The Good In Vitro Method Practices (GIVIMP) guidance aims to reduce the uncertainties surrounding in vitro method derived predictions, and was written jointly by the OECD Working Group on Good Laboratory Practices and the Working Group of the National Coordinators to the Test Guideline Program and coordinated by the European Union Reference Laboratory for alternatives to animal testing (EURL ECVAM) of the European Commission’s Joint Research Centre (JRC). It is a document comprised of best practices and points to consider in the design and execution of laboratory work using cells and tissues as the test system (OECD, 2018).

GIVIMP addresses the topics shown in the circles below. Many of the recommendations center around the test system itself. Other points raised focus on controls for the equipment used, documentation and standardization of processes, training of personnel, and data integrity and record retention. Following the GIVIMP guidance leads to reliable results, technologies that are more easily transferred from the laboratory of origin to others, and robust records and documentation supporting the science.

### What is GIVIMP?

- Begin utilizing GIVIMP to support data integrity and build evidence needed to document fit for purpose and establish scientific confidence in the method.
- Maintain high quality control standards, use instructions, and record performance of the test system.
- Retain ALL data in the associated raw data, data analysis, and transformed data for future regulatory validation activities or proficiency testing.
- Ensure the proficiency chemicals, where they are defined. Use calibrated equipment for each run.
- Use appropriate controls on data templates.
- Determine and report whether laboratory repeatability and reproducibility are met.
- Report the predictivity of the method.
- Retain raw data in testing media (i.e., export data from the lab to the lab). Include data capture machines.
- Retain metadata along with the associated raw data.
- Follow general principles of data integrity.
- Safeguard the quality of historical data.
- Retain ALL data in the archives.
- Follow general principles of data integrity.

### What to consider from GIVIMP for Test System Providers, Method Development, and Routine Use

- Use control items to assess performance of the test system in the method.
- Selection of positive control.
- Identify the highest acceptable concentration of test item and solvents used.
- Records describing the procedure in detail.
- Start a data set to track historical values for reference items and controls.
- Performance of in-house validation.
- SOPs in place to support the main activities of the laboratory.
- Procedures for adapting SOPs to changes in processes.
- Personal review revisions to data integrity.
- Determination of data quality, limitations, and exceptions.
- Determine cut-off values and the mean and SD for the acceptance criteria.
- Documented procedures for transformation of data and data analysis.
- SOPs in place to support the main activities of the laboratory.
- Procedures for adapting SOPs to changes in processes.
- Personal review revisions to data integrity.
- Explanation of applicability domain, limitations, and exceptions.
- Determine and report whether laboratory repeatability and reproducibility are met.
- Report the predictivity of the method.
- Retain raw data in testing media (i.e., export data from the lab to the lab). Include data capture machines.
- Retain metadata along with the associated raw data.
- Follow general principles of data integrity.

### ABSTRACT

The demand for toxicity data by human-relevant, New Approach Methodologies (NAMs) continues to increase. Fortunately, the scientific community has responded with new tools based on human tissues and cells. The creators of these systems and test methods have utilized them in their development and also in studies designed to demonstrate their reliability, reproducibility, and transferability. Despite these efforts, scientific confidence in these methods at the regulatory level remains comparatively low. In order to bridge the gap between development and acceptance, industry best quality practices need to be embraced by all stakeholders as early as possible in development and continue throughout the life cycle of a test method. The Good In Vitro Method Practices guidance document was published by the OECD in 2018 with an aim to "improve the reliability and robustness of in vitro methods, reducing the uncertainties of in vitro based predictions and therefore increasing the acceptance of the in vitro estimated safety measures by regulatory agencies." (OECD, 2018).

The magnitude of the information presented in GIVIMP has led to challenges in its uptake and use by the testing community. Incorporating GIVIMP standards into standard laboratory procedures to improve scientific confidence in NAMs, incorporating GIVIMP standards into standard laboratory procedures will improve the transparency and reproducibility of the methods developed and performed there, and increase the confidence of validation bodies, receiving authorities, and industry in NAMs.

### References


### Points to Consider from GIVIMP for Test System Providers, Method Development, and Routine Use

The OECD guidance document titled Good In Vitro Method Practices (GIVIMP) is divided into 10 chapters. These chapters are represented in the circles below with a summary of their content. Some key points to consider are extracted from the chapters and presented in the table. They are organized into three categories: 1) Test System Provider, 2) Method Development, and 3) Routine Use. Informed reviewers or providers of test system should review the items noted under the Test System Providers column as they are the appropriate party to provide the information noted here. The recommendations under the Method Development header are those items it would be beneficial to address while still in the development and early optimization phase of the method. Points raised in the Routine Use column can be addressed once the method is standardized and is performed often within a laboratory or has been transferred to a new laboratory.

### Test System Providers

- Provide test system users with adequate information to properly operate and use the system.
- Document that test system characterization.
- Provide documentation of identity.
- Provide users with information on acceptable performance limits of the test system.
- Document batch/lot acceptability.
- Train users where special training is warranted.
- Define laboratory requirements for use of the test system (BLS level, power).
- Describe acceptable disinfectant and cleaning procedures to users.
- Minimize the risk of mix-ups and cross-contamination.
- Understand the risk and mitigation needs for biological and chemical agents.
- Separate bacteria and yeast from cell and tissue culture work.
- Media details known and defined.
- Calibration of equipment prior to use.
- Appropriate labeling and storage of reagents.
- Is the cell line viable for routine cell culture work.
- Regular performance checks for pipettes.
- Retain documents related to the development of the test system.
- Provide users with reference items and controls.
- Describe the highest acceptable concentration of test item and solvents used.
- Media details known and defined.
- SOPs for test system handling.
- Procedures for mycoplasma testing.
- Characterization of test system.
- Documentation of absence of contamination with each batchlot.
- SOPs for test system handling.
- Cells and tissues from a certified provider.
- Establish go/no go points.
- Ensure both short and long term availability of the test system.
- Culture identification and contamination
- Importing of cell and tissue culture samples.
- Cultures stored from a certified provider.
- SOPs for test system handling.
- Procedures for mycoplasma testing.
- Retain raw data in testing media (i.e., export data from the lab to the lab). Include data capture machines.
- Retain metadata along with the associated raw data.
- Follow general principles of data integrity.
- Safeguard the quality of historical data.
- Retain ALL data in the archives.
- Follow general principles of data integrity.

### Method Development

- Clearly written method description.
- Consider IF guidelines and follow good licensing practices.
- Document competency to perform the work (e.g., proficiency chemicals).
- Media details known and defined.
- Record performance of the test system.
- Establish go/no go points (
- Analyze the accuracy and precision of the test.
- Relate deviations from the standard formal training on method validation activities.
- Make a plan to correct any deviations.
- Do a final performance check.
- Document results of the final check.
- Use appropriate controls on data templates.
- Determine the statistical power of the test.
- Identify the highest acceptable concentration of test item and solvents used.
- Records describing the procedure in detail.
- Start a data set to track historical values for reference items and controls.
- Performance of in-house validation.
- SOPs in place to support the main activities of the laboratory.
- Procedures for adapting SOPs to changes in processes.
- Personal review revisions to data integrity.

### Routine Use

- Communicate performance of the test system in the method.
- Selection of positive control.
- Identify the highest acceptable concentration of test item and solvents used.
- Validation of the test system.
- SOPs in place to support the main activities of the laboratory.
- Procedures for adapting SOPs to changes in processes.
- Personal review revisions to data integrity.

### Standards

- Documented procedures for test system use.
- Use robust in-life recording leads to early SOP drafts.
- Implement GIVIMP guidance to optimize the method and support continued use and dissemination to new laboratories.