

# SEURAT: Safety Evaluation Ultimately Replacing Animal Testing

## *Perspectives beyond SEURAT-1*

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The research programme of the first phase of the SEURAT initiative, SEURAT-1, will come to an end in December 2015. Much has already been achieved, and many lessons learned. From the outset, an important commitment of the SEURAT-1 cluster has been to disseminate research results as they appear and to report on the effectiveness and evolution of the SEURAT-1 research strategy. Although the SEURAT-1 annual book is a key instrument to achieve this, a Strategy Group was recently established (comprising the authors of this summary) to reflect on progress and advise on how SEURAT should evolve scientifically to ultimately realise its vision.

The group suggests two parallel work streams for a continuation of the SEURAT programme:

1. The first work stream would focus on integration of new approach methods for hazard (and risk) assessment within the current regulatory ‘paradigm’; aiming for acceptance of animal-free testing strategies by regulatory authorities (this is the applied part, i.e. translating scientific achievements into regulation). In essence, this would be to complete the SEURAT-1 “conceptual framework” for combining evidence, in particular from new-approach methods, in a biologically-rational manner to qualitatively and quantitatively predict traditional organ-based toxicity. Specific implementation of the framework includes contributing additional evidence of the biological basis for “read-across” and *ab initio* development of a safety assessment that relies only on the new *in silico* and *in vitro* methods. The aim is to develop guidelines (e.g. at OECD level) for the implementation of non-standard *in silico* and *in vitro* methods into regulatory risk assessment. The application in “real-world” decision-making process is an essential deliverable.
2. The second work stream would focus on developing new ‘paradigm’ approaches for regulatory science. The goal here is the identification of “critical biological molecules and pathways” relevant for toxicity and to test their suitability to be used as anchors for predicting toxicity. These critical molecules and pathways will not be restricted to effects on distinct organs or particular types of toxic effects. The idea is that independent of the nature of the adverse outcome of interest, be it cancer or developmental toxicity or acute or repeated dose toxicity, the disturbance of these pathways would indicate a likelihood for adversity and the dose at which this would occur. The aim would be to establish, at a proof-of-concept level, the suitability of this “critical pathway concept” to improve the predictive power of mechanism-based toxicity testing methods which might be applied in a future regulatory safety assessment.

There are a number of research areas that will need to be developed and/or perfected to deliver the components needed for these work streams. These include chemoinformatics, high throughput screening and high-content methods (e.g., toxicogenomics), systems biology approaches (both computational and lab-based (tissue chip) models) and pharmacokinetic modeling (including reverse-dosimetry and QVIVE).

A more detailed report from the Strategy Group is in preparation and is planned to be published soon in a peer-reviewed journal. For more information please send a message to:

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