Where NAMs are not Alternatives

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OECD TGs are validated Alternatives to Animal testing for defined toxicological endpoints : they are based on in vitro systems and currently used in different industrial sectors for chemical hazard classification and safety assessment after acute exposure. It is widely recognized within the scientific community that from the very beginning of their development (around the 90's) and increasing number of non regulatory models have been developped.

In a certain sense the regulatory requirements have opened the door to a more and more precise and specialized use of in vitro systems for pharmaco-toxicology investigations within the non clinical safety phase in drug development and globally in Life Sciences.

In vitro Science grew up so fast and today we no more take about NAMs exclusively in a replacement paradigm but in a more wide non clinical approach that includes the definition of new, unexplored or early toxicity endpoints and their mechanisms.

NAMs are increasingly encouraged in regulatory submissions, not only because animals models are not human relevant but also because they can improve the predictivity and ultimately enhance safety in clinical trials : some endpoints cannot investigated directly on humans in the clinical phase for practical, scientific and ethical reasons.

Some examples of in vitro models developped to address specific pharmaco-toxicological endpoints will be presented : epithelial barrier impairement as measure for gastrointestinal toxicity screening, mucociliary clearance impairment as early sign of viral infection, hair follicle organoids to recapitulate dermopapilla cycle, acid pH toxic action on oesophageal epithelium structure.