NanoHarmony

FROM SCIENCE TO REGULATION

The NanoHarmony White Paper on Test Guideline Development

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The NanoHarmony project, funded through Horizon 2020, has the mission to support the development of Test Guidelines and Guidance Documents for eight endpoints where nanomaterial-adapted test methods have been identified as a regulatory priority. NanoHarmony coordinates the collection and use of available data and information to support the finalisation of the test method development and to organise a sustainable network for the needed exchange, also for future regulatory development needs.

The 3.5-year project started on 1 April 2020 and brings together 14 expert partners from 10 European Countries and works alongside OECD and ECHA in accelerating the development of priority Test guidelines and Guidance Documents for nanomaterials.

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The NanoHarmony White Paper on Test Guideline Development

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Summary

International agreement on harmonised and standardised methodologies to test and characterise chemicals and innovative, advanced (nano)materials is essential to protect human health and the environment as well as to ensure sustainability. The OECD Mutual Acceptance of Data (MAD) agreement has clearly demonstrated the benefits of such an international approach. For this agreement to remain effective, however, OECD Test Guidelines (TGs) need to remain up to date and fit for purpose for new scientific and/or industrial developments and innovations, and for new and future regulatory needs. The European project NanoHarmony has analysed processes in test method development to identify obstacles and (unnecessary) delaying factors. This has resulted in recommendations to further streamline the processes of OECD TG development. To this end, NanoHarmony discussed with and collected feedback from stakeholders involved in these processes and identified overarching issues that need attention, not only for nanomaterials, but for OECD TG development in general. **Keeping pace with new developments** requires an effective strategy for prioritising, initiating, and coordinating TG developments and the funding for these activities. Many methods developed in the scientific domain will not reach the status of a harmonised and standardised test method, limiting or even preventing their use in regulatory setting. More general obstacles that hamper **engagement of the scientific community** in TG development were also identified, not in the least a lack of knowledge on the process towards OECD accepted TGs. Another hurdle is that once methods are developed, these generally still need extensive **validation** (including interlaboratory comparisons) for which **funding** is often lacking. Additional steps of reaching agreement with experts, and drafting a TG also require resources that may not be immediately available under current financing schemes. In this white paper, the NanoHarmony project provides recommendations to address the issues identified with the specific aim of ensuring engagement of all the relevant stakeholders, not least those in the academic community, and making the process of TG development more effective.

Recommendations

Ensure OECD Test Guidelines remain up-to-date

- Establish a formal structure for stakeholder engagement to allow a continuous early identification of required new or adapted OECD Test Guidelines.
- The European Commission, Member States and stakeholders should support the Malta Initiative's European Test Methods Strategy as proposed in its position paper.

Engage the scientific community

- OECD Member Countries should encourage universities, professional societies, industry sector bodies and other relevant stakeholders to include Test Guideline development in their curricula and training to help raise awareness of the role and importance they play in society.
- Funding agencies in OECD Member Countries should encourage and support the scientific community to improve the FAIRness of their research and data.

Validation of methods

- OECD and its Member Countries should encourage and support the validation of scientific research, e.g. by providing guidance and tools for researchers over and above that contained in OECD Guidance Document 34.
- The National Coordinators of lead countries for a Test Guideline in development should help ensure effective and efficient communication with all relevant stakeholders during validation and ensure that discussions and decisions are captured and shared.

Funding TG development

- OECD Member Countries should provide long-term, dedicated additional funding to help ensure that TGs are kept up-to-date and relevant to regulatory requirements, especially for new chemicals and materials, ensuring a prioritised and focussed approach.
- OECD Member Countries should encourage and (financially) support the translation of scientific progress into making Test Guidelines more effective and efficient, including addressing the 3Rs principles.

Introduction

To ensure safety of industrial chemicals, different jurisdictions have legislation in place that aim to protect human health and the environment against harmful effects of such chemicals. While differences may exist between different jurisdictions (e.g. TSCA in the US [1], REACH in Europe [2], Industrial Chemicals Act in Australia [3]), all of the different regulations rely on assessment of hazards, exposures and risks. In recent years also sustainability becomes more important in assessments (e.g. [4] [5]). All of these assessments, especially for regulatory use, require reliable testing data that are based on reliable and relevant test methods.

International agreement on methodologies to test and characterise advanced (nano)materials is essential to protect human health and the environment and ensure sustainability. Such agreement ensures that reliable and reproducible data and methods become available for the safety assessment of chemicals and materials and duplication of testing is minimised. For sustainability, however, methodology developments are generally in their infancy at the moment.

The OECD Mutual Acceptance of Data (MAD) agreement [6] clearly shows the benefits of an international approach. This MAD agreement reduces complexity and costs for industry and governments and minimises the need for (duplicate) testing. An important cornerstone under the MAD agreement is a set of OECD Test Guidelines for Chemicals (TGs) [7]. For the OECD MAD agreement to remain effective, these TGs need to remain up to date and fit for purpose for new developments, including new and future regulatory needs, e.g. on sustainability.

The **NanoHarmony** project (www.nanoharmony.eu) supported the development and adaption of OECD TGs for nanomaterials in different ways. It has expanded the scientific background in support of method development towards new OECD TGs and Guidance Documents (GDs) for eight endpoints where adaptations for nanomaterials were identified as a regulatory priority. These include endpoints on physicochemical properties (dissolution in water and biological media, surface chemistry, dustiness, and determination of nanomaterial concentrations in biological samples), on environmental endpoints (determining apparent bioaccumulation in fish, a scoping review on a tiered approach for bioaccumulation testing, recommendations for acute tests with nanomaterials in algae, daphnids and fish), and on human health endpoints (toxicokinetics, in vitro approach for intestinal fate).

NanoHarmony has analysed processes in test method development to identify obstacles and options

Furthermore, NanoHarmony has analysed processes in test method development to identify obstacles and options with the aim of further streamlining the TG development processes and to improve the engagement of key stakeholders therein. To this end, NanoHarmony discussed with and collected feedback from stakeholders involved in these processes in an online survey, by using interviews, and via webinars and workshops. Based on this input NanoHarmony identified four main issues that were highlighted for nanomaterials, but apply to OECD TG development in general. The following paragraphs briefly summarise these four issues.

For **keeping pace with new developments**, we need a better strategy for prioritising, initiating and coordinating TG developments and their funding. Different interrelated drivers determine whether OECD TGs are up to date. New materials, technological developments and improved insights on risks can all lead to new regulations. Conversely, new regulatory requirements and policy strategies prompt new method development. A strategy for prioritising, initiating and coordinating TG developments, therefore, requires a continuous exchange between the different stakeholders. These stakeholders include policy makers, regulators, industry, scientific researchers and others.

Many national and international research projects are establishing the scientific basis for the development of new techniques and methods. Such projects often aim for standardised methods as a desired outcome. However, many of these methods will not reach the status of

a harmonised and standardised test method that allows broad use, e.g. in regulation. This approach leads to a waste of resources, resulting in important information that may not be fully available or can only be used to a limited extent. For example, where new methods can replace more costly (animal) testing, but large uncertainties in their use remain due to lack of (extensive) validation. Hazard assessment may be incomplete and risk assessment may be more conservative compared to when all information would have been available, or risk may turn out to be insufficiently constrained. Both too conservative risk assessment and insufficiently constrained risks can have a negative effect on the market.

An important obstacle here is that the process for the development of harmonised and standardised test methods (e.g. OECD TGs) is still largely unknown by many within the scientific community. The NanoHarmony project has also identified other **obstacles that hamper engagement of the scientific community** in TG development.

A significant hurdle may be that towards harmonisation, the **developed method generally still needs extensive validation** beyond the projects' lifetime. Validation includes interlaboratory comparisons and needs (additional) funding. Additional steps for converting a test method into an OECD TG include TG drafting, agreement with experts, and responding to comments from OECD experts. These steps in the process also require **resources** that may not be immediately available, and they are not often eligible under current research project financing schemes, such as the European Union's research programmes.

In this white paper, the NanoHarmony project provides eight recommendations for these four key areas to address the issues identified above, with the specific aim of ensuring engagement of the relevant stakeholders, not least those in the academic community.

Ensure OECD Test Guidelines remain up to date

The need for new or adaptations of existing TGs are driven by three connected developments: 1) changes in regulations and policy strategies, 2) new material and chemical developments, and 3) scientific progress of technologies and in (new) methods. As these drivers are continuous processes, there is a need for a structure that allows a continuous exchange of information between the different stakeholders. Foresight is required to monitor these drivers and to identify and discuss future goals and needs for test method developments in time. Taking into account that method developments take time, this requires looking at goals and needs that may lay beyond a horizon of 6-7 years, about twice as long as most European and national research projects are funded for. This enables timely identification and prioritisation of the needs for development and adaptation of test methods that can enable compliance and enforcement of (future) regulatory requirements and provide clarity for all stakeholders.

Within such an exchange, the stakeholders have different roles in identifying whether existing TGs are still appropriate for safety evaluation, are up to date with technical progress, or challenged by newly developed materials.

Regulators should clearly define and continuously refine their needs for harmonised test methods to make regulation enforceable and enabling testing on a sound scientific level. Policies should take into account that safety perceptions may change over time, either towards higher or lower concerns, which may influence regulatory needs as well. Clarity is therefore needed on the answers that a certain TG must provide to cover the endpoint requested in a regulation. Furthermore, regulators need to communicate where they have difficulties in receiving acceptable information for specific relevant endpoints or materials. Preferably regulatory needs should be combined over different regulatory areas (e.g. food, medicine, cosmetics, chemicals), as the different regulations often have similar requirements with a similar need for method developments (e.g. [8] [9]). This clearly requires collaboration between the different regulatory areas, and preferably on a global level.

Industry needs to communicate any difficulties they experience in fulfilling regulatory requirements. For example, are there difficulties in implementing certain test methods in regulatory testing schemes under Good Laboratory Practices (GLP [10]) or Good In Vitro Method Practices (GIVIMP [11])? Is the method not applicable to certain (new) materials? In particular contract research organisations (CROs) can indicate where method description is unclear, or when methods are difficult to perform. Methods may be laborious to perform, or require specific (costly) equipment, or they are otherwise difficult to fit into a CRO's business model. Knowledge of these difficulties is essential to improve the definition of the applicability domain and the predictivity of test methods and reduce their uncertainties.

Stakeholders have different roles in identifying whether existing Test Guidelines are still appropriate for safety evaluation

Furthermore, industry may (need to) provide insights on specific (material) properties, e.g. of new materials. This can be beneficial for timely identification of potential issues in the applicability of existing methods and for timely identification of any regulatory needs. This can prevent regulatory uncertainties slowing down or even stopping industrial innovation.

Scientists should communicate information on progress in materials, technology and test method developments. The trigger for the development of a new test method should be made clear. This needs to touch upon questions on the use of the test. Which regulatory needs does the new method relate to? Is it covering a new endpoint or new materials? Which relevant specific answer can the test provide? If the method is intended to replace an existing test, it should be clarified what the benefits of the new test are in comparison with the established test. Once such triggers for development are clear, still further method developments may be

needed, including further (mandatory) validation to assure transferability and predictivity of the methods (see also section on "Validation of methods" below).

The informal structure of collaboration within the Malta Initiative (malta-initiative.org) has shown the benefits of stakeholder exchange in identifying and prioritising needs for test method development. This collaboration has accelerated adaptation of OECD TGs and GDs applicable to nanomaterials [12]. The Malta Initiative was established in 2017 for that specific purpose, i.e. to ensure that nanospecific issues are addressed in such OECD documents. This need was particularly felt in Europe. Here the chemicals regulation REACH [2] has been adapted specifically for nanomaterials [13] and the related test method regulation [14] refers directly to OECD TGs.

A more formal structure than that of the Malta Initiative, however, appears needed to ensure continuity in such collaborations and a scope beyond nanomaterials. Such a more formal structure can also provide an institutional memory and prevent (unnecessary) reiteration of earlier discussions. Such a memory can help to keep track of the reasons for certain decisions in the process of procedure or method developments, about efforts that did not work out, or why things failed in the past.

In a Position Paper [15] the Malta Initiative identified the need for such a formal and continuous structure. The Malta Initiative proposed to continue and expand its activities in a so-called 'European Test Methods Strategy'. This Strategy is foreseen to include funding of researchers for the development, validation, and harmonisation of test methods, while providing an international (global) platform for collaboration and exchange between stakeholders, including researchers, regulators and industry. To ensure an effective structure, however, active support is needed from the European Commission, Member States and stakeholders like industry, NGOs, and the scientific community. Support in terms of funding, coordination and seeking synergies, also reaching out to stakeholders outside of Europe, as well as researchers, regulators and industry outside of OECD, to ensure that all relevant latest innovations and developments can inform the discussions.

During a recent international meeting (24th-25th January 2023) on governance of nanomaterials, participants from Europe and other global regions supported the "*development of the European Test Methods Strategy as proposed by the Malta Initiative, to facilitate on international cooperation and continuous financial support for the systematic (further) development of OECD Test Guidelines*" [16]. Together with the signatures on the Position Paper [15], this acknowledges the need and willingness by stakeholders for continuous exchange to ensure up-to-date test methods.

Recommendations to ensure OECD Test Guidelines remain up-to-date

- Establish a formal structure for stakeholder engagement to allow a continuous early identification of required new or adapted OECD Test Guidelines.
- The European Commission, Member States and stakeholders should support the Malta Initiative's European Test Methods Strategy as proposed in its position paper.

Engage the scientific community

Many in the scientific community may still be unaware of the fact that their research can actually contribute to harmonised method development, while in particular young scientists may not even be aware that globally harmonised methods exist, or do not understand that lack of such harmonisation is often a reason why their own method is not (to be) used in regulatory risk assessment. On the other hand, some areas in this community show progress in this area, e.g. participants in the EU NanoSafety Cluster [17] become increasingly aware of the importance of translating their scientific findings into practice, including method developments. Here this may be related to the inevitable multidisciplinary teams necessary to address the nanosafety issues. Teams that also include regulatory risk assessors that rely on (data from) such harmonised methods. Nevertheless, even when they are aware, many academic scientists encounter difficulties in connecting with the OECD processes, while also (lack of) incentives may be a limiting factor for researchers to engage in OECD TG development.

The OECD TGs are published without the names of the authors/contributors, resulting in products that cannot be clearly attributed to an individual's academic record, which hampers transparency for documentation of effort. Moreover, acknowledgement of authors/contributors may allow the documents to be included in citation indices to provide further appeal to scientists. The European Food Safety Authority (EFSA) provides an example of how this could work. EFSA publishes its scientific output in a dedicated journal (efsa.onlinelibrary.wiley.com) where contributors are clearly identified (often as authors).

Recent developments, however, show that contributions of individuals to OECD documents become more visible. Latest publications in the OECD Series on Testing and Assessment can include specific acknowledgements of contributors (e.g. [18]), and the OECD has started developing co-operation with Scientific Journals for the review and publication of AOPs [19] [20]. For TGs such acknowledgements in the documents appear to remain difficult, although OECD has started to organise webinars on newly published TGs. Here TG developers are given a platform to introduce and advertise the TG and their own contributions to it [21].

Alternatively, or in parallel, journals may encourage scientists to publish their method developments (including difficulties or failures) and the factors that triggered such developments. These could be similar triggers as indicated above for scientific input in the discussions on necessary TG updates, e.g. new endpoints or materials, replacement of a test, regulatory need, etc. Allowing references to such method developments in OECD TGs may then create incentives for researchers to engage in OECD TG work.

NanoHarmony developed an educational training set to raise awareness on OECD and Test Guideline development

Awareness of the steps and timing of the OECD process is an obvious benefit for projects aiming to deliver OECD TGs. An educational process is recommended to accommodate this. Such education could then emphasise that excellent research practise should include excellent metrology and documentation, and thus provide broader skills than the OECD processes alone. Nevertheless, it should also include an introduction to the development of harmonised/standardised test methods. Details on procedures and requirements could be included, as well as a training in methods validation. In principle, such education appears highly beneficial for any experimentalist.

For an effective inclusion in the educational process, OECD Member Countries can encourage universities, career trainers, sector organisations, etc. to include the topic in their curricula. NanoHarmony has contributed to addressing this need by the development of an initial **educational training set** to make scientists familiar with TG developments in OECD. It is available on the NanoHarmony website (nanoharmony.eu), and would clearly benefit from further distribution, e.g. by OECD. OECD appears also best equipped to ensure such material remains up-to-date.

Many scientists are involved only once or twice in the development of a TG and will thus clearly benefit from such a training session. In particular for this group, it is also beneficial to contact more experienced experts on the process of the OECD Test Guidelines Programme, not in the least the National Coordinators (NCs). These NCs can be found on the OECD website (www.oecd.org/chemicalsafety/testing/national-coordinators-test-guidelines-programme.htm). They oversee the Test Guidelines Programme and take decisions on inclusion of new projects in the workplan and on TG (updates) approval. Based on their experience and interactions with other NCs, they can guide TG developers through the process, identify which of the stakeholders should be involved in which part of the process, and more generally point the TG developers towards the relevant information. Being in close contact with your NC can also bring the advantage of getting (early) aware of the start of ILCs, expert group discussions, and other activities or publications form OECD (e.g. when new TGs are published). When actually starting with the development of a TG, scientists that are willing to lead on such a project are obliged to reach out to their own NC, as only an NC can propose a project for inclusion in the Test Guideline Programme.

In addition, this 'novice' group of TG developers could benefit more generally from easily accessible information about the TG development process, e.g. in the form of training (see above), and/or through an interactive web-based tool that can provide available information in one place, preferably in smaller, focussed parts. The "**NanoHarmony OECD TG/GD Process Mentor**" has been developed to be such a tool that facilitates easy access to the relevant information. This tool has its own web domain (www.testguideline-development.org) and is also accessible via the NanoHarmony website (nanoharmony.eu). To ensure future longevity and accuracy, however, a role for OECD is foreseen, preferably also in hosting such an interactive tool.

The "NanoHarmony OECD TG/GD Process Mentor" facilitates easy access to the relevant information

TG development generally takes 5-7 years, resulting in a relatively high risk of scientists moving out of the project and the specific field. In particular, young scientists often move from one job to the next. Furthermore, scientific research is generally dynamic and increasingly steered by availability of funding. While other benefits exist, this dynamic nature of scientific research is an important reason for the recommendation that funding agencies like the European Commission encourage the scientific community to improve the FAIRness of research and data (including descriptions of methods used). This can mitigate against the potential loss of knowledge and data. Overall, data generated in research projects should be made FAIR (i.e. findable, accessible, interoperable and reusable) [22] [23], preferably with open access. Where open access is not possible (e.g. due to intellectual property issues), at least knowledge on existence of data and how to contact the owner should be available. In this way method descriptions, results, and interpretations can be accessed and understood even years after their completion. FAIR data may also form a useful source for retrospective evaluations.

Recommendations to engage the scientific community

- OECD Member Countries should encourage universities, professional societies, industry sector bodies and other relevant stakeholders to include Test Guideline development in their curricula and training to help raise awareness of the role and importance they play in society.
- Funding agencies in OECD Member Countries should encourage and support the scientific community to improve the FAIRness of their research and data.

Validation of methods

Validation is key to the successful development of new methods. It enables confidence and trust in the methods and the data generated by using these methods. Therefore, an essential part of the development of any OECD TG is the validation of the method(s) under consideration. OECD defines test method validation as “a process based on scientifically sound principles by which the reliability and relevance of a particular test, approach, method, or process are established for a specific purpose” [24]. This should provide evidence for reproducibility of results from a test within and among laboratories over time, as well as indicate regulatory need, usefulness and limitations of the test method [24].

Validation is key to the successful development of new methods.

Despite its importance, the validation process is perceived by many as being lengthy and expensive, which is discouraging to engage in the process. Furthermore, for many stakeholders information on the specific requirements of validation is often difficult to find. This is especially true for young researchers, as well as for stakeholders who are new to the field of OECD TG development and validation. They are in need of profound and reliable information about the different steps and requirements for successful validation of a new method.

The OECD document GD No. 34 [24], which is currently under revision, provides information on these aspects. As outlined in that document, the amount and type of information needed for validation and the criteria applied to a new test method will depend on a number of factors. An interactive tool to support this GD may be of great help for the community, especially for those new to the process. Such a tool can facilitate a more targeted approach to relevant validation aspects.

An interactive tool can provide additional suggestions and best practice tailored to the specific needs for validation in a particular project. The “NanoHarmony OECD TG/GD Process Mentor” developed by NanoHarmony can provide such suggestions. This tool provides comprehensive information about the process of OECD TG development [25] (see also previous section), including any validation requirements.

Close exchange between all different stakeholders during validation ensures a smooth process. The lead country for the TG development (effectively its NC) appears to be the best candidate to ensure smooth communication, keep track of updates, organise discussion, and ensure documentation of information exchanges.

Recommendations on validation of methods

- OECD and its Member Countries should encourage and support the validation of scientific research, e.g. by providing guidance and tools for researchers over and above that contained in OECD Guidance Document 34.
- The National Coordinators of lead countries for a Test Guideline in development should help ensure effective and efficient communication with all relevant stakeholders during validation and ensure that discussions and decisions are captured and shared.

Funding TG development

Obviously, development of test methods requires funding. While finding funding will remain challenging, investments now can save resources in the future, e.g. where new methods can replace more costly (animal) testing, or where harmonised test methods can minimise duplication of testing. These 3Rs principles (i.e. replace, reduce, refine) form an important driver for the OECD MAD agreement [6].

Data are needed to establish the scientific documentation used as a basis for TG development. Producing such data, as well as optimisation of test methods are often performed in projects supported under research funding (e.g. Horizon Europe). Many of these projects, however, finish before (pre-)validation activities or further formalisation of the method into a harmonised test method can actually start. Consequently, many (financial) efforts in method developments may have been in vain when the method will not be (broadly) used and researchers involved may move into other research projects or topics with different goals. Their previous work and results are then left in the scientific sphere, and not always picked up by others. Clearly depending on the method, but in general relatively small amounts of funding are needed to overcome this funding obstacle in the validation process towards a harmonised test method. In particular, when taking into account that a lack of validation can have important consequences for hazard and risk assessment.

Financial or in-kind support can come from different sources

Financial or in-kind support for some parts of the validation process may come from individual OECD Member Countries, interested industries and trade organisations, developers, or CROs. More institutionalised options exist as well. The latter may have the benefit of easier access and facilitating engagement of the different stakeholders during validation. For alternatives to animal testing, EURL ECVAM [26] has set up a system of 35 GLP certified laboratories within EU-NETVAL [27] for their validation exercises funded by Member States of the EU, although the conduct of testing itself generally requires additional funding. To organise the pre-validation of methods for characterising endocrine disruptors the French National Institute for Industrial Environment and Risks (Ineris) has set up the public-private PEPPER platform [28]. Similar to EURL ECVAM ,this platform organises parts of the testing, but again the actual conduct of the testing is often on in-kind basis. A similar, complementary institutionalised system may be an option in OECD, funded by its Member Countries. But also in this case clarity is needed in the various steps of the validation process and the required time and resources. It should be made transparent which different (funding) resources will be needed for which steps in the process (pre-validation, validation management, conduct of validation studies, production of reports, peer review, resources needed the answer questions from expert during the various commenting rounds), and who will or needs to provide such resources. Another interesting approach to long-term financing of testing has also been developed within the Open Innovation Test Beds (OITB) [29]. These have been established for several industrial sectors within European Union funded projects, with the aim to provide services to the market and foster the specific economic sector. Central part of the OITB programme is the long term-sustainability and the creation of new economic entities, i.e. in the form of spin-offs, which are expected to enable the activities to be carried over beyond the actual project period.

Another project that could serve as an example is the 7-year initiative PARC of the EU Commission (www.eu-parc.eu). Here European funding is complemented by an equal funding from national sources. Such complementary funding preferably for the full 7-years may help share the burdens of TG developments and their method validations. Unfortunately, PARC did not commit any funding of test methods beyond the stage of first evaluation. As a result, the huge amount of resources available for PARC are primarily used for research on test method developments, and not the transition of the results into test methods ready for regulatory use.

Again, transparency is needed here in which resources are allocated for which of the various steps of the process (within PARC or provided by others outside).

One or more lead countries for OECD TG developments often provide the funding from their national funds. This often primarily aims to enable drafting of TG documents and dealing with comments in various commenting and discussion rounds. Experts that contribute to expert groups are usually also funded by their respective OECD Member Countries, although also here in-kind options can contribute to the process.

Despite these funding possibilities that may be suitable for some (parts) of the TG developments, long-term dedicated additional funding is still required to keep the OECD TGs up-to-date and fit for purpose. Even recently OECD highlighted the urgent need for validated new methods (www.oecd.org/chemicalsafety/testing/urgent-mobilisation-national-regional-resources-to-support-the-validation-of-new-methods-safety-testing-of-chemicals.pdf). OECD indicates that although there are already mechanisms and processes in place to facilitate standardization and guarantee the good conduct of validation studies, they need sustainable and realistic financial support to continue to provide relevant and reliable methods that meet the needs of evolving chemicals regulations. Without such relevant and reliable methods regulation cannot be enforceable, and the safe innovation of products cannot take place.

Prioritisation and coordination are best served by a continuous structure with long-term dedicated funding

As outlined above, to ensure up-to-date OECD TGs that have a regulatory use, the exchange of knowledge and information requires a platform. Such a platform facilitates prioritisation and coordination of TG development towards OECD. It can (help) set a research agenda, and it can also function as an institutional memory. This is best served by a continuous structure (e.g. the European Test Method Strategy proposed by the Malta Initiative) with long-term dedicated funding, e.g. from the EU, OECD Member Countries and/or other relevant stakeholders that can steer and prioritise the necessary actions. Funds to maintain such a continuous structure will be relatively small compared to actual method developments, while it will ensure that investments in TG developments will be prioritised and focussed on the (most pressing) needs.

Recommendations on funding TG development

- OECD Member Countries should provide long-term, dedicated additional funding to help ensure that Test Guidelines are kept up-to-date and relevant to regulatory requirements, especially for new chemicals and materials, ensuring a prioritised and focussed approach.
- OECD Member Countries should encourage and (financially) support the translation of scientific progress into making Test Guidelines more effective and efficient, including addressing the 3Rs principles.

Conclusion

The NanoHarmony recommendations in this White Paper aim to bridge existing and perceived gaps between science and regulation. They are based upon extensive and in-depth liaison with relevant stakeholders from policy makers, NGOs, regulators, academia and industry. The implementation of the eight recommendations will help make the OECD TG development process more efficient and effective by ensuring that TGs are fit for purpose and better at anticipating future regulatory needs.

Continuous advances in chemical and materials research will result in new products coming onto the market. Identifying TG needs early on and helping streamline the OECD process will ensure that society is not waiting for new test methods to be developed to better manage hazards and risks of such new materials and products.

The better engagement of stakeholders, combined with easily accessible information and education on the TG development process, will ensure that more scientists are aware of OECD TGs and their use from an early stage of their career. This will enable them to not only develop new methods but being better equipped to see them used in the real world.

Finally, ensuring continuity in support through a new TG strategy will ensure that investments in methods development contributes to key societal goals like reducing animal testing. At the same time this supports introduction of safe chemical and material innovations for the benefit of society.

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