



# Epithelix

*in vitro* Solutions for Respiratory Diseases and Chemical Testing



## Toxicity assessment of construction materials *in vitro* on Human 3D Airway Epithelium (MucilAir™) using highly sensitive functional endpoints

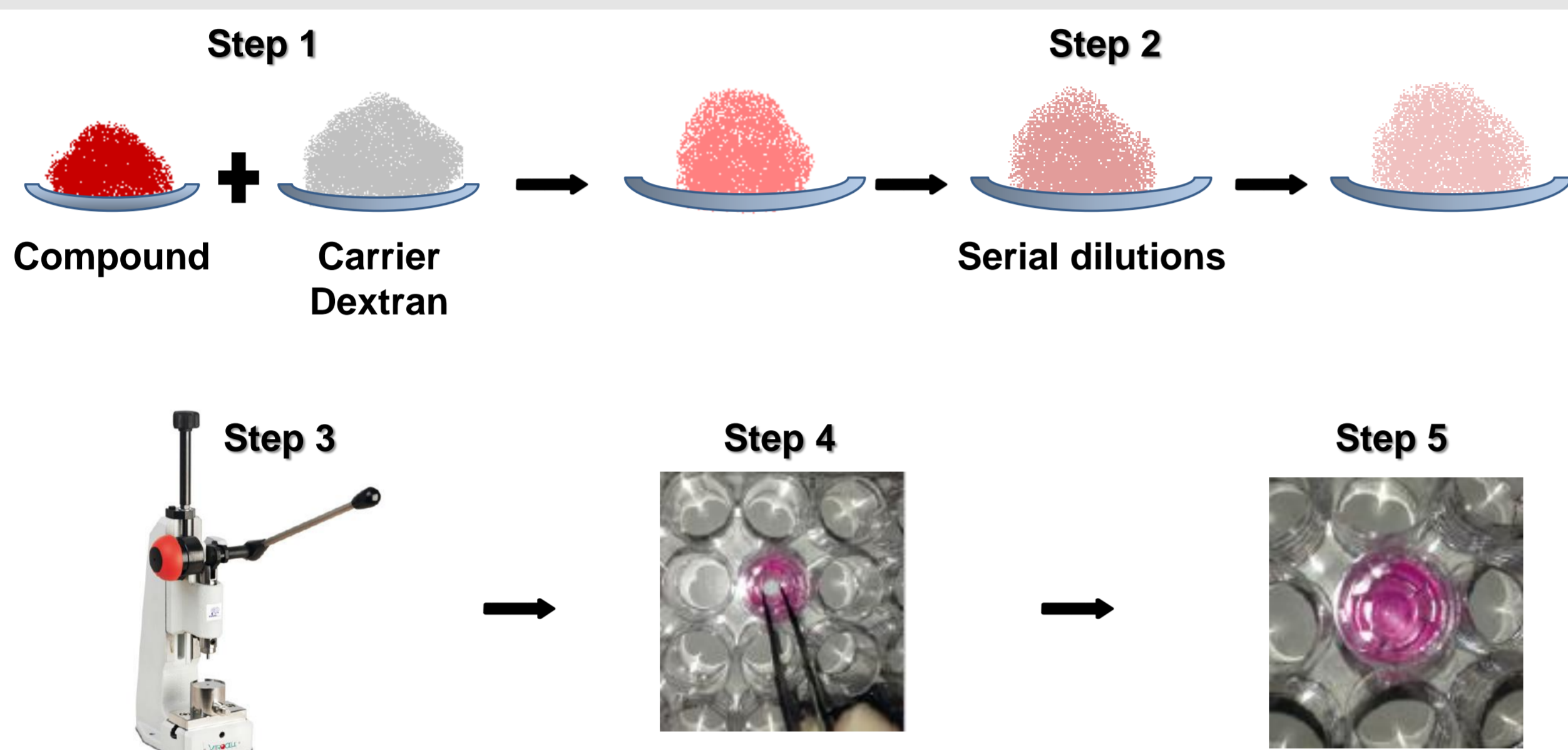
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Release of volatile compounds or particles from construction materials during their installation or during their life cycle is an occupational as well as a public health issue. The respiratory system is particularly sensitive and vulnerable due to repetitive and chronic exposures. One consequence is the steady increase of respiratory diseases such as asthma and COPD. The goal of this project is to develop an *in vitro* test using reconstituted human respiratory tissue (MucilAir™) to evaluate potential deleterious effect of construction materials. To this end, a multi-parametric analysis based on the quantification of cytotoxicity (LDH), tissue integrity (TEER), ciliary beating frequency (CBF), mucociliary clearance (MCC) and inflammation (IL-8) has been developed. In this study, 5 materials were selected: (i) 3 insulation panel materials (wood fibres (B); glass wool (C) and polyurethane panels (D)) and (ii) 2 types of insulating bulk products (wadding (A) and rape straw pellets (E)). End points were measured after 2 days (D2) exposure and recovery after 7 days (D7).

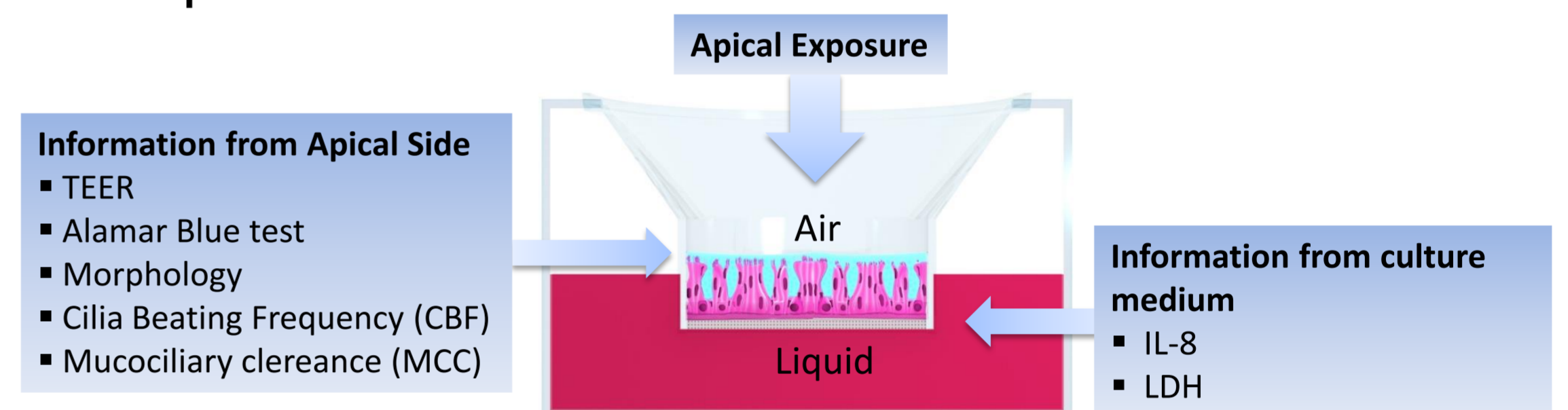
### Dextran Tablets Preparation



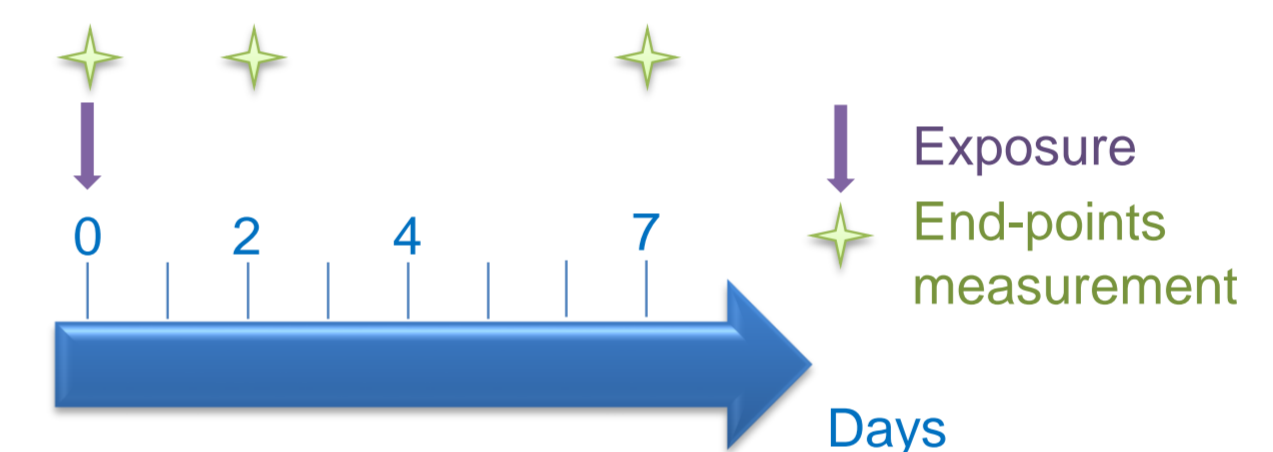
- 1- Dilute the compound with the Dextran at the targeted concentration and mix.
- 2- Make serial solid dilutions.
- 3- Compress the powder using the Epithelix-Vitrocell Nanopress to obtain a tablet.
- 4- Apply the tablet on the apical surface of MucilAir™ and incubate.
- 5- The tablet is entirely dissolved after 15 min.

### Testing Strategy

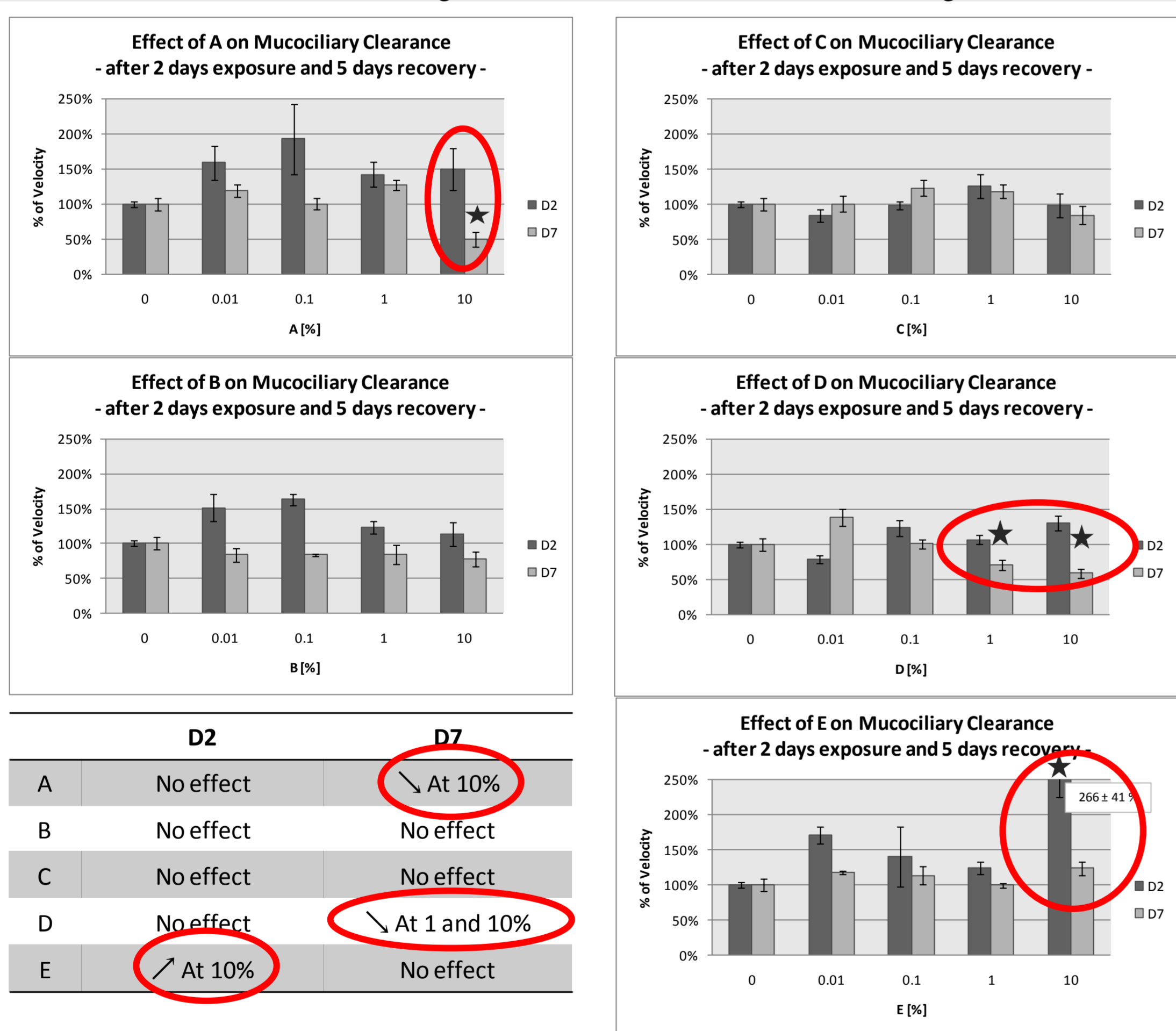
Multiple end-points:



Experimental scheme:

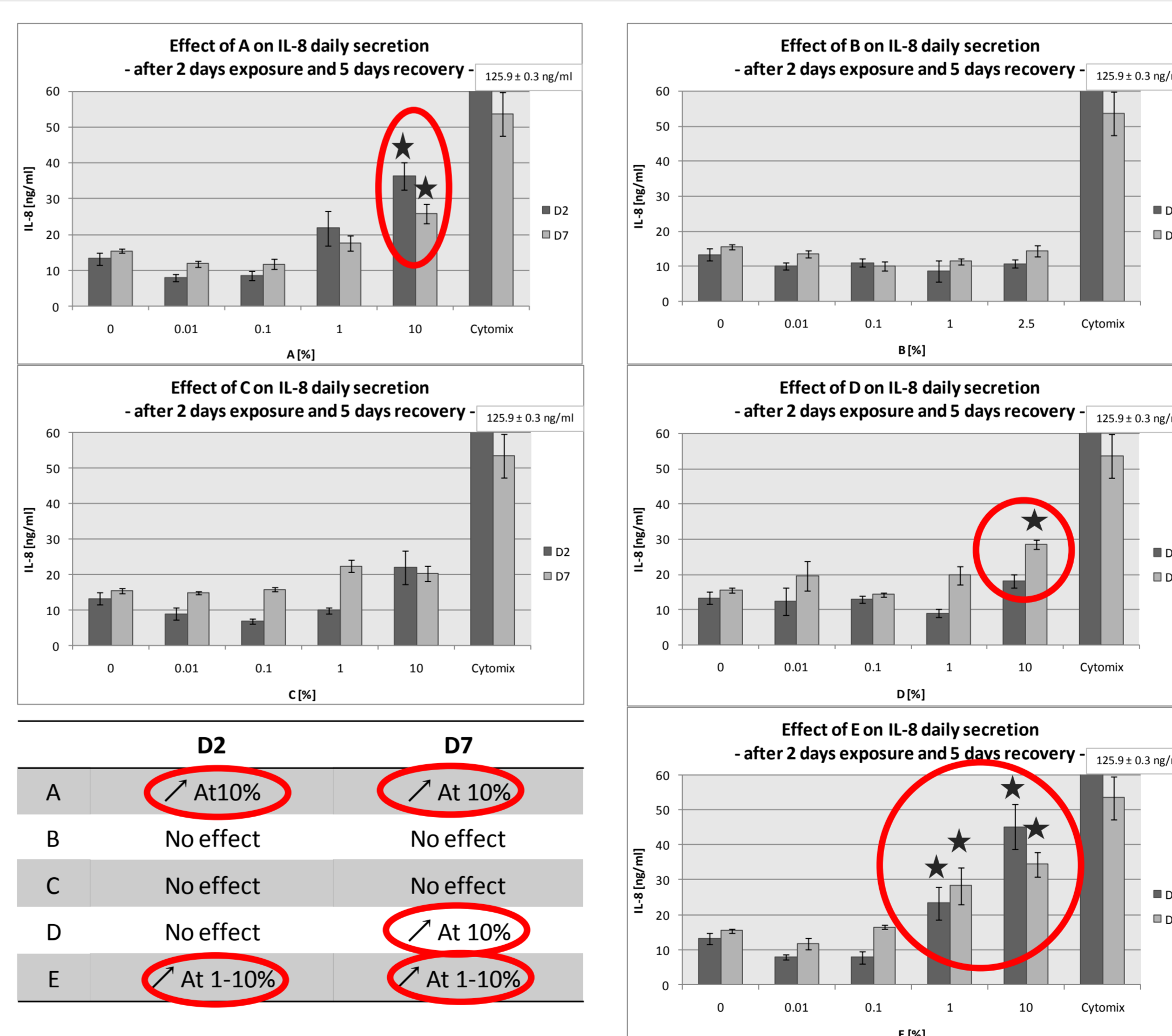


### Mucociliary Clearance Analysis



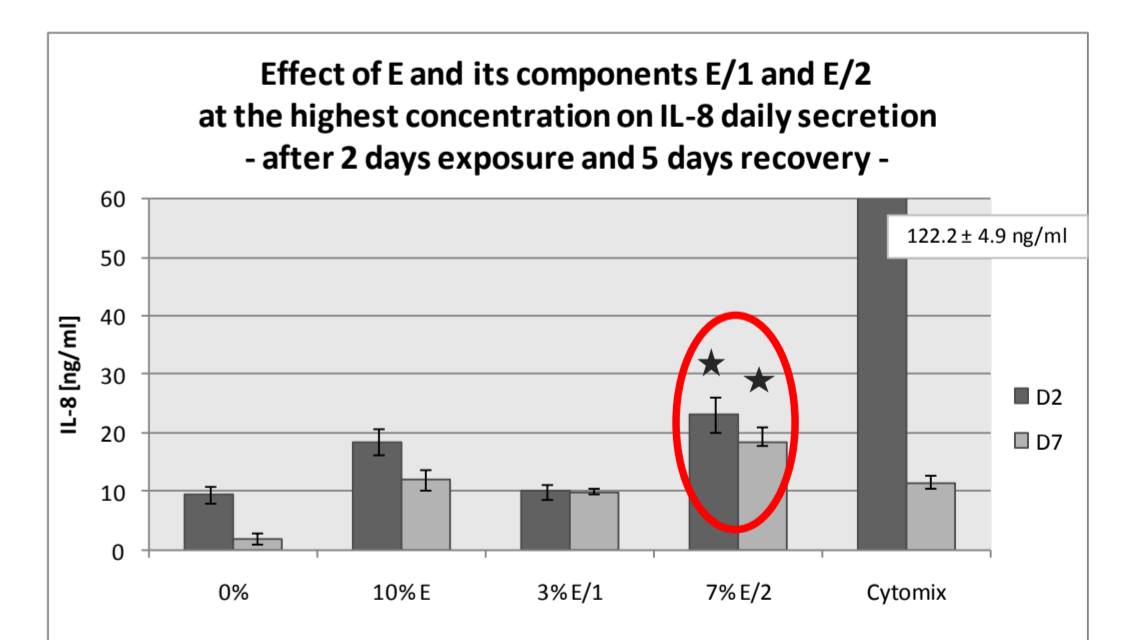
E induces a strong increased of MCC (+160%) at D2 which is reversible at D7. At D7, A and D at 1mg/cm<sup>2</sup>, MCC decrease (-50%). B and C don't affect MCC.

### IL-8 Release



A dose-dependent release of IL-8 was observed for A and E from 1mg/cm<sup>2</sup> to 10mg/cm<sup>2</sup> at D2 which stay upregulated until D7. D increases slightly IL-8 for 10mg/cm<sup>2</sup> at D7 but not at D2 suggesting a delayed effect. B had no effect and C induces a slight secretion of IL-8.

A series of experiments was performed on the base constituents of E. Indeed, E was pre-treated straw with slaked lime (30% dry mass).



The slaked lime treatment is not responsible for the pro-inflammatory nature of E.

### Conclusions

- 1: Selected endpoints are highly sensitive and relevant for detecting potential toxic effects of the construction materials.
- 2: The testing strategy described was able to discriminate the relative acute toxicity of the 5 materials and constituents (E > A > D ≈ C > B).
- 3: This new *in vitro* approach is particularly useful in the development of novel construction materials.

### Acknowledgements

