ERα	SV40 promotor and luciferase reporter plasmid.		SPSF submitted. Antagonist assay validation will start in 2008.	
	HeLa-9903 cells: hERα/pcDNA3.1 receptor expressing plasmid and ERE-AUG-Luc+ reporter plasmid	Transient, ag	Validated under domestic multi-lab. using same test chemicals as hERa-HeLa-9903 cell line. Should be considered for (preliminary) Peer review.	CERI/MHLW
	MELN. MCF-7 cells with endogenous ERα + luciferase stably transfected	ag/antag	Validation in 2008.	EC/ECVAM
	ER-CALUX. T47 D (human breast cancer) cells with endogenous ERα + luciferase stably transfected	ag/antag	Validation planned for 2008.	EC/ECVAM
	LUMI cell, BG1 cells with endogenous ERα + luciferase stably transfected (XDS Inc)	binding	Validation will done by May 2008. Slightly delayed by the EC due to contract issues.	US lead international collaboration study
ERβ	HeLa, hERß/pcDNA3.1, ERE-AUG-Luc+	Transient, ag	Completed data collection for 250 compounds	CERI/MHLW
AR	CV-1 cells hAR/pcDNA3.1 receptor expressing plasmid and ARE-AUG-Luc+ reporter plasmid	Transient, ag/antag	Pre-validated and validated in Japan in 4 labs, with 5 chemicals. Should be considered for (preliminary) Peer review.	CERI/MHLW
	AR-Ecoscreen™ stable CHO clone	Stable, ag/antag	Validation report available in March 2008. SPSF will be submitted.	CERI/MHLW
	PALM. PC-3 (prostate adenocarcinoma) cells stably transfected with hAR and luciferase reporter gene	ag/antag	Validation in 2008.	EC/ECVAM
	CALUX. U2-OS (bone cell) cells stably transfected with hAR and luciferase reporter construct	ag/antag	Validation in 2008.	EC/ECVAM
TRβ	RXR co-transfected CHO cells are used	Transient, ag/antag	Under development, 150 chemicals tested so far.	MHLW
Aromatase & Steroidogenesis Assays				
	Microsomal aromatase		Validated, and the peer	

	assay, KGN cells		review report available in early 2008	
	H295R cell-based Steroidogenesis assay		Validation and peer review completed by December 2008. SPSF submitted.	US lead international collaboration study

THURSDAY 15 NOVEMBER

23. Christian Pelizzer of ECVAM presented of the ReproTect programme aiming at developing and optimising *in vitro* tests for reproductive toxicity endpoints. This is a EU project coordinated by ECVAM with a total budget 13 million €.

Continued Discussions on PBTG Issues

24. Steve Bradbury introduced the subject and concluded the previous days discussion and that MAD is probably the most important underlying requirement that may influence how we want to move this forward. With quickly emerging new strategies and new methods coming quickly we need to be adaptable without lowering the bar of acceptance and validation. The actual commenting round of new test methods is probably the most labour-some step after the actual validation. Steve introduced a set of three options based on Gary Timm's proposal.

> Option 1. *Status quo.* Keep the OECD adoption process as it is and develop individual Test Guidelines for all new test methods but the aim should be to have an expedited procedure for the adoption of me-too tests that meet the Performance Standards. No effects on MAD but will cause problems since the process is slow, and therefore tests could be outdated scientifically before they have been validated and adopted.
>
> Option 2. Develop PBTG for a specific endpoint with a separate compendium with detailed descriptions/SOP's for similar studies. There would be a streamlined way to have these "similar test methods" (me-too tests) accepted. One way could be to have a specific expert group (VMG NA, EDTA or a new Expert Group established for this particular purpose) that only examines these types of similar test methods and makes recommendations to the WNT for their adoption, or the specific expert group would make the decision whether the me-too test meet the requirements of the Performance Standard. Probably considerably quicker but may affect MAD.
>
> Option 3. PBTG approved by OECD but the "me-too-tests" could be adopted outside of the OECD procedures. Probably very vulnerable to MAD but would probably be a good procedure for some member countries that wants to keep up with the latest developments. This would give a self-certifying process by individual member countries.

25. The group discussed the different options and leaned towards option 1 and 2, however, with an emphasis of a quicker and smoother adoption process. The Secretariat explained that there are several projects were performance standards will be developed and ECVAM is setting up a special organisation to meet this challenge in the future. The Secretariat suggested that maybe another broader group with expertise in validation and performance standards should be involved in the development of performance standards and probably not the experts that have been involved in the validation of the test methods. The group generally agreed to the proposal, especially in the light of the fact that criteria for performance standard developments and how me-too tests can be used is an international issue that needs to be resolved relatively quickly. The group asked Laurence Musset to also consider discussions with legal services in

order to evaluate processes encompassing MAD yet greatly speeding up the process of validation and adoption without having too many layers of discussions and decisions.

26. The meeting suggested to establish a Performance Standards Issues Group (PSIG) (Secretariat, Gary Timm, Steve Bradbury, Alexius Freyberger, Dan Dietrich, Kate Willett) that would develop an issues paper for the WNT. The Secretariat explained that a consultation with OECD legal services regarding issues on MAD needs to be completed before an issues paper is developed. Therefore, it is probably more appropriate if the Secretariat develop a draft issue paper for review, discussion and comment by the PSIG before any recommendations provided to the WNT. Based on initial comments from the member countries the Secretariat may consider invitation one of the co-chairs of the VMG NA to the WNT meeting.

Discussion on the Fish *In Vitro* DRP

27. The meeting acknowledged the draft DRP but felt that a number of issues needs to be addressed in the DRP before it can be considered finalised and sent out for commenting to member countries. A Fish *In Vitro* Working Group comprising Dan Dietrich (coordination) Miriam Jacobs, Pat Schmieder, Jose Maria Savas, Susan Laws, Kate Willett and Les Touart will work on the document and submit an updated version to the Secretariat preferably by December 15, 2007 December. The Secretariat will share the document with the Japanese authors and will be asking them for revisions.

Update on EU CASCADE.

28. Lars-Arne Haldosen (Sweden) gave an update of the ongoing activities of the EU Network of Excellence

Follow-Up Work of the STTA

29. *PC10 and the wobbly base-line.* Yumi Akahori had a look at the raw data and it may not be so easy to resolve but need to get back to Japan before she can get the whole picture. Dan Dietrich and Alexius Freyberger emphasized that not interconnecting single values should be used to determine the PC10 but rather a curve should be optimized and integrated to lie within the data-points and therefore would cut the PC10-line only once.

Perfomance Standard for the agonist STTA.

30. Yumi Akahori gave a short presentation and suggested how to remove some outliers depending on the "zig-zag response". The feeling was that the PC10 was too close to the baseline. Yumi will check and put in some additional text. A compiled list of reference chemicals will be sent to Ray Tice from CERI and a selection of 10-15 reference chemicals will be used. Issues on true negatives came up, especially since the test has not been validated with maximum solubility, so it might be difficult to trust the data, why some negatives have to be cross-checked with other sources. Ray insisted that some of the test compounds have to be tested up to solubility.

31. Synopsis by the chair: Data needs to be gathered ASAP and Miriam will collate this but the Secretariat will have to give some justifications to the WNT why work is still ongoing and yet the draft Test Guideline is out for commenting. The final version with a complete list of chemicals will be available in February 2008 for the final review before the WNT20. Hopefully, no laboratory work needs to be done but this will follow the evaluation by Miriam Jacobs and Ray Tice.

Guidance on Chemical Selection for the STTA Antagonist Validation Study.

32. Hajime Kojima introduced the subject. The group decided that a chemical selection group comprising Hajime, Ray Tice and Miriam Jacobs will get together and clarify numbers of participating laboratories and the chemicals selected. The group will communicate with the Secretariat and the Secretariat will circulate this to the VMG NA for comments.

H295R Discussion

33. Gary Timm reintroduced the H295R issues and asked for input how should the data be interpreted? He will send his questions by e-mail to the group.

COMMITMENTS AND TIME FRAMES

34. The STTA-SC will develop a compilation of comments with expert's responses and a revised STTA TG including performance standards for the agonist assay within 2 weeks after the meeting for submission to the WNT for comments. The Secretariat will explain the issue with the chemical selection to the WNT in the accompanying letter.

35. The Fish *In Vitro* Working Group will report to the Secretariat preferably before 15 December and the Secretariat will communicate with the lead country, Japan.

36. The issues paper for the PBTG will be further developed by the Secretariat and circulated to the PSIG prior finalisation and submission to the WNT.

37. The VMG NA6 will be held in Paris in November 2008 and a suggestion for the 2009 meeting to be held in the US was presented and preliminary accepted.

38. A meeting report will be made available to participants for a short commenting period.

39. The VMG-NA thanked Patric Amcoff for his years of service, support and excellent advice and counsel to the validation group. All wished him well for the future.

Patric.Amcoff@oecd.org
Paris, 19 December 2007

ANNEX 1

List of Participants
(Only available for governmental representatives)

Patric.Amcoff@oecd.org
Paris, 19 December 2007

5TH MEETING OF THE VALIDATION MANAGEMENT GROUP FOR NON-ANIMAL TESTING (VMG-NA)
13-15 November 2007, ECVAM-DG JRC, Ispra Italy

DRAFT AGENDA (Version 1.2)

Monday 12 November The meeting of the PBTG sub-committee and the STTA working group will take place at 15.45-18.00 at the Hotel Conca Azzurra, Via Alberto, 53, Ranco. Participants will meet in the lobby of the hotel for further information.		
Tuesday 13 November		
09h30-09h40	**Opening of the Meeting, Explanation of OECD Procedures** - There will be a brief explanation of the role of the members, the status of documents and other general procedures. Listing of Meeting documents.	
09h40-09h50	**Welcoming on behalf of the Hosting Institute (Thomas Hartung, ECVAM)**	
09h50-10h00	**Approval of the Draft Agenda**	
10h00-10h15	**Introduction of the Membership of the VMG-NA**	
10h15-10h30	**Introduction of the Special Activity on ED Testing by the Test Guidelines Programme** - There will be a brief summary of the history of the VMG's and the EDTA (Secretariat).	**Meeting documents 1 and 2**
10h30-10h45	**Update on Japanese activities** - Presentations of activities by CERI (Mashiro Takeyoshi)	**Meeting Documents 8, 9, 14**
10h45-11h15	**COFFEE/TEA BREAK**	
11h15-11h30	**Continued update on Japanese activities** - Presentations of activities by MHLW (Dr. Kojima or Dr. Ono) - The Draft Fish In Vitro Receptor DRP (Secretariat)	**Meeting Documents 8, 9, 14**
11h30-12h00	**Update on ECVAM activities** - Presentation by ECVAM on validation status of ED *in vitro* ER and AR TA assays (Miriam Jacobs) - Discussions	**Meeting document 9**

12h00-12h30	**Status of the DRP on Metabolism** - Presentation by Miriam Jacobs (ECVAM)	**Meeting Document 7**
12h30-13h45	**LUNCH BREAK**	
13h45-14h15	**The H295R Validation Study Plan** - Presentation by Gary Timm (US EPA) - Discussions	**Meeting Document 12**
14h15-15h00	**The LumiCell Pre-validation Report** - Presentation by Ray Tice (US NICEATM) - Discussions	**Meeting Document 15**
15h00-15h30	**COFFEE/TEA BREAK**	
15h30-16h30	**The Validation Plan for the Human Recombinant ER-Binding Assay** - Presentation by Shirlee Tan (US EPA) - Discussions	**Meeting Document 12**
16h30-17h10	**Presentation on the US EPA ToxCast Programme** - Presentation by US EPA (David Dix)	**Meeting Document 15**
17h10-17h30	**Presentation on Progress of the QSAR Group** - Presentation by Pat Schmieder (US EPA)	
17h30	**ADJOURN FOR THE DAY**	
Wednesday 14th November		
09h30-09h40	**Review Day 1 and Objectives for Day 2**	
09h40-10h30	**Over view of the Work of the Stably Transfected ER Transcriptional Activation Assay Sub-Committee (STTA SC)** - The work and proposed strategy of the STTA SC will be presented by Masahiro Takeyoshi (CERI) - Discussions	**Room Documents 2 and 3**
10h30-11h00	**COFFEE/TEA BREAK**	
11h00-12h30	**Continued Discussions on the STTA SC**	
12h30-13h45	**LUNCH BREAK**	

13h45-14h45	**Over view of the Work of the Performance-Based Test Guidelines Working Group (PBTG WG)** - The work and proposed strategy of the PBTG WG will be presented by Miriam Jacobs (ECVAM) - Performance Standards at the OECD (Secretariat) - Discussions	**Room Documents 1, 2 and 3**
14h45-15h15	**COFFEE/TEA BREAK**	
15h15-16h00	**Continued Discussions on the PBTG WG**	
16h00-17h30	**Standard Project Submission Forms** - The Secretariat will introduce the topic - Discussions	**Meeting Documents 9, 10, 11**
Thursday 15th November		
09h30-09h40	**Review Day 2 and Objectives for Day 3**	
09h40-11h00	**Continued Discussions on the STTA and PBTG Activities and ways forward** - Discussions - Work plans, establishment of sub-groups, dead lines, etc,	
11h00-11h30	COFFEE/TEA BREAK	
11h30-12h00	**Any Other Business**	
12h00-13h00	**Concluding Discussions Time Frames and Commitments for Activities**	
13h00	**MEETING ADJOURNED**	

Meeting Documents

Documents are available on the protected website:
http://webdomino1.oecd.org/comnet/env/tf-edta.nsf?OpenDatabase
User name <<more>>, Pass word <<estrogen>>; and then go to VMG NA5

Meeting Document #1	**Meeting Report from EDTA 10, 27-28 March, 2007, Paris [ENV/JM/TG/EDTA/M(2007)3/REV 1]**
Meeting Document #2	**Meeting Report from the 4th Meeting of the VMG-NA, December 2006 [ENV/JM/TG/EDTA/M(2006)4]**

Meeting Document #3	**Guidance Document No. 34 on the Validation and International Acceptance of New or Upgraded Test Methods for Hazard Assessments**
Meeting Document #4	**Test Guidelines 435 on In Vitro Membrane Test for Corrosivity Testing**
Meeting Document #5	**Test Guidelines 430 "EPISKIN"**
Meeting Document #6	**Test Guidelines 431 "TER"**
Meeting Document #7	**Draft Detailed Review Paper for the Use of Metabolising Systems for In Vitro Testing of Endocrine Disrupters.**
Meeting Document #8	**Draft Detailed Review Paper for Fish In Vitro Receptor Binding Assays**
Meeting Document #9	**SPSF for Stably Transfected Transcriptional Activation Assay for the Detection of Estrogen Receptor Agonists and Antagonists**
Meeting Document #10	**SPSF for Human Recombinant Estrogen Receptor Alpha Binding Assays**
Meeting Document #11	**SPSF for H295R Cell-based Steroidogenesis Assay**
Meeting Document #12	**Update on US EPA's In Vitro Method Developmental Activities**
Meeting Document #13	**Status report on the human recombinant ERα-binding pre-validation effort (2007)**
Meeting Document #14	**Update Validation Status of Non-animal Testing in Japan by CERI, METI, NIHS. MHLW and MOE.**
Meeting Document #15	**Update on US-EPA's VMG NA In Vitro Activities**
ROOM DOCUMENTS	
Room Document #1	**Minutes of the Performance Based Test Guidelines Task Group (PBTG TG) Teleconference, Tuesday 23 October 2007.**
Room Document #2	**Minutes of the STTA sub-committee telephone conference, Tuesday 23 October 2007**
Room Document #3	***Documents for the STTA sub-committee:*** **3.1: Letter PA.2007.15_STTA PRP_12 September_ 07** **3.2: Letter PA.2007.13 STTA PRP and Comments** **3.3: Validation Report STTA** **3.4: STTA Test Guidelines draft** **3.5: JM Letter by Rob Visser** **3.6: WNT19-JM-Declass-PRP-STTA**

OECD TEST GUIDELINES PROGRAMME

Standard Project Submission Form

If you require further information please contact the OECD Secretariat
Return completed forms to:
env.tgcontact@oecd.org

PROJECT TITLE

Stably transfected Transcriptional Activation (TA) assay for detection of anti-estrogenic activity of chemicals

SUBMITTED BY (Country / European Commission / Secretariat)

Yumiko Nomura and Ayumi Kodama

DATE OF SUBMISSION TO THE SECRETARIAT

January 2008

DETAILS OF LEAD COUNTRY/CONSORTIUM

Country /Organisation:	Japan
Agency/ministry/Other:	Ministry of Health, Labour and Welfare (MHLW), Japan and Ministry of Economy, Trade and Industry (METI), Japan
Mail Address:	Kasumigaseki 1-2-2, Chiyoda-ku Tokyo, Japan and Kasumigaseki 1-3-1, Chiyoda-ku Tokyo, Japan
Phone/fax:	81-3-3595-2298/81-3-3593-8913 and 81-3-3501-0080/81-3-3580-6347
Email:	nomura-yumiko@mhlw.go.jp and kodama-ayumi@meti.go.jp

PROJECT OUTCOMES

☒ New Test Guideline	☐ Guidance document
☐ Revised Test Guideline	☐ Detailed Review Paper
☐ Deletion of an existing Test Guideline	☐ Other, please specify below

PROPOSED WORK PLAN and RESOURCE NEEDS:

1. Draft workplan for development of the proposal, including any need to establish Ad Hoc Expert Group and mode of meetings (face-to-face, teleconference; electronic discussion group). Indicate key milestones, including first and subsequent drafts of documents and timing of meetings.

The validation study for a method using estrogen responsive stable cell line using HeLa9903 cell line to detect anti-estrogenic activity will be completed by early 2009 and its validation report and its draft guideline will be available by middle 2009. At the same time, the scientific peer review will be initiated and the report from the scientific peer review will be prepared until late 2009.

2. Will additional information, including generation or collection of data, be required? If yes, please describe the anticipated process and timelines.

The multi-lab validation study using 10-12 coded chemicals including 3-4 laboratories under the lead of JaCVAM (Japanese Center for the Validation of Alternatives) will be initiated in early 2008. The participation from Japanese and European laboratories is planed.

3. Indicate the estimated overall resource need (time/money) for member country / consortium and Secretariat

- Time: At least, six weeks of peer review process 3-4 weeks for the consultant to prepare and finalize the peer review report.
-
- Money: At least, 20,000-EUR would be needed if employ independent consultant for the peer review process.

4. Is this proposal intended to replace an existing Test Guideline or lead to the deletion of an existing Test Guideline?

No

ESSENTIAL INFORMATION

In this section, please provide the information required by the Working Group of National Coordinators of the Test Guidelines Programme to assess the suitability of the project for the workplan of the Test Guidelines Programme

1. What is the existing or expected regulatory need/data requirement that will be met by the proposed outcome of the project? Please provide details below or as an attachment.

The proposed assay will provide data for Level2 assay (in vitro assays providing mechanistic data) in OECD EDTA conceptual framework

or as attachment No.__

2. How will the work contribute to further international harmonisation of hazard and risk assessment? Please provide details below or as an attachment.

Approaches for endocrine disrupters testing and risk assessment will be more harmonized.

or as attachment No.__

3. How will the proposed project address issues and /or endpoints which are of major human health or environmental concerns? Please provide details below or as an attachment.

The proposed assay can be used for the screening of potential endocrine modulating chemicals through ER

or as attachment No.__

4. Will the project have general support from OECD member countries or is the outcome relevant for just one or a few member countries / stakeholders? Provide details of the countries and the rationale for this view below.

☒ Many countries ☐ A few countries ☐ Only for the submitting country

Japan, United States, EU countries

5. If the Test Guideline is not intended for general use, indicate if the Test Guideline would be intended for:

☐ Specific (limited) applications such as pesticide usage, or

☐ for specific classes of chemicals (e.g. surfactants) rather than for chemicals in general.

6. If the expected outcome of this proposal is a Test Guideline or a Guidance Document, provide information on the intended use, applicability and limitations of the test method.

The test method is applicable for use as a Level 2 *in vitro* screening assay as described in the OECD Conceptual Framework for the Testing and Assessment of Endocrine Disrupting Chemicals. Applicability and limitations will be determined taking into account the results of the validation study.

7. Provide supporting information on the validation status (i.e. relevance and reliability) of the method. Principles for validation of test methods for OECD Test Guidelines are described in Guidance Document 34.

Provide justification and rationale for the test, including data.

If there are no or limited data available to support the reliability and relevance of the proposed test, indicate if validation work is included in the project.

If there is no need for validation provide a detailed justification.

The revised draft TG for detecting "estrogenic" activity using HeLa-9903 is under circulation. Since there are urgent needs for detecting anti-estrogenic activity using the validated cell, the pre-validation study for anti-estrogenic activity using HeLa-9903 cell line has been conducted, and highly reproducible results have been obtained using 7 known ER antagonists. The standardized protocol will be formalized in early 2008.

The multi-lab validation study using 10-12 coded chemicals including 3-4 laboratories under the lead of JaCVAM (Japanese Center for the Validation of Alternatives) will be initiated in early 2008. The participation from Japanese and European laboratories is planed.

ADDITIONAL INFORMATION

In this section please provide further information to allow the Working Group of National Coordinators of the Test Guidelines Programme to assess the suitability of the project for the workplan of the Test Guidelines Programme

1. If the expected outcome of the project proposal is a Test Guideline and is based on existing, regional or international documents such as guidelines, protocols or guidance material, please provide that information here or as an attachment.

ER antagonist effect is one of important mechanisms in endocrine disruption. There is no test guideline for ERTA assay to detect ER antagonist effect of chemicals, although TG of ERTA assay for ER agonist is under consideration in OECD test guideline program. This project will provide the complementary TG for ERTA assay and also will provide additional information to the requirement arisen from the peer review panel of the ERTA agonist assay using HeLa-9903 cell line.

or as attachment No.__

2. If Animal Welfare considerations are addressed in the project proposal, provide details below or as an attachment. Explain if the project is aimed at refining, reducing and/or replacing the use of animals.

If the project is not specifically developed for animal welfare purposes, indicate if the animal welfare considerations have been a component of the project proposal.

Indicate if animal welfare considerations are irrelevant to the project, for example for physico-chemical properties.

Although not aimed at the issue of animal welfare it will certainly be considered

or as attachment No.__

3. Provide information on expected or possible resource savings in member countries as a result of this project.

Harmonized approach for assessment of endocrine disrupters would save time and resources in Member countries.

4. If the expected outcome of the proposed project is a Guidance Document or Detailed Review Paper, will it be directly linked to the development of a particular Test Guideline or a series of Test Guidelines?

☒ Yes, it is the initial step in the development of a new or revision of existing Guidelines.

☐ Yes, additional guidance is needed for the most appropriate selection of the Guidelines on the subject.

☐ No, the guidance is on issues related to testing or the development of Test Guidelines in general.

There are ___ attachments added to this form.

ASSESSMENT OF PROJECT PROPOSAL

(To be completed by all member countries /stakeholders except the submitter)

Country / Organisation:	

Representative: (Preferably NC):	

Taking into account the project information, requested above, does this project meet the needs of the member countries for addition to the workplan of the Test Guidelines Programme

☐ Yes ☐ No ☐ Further information needed

If the response is "No" or "Further information needed", please provide justification:

Remarks as appropriate, including further information needs, if any:

OECD TEST GUIDELINES PROGRAMME

Standard Project Submission Form

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PROJECT TITLE

Stably transfected Transcriptional Activation (TA) assay for detection of androgenic and anti-androgenic activity of chemicals

SUBMITTED BY (Country / European Commission / Secretariat)

Yumiko Nomura and Ayumi Kodama

DATE OF SUBMISSION TO THE SECRETARIAT

January 2008

DETAILS OF LEAD COUNTRY/CONSORTIUM

Country /Organisation:	Japan
Agency/ministry/Other:	Ministry of Health, Labour and Welfare (MHLW), Japan and Ministry of Economy, Trade and Industry (METI)
Mail Address:	Kasumigaseki 1-2-2, Chiyoda-ku Tokyo, Japan and Kasumigaseki 1-3-1, Chiyoda-ku Tokyo, Japan
Phone/fax:	81-3-3595-2298/81-3-3593-8913 and 81-3-3501-0080/81-3-3580-6347
Email:	nomura-yumiko@mhlw.go.jp and kodama-ayumi@meti.go.jp

PROJECT OUTCOMES

☒ New Test Guideline	☐ Guidance document
☐ Revised Test Guideline	☐ Detailed Review Paper
☐ Deletion of an existing Test Guideline	☐ Other, please specify below

PROPOSED WORK PLAN and RESOURCE NEEDS:

1. Draft workplan for development of the proposal, including any need to establish Ad Hoc Expert Group and mode of meetings (face-to-face, teleconference; electronic discussion group). Indicate key milestones, including first and subsequent drafts of documents and timing of meetings.

The validation study for a method using androgen responsive stable cell line (AR-EcoScreen^{TM}) to detect androgenic and anti-androgenic activity of chemicals has been completed and its validation report and its draft guideline will be available in March, 2008. The scientific peer review will be initiated within the 2008 JFY and the report from the scientific peer review will be prepared until early 2009.

2. Will additional information, including generation or collection of data, be required? If yes, please describe the anticipated process and timelines.

Not planned

3. Indicate the estimated overall resource need (time/money) for member country / consortium and Secretariat

- Time: At least, six weeks of peer review process 3-4 weeks for the consultant to prepare and finalize the peer review report from the submission of Validation report and draft test guideline.

- Money: At least, 20,000-EUR would be needed if employ independent consultant for the peer review process.

4. Is this proposal intended to replace an existing Test Guideline or lead to the deletion of an existing Test Guideline?

No

ESSENTIAL INFORMATION

In this section, please provide the information required by the Working Group of National

Coordinators of the Test Guidelines Programme to assess the suitability of the project for the workplan of the Test Guidelines Programme

1. What is the existing or expected regulatory need/data requirement that will be met by the proposed outcome of the project? Please provide details below or as an attachment.

The proposed assay will provide data for Level2 assay (in vitro assays providing mechanistic data) in OECD EDTA conceptual framework

or as attachment No.__

2. How will the work contribute to further international harmonisation of hazard and risk assessment? Please provide details below or as an attachment.

Approaches for endocrine disrupters testing and risk assessment will be more harmonized.

or as attachment No.__

3. How will the proposed project address issues and /or endpoints which are of major human health or environmental concerns? Please provide details below or as an attachment.

The proposed assay can be used fro the screening of potential endocrine modulating chemicals through AR

or as attachment No.__

4. Will the project have general support from OECD member countries or is the outcome relevant for just one or a few member countries / stakeholders? Provide details of the countries and the rationale for this view below.

☒ Many countries ☐ A few countries ☐ Only for the submitting country

Japan, United States, EU countries

5. If the Test Guideline is not intended for general use, indicate if the Test Guideline would be intended for:

☐ Specific (limited) applications such as pesticide usage, or

☐ for specific classes of chemicals (e.g. surfactants) rather than for chemicals in general.

6. If the expected outcome of this proposal is a Test Guideline or a Guidance Document, provide information on the intended use, applicability and limitations of the test method.

The test method is applicable for use as a Level 2 *in vitro* screening assay as described in the OECD Conceptual Framework for the Testing and Assessment of Endocrine Disrupting Chemicals. Applicability and limitations /////

7. Provide supporting information on the validation status (i.e. relevance and reliability) of the method. Principles for validation of test methods for OECD Test Guidelines are described in Guidance Document 34.

Provide justification and rationale for the test, including data.

If there are no or limited data available to support the reliability and relevance of the proposed test, indicate if validation work is included in the project.

If there is no need for validation provide a detailed justification.

At the present time, there is global concern regarding endocrine disruption effects, particularly mediated by the andorogen receptor (AR) resulting from chemical exposure. Several *in vitro* AR binding and transfected cell line assay methods are currently or imminently being (pre) validated at national, regional and international levels, but are some way away from completion and full assessment of their validation status. Currently, no *in vitro* screening assay for AR activity that can be used for OECD regulatory purposes has been peer reviewed for potential test guideline development, although the need is urgent. Recognizing this urgency, Japan has made an extensive effort to establish and domestically validate a new *in vitro* pre-screening procedure, the Andorogen Receptor (AR) Transcriptional Activation (TA) Test for detecting the andorogenic and anti-andorogenic activities of chemicals for a level 2 screening test in the OECD Conceptual Framework for the Testing and Assessment of Endocrine Disrupting Chemicals. The with-in Japan multi-laboratory validation process of Japanese ER TA Assay was completed as an activity of the Validation Management Group (Non -Animal) (VMG-NA) and the results were presented at the 3rd and 5th VMG-NA held in November 2007.

The assay is based on an andorogen responsive stable cell line, AR EcoScreen cell, which was developed by the Otuka Permaceutical Ltd. in Japan. An initial test protocol of the assay system was developed and optimized in the Otuka Permaceutical. Using the optimized protocol, a pre-validation of the test system was conducted by the same company as an initial assessment exercise in order to identify the reliability, relevance and performance (accuracy) of the assay system. Following this initial assessment of the assay system, CERI led an inter-laboratory validation involving four participating laboratories, all of which used coded chemicals under GLP compliance conditions. The data produced indicated good reproducibility and technical transference between laboratories.

ADDITIONAL INFORMATION

In this section please provide further information to allow the Working Group of National Coordinators of the Test Guidelines Programme to assess the suitability of the project for the workplan of the Test Guidelines Programme

1. If the expected outcome of the project proposal is a Test Guideline and is based on existing, regional or international documents such as guidelines, protocols or guidance material, please provide that information here or as an attachment.

AR agonist and antagonist effects are one of important mechanisms in endocrine disruption. There is no test guideline for ARTA assay to detect AR agonist and antagonist effect of chemicals, although TG of ERTA assay for ER agonist is under consideration in OECD test guideline program. This project will provide the useful TG to detect AR mediated endocrine

modulating effect.

or as attachment No.__

2. If Animal Welfare considerations are addressed in the project proposal, provide details below or as an attachment. Explain if the project is aimed at refining, reducing and/or replacing the use of animals.

If the project is not specifically developed for animal welfare purposes, indicate if the animal welfare considerations have been a component of the project proposal.

Indicate if animal welfare considerations are irrelevant to the project, for example for physico-chemical properties.

Although not aimed at the issue of animal welfare it will certainly be considered

or as attachment No.__

3. Provide information on expected or possible resource savings in member countries as a result of this project.

Harmonized approach for assessment of endocrine disrupters would save time and resources in Member countries.

4. If the expected outcome of the proposed project is a Guidance Document or Detailed Review Paper, will it be directly linked to the development of a particular Test Guideline or a series of Test Guidelines?

☒ Yes, it is the initial step in the development of a new or revision of existing Guidelines.

☐ Yes, additional guidance is needed for the most appropriate selection of the Guidelines on the subject.

☐ No, the guidance is on issues related to testing or the development of Test Guidelines in general.

There are ___ attachments added to this form.