The European Commission's Science and Knowledge Service

Joint Research Centre

Good *In Vitro* Method Practices (GIVIMP) and its implementation

Sandra Coecke,

Gerard Bowe, Patience Browne

European Commission

.....and the use of cooking pots in the experimental design

Human liver perfusion, Marseille, April 1992

European Commission

.....and the use of cooking pots in the experimental design

Human liver perfusion, Marseille, April 1992

MiniReview

Basic & Clinical Pharmacology & Toxicology, 2016, 123, 42–50

Cytochrome P450 Induction and Xeno-Sensing Receptors Pregnane X Receptor, Constitutive Androstane Receptor, Aryl Hydrocarbon Receptor and Peroxisome Proliferator-Activated Receptor α at the Crossroads of Toxicokinetics and Toxicodynamics

Jukka Hakkola[1,2], Camilla Bernasconi[3], Sandra Coecke[3], Lysiane Richert[4], Tommy B. Andersson[5,6] and Olavi Pelkonen[1,2]

[1]Research Unit of Biomedicine, Pharmacology and Toxicology, Faculty of Medicine, University of Oulu, Oulu, Finland, [2]Medical Research Center Oulu, University of Oulu, Oulu, Finland, [3]European Commission Joint Research Centre, EURL ECVAM, Ispra, Italy, [4]Kal.y-Cell, Plobsheim, France, [5]Drug Metabolism and Pharmacokinetics, Cardiovascular and Metabolic Diseases, IMED Biotech Unit, AstraZeneca, Gothenburg, Sweden and [6]Department of Physiology and Pharmacology, Section of Pharmacogenetics, Karolinska Institutet, Stockholm, Sweden

Toxicology in Vitro 60 (2019) 212–228

Contents lists available at ScienceDirect

Toxicology in Vitro

journal homepage: www.elsevier.com/locate/toxinvit

Validation of *in vitro* methods for human cytochrome P450 enzyme induction: Outcome of a multi-laboratory study

Camilla Bernasconi[a], Olavi Pelkonen[b,i], Tommy B. Andersson[c,d], Judy Strickland[e], Iwona Wilk-Zasadna[a], David Asturiol[a], Thomas Cole[a], Roman Liska[a], Andrew Worth[a], Ursula Müller-Vieira[f], Lysiane Richert[g], Christophe Chesne[h], Sandra Coecke[a,*]

[a] European Commission, Joint Research Centre (JRC), Ispra, Italy
[b] Research Unit of Biomedicine/Pharmacology and Toxicology, Faculty of Medicine, Aapistie 5B, University of Oulu, FIN-90014, Finland
[c] Drug Metabolism and Pharmacokinetics, Cardiovascular, Renal and Metabolism, IMED Biotech Unit, AstraZeneca, Gothenburg, Sweden
[d] Department of Physiology and Pharmacology, Section of Pharmacogenetics, Karolinska Institutet, SE-171 77 Stockholm, Sweden
[e] Integrated Laboratory Systems (contractor supporting NICEATM), Research Triangle Park, North, Carolina, 27709, USA
[f] Boehringer Ingelheim, Germany. Department of Drug Discovery Sciences, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach, an der Riss, Germany
[g] Kal.y-Cell, 20A, rue du Général Leclerc, 67115 Plobsheim, France[e] Biopredic International, Parc d'activité de la Bretèche Bâtiment A4, 35760 Saint Grégoire, Fr
[h] Biopredic International, Parc d'activité de la Bretèche Bâtiment A4, 35760 Saint Grégoire, France
[i] Clinical Research Center, Oulu University Hospital, Finland

https://tsar.jrc.ec.europa.eu/search-test-methods-a?search_combined_anonymous=cyp+induction

NO Foetal Bovine Serum

1. Underlying mechanisms

DNA level, protein level, enzyme level

2. Reproducibility

Within and between lab reproducibility

Obtaining relevant and reliable methods

EURL ECVAM European Union Reference Laboratory for Alternatives to Animal Testing

European Commission

In vitro method development based on GOOD PRACTICES safeguarding scientific integrity *(Relevance)* and quality *(Reproducibility)*

Trusted by decision makers
Used by industry

Need approaches and tools to stimulate "scientific reproducibility"

https://plato.stanford.edu/entries/scientific-reproducibility/
First published Mon Dec 3, 2018

Importance of the way *IN VITRO* METHODS are described and how they are performed!!!

European Commission

ATLA 33, 261–287, 2005

REFERENCE 02 from EURL ECVAM

Guidance on Good Cell Culture Practice

A Report of the Second ECVAM Task Force on Good Cell Culture Practice

Sandra Coecke,[1] Michael Balls,[2] Gerard Bowe,[1] John Davis,[3] Gerhard Gstraunthaler,[4] Thomas Hartung,[1] Robert Hay,[5] Otto-Wilhelm Merten,[6] Anna Price,[1] Leonard Schechtman,[7] Glyn Stacey[8] and William Stokes[9]

- In 2015, OECD approached **EURL ECVAM to coordinate the drafting** of a guidance document on Good in Vitro Method Practices.
- **Joint effort** by the Working Group of GLP inspectors & the Test Guideline Program.
- **Formally adopted by all OECD countries in August 2018**, to be used within the context of the OECD Test Guidelines Programme.

36 **Member Countries** + EC
Accession countries: Russia, Columbia, and Costa Rica
Key Partners: Brazil, India, China, South Africa and Indonesia

GIVIMP OECD Guidance Document on Good *In Vitro* Method Practices

Scope: provide guidance for THE DEVELOPMENT, USE AND IMPLEMENTATION OF IN VITRO METHODS

- This **tool** helps to **implement good practices** early in the in vitro method development process.
- When GIVIMP is properly implemented, it will **increase credibility** of mechanistic data, **increase the reliability and integrity** of the generated data and will **improve the efficiency** of in vitro method development and use for regulatory purposes.

European Commission

GIVIMP

OECD Guidance Document on Good *In Vitro* Method Practices

- **GIVIMP gives a systematic, logic and sequential framework to avoid bad practices in cell and tissue-based *in vitro* method work and all related processes.**

- **It is important to properly read, practice and routinely implement the GIVIMP guidance in all its aspects to ensure a globally harmonized approach.**

European Commission

EURL ECVAM
European Union Reference Laboratory for Alternatives to Animal Testing

GIVIMP OECD Guidance Document on Good *In Vitro* Method Practices

OECD
BETTER POLICIES FOR BETTER LIVES

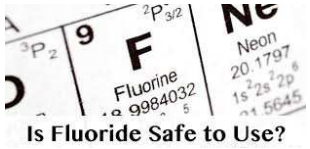
The GIVIMP GD is divided into 10 sections covering:

1. Roles and responsibilities
2. Quality considerations
3. Facilities
4. Apparatus, material and reagents
5. Test systems
6. Test and reference/control items
7. Standard operating procedures (SOPs)
8. Performance of the method
9. Reporting of results
10. Storage and retention of records and materials

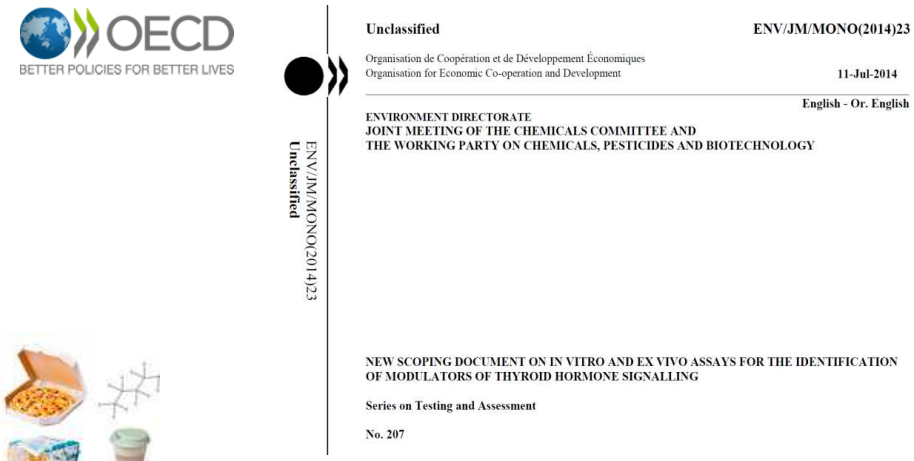
European Commission

Thyroid Validation Study

manage metabolism & regulate vital body functions
including breathing, heart rate, central and peripheral nervous systems, body weight, muscle strength, menstrual cycles, body temperature and cholesterol levels



Perchlorate Information Bureau



Natural and man-made chemicals have the potential to interfere with the functioning of the thyroid and related hormone signalling processes, which can result in adverse health effects in humans and other organisms

European Commission

13 method developers

14 EU-NETVAL labs

EU-NETVAL
Validation study to identify potential thyroid disruptors assessing 17 mechanistic methods



DSMZ

Universiteit Utrecht

ISCBI

ECVAM SCIENTIFIC ADVISORY COM. MEMBERS

Universiteit Utrecht

GIVIMP OECD Guidance Document on Good *In Vitro* Method Practices

European Commission

GIVIMP OECD Guidance Document on Good *In Vitro* Method Practices

Thyroid Validation Study

1.1 *In vitro* method developers

- Sign declaration; inform on IPR
- Declare GM elements
- Provide input to first draft of the outline protocol
- Provide input for choice of reference and control items

1.2 Test system providers

- Sign Material Transfer Agreement, IPR
- Declare GM elements

1.3. Validation bodies (EC JRC EURL ECVAM)

- Overall coordination (incl. all legal agreements…35)
- Provision test systems (characterisation and Qc), compounds, outline protocols

1.5 Suppliers of equipment, materials and reagents

European Commission

GIVIMP OECD Guidance Document on Good *In Vitro* Method Practices

Thyroid Validation Study

2. Quality considerations

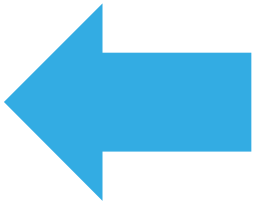
- Discusses quality assurance versus quality control
- Examines quality risk-based assessment and quality control requirements for development and implementation of *in vitro* methods
- Provides quality considerations regarding the integrity of the data

2.4 Quality control of test systems

2.5 Quality control of consumables and reagents

Applicability of integrity checks on cell cultures

Attributes	Original Source	Early Stocks	Cell Banks	Routine Cultures
Morphology	✓	✓	✓	✓
Viability	✓	✓	✓	✓[a]
Identity	✓	✓	✓	
Doubling time[b]	✓	✓	✓	✓
Mycoplasma	✓	✓	✓	✓
Viruses	✓ (donor only)		✓ (master bank only)	
Bacteria and Fungi			✓	✓[c]
Function/phenotype		✓	✓	✓[d]
Genetic stability			✓	✓[e]
Absence of reprogramming vectors (iPSC[f] lines)		✓	✓	

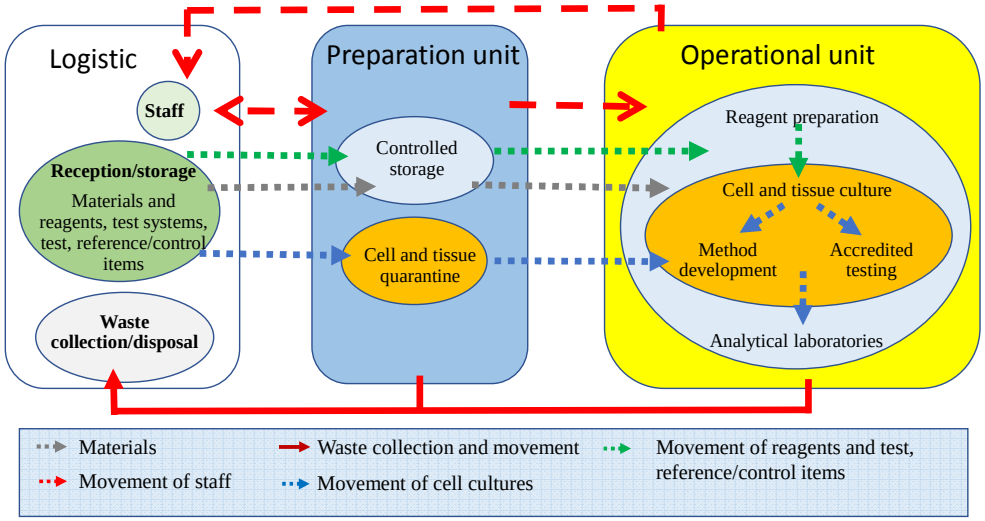


European Commission

Thyroid Validation Study

3. Facilities

- Recommends fit for purpose facilities and a detailed understanding of the work flow
- Indicates that facility design and safety risk assessment and management should be adequate
- Prescribes strategies to avoid cross-contamination



European Commission

GIVIMP OECD Guidance Document on Good *In Vitro* Method Practices

Thyroid Validation Study

4. Apparatus, materials and reagents

- Highlights the importance of regular maintenance, calibration, and validation
- Instructs on sourcing of materials and reagents (e.g. from well-established suppliers) to ensure the integrity and reliability
- Discusses the use of media in cell culture, including alternatives to animal-sourced serum

Antibiotics

…may arrest or disrupt fundamental aspects of cell biology, and, while they are effective against prokaryotic cells (i.e. bacteria), they can causing toxic effects in mammalian cells.

Foetal bovine serum

Consensus Report ALTEX. 2018;35(1):99-118

Fetal Bovine Serum (FBS):
Past – Present – Future

Jan van der Valk[1], Karen Bieback[2], Christiane Buta[3], Brett Cochrane[4], Wilhelm G. Dirks[5], Jianan Fu[6], James J. Hickman[7], Christiane Hohensee[8], Roman Kolar[9], Manfred Liebsch[10], Francesca Pistollato[11], Markus Schulz[12], Daniel Thieme[13], Tilo Weber[9], Joachim Wiest[14], Stefan Winkler[15] and Gerhard Gstraunthaler[16]

- The use of serum has been discouraged: the undefined nature of the medium
- batch variability
- potential limitation
- availability of supply.

https://fcs-free.org/

European Commission

Toxicology in Vitro 57 (2019) 143–144

Contents lists available at ScienceDirect

Toxicology in Vitro

journal homepage: www.elsevier.com/locate/toxinvit

What is understood by “animal-free research”?

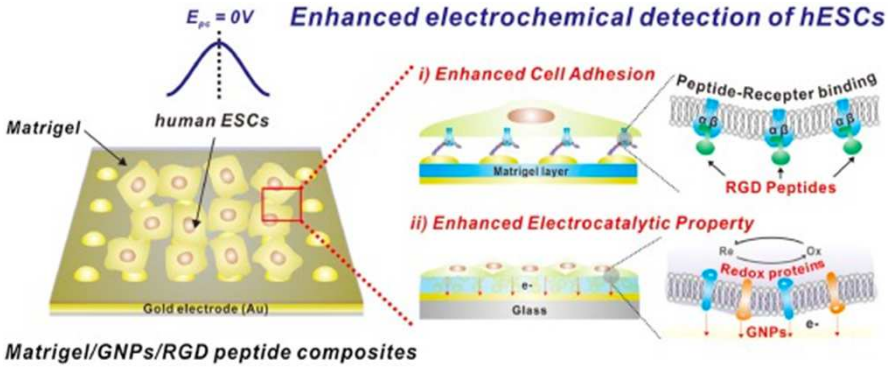
Stina Oredsson[a,*], Sandra Coecke[b], Jan van der Valk[c], Mathieu Vinken[d,e]

[a] Department of Biology, Lund University, Lund, Sweden
[b] European Commission, Joint Research Centre, Ispra, Italy
[c] 3Rs-Centre Utrecht Life Sciences, Utrecht University, Utrecht, the Netherlands
[d] European Society of Toxicology In Vitro, the Netherlands
[e] Department of In Vitro Toxicology and Dermato-Cosmetology, Vrije Universiteit Brussel, Brussels, Belgium

European Commission

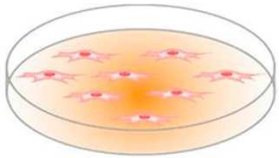
Other Animal-Derived Reagents

antibodies

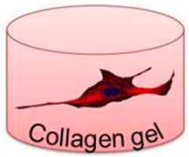


Tissue extracts
Proteolytic enzymes

3D collagen cell culture



2D cell culture



3D cell culture

European Commission

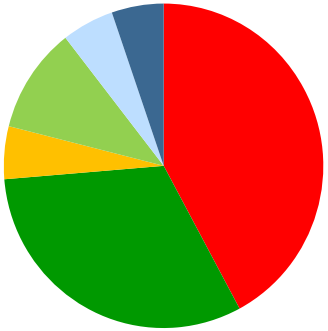
GIVIMP OECD Guidance Document on Good *In Vitro* Method Practices

Thyroid Validation Study

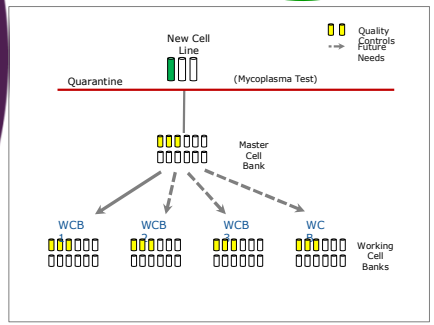
5. Test systems

- Elaborates the importance of Good Cell Culture Practice (GCCP)
- Advises the setting of acceptance criteria already at the development stage
- Describes identification and characterisation, sourcing, cell-banking and cryopreservation
- Suggests good practices for contaminants screening, including sterility, mycoplasma, virus testing

19 Test systems



- 8 animal cell lines (5 with human inserts)
- 6 human cell lines
- 1 human primary cells
- 2 proteins
- 1 cellular fraction
- 1 whole organism



Methodologies test system QC

Annex 1

ATLA 33, 261–287, 2005 REFERENCE 02 from EURL ECVAM

Guidance on Good Cell Culture Practice

A Report of the Second ECVAM Task Force on Good Cell Culture Practice

Sandra Coecke,[1] Michael Balls,[2] Gerard Bowe,[1] John Davis,[3] Gerhard Gstraunthaler,[4] Thomas Hartung,[1] Robert Hay,[5] Otto-Wilhelm Merten,[6] Anna Price,[1] Leonard Schechtman,[7] Glyn Stacey[8] and William Stokes[9]

Annex 2

ALTEX 34(1), 2017

transatlantic think tank for toxicology

t4 workshop report*

Good Cell Culture Practice for Stem Cells and Stem-Cell-Derived Models

David Pamies[1], Anna Bal-Price[2], Anton Simeonov[3], Danilo Tagle[3], Dave Allen[4], David Gerhold[3], Dezhong Yin[5], Francesca Pistollato[2], Takashi Inutsuka[6], Kristie Sullivan[7], Glyn Stacey[8], Harry Salem[9], Marcel Leist[10], Mardas Daneshian[10], Mohan C. Vemuri[11], Richard McFarland[12], Sandra Coecke[2], Suzanne C. Fitzpatrick[12], Uma Lakshmipathy[11], Amanda Mack[13], Wen Bo Wang[13], Daiju Yamazaki[14], Yuko Sekino[14], Yasunari Kanda[14], Lena Smirnova[1] and Thomas Hartung[1,10]

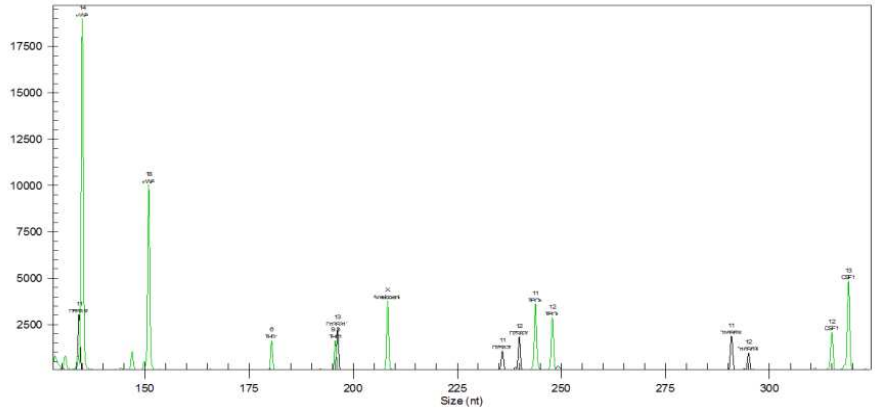
European Commission

Cell line identity & purity

Authentication of human cell lines with DNA profiling using 8 different and highly polymorphic short tandem repeat (STR) loci.

Human samples also tested for presence of mitochondrial DNA sequences from rodent cells as mouse, rat, Chinese and Syrian hamster. At a detection limit of $1:10^5$ mitochondrial sequences from mouse, rat or Chinese and Syrian hamster cells were not detected in the samples.

Identification of animal species with DNA Barcoding of Cytochrome Oxidase subunit 1.



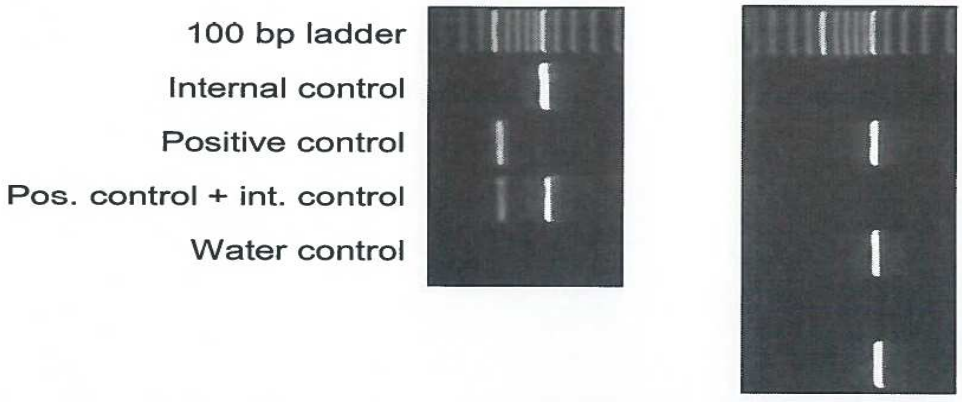
5`- TTTANAGTACACNTATAGTCTCACCCACCCACCAAGAATATCGGTACTTTATACTTACTA
TTGGGAGCATGAGCCGGTATAGTAGGCACTGCCTTGAGCCTCCTCATCCGAGCCGAACTA
GGTCAGCCCGGTACTTTACTAGGTGACGATCAAATTTATAATGTCATCGTAACCGCCCAT
GCTTTCGTAATAATCTTCTTCATAGTCATGCCCATCATAATTGGGGGCTTTGGAAACTGA
CTAGTGCCGTTAATAATTGGTGCTCCGGACATGGCATTCCCCCGAATAAATAACATGAGC
TTCTGACTCCTTCCTCCATCCTTTCTTCTACTATTAGCATCTTCTATGGTAGAAGCAGGT
GCAGGAACGGGATGAACCGTATACCCCCCACTGGCTGGCAATCTGGCCCATGCAGGAGCA
TCCGTTGACCTTACAATTTTCTCCTTACACTTAGCCGGAGTCTCTTCTATTTTAGGGGCA
ATTAATTTCATCACTACTATTATCAACATAAAACCCCCTGCAATATCCCAGTATCAAACT
CCCCTGTTTGTATGATCAGTACTAATTACAGCAGTTCTACTCTTACTATCCCTGCCTGTA
CTGGCTGCTGGAATTACAATACTTTTAACAGACCGGAATCTTAATACAACATTTTTTGAT
CCCGCTGGAGGAGGAGACCCAATCCTATATCAACACCTATTCTGATTCTTCGGCCAGCCA
AGAGTA-3`

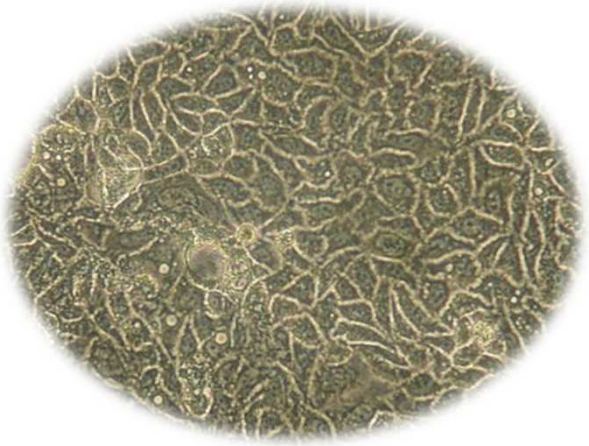
Example of results; STR profile of a human cell line (left) and DNA sequence of an animal cell line (right)

European Commission

Freedom of contamination

- Culturing without antibiotics + microscopic detection of bacteria, fungi, yeast
- Mycoplasma test (PCR and broth agar)
- Presence of human pathogenic viruses (PCR)





The following viruses are checked in rodent cell lines

- Retroviruses (with RT-PCR and ELISA)

The following viruses are checked in human cell lines

- Human Immunodeficiency Virus types 1 and 2
- Hepatitis B and C Viruses
- Human Papilloma Virus
- Xenotropic murine leukemia virus

Example of results; Mycoplasma PCR (left) and microscope image (right)

European Commission

Thyroid Validation Study

	sample	parental/ reference line	comment/match
1b	CHO-R, JP09	Puck et al, 1958	COI Barcoding analysis revealed Cricetulus barabensis species, species-specific
5a	MDCK1-MCT8	Gaush et al., 1966	COI Barcoding analysis revealed Canis lupus species, species-specific
5a	MDCK1-pcDNA	Gaush et al., 1966	COI Barcoding analysis revealed Canis lupus species, species-specific
6b	TRβ-CALUX	U-2-OS (DSMZ ACC 785)	full-matching STR profile of cell line U-2-OS in the reference database, authentic

Thyroid Validation Study

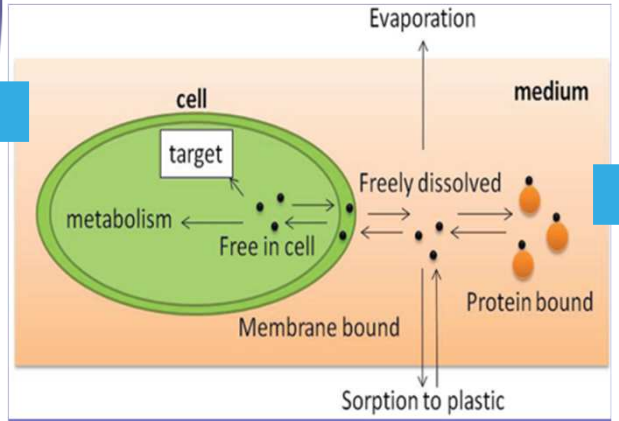
6. Test and reference/control items

- Illustrates the preparation and characterisation of test, reference and control items
- Defines the applicability and limitations of the method
- Recommends to identify potential sources of interference with the test system and/or method endpoint

Comparison between solubility determination methods

Method	Limitations	Specificity	Cut off	Rapidity
Nephelometry (Light scatter)	• Sticky precipitates • Impurities	Low	No	High
UV/VIS 1 (Absorbance)	• Compound must have chromophore • Sticky precipitates • Impurities	Low	<500 nm	High
UV/VIS 1* (Filtration + Absorbance)	• Compound must have chromophore • Sticky precipitates • Impurities • Loss due to filter absorption	Medium	<250 nm	Medium
HPLC-UV*^	• Sticky precipitates	High	No	Low
LC-MS*^	• Sticky precipitates	High	No	Low

** Requires Calibration* *^ High Cost*



Representation of some processes that can cause the final target concentration to be different than the nominal concentration in an in vitro test (Kramer et al., 2012)

6. Test and reference/control items

6.1 Reference and control items

6.3 Test item preparation

6.4 Concentration range

6.5 Solubility

6.6 Stability

6.7 Solvents

European Commission

GIVIMP OECD Guidance Document on Good *In Vitro* Method Practices

7. Standard operating procedures

- Provides guidance on the development and preparation of *in vitro* method standard operating procedures (SOPs) to ensure consistency and reproducibility of data acquired
- Describes the evolution of a SOP from initial method description to method optimisation and validation

Thyroid Validation Study

Evolution of a Standard Operating Procedure (SOP)

No SOP
Limited reproducibility (operator dependant)

Method optimisation
Describe the in vitro method procedure
Method optimised
Historical data of reference items are generated in a controlled way

SOP Version 01
Advanced in vitro method description
Acceptance criteria for valid/invalid experiments
Lists of needed equipment, reagents, consumables and reference items
Calculation of results

SOP Version xx
Further optimised procedure
Acceptance criteria for valid/invalid experiments
Calculation of results for test items
Data recording Forms, Data Calculation forms
SOP is robust

European Commission

GIVIMP OECD Guidance Document on Good *In Vitro* Method Practices

Thyroid Validation Study

8. Performance of the method

- Analyses development of acceptance criteria for components (e.g..positive and negative controls)
- Reviews the elements of experimental design such as plate layout, the number of replicates, outlier detectin, data analysis
- Examines how to determine the performance of the method, including the assessment of linearity, range, accuracy

Performance of the method

8.1 Acceptance criteria

8.2 Experimental design

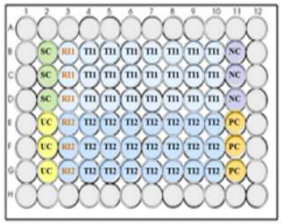
- 8.2.1 Plate layout
- 8.2.2 Data analysis
- 8.2.3 Outlier detection and removal
- 8.2.4 Non-monotonic dose and U-shaped curves

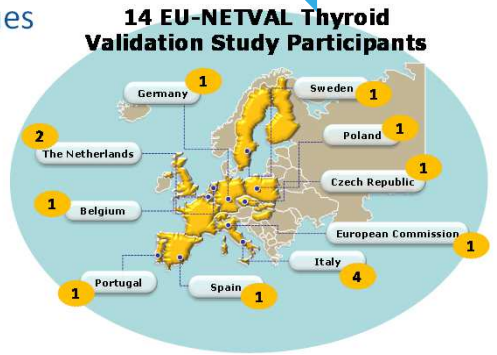
8.3 In-house validation of the measurement endpoint(s)

- 8.3.1 Detection Limits and Cut-off values
- 8.3.2 Linearity and dynamic range
- 8.3.3 Accuracy and precision
- 8.3.4 Sensitivity and specificity
- 8.3.5 Repeatability

8.4 Proficiency chemicals

8.5 Data-intensive *in vitro* methods

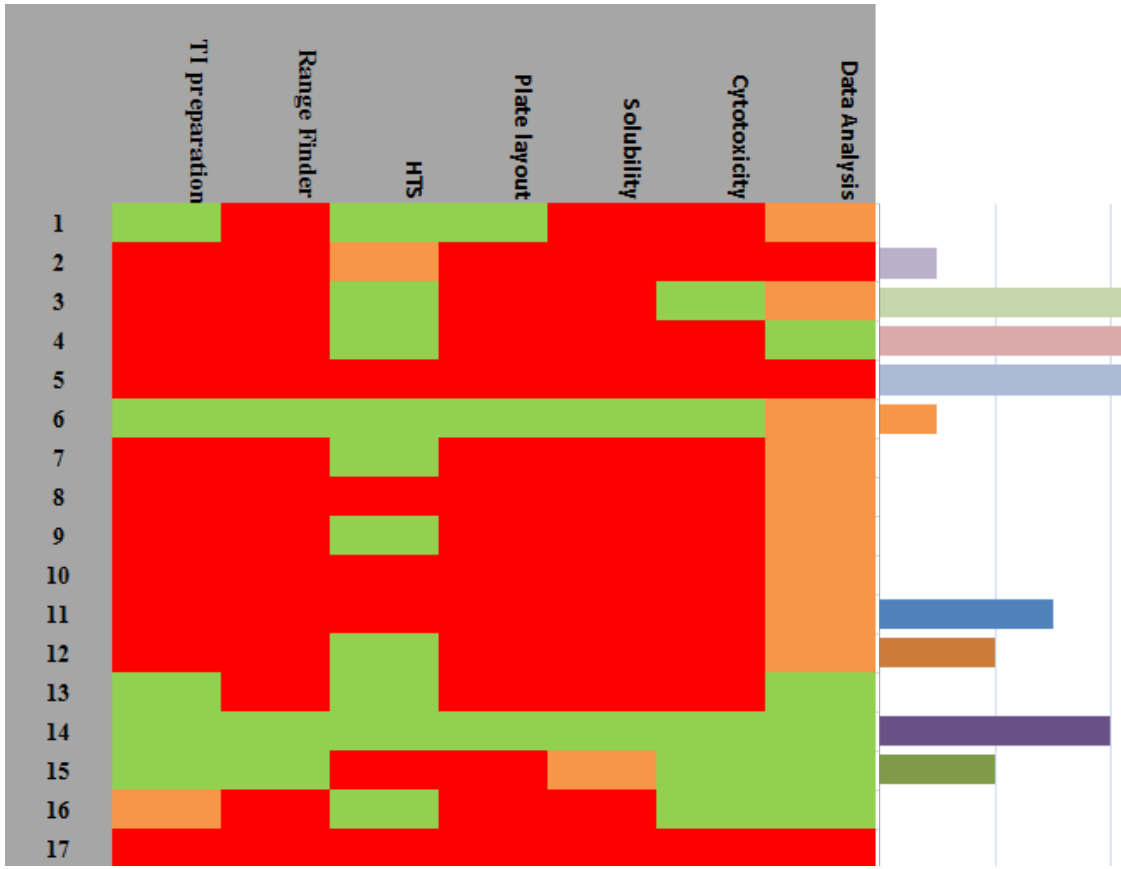




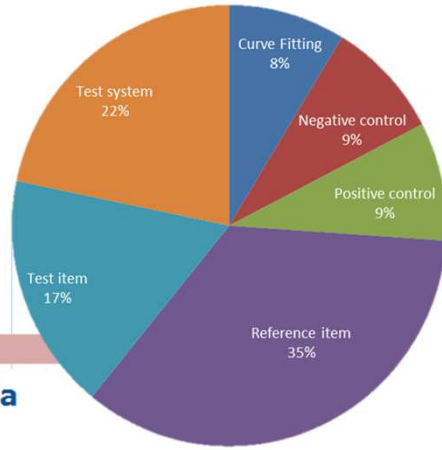
European Commission

Thyroid Validation Study

Completeness of methods



Distribution of **acceptance criteria**



Examples of acceptance criteria

- ✓ 20% reduction in cell viability
- ✓ 80-90% confluency after 3 days
- ✓ Passage number > 2 and < 30
- ✓ solvent concentration should be ≤0.1%
- ✓ Absolute fluorescence value of the solvent control has to be above 30000 RFU
- ✓ Replicates CV of 20% or less
- ✓ Minimum six valid triplicate samples
- ✓ TPO activity - dynamic range of 25.4 ± 4.3
- ✓ IC_{50} range reference item 1×10-7 – 1×10-6 M
- ✓ Z′ factor of 0.74 ± 0.021
- ✓ CV of estimated log(IC_{50}) reference item < 3%
- ✓ Pearson's coefficient (r2) of 0.8 or higher
- ✓ Maximum 2 concentrations may be excluded from RI curve

GIVIMP OECD Guidance Document on Good *In Vitro* Method Practices

Thyroid Validation Study

Publication of method procedures in on-line repositories

Major required elements to be reported:

1. Aspects of test system
2. and *in vitro* method details (e.g. complete SOPs)
3. Generated data

Transparency

The Transparency and Openness Promotion (TOP) guidelines https://osf.io/ud578/
The Journal of Negative Results in BioMedicine
https://jnrbm.biomedcentral.com/
Etc.

European Commission

GIVIMP OECD Guidance Document on Good *In Vitro* Method Practices

Annex 1

ATLA 33, 261–287, 2005 REFERENCE 02 from EURL ECVAM

Guidance on Good Cell Culture Practice

A Report of the Second ECVAM Task Force on Good Cell Culture Practice

Sandra Coecke,[1] Michael Balls,[2] Gerard Bowe,[1] John Davis,[3] Gerhard Gstraunthaler,[4] Thomas Hartung,[1] Robert Hay,[5] Otto-Wilhelm Merten,[6] Anna Price,[1] Leonard Schechtman,[7] Glyn Stacey[8] and William Stokes[9]

Table 5: Details to be included in papers for publication in journals, using an example of primary/early passage human cell culture

	Details	Supplier details
Type of culture	Primary cell culture	na
Cell/tissue type	Keratinocyte	na
Species	Human	na
Origin	Foreskin	QMC Hospital Trust, Nottingham, UK
Ethical permission	Required	Ethics Committee, QMC Hospital Trust
Supply to other users	Not permitted	
Transport solution	Phosphate-buffered saline	Gibco, Paisley, Scotland
Basic culture medium	Epi-Life® Medium	Cascade Biologics, Mansfield, Notts., UK
Serum	None	na
Antibiotics	100U/ml penicillin, 100µg/ml streptomycin	Gibco
Other additives	HKGS Kit (5-001 5) Calcium chloride	Cascade Biologics In-house
Complete medium	No further comment	na
Frequency of medium change	Every 2 days and at subculture	na
Culture flasks for establishing cultures	24cm² tissue culture flasks (163371)	Nunclon, Roskilde, Denmark, or Scientific Laboratory Supplies, Nottingham, UK
Inserts	Not used	na
Surface coating	Not used	na
Subculture	When 50–80% confluent (not when 100% confluent)	na
Subculture split ratio	1:5 or 1:10	na
Detachment solution	0.25% trypsin/EDTA (R-001-100) with trypsin-neutralising solution (R002-100)	Cambrex Bio Science, Wokingham, Berkshire, UK
Usable passage range	1–4	na
Maintenance conditions	37°C, 5% CO_2 in air	na
Storage conditions	Stock cells in liquid nitrogen, in 90% fetal calf serum/10% DMSO	na
Passage number at use	3	na
Culture plates for use	96-well plates (167008)	Nunclon
Use	3T3-NRU phototoxicity test	na
Relevant Standard Operating Procedures/guidelines	OECD TG 427, EU B.29	na
References	14, 15	na
Further comments	None	na

na = not applicable.

European Commission

GIVIMP OECD Guidance Document on Good *In Vitro* Method Practices

Data sharing

- Public repositories – guarantee data integrity and access
- Electronic data – format critical for future retrieval

European Commission

GIVIMP OECD Guidance Document on Good *In Vitro* Method Practices

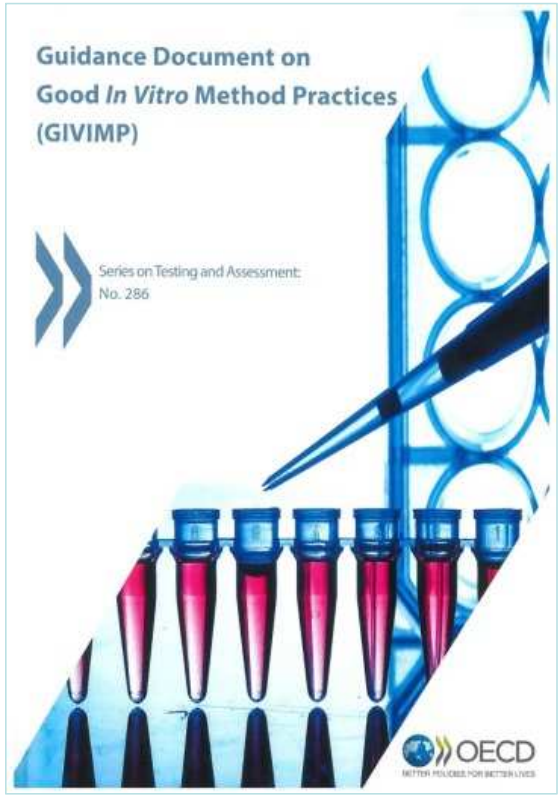
Applying GIVIMP during the development and use of in vitro methods is one of the tools used to improve the reproducibility and reliability of in vitro methods and their resulting data

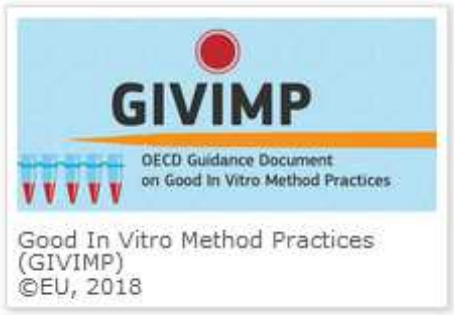
It's important that methods can be reproduced by others by making publically available the method details (e.g. SOPs incl. acceptance criteria to describe methods as complete as possible) and test system characterisation (e.g. specific characteristics, authentication and freedom of contamination)

Proving method reproducibility (in-house and ideally between laboratories) is recommended GOOD PRACTICE prior to using the methods to generate data

This allows for detailed systematic review of mechanistic data when evaluating their validity

European Commission





Download GIVIMP here

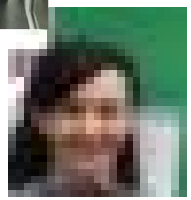
Available on OECD e-Library https://doi.org/10.1787/20777876

Also available on the
OECD Series for Testing and Assessment No. 286

Collaboration = faster progress

EC JRC Chemicals Safety and Alternative Methods hosting EURL ECVAM

Thyroid team



OECD team

EURL ECVAM first GIVIMP writing team

EU-NETVAL meeting participants

DG ENV

OECD GIVIMP expert group

et al.

European Commission

Stay in touch

EU Science Hub: ***ec.europa.eu/jrc***

Twitter: ***@EU_ScienceHub #ECVAM***

YouTube: ***EU Science Hub***

LinkedIn: ***Joint Research Centre***

Facebook: ***EU Science Hub - Joint Research Centre***

sandra.COECKE@ec.europa.eu

Twitter: **@SandraCoecke**

LinkedIn: **Sandra Coecke**

European Commission