DRAFT GUIDING PRINCIPLES ON GOOD PRACTICES FOR THE AVAILABILITY/DISTRIBUTION OF PROTECTED ELEMENTS IN OECD TEST GUIDELINES

- 18 December 2018-

FOREWORD

This document describes good practices for the licensing of protected elements included in OECD Test Guidelines (TGs) and specifies the information required from a test method developer when submitting a proposal for a new TG that contains protected elements. Following the workshop organised at OECD in September 2017 (OECD, 2018a), there was agreement that more guidance, transparency and communication are needed around protected elements resulting from innovation in sciences and techniques that are gradually integrated in OECD Test Guidelines (TGs). The aim of the present document is to serve as a guide for organisations (e.g. private companies, universities, etc.) having developed and claimed intellectual property on material and techniques that could be readily used to fulfil a regulatory need, if it was integrated in an OECD Test Guideline. By observing and following the guiding principles, test developers would join the Programme with increased awareness of expectations and requirements.

These Guiding Principles were elaborated in 2018 by a group of experts in intellectual property issues and in various sectors ranging from biotechnology applications to standards development, and experts in anti-trust/competition law. Experts were nominated by their National Coordinators and are practitioners generally representing national patent offices, lawyers in private companies, or IP experts in regulatory agencies.

This document contains a broad overview of the intellectual property and similar protections that affect the OECD Test Guidelines Programme. Laws governing intellectual property and similar rights vary widely from jurisdiction to jurisdiction; anyone seeking to answer specific questions about the interpretation of the concepts in this paper in a specific jurisdiction must seek the advice of a specialised lawyer. Therefore, the OECD shall in no way be held liable for the content of this document, which is intended as a general overview only and should not be interpreted as legal advice.

Introduction – Setting the scene

1. The OECD Test Guidelines for the testing of chemicals are a collection of the most relevant internationally agreed testing methods used by governments, industry and independent laboratories to assess the safety of chemical products. They are primarily used in regulatory safety testing and subsequent chemical notification and registration. The set of Test Guidelines are updated on a regular basis to keep pace with progress in science and countries' regulatory needs.

2. With the development of new technologies, new ways of testing chemicals have emerged and will increasingly develop. These new methods generally include elements covered by intellectual property rights (IPR). IPR aim at stimulating innovation by enabling inventors to seek the returns on their investments. To date, many Test Guidelines for *in vitro* methods already include protected elements. This should not hamper their use for generating chemical safety data but should be accompanied by good licensing practices, as encouraged by OECD. In September 2017, the OECD held a workshop to present and discuss issues of availability, distribution and transparency associated with access to protected elements in OECD Test Guidelines (TGs) (OECD, 2018a). The workshop report includes a number of recommendations for further activities, one of which is to develop guidance at the OECD level on best practices for licensing protected elements in OECD Test Guidelines.

3. The Guiding Principles described in this document explain the functioning of the OECD Test Guidelines Programme, they specify the types of protected elements commonly encountered and the information to provide to OECD when submitting a project proposal to develop a new Test Guideline. Finally, the Guiding Principles promote the terms and conditions that should be followed to guarantee accessibility of these elements to the end-users when such elements are integrated in OECD Test Guidelines. A glossary of terms is available in Annex 1, as well as a model form for a licensor to commit to Fair, Reasonable and Non-Discriminatory conditions (see Annex 2).

The OECD Test Guidelines Programme: functioning principles

Purpose, Benefits of Harmonisation, Mutual Acceptance of Data

4. Accepted internationally as standard methods for safety testing, the Guidelines are used by industry, academic and government professionals involved in the testing and assessment of chemicals (industrial chemicals, pesticides, personal care products, etc.). These Guidelines are regularly updated with the assistance of national experts from OECD member countries. OECD Test Guidelines are covered by the Mutual Acceptance of Data (MAD), implying that data generated in the testing of chemicals in an OECD member country or a partner country having adhered to the Decision, in accordance with OECD Test Guidelines and Principles of Good Laboratory Practice (GLP), be accepted in other OECD countries and partner countries having the same data requirement.

Availability/Accessibility

5. One characteristic of the OECD Test Guidelines is their public availability, free of charge to the users' community. The OECD Test Guidelines are mainly intended to be used by laboratories performing the tests for regulatory purposes, at the request of authorities in member and adhering countries. The OECD i-library references all current Test Guidelines, and these can be downloaded as PDF without payment or any sort of privilege (https://www.oecd-ilibrary.org/books).

6. A number of supporting documents are also published free of charge in the Series on Testing and Assessment (validation reports, guidance documents, performance standards, workshop reports, review papers,…) (http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm).

Relevance (biological/mechanistic/predictive)

7. The relevance of a test method is indicated by the relationship of the test to the effect of concern and whether it is meaningful and useful for a particular purpose. It is the extent to which the test correctly measures or predicts the biological effect of interest. Relevance incorporates consideration of the accuracy (concordance) of a test method (OECD, 2005).

8. The biological relevance and scientific basis of test methods that are candidates for OECD Test Guidelines need to be established and documented, usually in peer-reviewed scientific literature. The Programme on the development of Adverse Outcome Pathways (http://www.oecd.org/chemicalsafety/testing/adverse-outcome-pathways-molecular-screening-and-toxicogenomics.htm) also provides a basis for describing the underlying biologic and mechanistic basis that should be modelled by assays. Scientific articles explaining the basis and mechanistic relevance of an assay are published, generally preceding experimental validation of test methods. The number of articles usually increases after the validation process with any new findings on the applicability and predictive capacity of the method to different categories or classes of chemicals.

Transferability and reliability

9. The transferability of a test method is demonstrated by the reproducibility of results expected when the test is repeated, outside of the laboratory that initially developed the test. The reliability is a measure of the extent that a test method can be performed reproducibly within and between laboratories over time, using the same protocol. It is assessed by calculating within- and between-laboratory reproducibility and within-laboratory repeatability (OECD, 2005).

10. For a test method to be considered valid and fit for Test Guideline development, its relevance and reliability need to be demonstrated experimentally and results made available for an independent review.

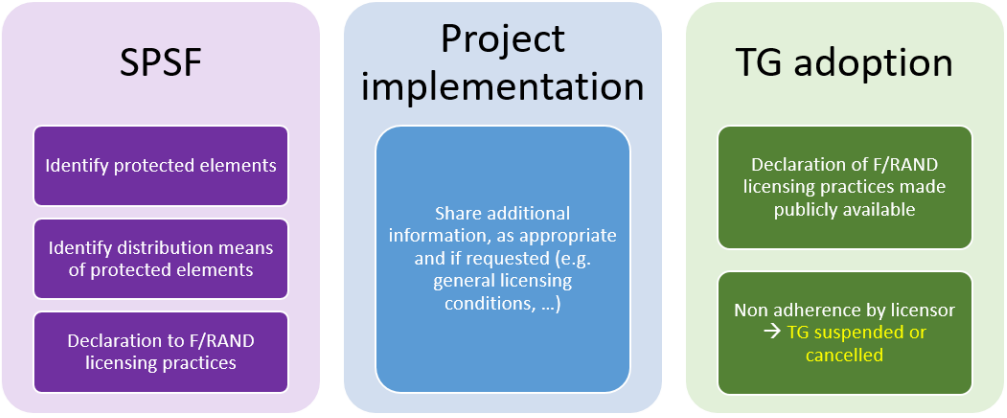
Transparency

11. All documentation establishing the validity of a test method is made available for review prior to the method gaining acceptance by the OECD. The documentation is published when the method becomes an OECD Test Guideline. If a test method contains protected elements (see following section), the developer of the method is explicitly required to be transparent and indicate at the stage of the initial proposal to the Test Guidelines Programme what these elements are and how the user can access these elements.

12. Protection and secrecy are distinct concepts. While protection of test method elements is not a problem in itself, the secrecy that some intellectual property rights (IPR) owners will claim under the label of confidential business information may impede the transparency that regulators want and need to understand the functioning, relevance, reliability of a key element of a test system they endorse.

13. Transparency is required from the moment a project proposal is submitted to the Test Guidelines Programme. Not disclosing information and claiming confidentiality or trade secret is against the principle of transparency and there is a risk that the project will not be taken up in the Programme. Similarly, hiding or changing access rights to protected elements during the course of a project or after a Test Guideline is adopted will result in suspension of the project or cancellation of the Test Guideline (see Figure 1 below).

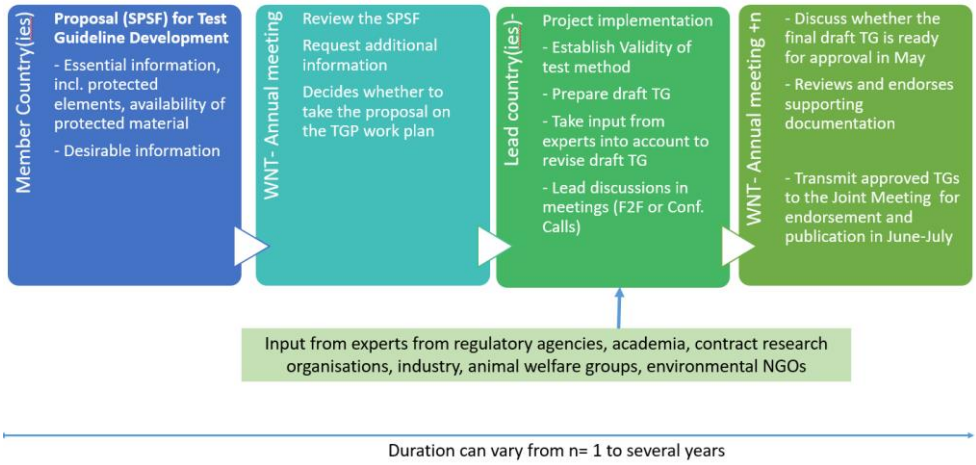
Figure 1. Documentation and Transparency



Overview of the Test Guidelines development process from proposal to adoption

14. The following Figure 2 illustrates the process for Test Guidelines development and publication, following an annual cycle, at the OECD. The initial proposal always comes from a National Coordinator, representing the regulatory authority in his/her country. The content of the proposal can be jointly prepared with the developer of a test method, but the National Coordinator has the responsibility for the Standard Project Submission Form. The initial proposal should be accompanied by all relevant information available and timelines for the project implementation.

Figure 2- OECD Test Guidelines development process



15. If the proposed test method contains protected elements, the initial proposal is explicitly required to indicate this and the means foreseen to make these protected elements available to users if the method becomes a Test Guideline. Further detail on the specific information requested on protected elements is described in paragraphs 49-50.

16. Depending on the validation status of the test method when initially proposed to the Test Guidelines Programme, additional experimental work, data retrieval or analysis may be necessary. Following experimental work to establish the validity of the test method, a draft Test Guideline is prepared by the lead country(ies). Several rounds of review and commenting on the draft Test Guideline are organised, during which experts and regulators provide input for the improvement of the final product. The Test Guideline is also expected to describe how and where end users can obtain the test material, including any protected element.

Performance Standards as the work-around solution for monopoly situations

17. A new test method, presenting unique and attractive features and containing protected elements, is likely to benefit from a privileged position, as a reference method, for a certain period following its adoption; and a potential market monopoly situation may arise. In such cases, the OECD currently requests the development of performance standards (PS) to enable the development and validation of similar methods proposed by other organisations or companies. As the choice of similar methods addressing the same

hazard area increases, the monopoly situation gets diluted through the emergence of competitor methods. However, the possibility for developing similar methods on the basis of these performance standards should not be hampered by IPR (e.g. patents) that have a very wide coverage or by abusive licensing conditions (e.g. excessive fees).

18. Once several alternative methods are available on the market, the utility of performance standards for single methods becomes less relevant, even in the presence of protected elements. As the field of alternative methods for specific hazard testing areas evolve, issues related to intellectual property and accessibility tend to fade away, following the normal cycle of innovation.

Protected elements in OECD Test Guidelines

Concepts

19. Access to innovation is critical to progress in toxicology testing, where alternative methods and techniques are needed for the generation of relevant and reliable safety data for the protection of human health and the environment. Innovative techniques are increasingly integrated in testing methods as they offer insight into more mechanistic and biologically relevant effects compared to the traditional apical endpoints such as organ weight and anatomo-pathology; these techniques may offer humane alternatives to the less ethical animal testing. These new techniques and technologies result from costly investments. Intellectual property rights, such as patents and trade marks, are an important driver of innovation in many fields, including the development of new test methods. They represent a key asset with which companies are able to attract investment and recoup the significant costs incurred to develop and validate new tests. However, if used in OECD Test Guidelines, it is in the common interest to set up reasonable conditions so that users can access and benefit from innovations, and regulators can base their decisions on best available techniques and data.

20. In the context of OECD Test Guidelines, a "protected element" may be regarded as any feature or aspect of a test method which use is protected by intellectual property (IP) rights, e.g. patents, such that it is not available to the public without the consent of the holder of the IP rights. Such protected elements exist particularly within *in vitro* and *in silico* method, but also in *in vivo* test methods (see Table 1 for examples).

21. In the last few years, toxicology testing methods have progressively integrated techniques and products such as e.g. *in vitro* cell culturing wherein engineered cell lines are often protected (OECD, 2018b). Likewise, *in vivo* methods have been developed comprising the use of transgenic animals having knocked-out genes that make them attractive models for e.g. genotoxicity testing, wherein the transgenic animals themselves constitute protected IP. In addition, in more recent developments *in vitro* test methods have been protected by patents (and/or other IP) rights that comprise measurement of the expression of a set of genes (*i.e.* a biomarker signature) in a specified cell system. The increasing use by innovator companies of IP rights such as patents to protect investments in the research and development of such new methods can complicate the accessibility of such new methods and the applicability of the current principle of using performance standards to circumvent monopoly situations. Consequently, there is a pressing need to find a way of allowing accessibility to new and improved testing methods whilst, at the same time, protecting and encouraging investment in R&D by innovator companies.

22. The use of these techniques and products is made possible when there is a reasonable agreement between the rights owner, any intermediate player, and the end user

in the laboratory. As these techniques are progressively penetrating regulatory safety testing, it becomes important to be more explicit about the so-called 'reasonable' conditions alluded to earlier. Indeed, in the absence of agreed guiding principles and good practices, there is a risk that IP rights owners could be tempted to take major advantage of the incorporation of their invention in a standard-setting program such as the Test Guidelines Programme; they may want to apply conditions to the use of their intangible asset that would prevent or restrict potential users from using the Test Guideline.

23. Access to innovation is critical to progress in toxicology testing, where alternative methods and techniques to animal testing are needed for the generation of relevant, reliable and humanely generated chemical safety data for the protection of human health and the environment.

Types of protection

24. An invention or a product can be protected in different ways. The types of IP protection underlying a "protected element" of an assay or test include but are not limited to the following:

- Patents – provide protection for technical inventions (products, processes, apparatus or uses), such as new chemical reagents, cell lines, process for performing a test, and depending on the jurisdiction, computer software associated with a technical effect, medical and laboratory devices, etc.
- Registered (and unregistered) designs – provide protection for the shapes of objects, such as medical devices and laboratory equipment;
- Trade marks – provide protection for the names and logos associated with products and companies;
- Copyright – provide protection for written and artistic work, including marketing material, computer programs/software, website layout and the like;
- Database rights – provide protection for collections and compilations of data.

25. Some forms of IP protection, such as patents, registered trade marks and designs, may require a formal application to be filed and an examination process to be conducted by the relevant national or regional authority. Other IP rights, such as copyright and unregistered trade marks and designs, may subsist automatically upon the creation and/or use of the article, with or without registration with an authority. However, these practices vary from jurisdiction to jurisdiction.

26. IP rights are territorial in the sense that they must be obtained and enforced on a country by country basis (or, in some cases, on a region by region basis). In the case of patents, for example, a singular worldwide patent as such does not exist. Thus, it is incumbent upon the test developer to apply for patent rights at the national IP office in each country/region in which protection is desired (although this process may be commenced by filing a single international, or PCT, patent application). Thereafter, the national/regional IP office will examine the merits of the application and, if satisfied, may allow it to proceed to grant as a patent. Once the patent has been granted, and the scope of protection defined therein, it is possible for those IP rights to be enforced against other parties (although certain rights to damages for infringement may also accrue prior to grant of a patent upon publication of the application, *i.e.* provisional protection). The conclusions of the examination process by each of the national/regional IP offices may differ, not least

because there are differences in the patents systems across regions. Consequently, the scope of protection can vary between jurisdictions.

27. One of the legal requirements for obtaining patent protection is that the patent application must contain enough information to enable a skilled person to put the invention into effect (i.e. the disclosure of the invention must be "enabled" or "sufficient"). Consequently, if the gene combination and/or algorithm is essential for putting the invention into effect, then these aspects must be fully disclosed in the patent application.

28. The disclosure of essential information, through a patent protection for example, is important to guaranteeing transparency and gaining acceptance of the invention's application in the regulatory domain.

29. Other types of protection identified above do not come automatically with the same level of transparency to the public.

Existing distribution, release and dissemination models

30. For a protected invention to be used by a third party, the rights owner will have to develop means, define conditions and establish contractual agreement(s) so that potential users can access the innovative material, by agreeing to the conditions. The most common types of means and models that exist in the area of science are the material transfer agreement (MTA), licence agreement, and open source, and patent pools in the area of drug development (i.e. an agreement between two or more patent owners to license one or more of their patents to one another or to third parties, often associated with complex technologies that require complementary patents in order to provide efficient technical solutions).

Key players

31. In relation to OECD Test Guidelines, the following key players exist:

- IP rights owner – often, this will be the test method developer, but it is conceivable that the IP rights have been assigned (i.e. transferred) to or from another legal entity, or that third parties hold additional relevant IP rights;
- Test method developer – this may be, for example a small or medium enterprise (SME), established based upon the development and commercialisation of a new test method;
- Test method provider – sometimes, this will be the test method developer but often the methods will be offered under licence by distribution agents such as contract research organisations (CROs);
- End user –this can be a manufacturer (or possibly a research company) seeking to identify and/or characterise an element within their products, such as chemicals or cosmetic formulations, or it can also be a CRO (who may conduct tests on behalf of the chemical manufacturer for example);
- Regulatory authorities implementing chemicals regulations in member countries, and setting the data requirements determining the use of the Test Guidelines;
- Working Group of the National Coordinators of the Test Guidelines Programme (WNT), who oversees the development of OECD Test Guidelines, from proposal to approval (see Figure 2 above).

32. The owner of IP rights on protected elements included in a test method will not usually be dealing with users of the OECD Test Guideline directly. The right owner must ensure that the protected elements of a test method are available to the user via a registered entity (e.g. a cell bank or repository), and not block any request to use the protected element, if requested. If royalty fees are requested by the IP rights owner, they should remain reasonable. For protected material that has not implied financial investment, royalty fees should be graciously waived, for purposes of generating safety data for the protection of human health and the environment.

33. The test method developer may not be the original IP rights holder, but may be an intermediate player who assembled the protected elements into a test method in such a way that it can be useful in a regulatory context. It will be important for the end user of a Test Guideline (e.g. a contract research organisation) to know what type of agreement, under what conditions and with whom s/he has to sign, regardless of who is the original inventor or IP owner.

34. The test method provider or the provider of the protected elements may be identified as the entity distributing/selling/commercialising the test method or the protected elements of the test method. This entity should have obtained the rights to do so directly or indirectly from the owner of IP rights or from the test method developer. It can act as a repository, e.g. a cell bank in the case of cell lines or a biological resources centre for any biological material, or a company who has the legal rights to exploit the protected material and to distribute the commercial product containing the protected element(s).

35. The end user is the entity applying the test method described in an OECD Test Guideline for the purpose of generating chemical safety data for submitting them to a regulatory authority.

36. The regulatory authorities are responsible for defining the standard (i.e. Test Guideline) that should be used to satisfy a data requirement set in their chemical legislation. The regulatory authorities also have responsibility in accepting and using the data generated to evaluate the risk and take measures to protect human health and the environment from the unwanted hazards of chemicals.

37. The Working Group of the National Coordinators of the Test Guidelines Programme (WNT) is composed of National Coordinators (countries' representatives) who decide on the approval of new or revised Test Guidelines, or their deletion, and review and decide on project proposals in the place. In the WNT, there are also industry representatives and animal welfare and environmental non-governmental organisations, and a Secretariat.

Examples of protected elements in Test Guidelines

38. The following are typical examples of protected elements:

- A method of measuring a biological marker which is indicative of a property of a compound, e.g. toxicity, biocidal efficacy, etc.,
- A cell line or a composite tissue model for use in a test method,
- A chemical or biological reagent for use in test method,
- A device or instrument for use in test method,
- A computer algorithm for use in the interpretation of data obtained using a test method.

39. The following Table l 1ists many of the recently adopted OECD Test Guidelines that contain protected elements currently contained in OECD Test Guidelines, as of 2018. Please note that the information was provided to the OECD on a voluntary basis by the relevant rights holders (or test method developers) and the OECD makes no guarantees as to its accuracy or completeness, which the OECD is unable to independently verify. Users should verify the information independently before taking any actions in relation to the below.

Table 1 – TGs including protected elements (as of 2018)

TG Nb (date of last update)	TG title	Protected elements and type of protection	Type of agreement	Elements can be obtained from:
TG 431 (2016)	*In vitro* skin corrosion: reconstructed human epidermis (RHE) test method	- EpiSkin™ - EpiDerm™ - SkinEthic™ RHE - epiCS® Trademarked tissues	No agreement needed; tissues can be purchased on a commercial offer/ pricelist.	Commercial companies
TG 435 (2015)	*In Vitro* Membrane Barrier Test Method for Skin Corrosion	Corrositex® Registered trademark Proprietary biomembrane and chemical detection technology	No agreement needed; tissues can be purchased on a commercial offer/ pricelist.	Commercial companies
TG 439 (2015)	*In Vitro* Skin Irritation: Reconstructed Human *Epidermis* Test Method	- EpiSkin™ - EpiDerm™ SIT (EPI-200) - SkinEthic™ RHE - LabCyte EPI-MODEL24 SIT Trademarked tissues	No agreement needed; tissues can be purchased on a commercial offer/ pricelist.	Commercial companies
TG 442D (2015)	*In Vitro* Skin Sensitisation: ARE-Nrf2 Luciferase Test Method	KeratinoSens™: Luciferase gene contained in the cell line is patented by a commercial company. The laboratory providing the cells holds a licence from the commercial company to transfer the cells under defined conditions - Trademarked assay - Patented detection gene	Licence agreement (free licence).	Commercial companies
TG 442D (2018)	*In Vitro* Skin Sensitisation: ARE-Nrf2 Luciferase Test Method	LuSens: Luciferase gene contained in the cell line is patented by a commercial company. - Patented detection gene	Licence agreement (free limited use label license) with Promega.	Commercial companies
TG 442E (2015)	*In Vitro* Skin Sensitisation: h-CLAT assay	- Human monocytic leukaemia cell line, THP-1 Each cell bank has their own registered cells - Antibodies (FITC Mouse Anti-Human CD86, CD54, or mouse IgG1 antibodies)	No agreement needed; tissues can be purchased on a commercial offer/ pricelist.	Cell Banks Commercial companies
TG 442E (2017)	*In Vitro* Skin Sensitisation: U-SENS assay	Human histiocytic lymphoma cell line, U937 clone CRL1593.2.	ATCC specifies that "commercial entities are allowed to purchase and use the U-937 cell line, without further licensing fee with	Cell Banks

TG Nb (date of last update)	TG title	Protected elements and type of protection	Type of agreement	Elements can be obtained from:
		Each cell bank has their own registered cells Trademarked assay	ATCC or with Professor Nilsson, for testing in OECD member countries for purposes of assessment and other uses relating to the protection of man and environment; …"	
TG 442E (2017)	*In Vitro* Skin Sensitisation: IL8-Luc assay	Recombinant THP-G8 cell line	MTA Initially patented cell line - The Secretariat was informed in February 2017 that an Application for cancellation of registration of patent rights per waiver had been submitted and accepted. Accordingly, no licence is needed to get the cells, but requires the execution of a MTA.	Commercial company
TG 455 (2016)	PBTG for STTA *in vitro* assays to detect estrogen receptor agonists and antagonists - HeLa assay	Stably transfected hERa-HeLa-9903 cell line	MTA	Cell banks
TG 455 (2016)	PBTG for STTA *in vitro* assays to detect estrogen receptor agonists and antagonists - VM7Luc4E2 assay	Stably transfected VM7Luc4E2 cell line	Licence agreement	One University and one commercial company
TG 455 (2016)	PBTG for STTA *in vitro* assays to detect estrogen receptor agonists and antagonists - ERa CALUX assay	Stably transfected U2OS ERa CALUX cell line	Licence agreement	Commercial company
TG 456 (2011)	H295R Steroidogenesis Assay	NCI-H295R [H295R] CRL-2128™ Trademarked cell clone	MTA however, this condition is not specified on the ATCC website	Cell bank (ATCC)
TG 458 (2016)	Stably Transfected Human Androgen Receptor Transcriptional Activation Assay for Detection of Androgenic Agonist and Antagonist Activity of Chemicals	AR-EcoScreen™ cell line Trademarked cell line	MTA Although the AR-EcoScreen™ cell line was initially claimed as only needing signature of a MTA it appears that there are licencing fees associated with its use. These fees have been temporary waived until Performance Standards are developed	Cell bank (JCRB)

TG Nb (date of last update)	TG title	Protected elements and type of protection	Type of agreement	Elements can be obtained from:
			and approved by the Working Group of the National Coordinators of the Test Guidelines Programme (WNT). The TG will then be revised accordingly.	
TG 488 (2013)	Transgenic Rodent Somatic and Germ Cell Gene Mutation Assays	- Muta™Mouse - Big Blue™ Trademarked animals	No agreement needed; tissues can be purchased on a commercial offer/ pricelist.	Commercial companies
TG 490 (2015)	*In Vitro* Mammalian Cell Gene Mutation Tests Using the Thymidine Kinase Gene	For MLA: L5178Y TK+/- clone (3.7.2C) Each cell bank has their own registered cells	A disclosure is present in the ATCC description for a specific TM clone: "This material is cited in a US or other Patent and may not be used to infringe the claims. Depending on the wishes of the Depositor, ATCC may be required to inform the Patent Depositor of the party to which the material was furnished. This material may not have been produced or characterized by ATCC." Such disclosure is not mentioned in the Japanese Collection of Research Bioressources (JCRB) description where the cells can also be obtained.	Cell banks
TG 491 (2015)	Short Time Exposure *In Vitro* Test Method for Identifying i) Chemicals Inducing Serious Eye Damage and ii) Chemicals Not Requiring Classification for Eye Irritation or Serious Eye Damage	Rabbit cornea cell line SIRC [Statens Seruminstitut Rabbit Cornea] Each cell bank has their own registered cells.	No agreement needed; cell line can be purchased on a commercial offer/ pricelist.	Cell Banks
TG 492 (2017)	Reconstructed human Cornea-like Epithelium (RhCE) test method for identifying chemicals not requiring classification and labelling for eye irritation or serious eye damage	- EpiOcular™ tissue - SkinEthic™ HCE tissue Trademarked tissues	No agreement needed; tissues can be purchased on a commercial offer/ pricelist.	Commercial companies

Overview of conditions often applied to protected elements present in standards

F/RAND conditions applied in other regulated sectors

40. Reasonable and non-discriminatory ("RAND") terms, known in the European Union as fair, reasonable, and non-discriminatory ("FRAND") terms, denote a voluntary licensing commitment that standards organisations often request from the owner of an intellectual property right (usually a patent) that is, or may become, essential to practice a technical standard. Put differently, a F/RAND commitment is a voluntary agreement between the standard setting organisation and the holder of standard-essential patents. The view of courts in several jurisdictions is that, in appropriate circumstances, the licensee of a standard that is, a company or entity that uses a standard to render a service or manufacture a product is an intended third-party beneficiary of the F/RAND agreement, and, as such, is entitled to certain rights conferred by that agreement. The principle of F/RAND licensing is well-established in other technical fields in which standard essential patents (SEPs) are utilised, most notably within mobile telecommunication sector.

41. Because a patent, under most countries' legal regimes, grants its owner an exclusive right to forbid others from using (prevent from using) the covered technology, a standard setting organisation generally must obtain permission from the patent holder to include a patented technology in its standard. So, it will often request that a patent holder clarifies its willingness to offer to license its standard essential patents on F/RAND terms. If the patent holder refuses upon request to license a patent that has become essential to a standard, then the standard setting organisation must exclude that technology. When viewed in this light, the F/RAND commitment serves to harmonise the private interests of patent holders and the public interests of standard setting organisations.

42. Standard setting organisations commonly adopt policies that govern the ownership of patent rights that apply to the standards they adopt (the patent policy). One of the most common policies is to require a patent holder that voluntarily agrees to include its patented technology in the standard to license that technology on "reasonable and non-discriminatory terms" (RAND) or on "fair, reasonable, and non-discriminatory terms" (FRAND). The two terms are generally interchangeable; but FRAND is preferred in Europe and RAND in the US.

43. The F/RAND obligations are often adopted by a standard setting organization's bylaws primarily as a means of enhancing the pro-competitive character of their industry. They are intended to prevent members from engaging in licensing abuse based on the monopolistic advantage generated as a result of having their intellectual property rights (IPR) included in the industry standards. Once an organisation offers a F/RAND licence, it is required to offer that licence under equal/comparable terms to anyone wishing to access the standard. Without such commitment, members could use monopoly power inherent in a standard to impose unfair, unreasonable and discriminatory licensing terms that would damage competition and inflate their own relative position.

44. On the other hand, the F/RAND commitment also serves to ensure that the holder of a patent that becomes essential to the standard will receive royalties from users of the standard that adequately compensate the patent holder for the incremental value that its technology contributes to the standard. The development of a patented technology typically requires significant investment in research, and contributing that technology to a standard is not the only option by which a patent holder can recoup that investment and thus

monetize its invention. F/RAND royalty will mean that the patent holder will typically agree to contribute its technology to the standard, thus forgoing the exclusive use or the exclusive licensing of its technology, in exchange for the assurance that it will receive adequate compensation in reasonable royalties.

45. The individual terms are often defined as follows[1], [2]:

- Fair relates mainly to the underlying licensing terms. Drawing from anti-trust/competition law; fair terms means terms which are not anti-competitive and that would not be considered unlawful if imposed by a dominant company in their relative market. Examples of terms that would breach this commitment are: requiring licensees to buy licences for products that they do not want in order to get a licence for the products they do want or requiring licensees to take licences to certain unwanted or unneeded patents to obtain licences to other desired patents (bundling); requiring licensees to license their own IP to the licensor for free (free grant backs); and including restrictive conditions on licensees' dealings with competitors (mandatory exclusivity).

- Reasonable refers mainly to the licensing rates. According to some, a reasonable licensing rate is a rate charged on licences which would not result in an unreasonable aggregate rate if all licensees were charged a similar rate. According to this view, aggregate rates that would significantly increase the cost to the industry and make the industry uncompetitive are unreasonable. Similarly, a reasonable licensing rate must reward the licensor with adequate compensation for contributing its essential patents to a standard. Compensation is adequate if it provides the licensor with the incentive to continue investing and contributing to the standard in future time periods[3].

- Non-discriminatory relates to both the terms and the rates included in licensing agreements. As the name suggests this commitment requires that licensors treat each individual licensee in a similar manner. This does not mean that the rates and payment terms cannot change dependent on the volume and creditworthiness of the licensee. However, it does mean that the underlying licensing condition included in a licensing agreement must be the same regardless of the licensee. This obligation is included in order to maintain a level playing field with respect to existing competitors and to ensure that potential new entrants are free to enter the market on the same basis.

[1] **Interpreting and Enforcing the Voluntary FRAND Commitment** by Roger G. Brooks and Damien Geradin (Cravath, Swaine & Moore LLP), Tilburg Law & Economics Center (TILEC); University College London - Faculty of Laws, Posted: 20 Jul 2010

[2] **THE MEANING OF FRAND, PART I: ROYALTIES**, by J. Gregory Sidak, *Journal of Competition Law & Economics*, Volume 9, Issue 4, 1 December 2013, Pages 931–1055, https://doi.org/10.1093/joclec/nht040

[3] **A SIMPLE APPROACH TO SETTING REASONABLE ROYALTIES FOR STANDARD-ESSENTIAL PATENTS** by Mark A. Lemley & Carl Shapiro, 30 March 2013

Transposing the RAND/FRAND conditions to the OECD Test Guidelines Programme

46. The main concept of F/RAND as described in Communication from the Commission on Setting out the EU approach to Standard Essential Patents[4] assumes that both parties must be willing to engage in good faith negotiations, with the view to establishing licensing conditions that are fair, reasonable and non-discriminatory.

47. The parties to the negotiations are in the best position to establish what F/RAND conditions will be in a specific situation. In the specific context of the OECD Test Guidelines, the following IP valuation principles should be taken into account when determining the Fair and Reasonable elements of a licence fee:

- clear relationship to the economic value of the protected elements in the OECD Test Guidelines. In this approach the value should not include any element resulting from the decision to include the protected elements into the Test Guideline and focus should be placed on the value of the protected elements themselves;
- in cases where the protected element is developed mainly for the purpose of being included in the Test Guideline and has little market value outside of it, alternative evaluation methods, such as the relative importance of the protected element in the Test Guideline compared to other contributions to the Guideline, should be considered;
- determining F/RAND should also require taking into account the value added by the protected element to the Guideline, irrespective of its commercial value / market success of the protected element itself;
- F/RAND value obtained should insure that it constitutes a further incentive for the developers of protected element;
- the Non-Discriminatory element of F/RAND provides for non-discrimination between parties that are "similarly situated";
- to avoid entry barriers for small enterprises or laboratories, licensing conditions should not include large base-fees and upfront payments for setting up the technology, but rather be based on turn-over and/or cost per test.

48. Furthermore, the Communication from the Commission on Guidelines on the applicability of Article 101 of the Treaty to horizontal co-operation agreements requires the holders of the IPR embodied in a standard to subject themselves to a F/RAND commitment[5]. In the context of the OECD Guidelines, F/RAND commitment can be applied in order to ensure effective access to the protected elements, and therefore a wide access to the Test Guideline. The IPR policy will require participants wishing to have their protected elements included in the Test Guideline to provide an irrevocable commitment

[4]Communication From The Commission To The European Parliament, The Council And The European Economic And Social Committee on Setting out the EU approach to Standard Essential Patents COM(2017) 712 final

[5] Communication from the Commission Guidelines on the applicability of Article 101 of the Treaty on the Functioning of the European Union to horizontal co-operation agreements, 2011/C 11/01

in writing to offer to license their protected elements to all third parties on fair, reasonable and non-discriminatory terms ('F/RAND Commitment').

49. The non-commitment of the test method developer to license under FRAND/RAND terms or the non-compliance during the course of Test Guideline implementation will be reported and addressed under the Programme and the possible cancellation of the Test Guideline if it cannot be used under the FRAND/RAND terms and conditions.

Information on protected elements to be provided by a developer when submitting a project proposal for the development of a Test Guideline at OECD

50. The Test Guidelines Programme (TGP) is fed annually, usually in November, by proposals to develop new or updated Test Guidelines or supporting documents. These proposals can be submitted by the National Coordinators to the TGP. Test developers may contact their National Coordinator (list publicly available) with a proposal and address the following requirements in the Standard Project Submission Form:

- Identify components (e.g. test system, reagent, etc.), equipment or other scientific procedures that are covered (or pending) by Intellectual Property Rights (IPR) (e.g., patents, patent applications, industrial designs and trade marks, copyright on protected software or prediction model, etc.). Information should be provided on the overall availability of the IPR-protected components including whether they are commercially available or require a Material Transfer Agreement (MTA) or other licensing agreements. In addition, a description of the IPR-covered component/test system should be disclosed, and it should be indicated whether Performance Standards have been developed for the test method.
- In particular, in section 8 of the SPSF, the following is requested:
    - 8.1 Nature of protected elements (e.g. reagent identity, cell line identity, specific process, etc.), providing as much detail as needed depending on the element;
    - 8.2 Form of protection (e.g. trade mark, patent, etc.) for each protected element,
    - 8.3 For users to access protected elements, please tick the relevant box(es): MTA/ License requirement/ other/No agreement required,
    - 8.4 Are you providing the agreement document(s) referred to in 8.3 with the Standard Project Submission Form (SPSF):
    - 8.5 How and where can users get access to protected elements (organisaiton or company contact information)?
    - 8.6 Has any search for existing patent(s) possibly associated with this test method been performed (e.g. through patent search or Freedom-To-Operate search). If yes, please provide a list of the relevant patents and if possible further related information and documents. ?
    - 8.7 Have Performance Standards been developed?

51. A test method developer is encouraged to provide as much relevant information as possible. The National Coordinator can advise in case of doubt. Transparency is essential, as it helps the regulator to understand the relevance and reliability of the test method he/she is requested to endorse.

Current and intended distribution, dissemination, and release model for protected elements when a test method becomes an OECD Test Guideline

Licensing agreement

52. A licensing agreement is a legal contract between at least two parties, known as the licensor and the licensee. In a typical licensing agreement, the licensor grants the licensee the right to produce and sell goods, apply a brand name or trade mark, or use patented technology owned by the licensor. In exchange, the licensee usually submits to a series of conditions regarding the use of the licensor's property, which may include the obligation to make payments known as royalties.

53. Due to the legal ground it must cover, licensing agreements can be lengthy and complex documents. Most such agreements cover the same basic points. These include, but are not limited to, the scope of the agreement, including exclusivity or territorial restrictions, financial aspects including required advances, royalty rates, and how royalties are calculated, guarantees of minimum sales, time schedules involving "to market" dates, length of contract, and renewal options, the licensor's rights of monitoring and quality control, including procedures to be followed, minimum inventories required to be maintained, limitation of liabilities, escrow arrangement for source codes, dispute resolution and finally, returns and allowances.

54. One of the most important elements of a licensing agreement covers the financial arrangement. Payments from the licensee to the licensor usually take the form of guaranteed minimum payments and royalties on sales. Not all licensors require guarantees, although some experts recommend that licensors get as much compensation up front as possible. In some cases, licensors use guarantees as the basis for renewing a licensing agreement. If the licensee meets the minimum sales figures, the licence is renewed; otherwise, the licensor has the option of discontinuing the relationship.

55. Another important element of a licence agreement establishes the time frame of the deal. Many licensors insist upon a strict market release date for products licensed to outside manufacturers or use. After all, it is not in the licensor's best interest to grant a license to a company that never markets or use the product. The licensing agreement will also include provisions about the duration of the contract, renewal options, and termination conditions.

56. Most licensing agreements also address the issue of quality. The best form of quality control is usually achieved before the fact—by carefully checking the reputation of the licensee.

57. Another common element of licensing agreement covers which party maintains control of copyrights, patents, or trade marks. Many licences also include a provision about territorial rights, or who manages distribution in various parts of the country or the world. In addition to the various clauses inserted into agreements to protect the licensor, some licensees may add their own requirements. They may insist on a guarantee that the licensor owns the rights to the property, for example, or they may insert a clause prohibiting the licensor from competing directly with the licensed property in certain markets.

Material Transfer Agreement

58. A Material Transfer Agreement (MTA) is a contract that governs the transfer of tangible research materials between two organisations, whether the recipient intends to use it for his or her own research purposes or not. The MTA defines the rights of the provider and the recipient with respect to the materials and any derivatives. Biological materials, such as reagents, cell lines, plasmids, and vectors, are the most frequently transferred materials, but MTAs may also be used for other types of materials, such as chemical compounds and even some types of software.

59. The types of MTAs that are most common are MTAs concerning, e.g. transfer between academic or research institutions, transfer from academia to industry, transfer from industry to academia and transfer from industry to industry. Each call for different terms and conditions.

60. Material Transfer Agreements (MTAs) are contractual documents used for the acquisition of various biological and research materials, and occasionally, data, developed by non-profit, government and private industry. Often these materials are a necessary component of a research project and are available only from a sole source, often industry. Industry may view their materials as important proprietary resources and may want to assert ownership of any inventions made with those materials or restrict publication of unfavourable results. Universities will want to ensure that MTA terms permit full dissemination of research results, and do not conflict with other university policies. Because of these differing views, the negotiations necessary to accommodate the needs of both parties can be time consuming. The usual areas of negotiation relate to publications, use of the research results, the ownership of the technology generated by the research and regulations of how the generation and ownership of any new IPR should be handled.

61. The main element of a typical MTA cover, e.g. the scope of the agreement and use of the material, including whether or not the MTA shall be exclusive, confidentiality, warranties, financial aspects, length of contract, and renewal options, limitation of liabilities, escrow arrangement for source codes, dispute resolution, the parties' option of discontinuing the relationship and finally, returns and allowances.

62. One of the most important elements of an MTA concerns research restrictions and directives, reporting requirements, handling of results, publishing of results and the parties right to purchase the other party's results.

63. Another common element of MTA covers which party maintains control of copyrights, patents, or trade marks and the prohibiting of either party from competing directly with the other party's business or activities.

64. The OECD has developed a template MTA with the typical conditions for the transfer of protected material. Although this MTA is not an obligation, it can be used as a reference or starting point for parties willing to sign an agreement (http://www.oecd.org/env/ehs/testing/Example_TG_Material_Transfer_Agreement_(MTA)_Template.pdf).

Supporting documentation requested at the proposal submission stage

65. Although it is not an absolute obligation to share the licensing agreement when submitting a project proposal to the OECD, method developers will have to commit to adhere to F/RAND terms and conditions through a declaration (see Annex 2). When such declaration is submitted, it will be shared with the Working Group of the National

coordinators of the Test Guidelines Programme, and its availability made publicly available upon request on the OECD Internet site (see Table 1).

Cost model for the distribution (including cost range)

66. General or specific information related to the cost model envisaged should be shared with the WNT for information and transparency purposes. Such information provides an indication of the accessibility of the test method to potential end users at reasonable conditions.

Sharing of relevant information:

Sharing with the WNT community

67. The SPSF and supporting information are shared with the Working Group of the National Coordinators of the Test Guidelines Programme, via a protected site.

Sharing with the public

68. Upon publication of a Test Guideline, limited but useful information on protected elements, type of protection and distribution means is published in the form of a table listing the same information for all Test Guidelines concerned (http://www.oecd.org/chemicalsafety/testing/protected-elements-in-test-guidelines.htm).

69. It is expected that if changes occur to the distribution means, it will only be under more favourable conditions for the users, and in line with F/RAND terms.

Conclusions and Recommendations

70. The following summarises the recommended best practices that must be taken into consideration when protected elements are included in a proposal to develop an OECD Test Guideline:

- The SPSF should identify the protected elements, the type of protection, and disclose the relevant information that enable the regulator to trust the relevance and reliability of the protected element; transparency over the protected elements and access to relevant information upon request should be enabled;
- The SPSF should describe the means to obtain the protected elements and the conditions at which these elements are obtainable;
- In the case of a licence, the SPSF should describe the licensing conditions;
- The test method developer should commit to licensing under F/RAND terms and conditions (see Annex 2 for the declaration), and not deviate during the course of the project and when the Test Guidelines are implemented.

Glossary of terms and acronyms

Material Transfer Agreement (MTA): An MTA is an agreement between the cell bank (provider) owning the biological materials concerned and the recipient of such materials. It is used to document the transfer of protected materials and may include a number of terms and conditions.

Intellectual property rights (IPR): the rights given to persons over the creations of their minds. They usually give the creator an exclusive right over the use of his/her creation for a certain period of time.

Performance Standards (PS): The purpose of performance standards is to communicate the basis by which new test methods, in particular those containing protected elements (i.e., patented, copyrighted, trade marked, registered elements) can be determined to have sufficient accuracy and reliability for specific testing purposes. These performance standards, based on validated and accepted test methods, can be used to evaluate the accuracy and reliability of other analogous test methods that are based on similar scientific principles and measure or predict the same biological or toxic effect. Performance Standards currently include three elements: essential test method components, minimum list of reference chemicals, accuracy and reliability values. A patented test may be adopted as an OECD Test Guideline provided a detailed generic description of the method is provided as well as proper reference to the validated, patented version of the method, and usually together with a set of performance standards (OECD, 2005). [Note for the reader: in the last 15 years, many PS have been developed for several *in vitro* methods containing protected elements; as more innovative methods develop and also contain more innovative IP protection means, there will be discussions to adapt PS, as appropriate, taking them to the level of the hazard endpoint to predict (i.e. less specific), and not the individual method itself.]

Standard project Submission Form (SPSF): format used by the National Coordinators of the Test Guideline Programme to describe and submit project proposals to develop new or revised Test Guidelines, Guidance or other supporting documents.

Working Group of the National Coordinators of the Test Guidelines Programme (WNT): Group of representatives from regulatory authorities in member countries, representatives from industry and from non-governmental organisations who take part in the oversight of the OECD Test Guidelines programme.

ANNEX 1 - Typical terms foundin Licence contracts or Material Transfer Agreements

The following definitions are often found in licence contracts relevant to the Test Guidelines Programme. They are given by way of example and are not intended to serve as a model. Given the variations in laws governing intellectual property from jurisdiction to jurisdiction, in every case licensors and licencees must seek the advice of a specialised lawyer and should not rely on the below when drafting such agreements.

A selection of the definitions that are to be expected in a licence contract or when dealing with such contracts are:

- "[Trade mark of the concerned] Assay" shall mean the [description of the Trade mark of the assay that is concerned] assay.
- "[insert the trade mark of the concerned] Assay SOP" shall mean the latest and submitted version of Licensor's assay Standard Operating Procedure set out in Agreement. The version number on the [insert the trade mark of the concerned] Assay SOP will indicate which version that shall apply.
- "Cell Line" shall mean the biological material specified in the Handover Specification.
- "Confidential Information" shall include technical, financial and business information disclosed by either Party to the other in any form for the purpose of this Agreement, including without limitation, information pertaining to the [name of the referred to IPR, if any] Technology Platform, the Licensor Know How, the Licensor Software, the Cell Line and other information in relation to the Services such as documents, data or information relating to the Equipment, devices, methods, formulae, compositions, materials, apparatus, techniques, production methods, processes, designs, research, specifications and other technical and/or commercial data.
- "Equipment" shall mean the equipment for performing the Services presented in the Assay SOP (i.e. Standard Operation Procedure).
- "Escrow Agreement" means the escrow agreement that shall be entered into between the Parties and the Escrow Agent in regard to the retention of the Licensor Software source code.
- "Escrow Agent" means the mutually agreeable escrow agent that the Parties have appointed and with whom the Parties have entered into an Escrow Agreement.
- "Escrow Material" means the information and data to be subject to an escrow arrangement.
- "Handover Specification" shall mean the specification of the Licensor Know-how, the Licensor Software and the Cell Line to be handed over by Licensor to the Licensee on a date to be agreed upon in writing for the purpose of the License.
- "Improvement" shall mean any modification or development of the [insert the trade mark of the concerned] Technology Platform, the Licensor Know-how, the Licensor Software and the Cell Line as the case may be in the form of patentable

or non-patentable inventions, improvements, ideas, technology, know-how or other Intellectual Property Rights.

- "Intellectual Property Rights" shall mean the rights to patents, patent applications, technology, techniques, designs, utility models, trade secrets, copyrights, trade marks, trade names, know how or the like.
- Licence (or IP rights)": A legal contract between two or more parties wherein the holder of IP rights grants to one or more other parties the right to exploit or use those IP rights in return for a consideration, e.g. a licence fee.
- "Licencing Fees": Fees payable to the IP rights holder under the terms of a licence in return for access to those IP rights. The fees may include one-off "milestone' payments and/or royalties based on sales.
- "Marketing Commitment" shall mean the marketing commitments and activities to be performed by the Licensee when marketing the Services during the term of this Agreement.
- "Licensor Know-how" shall mean Licensor's knowledge, experience, data, techniques, and other information relating to the Services, owned or controlled by Licensor at the time of execution of this Agreement and which Licensor is entitled to disclose and license to the Licensee, including [insert the trade mark of the concerned] Assay SOP as listed in the Handover Specification.
- "Licensor Software" shall mean the software developed and owned by Licensor used for the analysis in connection with the Services as further set out in the Handover Specification.
- "Price Adjustments" shall mean the price adjustments mechanism set out in Agreement
- "Price List" shall mean the price list of Licensor set out in the Agreement.
- "Services" shall mean the assessments and services, which the Licensee is entitled to perform by utilizing the [insert the trade mark of the concerned] Technology Platform, the Licensor Know-how, the Licensor Software and the Cell Line as described in the Handover Specification.
- "[Trade mark of the concerned] Technology Platform" shall mean a [insert description of the concerned method] method for safety assessment of chemicals, a patented technology developed and owned by Licensor.
- "Test Substance" shall mean each substance that is tested and invoiced by the Licensee to their customers.
- "Trademarks" shall mean the trade marks specified in the Agreement.

Typical definitions in a Material Transfer Agreements (MTA)

A selection of the definitions that are to be expected in a MTA or when dealing with such agreements are:

- "Materials" means (a) those materials listed in Schedule 1 hereto, in the aggregate quantities specified in the Agreement; (b) any substance or compound that is a derivative or modification thereof or is replicated therefrom, and any other compositions made using such substance or compound; and (c) any associated know-how and data that is transferred to Recipient by Provider.
- “Material Transfer Agreement” (MTA): A legal contract that governs the transfer of tangible research materials between two parties, typically when the recipient intends to use it for his or her own research purposes. The MTA defines the rights of the provider and the recipient with respect to the materials and any derivatives.
- “Recipient's Technology" means the [insert the trade mark of the concerned] assay an animal free genomic testing for prediction and classification of chemical sensitizers, which is a proprietary technology of Recipient, including thereto related test services.
- "Research" means those tests, studies and other activities set forth in the Agreement carried out by Recipient.
- "Research Documentation" means any and all documents, records, accounts, notes, reports (including, without limitation, the progress reports and the final report prepared in accordance with the concerned provisions in the Agreement) and other data from the Research related to the Materials, whether in written, electronic, video or other tangible form created by or by a third party on behalf of Recipient.
- "Researchers" means all employees or agents of Recipient who are engaged in carrying out the Research.
- "Results" means any ideas, improvements, inventions, discoveries, know-how, data, documentation, reports, materials, writings, designs, computer software, processes, principles, methods, techniques and other information, recorded in any form, that are discovered, conceived, reduced to practice or otherwise generated as a result of or in connection with the Research or any other use of the Materials by, or by a third party on behalf of, Recipient (whether solely or jointly with others), and any patent, trade secret, copyright or other intellectual property rights pertaining to any of the foregoing; provided, however, that "Results" shall exclude any substance or structure that is a derivative, modification or replication of the Materials and any other compositions made using the Materials, which derivatives, modifications, replications and compositions form part of the Materials pursuant to the Agreement and are owned by Provider.

ANNEX 2 - IPR Licensing Declaration Form (see separate file attached)

References

OECD (2005). Guidance Document on the Validation and International Acceptance of New or Updated Test Methods for Hazard Assessment. Series on Testing and Assessment, No. 34. ENV Publications. OECD, Paris.

OECD (2018a). Report of the OECD Workshop on Intellectual Property Issues in OECD Test Guidelines. Series on Testing and Assessment, No. 278. ENV Publications. OECD, Paris.

OECD (2018b). Guidance on Good *In Vitro* Methods Practices. Series on Testing and Assessment, No. 286. ENV Publications. OECD, Paris.