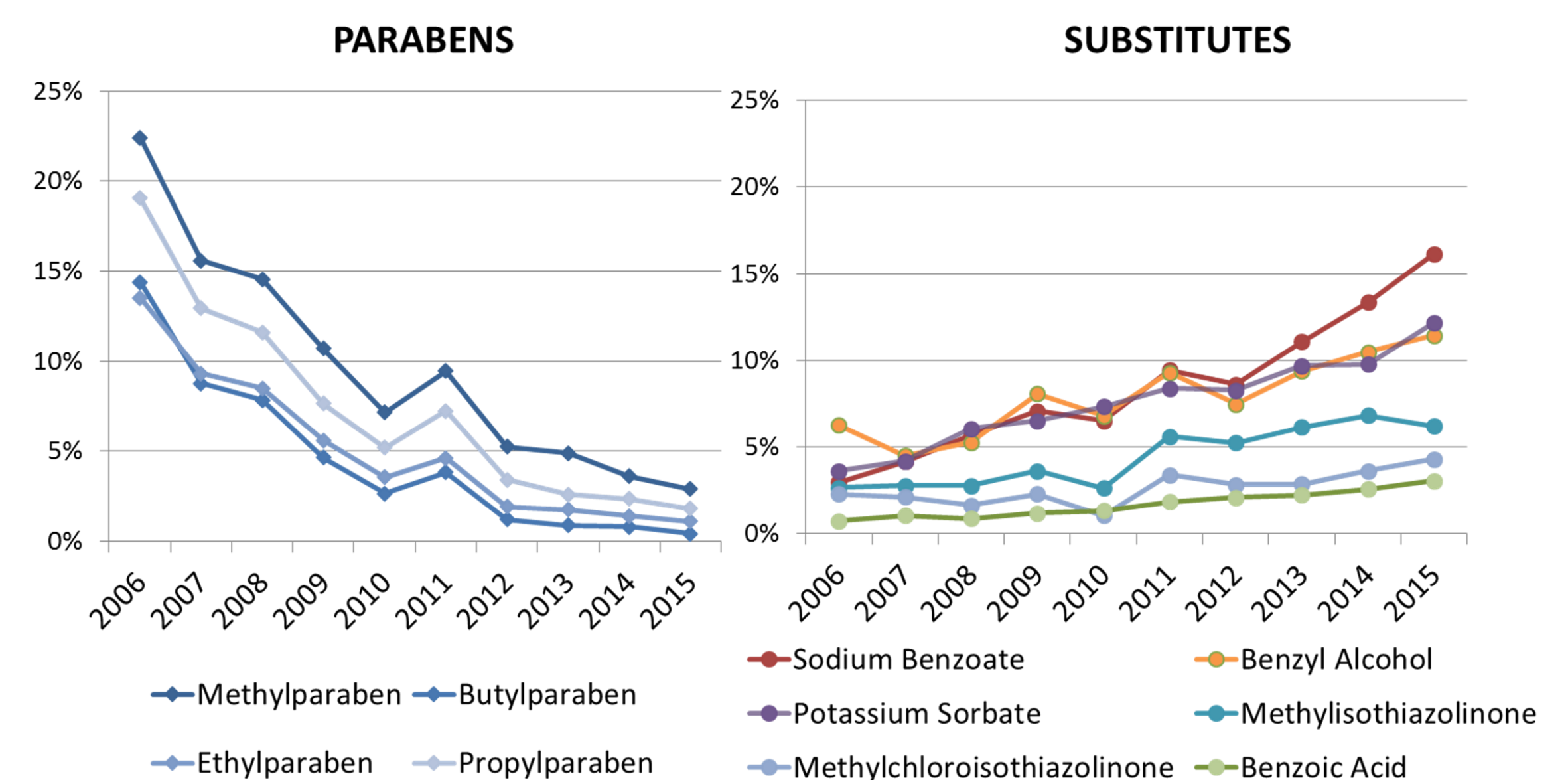
## Objectives

- Determination of which chemicals replace parabens
- Evaluation of the toxicity of these molecules on the development and the behavior of zebrafish (*Danio rerio*) larvae.

## Substitution of parabens in cosmetic products

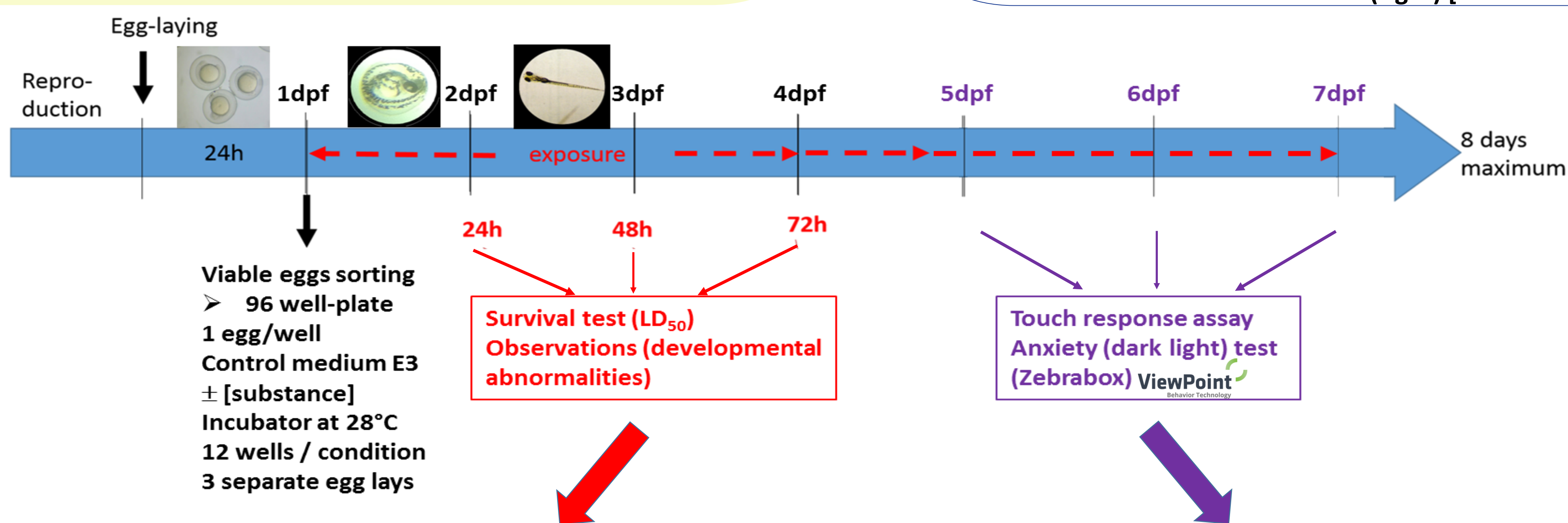
### Bibliography and industrial survey :

- Identification of parabens substitutes
- Potentially hazardous effect of some substitutes on aquatic organisms : phenoxyethanol (PE), methylisothiazolinone (MIT), chlorphenesin (CPN)..



Yearly evolution of marketed cosmetics containing parabens (left) and substitutes (right) [Mintel database, 2015]

## Methodology



### Substances:

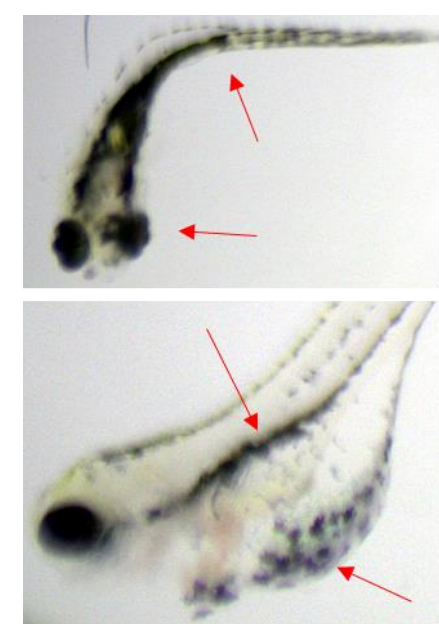
- Methyl Parabene (MeP)
- Chlorphenesin (CPN)
- MethylIsoThiazolinone (MIT)
- Phenoxyethanol (PE)

## Impact on zebrafish larvae development and survival

Non-environmental concentrations

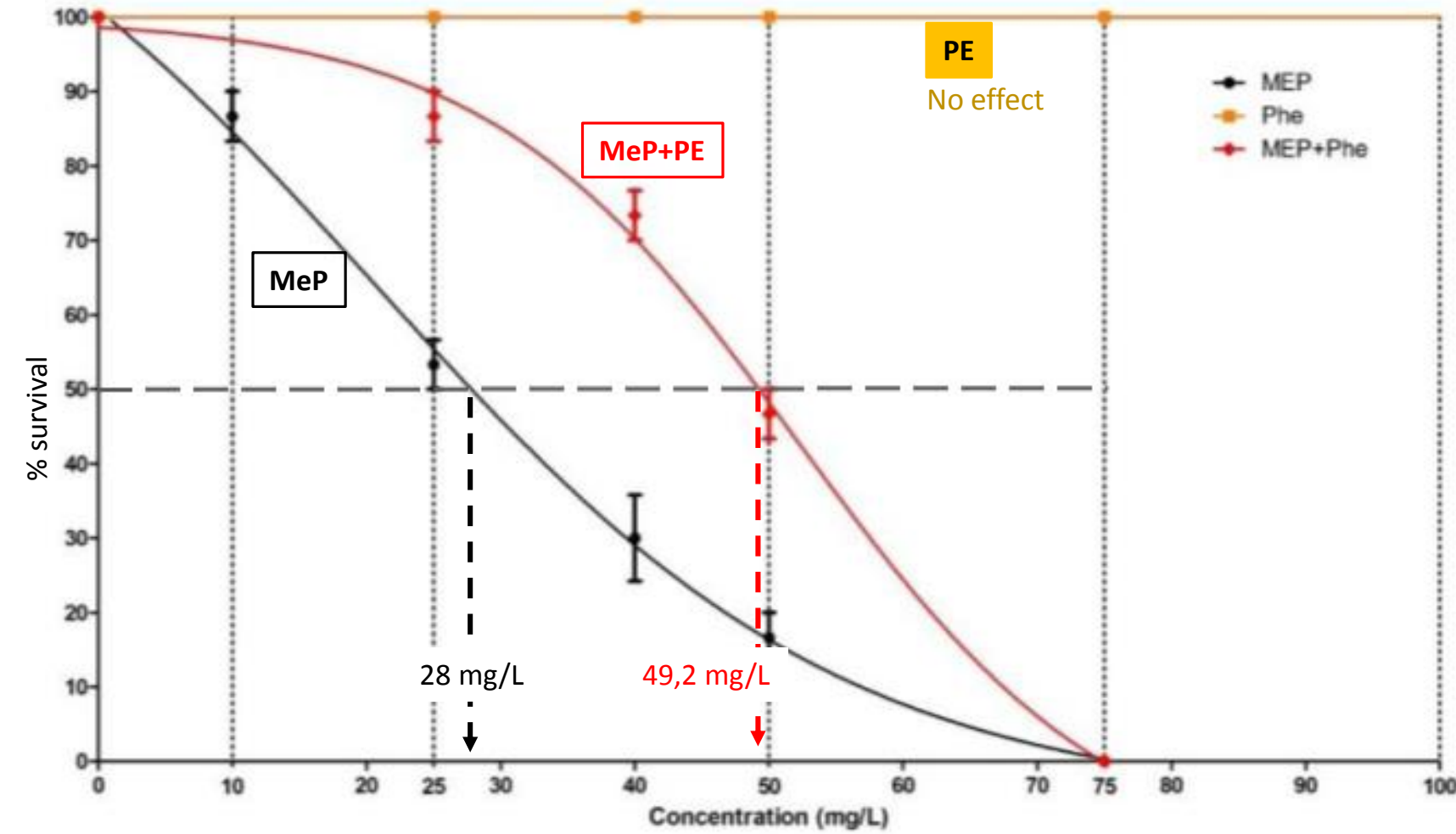
LD <sub>50</sub>	MeP	MIT	CPN	PE
48h	75.8 mg/L	40.9 mg/L	167 mg/L	-
72h	10.9 mg/L	33.5 mg/L	153 mg/L	-
Developmental abnormalities	- Edemas - Death <i>in ovo</i>	- Edemas - Weak heart beats - Accelerated larvae decay	- Edemas - Curved tails - Red blood cells accumulation	- No gross abnormalities

- MeP, MIT & CPN affect survival and development
- No obvious effect for PE



- Head malformation
- Curved tails
- Edemas
- Deflated swim bladder

### Cocktail effect : MeP-PE at 6dpf

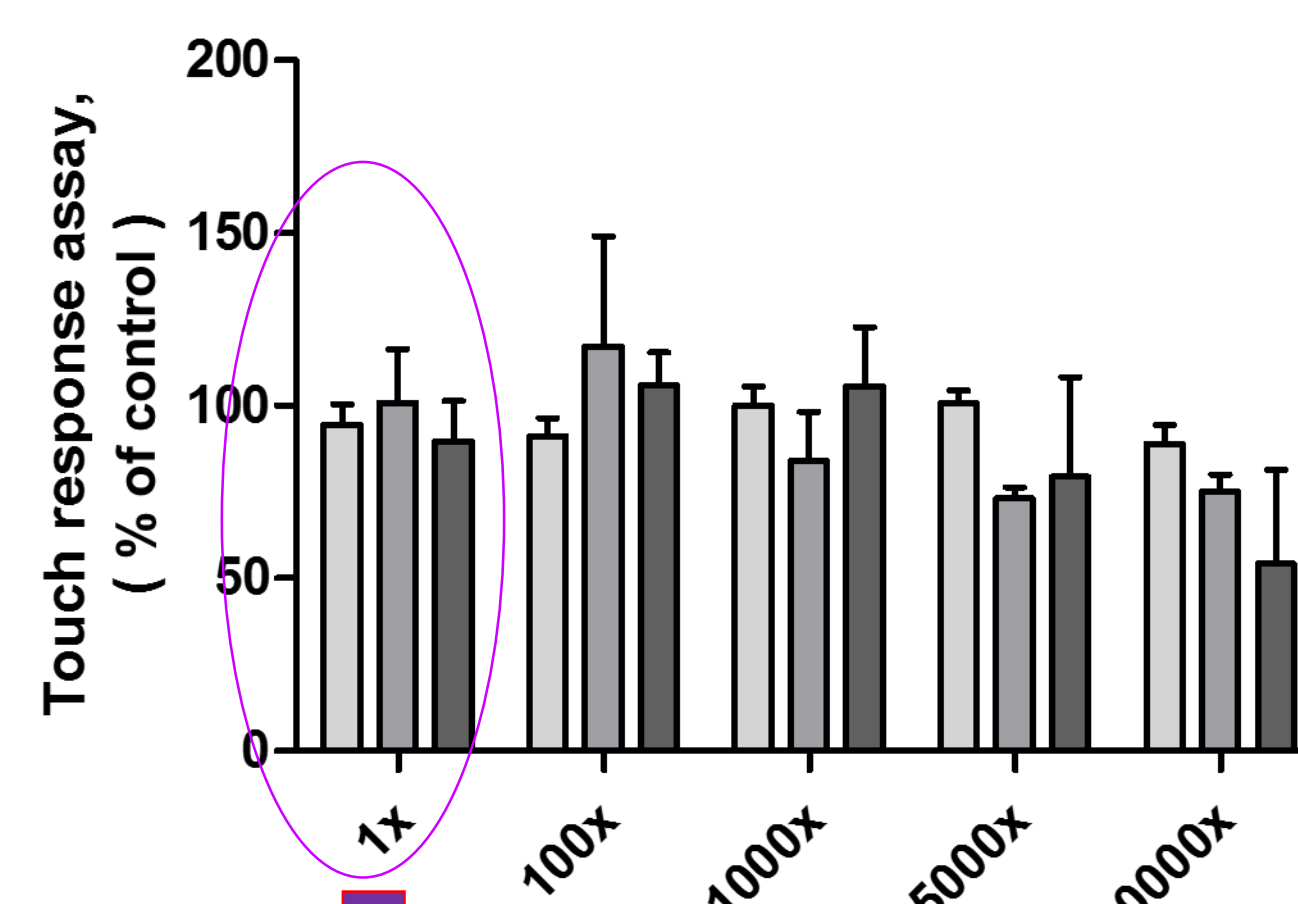


Dose-response between 0 - 75mg/L (MEP) + 2[MEP] (PE)

- PE presence alters MeP ecotoxicity :
- Increased survival rate
- Apparitions of important abnormalities, unseen for MeP alone

## Impact on zebrafish larvae behavior and stress

### Touch Response Assay

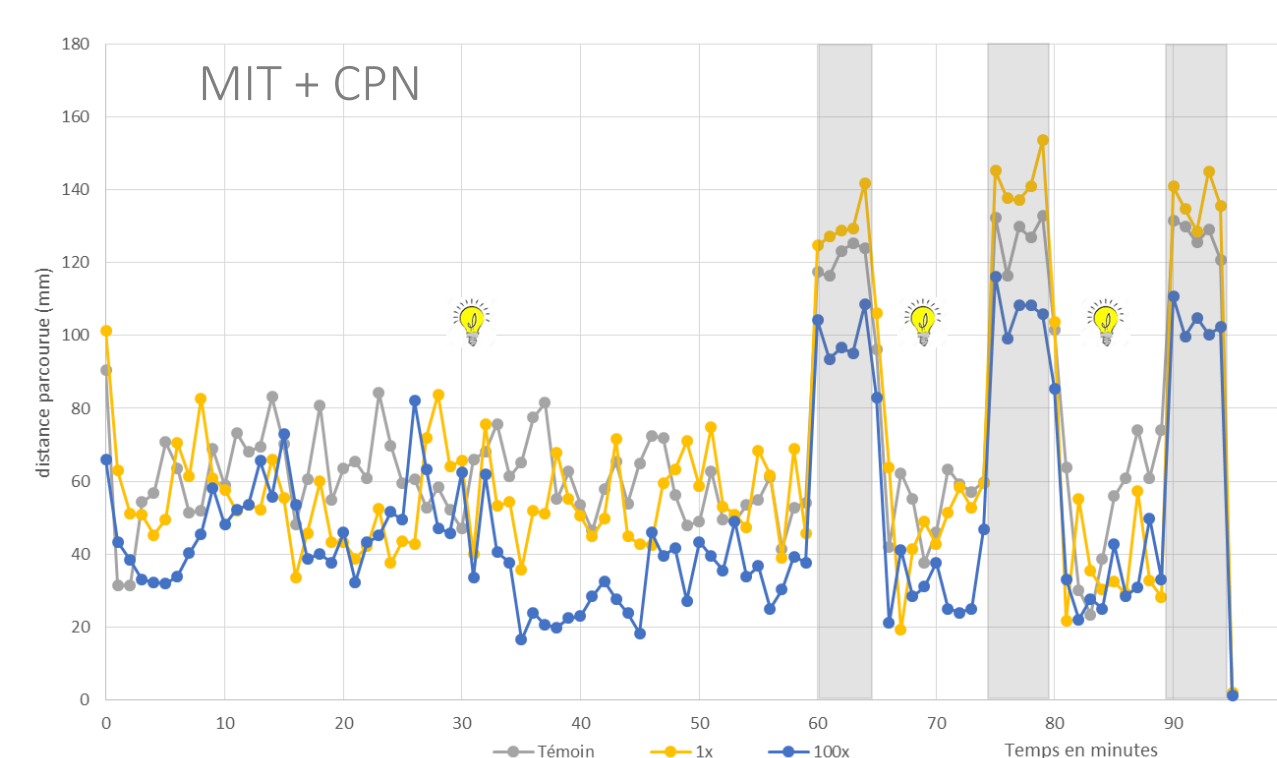


Substances (1X)	Concentration (µg/L)
MeP	0.7
MIT	0.05
CPN	0.16
PE	14

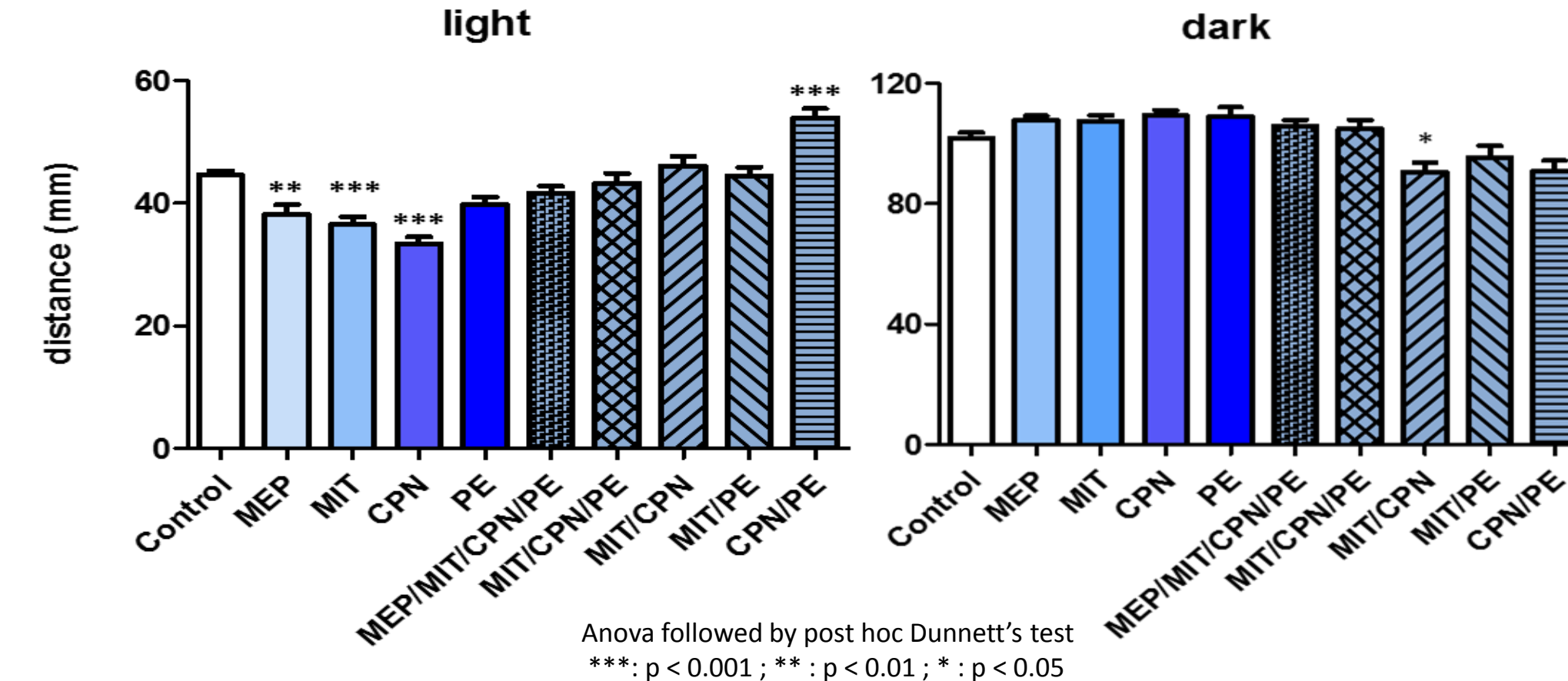
Kimura et al., Chemosphere (2014) 107, 393-99;  
Peng et al, 2016, Pharmacology, Biochemistry and Behavior 145 (2016) 55-65;  
Rafath J, Chromatogr A 1164, (2007), 74-81

Environmental concentration (1X) : Light-dark stress assay

### Example of profile



### Statistical analysis



- Single molecules, but not mixes, produce a significant hypolocomotion during the light periods, except PE
- Significant hyperactivity of the larvae with the mix CPN/PE during the light periods
- No significant effect observed during the dark periods, except MIT/CPN
- Unpredictable effect of combination of molecules
- Sensitive test suitable for concentrations found in the environment

## Conclusion

These original results clearly connect the domestic consumption practices with potential ecotoxic discharges in receiving water and raise questions about the substitution after regulation. Our results show that paraben and some of its substituents have negative effects on survival, development and behavior of zebrafish larvae, potentialized by "cocktail effect" even at environmental concentrations. The use of zebrafish larvae is a promising and robust tool to assess toxicological impacts of parabens and their substituents in the environment. In particular, this model could enable to generate valuable data on cocktail effects, which remain to date poorly documented in environmental conditions.

## Acknowledgements

This study is part of the Cosmet'eau project which is funded within the framework of a French call for project about "Micropollutants: innovation and changes of practices" launched in 2013 by the French Ministry of Environment, The French National Agency for Biodiversity (AFB) and a French water agency (Agence de l'Eau Seine-Normandie).