Mucilair™: An *In Vitro* 3D Human Cell Model for Repeated Dose Inhalation Toxicity Assessment

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Most of the *in vitro* cell models for long term testing of chemicals suffer of at least two shortcomings: 1. The failure of reproducing the *in vivo* physiological characteristics of the corresponding tissues, such is the case for the immortalized cell lines. 2. A limited shelf-life, for example, the freshly established primary cell cultures. Our company, Epithelix, has developed and is commercializing a novel *in vitro* cell model of the human airway epithelium (MucilAir[™]) made of primary cells which is free of these limitations.

MucilAirTM is morphologically and functionally differentiated and it can also be maintained at a homeostatic state for more than one year. The typical ultra-structures of the human airway epithelium, such as the tight junctions, the cilia, the basal cells, the mucous cells can be observed. The epithelium is electrically tight (TEER $\approx 450 \ \Omega.cm^2 \pm 5 \ (N=1470)$). The ion channels are fully functional and respond normally to their specific inhibitors and activators. Moreover, the epithelial cells react to pro-inflammatory mediators in a physiological manner. Remarkably, the epithelium has a strong capacity of regeneration after mechanical or chemical injuries. Epithelia from several different pathologies can be reconstructed (e.g. Asthma, COPD, CF, smoker, etc.).

Due to its unique long shelf-life of one year, this model is used for studying the human respiratory diseases, and for testing the long-term/repeated dose effects of drugs/chemicals on the respiratory tract. Several applications of MucilAir[™] relevant to inhalation toxicity assessment will be presented:

- Acute, Long-Term and Repeated Dose Toxicity testing
- Inflammatory effect assessment
- Wound healing experiments