# *Executive summary*

The rapid expansion in *in vitro* methods, along with improved understanding of the biological processes involved in toxicological sequelae, have facilitated the development of a variety of predictive *in vitro* methods. These *in vitro* methods can be robust alternatives to using animals to identify and characterise chemical safety hazards. In some regulatory sectors, recent changes in regulation now accept, or in some cases, require, *in vitro* data in lieu of data from animal studies. When the scientific suitability has been demonstrated, the use of *in vitro* methods can reduce the resources required and increase the efficacy of chemical safety evaluation. In order for these alternatives to be used in regulatory decision making the scientific integrity and quality assurance must be assured.

The Guidance Document on Good *In Vitro* Method Practices (GIVIMP) for the development and implementation of *in vitro* methods for regulatory use in human safety assessment was developed as a reference for best practices and as a tool to avoid a reproducibility crisis in *in vitro* toxicological science. The project was a joint activity of the Working Group on Good Laboratory Practises and the Working Group of the National Coordinators to the Test Guidelines Programme. The document includes guidance for developing and using *in vitro* methods for chemical safety assessment, as well as guidance for the laboratory environment in which test data are generated and recorded. The project was coordinated by the European Union Reference Laboratory for alternatives to animal testing (EURL ECVAM) of the European Commission's Joint Research Centre (JRC) with the aim of reducing the uncertainties in cell and tissue-based *in vitro* method derived predictions. The GIVIMP includes a glossary of terms to assure developers and end users begin with a common understanding and tackles ten important aspects related to *in vitro* work.

Chapter 1: Roles and responsibilities, describes the roles of key players over the life cycle of *in vitro* method development and use for safety assessment and provides guidance for improving regulatory acceptance of the method and resulting data. Chapter 2: Quality considerations discusses requirements for development and implementation of *in vitro* methods and considerations to assure the integrity of resulting data. Chapter 3: Facilities, details considerations for the physical environment in which *in vitro* cell and tissue culture are performed to limit impacts that may adversely impact the science. Chapter 4: Apparatus, material and reagents indicates quality requirements for equipment and reagents and includes recommendations to improve reproducibility of the method and results. Chapter 5: Test systems, describes best practices for storage, handling, authentication and characterisation of cell and tissue-based test systems. Chapter 6: Test and reference/control items, provides information on how to assess test system and test item interactions to assure accurate and reliable exposure and avoid *in vitro* method interference due to insolubility and other limitations. Chapter 7: Standard operating procedures, recommends a process for simplifying the work of personnel using the *in vitro* method to assure similar process is followed each time the *in vitro* method is used and reduce variability due to deviations from a fixed methodology. Chapter 8: Performance of the method, describes elements of the experimental design such as plate

layout, data analysis, assessment of linearity, and accuracy to ensure the method is preformed correctly and the endpoint is reliable. Chapter 9: Reporting of results includes guidance on including appropriate detail and recording practises in scientific publications, as well as all related documents, to improve transparency and reproducibility of the method and results. Chapter 10: Storage and retention of records discusses requirements for traceability, storage, verification and transmission of data throughout the life cycle of the *in vitro* method. Key messages and content are highlighted at the beginning of each of the ten sections. Also included in the GIVIMP are eight annexes that provide detailed and directed guidance on specific topics related to good *in vitro* methods practices.