3. Non-quantifiable benefits of the Environment, Health and Safety Programme

This chapter discusses the more qualitative, non-quantifiable benefits for governments and industry of participating in the OECD Environment, Health and Safety Programme. These include easier access to information on chemicals, access to harmonised templates, improved safety of manufactured nanomaterials, harmonisation of biotechnology safety assessment methods, harmonised tools to manage the risks of endocrine disrupters, reduced needs for governmental inspections of test facilities in other countries, enhanced hazard assessment methods, facilitation of the exchange of information on chemical accidents, advanced harmonisation of biocides regulation, reduced potential for repeat testing for new pharmaceuticals, and counteraction towards illegal trade of pesticides.

The previous chapter calculated the monetary savings for industry and governments as a result of the OECD's Environment, Health and Safety (EHS) Programme were calculated. This chapter discusses the more qualitative (but significant) benefits of the EHS Programme.

3.1. Facilitating access to information on chemicals

In collaboration with other key players in the area of chemicals management, the OECD has developed information systems and other tools to enhance public access to chemical hazard data and risk information prepared by government chemical review programmes.

Together with the European Chemicals Agency (ECHA), the OECD developed and maintains the eChemPortal[1] – the Global Portal to Information on Chemical Substances – in order to support regulators and industry, academics and the public in taking health and environment decisions concerning chemicals. This online portal provides direct links to multiple websites compiling information on chemical hazards, risk, exposure and use as well as chemical classifications prepared for national, regional and international chemical programmes worldwide. By facilitating access to this information, the eChemPortal helps governments achieve resource efficiencies, share the burden and avoid duplication of work across national and regional assessment programmes and, therefore, reduce animal testing.

Through the eChemPortal, governments and industry can rapidly identify publically available and relevant information (including reports, webpages and data sets) on a chemical substance, the properties and effects (for example physical properties and toxicity) of a specific substance, or substances with specific properties and effects, in addition to getting access to direct links to full data sets. The portal also contains information on chemical hazard classifications in accordance with the Globally Harmonized System of Classification and Labelling and which have undergone a review by a regulatory body or international organisation as well as information on where these classifications differ. Further, the eChemPortal provides authorities with an additional channel through which they can disseminate information from their chemical programmes widely, particularly if they have structured chemical data in, or mapped to, the OECD Harmonised Templates (see below).

3.2. Providing OECD Harmonised Templates

Writing dossiers for the electronic submission of health and safety data to regulatory authorities can be very resource-intensive. Therefore, the OECD has developed the OECD Harmonised Templates[2] for reporting information used for the risk assessment of chemicals, mainly studies conducted on chemicals to determine their properties or effects on human health and the environment, but also for storing data on use and exposure. As countries increasingly implement the OECD Harmonised Templates in their IT systems, the costs of preparing different data sets for different national/regional regulatory assessment schemes are reduced.

The OECD Harmonised Templates allow companies to gather and store their chemical test summaries in a single database and submit the same information to different authorities without having to re-enter or reformat any data. They also allow governments to easily exchange information on chemicals in a structured and harmonised format, without costly data reformatting.

3.3. Ensuring the safety of manufactured nanomaterials

The EHS Programme offers many benefits to the new and growing area of nanomaterial production and other advanced materials. These materials – which have physical, chemical and biological properties which may differ in fundamental ways from those of individual atoms and molecules – hold much promise for improving people's lives. However, the special features that make nanomaterials so useful may also pose risks to human health and/or the environment. Thus, their risks need to be properly assessed. But given the innovative structure of nanomaterials, the traditional testing and assessment methods for conventional chemicals may not always be appropriate.

OECD countries began working together to share knowledge and expertise when the use of manufactured nanomaterials was emerging as a possible concern. By co-operating on this issue before governments had fully developed programmes in response, the EHS Programme was able to ensure that the approaches for hazard, exposure and risk assessment for manufactured nanomaterials were internationally harmonised, science-based and of high quality.

The OECD's EHS Programme ensures cost savings to governments and industry in the area of safety of nanomaterials in several ways. Among others, under the Testing Programme of Manufactured Nanomaterials, OECD member countries, along with some non-member economies and other stakeholders, pooled their expertise and organised the safety testing of specific manufactured nanomaterials, seeking to identify the need for developing new Test Guidelines or adapting existing Test Guidelines to nanomaterials.

In 2013, the OECD adopted a *Recommendation of the Council on the Safety Testing and Assessment of Manufactured Nanomaterials* (OECD, 2013). An important consequence of this Recommendation is that much of the data collected as part of the safety assessment of nanomaterials will fall within the scope of the OECD Mutual Acceptance of Data (MAD) system. With OECD guidance increasingly being adapted to nanomaterials, this implies that savings similar to those generated for traditional chemicals due to MAD (as outlined in Chapter 2) eventually will also apply to nanomaterials.

The EHS Programme has developed new test methods for manufactured nanomaterials (or adapted existing methods) so that no individual government will have the burden of developing these new methods. The OECD adopted the first Test Guidelines developed specifically for nanomaterials in 2017.[3] Testing using the guidelines adopted by the OECD will fall under the MAD system and hence eliminate any duplicative testing costs.

3.4. Harmonising biotechnology safety assessments

Modern biotechnology is becoming increasingly important for agriculture, livestock farming, fisheries, forestry, industrial production and public health. Every year, more and more species are modified for various traits, including resistance to biotic and abiotic stresses, tolerance to herbicides/insecticides, and improved nutritional content for crops. Each new host organism (plants, animals and micro-organisms) and trait combination developed by a company is a new product. In the absence of an internationally harmonised approach for commercial approvals, each company must obtain approval for its engineered products in every country in which it expects to market them for production and/or use in foods or feeds. As with industrial chemicals and pesticides, the cost to industry to prepare dossiers, and to governments to review each application, can be substantial.

A considerable portion of the cost of product approval involves environmental risk (biosafety) assessments. These examine three aspects of the product: 1) its biology; 2) the specific trait introduced (e.g. virus resistance); 3) the potential impact on the environment in which it is intended to be released. Since the environmental information required is largely the same in every country, national authorities and experts involved in the EHS Programme develop "consensus documents"[4] that contain common technical elements for use during the regulatory assessment of products of modern biotechnology. Similarly for novel foods and feeds derived from these products, consensus documents are elaborated for each bioengineered crop species to provide information on compositional and nutritional parameters that are critical in comparative safety assessments.

To date, these OECD consensus documents constitute official reference tools in risk/safety assessment of the regulatory systems of many economies worldwide. Their use can contribute to mutual recognition of assessments among countries, therefore facilitating the international trade of the products. There is a reported case where the competent authority of a non-OECD country, Viet Nam – which participates as an observer in the EHS Programme – accepts the food/feed safety approvals issued by other participating authorities for granting its own national approvals for food/feed use without requiring additional tests, therefore drastically reducing the safety assessment cost. Further, the Argentinian regulation on the commercialisation of genetically modified organisms, issued in 2018, explicitly lists the situations of low level presence of transgenic grains in bulk commodities where the OECD related guidelines should be taken into account (Government of Argentina, 2018). This allows for savings in the safety assessment process by providing internationally recognised approaches to information sharing on the transgenic plant unauthorised in the importing country, with guidance on how to establish a risk profile for environmental safety, and proposing potential ways to proactively address the low level presence situation.

Hundreds of genetically engineered crop varieties and other organisms are currently in the development pipeline, each requiring a separate notification or authorisation in each country. The *BioTrack Product Database*,[5] developed by the EHS, collates information on these varieties approved for cultivation and for use in foods and feeds in OECD countries and other economies associated with the work. With the increasing commercialisation potential for these products, the use of OECD consensus documents and database information leads to significant savings for government and industry and also accelerate the assessment of these products.

In addition, the EHS Programme facilitates cross-country discussions on solutions to common emerging issues, such as new plant breeding techniques (e.g. genome editing), which in turn will reduce the possibility of differences in regulatory responses across countries. The programme ensures regular information sharing on these techniques, including through workshops such as the Conference on Genome Editing Applications in Agriculture held in June 2018.[6]

3.5. Providing harmonised tools to identify endocrine disrupters

Over the last two decades, the OECD has emerged as a key player associated with the issue of endocrine disrupters testing and assessment. In 1996, the OECD set up an Advisory Group on Endocrine Disrupters Testing and Assessment to develop new and update existing OECD Test Guidelines to identify chemicals with endocrine disrupting properties. The Advisory Group has overseen the validation of about 35 OECD Test Guidelines with endpoints that are specific for endocrine disrupters, including a variety of *in vitro* Test Guidelines that

provide information on endocrine modes of action. One of the most important outcomes of the Advisory Group's work was the 2012 publication of *Guidance Document 150* (GD 150) (OECD, 2012), which was the first comprehensive, international guide for identifying endocrine disrupting chemicals. GD 150 provides guidance for analysing test results, evidence for a chemical mode of action, support for regulatory authorities' decisions on whether a substance is an endocrine disrupter, and, in some cases, recommendations for follow-up testing if a conclusion cannot be made. GD 150 also includes a conceptual framework for organising OECD Test Guidelines and other standardised test methods into levels of increasing biological complexity and may help evaluations of endocrine disrupters. The OECD updated both GD 150 and the conceptual framework in September 2018 (OECD, 2018b).

The OECD's validated methodologies on screening and testing chemicals for their endocrine disrupting potential allow governments to implement policies for assessing and managing the risk of potential endocrine disrupters, using internationally harmonised tools. Table 3.1 lists the United States Environmental Protection Agency's (US EPA) estimates of the cost of Tier 1 and Tier 2 assays carried out as part of its Endocrine Disruptor Screening Program. Those indicated in bold in the table are OECD Test Guidelines. (The table does not include estimates for Test Guidelines 407, 408, 414 and 421/422 as the United States requires these for other types of testing and they are thus not included in endocrine screening costs.)

Table 3.1. **Estimated costs of US EPA Endocrine Disruptor Screening Program Tier 1 and Tier 2 Assays**

	Estimated cost/assay (USD)
Tier 1 *in vitro* assays[1]	
OECD TG 458/OCSPP 890.1150 – Androgen Receptor Binding (Rat Prostate)*	27 700
OCSPP 890.1200 – Aromatase (Human Recombinant)	34 700
OECD TG 493/OCSPP 890.1250 – Estrogen Receptor Binding	27 100
OECD TG 455/OCSPP 890.1300 – Estrogen Receptor Transcriptional Activation (Human Cell Line HeLa-9903)	27 800
OECD TG 456/OCSPP 890.1550 – Steroidogenesis (Human Cell Line – H295R)	20 300
Total	137 600
Tier 1 *in vivo* assays[2]	
OECD TG 231/OCSPP 890.1100 – Amphibian Metamorphosis (Frog)	145 000-187 000
OECD TG 230/OCSPP 890.1350 – Fish Short-Term Reproduction	197 000-203 000
OECD TG 441/OCSPP 890.1400 – Hershberger (Rat)	154 000-192 000
OCSPP 890.1450 – Female Pubertal (Rat)	228 000-250 000
OCSPP 890.1500 – Male Pubertal (Rat)	234 000-261 000
OECD TG 440/OCSPP 890.1600 – Uterotrophic (Rat)	139 000-150 000
Total	1 152 000-1 188 000
Total cost range for US EPA Tier 1 battery	1 289 600-1 325 600
Tier 2 *in vivo* assays[2]	
OCSPP 890.2100 – Avian Two-Generation Toxicity Test in the Japanese Quail (JQTT)	473 000-643 000
OECD TG 240/OCSPP 890.2200 – Medaka Extended One-Generation Reproduction Test (MEOGRT)	488 000-669 000
OECD TG 241/OCSPP 890.2300 – Larval Amphibian Growth and Development Assay (LAGDA)	227 000-438 000
OECD TG 443 – Extended One-Generation Reproduction Toxicity Test (EOGRT) (Rat). (*Note:* May be substituted for Two-Generation Reproduction Toxicity Test in Rat, OCSPP 870.3800.)	1 274 000-1 600 000
Total cost range for US EPA Tier 2 tests	2 462 000-3 350 000

Notes: OECD Test Guidelines are highlighted in bold. Estimated costs include, but are not limited to, chemical purchase, sampling and shipment, analytical method development and measurements, range-finding assay, in-life assay, histopathology, biochemical analyses, statistical assessment, quality assurance, project management, paperwork (e.g. reports), and clerical costs.
1. Figures are from 2012 and from US EPA (2013), adjusted to 2018 USD using the US Department of Labor inflation calculator.
2. Estimates provided by the US EPA, based on the range of contract offers submitted to the US EPA in April 2015.

Other countries are setting up endocrine disrupting chemicals programmes requesting testing according to OECD Test Guidelines. One example is the European Union's endocrine disrupting chemicals criteria for pesticides and biocides, adopted in 2018 (European Commission, 2018). As more countries set up their programmes using results from OECD Test Guidelines, the potential for savings will increase. That is, as many countries will be requesting and using the same new OECD Test Guidelines the cost of testing will be less than it might otherwise have been if governments developed and used different tests developed outside of the OECD (i.e. without MAD).

3.6. Reducing the need for governmental inspections of test facilities in other countries

The OECD MAD system not only reduces duplicative testing and allows governments to share data, it also eliminates the need for governments to inspect test facilities outside their country. In the past, if a government that relied on critical health and safety test data generated in another country had concerns about the quality of that data, it needed to travel to the other country to conduct an inspection of the test facility that produced the data or conduct a study audit to verify the quality of the data. However, with the adoption of the 1989 *Decision-Recommendation of the Council on Compliance with the Principles of Good Laboratory Practice* (OECD, 1989) – which is one of the three Council acts[7] related to MAD – countries adhering to MAD can request another country to conduct an inspection of a test facility or a study audit for test facilities located in the other country. This has significantly reduced the cost of travel for the requesting country.

3.7. Enhancing hazard assessment methods

Current regulatory toxicity testing and assessment approaches largely remain based on a checklist of *in vivo* tests, conducted in accordance with standardised test guidelines or protocols such as the OECD Test Guidelines. While this approach has evolved over the past half century, it is unlikely to meet, in an efficient manner, legislative mandates that require increased numbers of chemical assessments to be undertaken without a concomitant increase in the use of animals and resources. New approaches are necessary to close the gap between the number of chemicals in use and the number assessed to date.

The OECD Cooperative Chemicals Assessment Programme, which originally was established based on the previous High Production Volume (HPV) chemicals work, was revised in 2014 to better respond to the changing needs of member countries. It addresses a number of member country challenges, such as: assessing more chemicals in a shorter period of time; addressing all chemicals on the market; and avoiding duplication of ongoing work in other countries. Recently, such work has focused on enhancing the development and application of Integrated Approaches to Testing and Assessment (IATA). IATAs are pragmatic, science-based approaches for chemical hazard characterisation that rely on an integrated analysis of existing information coupled with the generation of new information using testing strategies. IATAs can include a combination of methods and can be informed by integrating results from one or many methodological approaches, such as (Quantitative) Structure-Activity Relationship, i.e. (Q)SARs, read-across, *in vitro*, *ex vivo*, *in vivo* or omic technologies (e.g. toxicogenomics). (See further information on the OECD's work on "omics" technologies in Section 5.8.) Read-across and similar approaches can fill data for requirements for chemical categories as well as eliminate the need for many animal tests (Stanton and Kruszewski, 2016).

The EHS Programme also supports the development of Adverse Outcome Pathways (AOPs), which helps harmonise IATAs. AOPs are tools that involve capturing the underlying biology of how chemicals interact with organisms to cause adverse effects in a practical, modular format. AOPs provide decision makers with enhanced scientific understanding and greater confidence, and can thus enable the increased integration and acceptance of read-across, new approach methods and the use of *in vitro* assays.

As discussed in Chapter 2, the EHS Programme has developed, and continues to develop, guidance documents and tools for the use of alternative methods such as (Q)SARs and grouping of chemicals. The goal is that over time these new approach methodologies will not only provide a more mechanistically informed process for chemical assessment, but will also reduce the cost of testing and the need for tests on animals. In addition, moving to more harmonised approaches for hazard assessment and their technological convergence will allow countries to more readily draw upon other countries' assessments of chemicals, reducing duplication of effort.

The *Decision-Recommendation of the Council on the Co-operative Investigation and Risk Reduction of Chemicals* (OECD, 2018a), developed through the EHS Programme, was adopted on 25 May 2018 by the OECD Council. The Decision-Recommendation (which is an updated version of a 1991 Decision-Recommendation) promotes collaboration between adherents in the development of harmonised hazard and exposure assessment methodologies, and facilitates information dissemination and the sharing of the burden associated with information generation. Such collaboration will improve the quality of assessments, and reduce the time and effort required to conduct them.

3.8. Facilitating the exchange of information on chemical accidents to support prevention, preparedness and response

The potential for major industrial accidents has increased with the expansion of production, storage and use of hazardous substances. Over the past decades, such accidents have caused deaths, numerous injuries, significant environmental pollution and massive economic losses, highlighting the need for a systematic approach to the control of hazardous substances. There are also hundreds of small-scale, but recurrent, chemical accidents every year that cause severe harm to workers, communities, municipalities, businesses and the environment. In order to gauge the number and scale of accidents globally over one year, the European Commission's Joint Research Centre examined the number of accidents reported in the media from 1 October 2016 to 30 September 2017 (Wood, 2017). The study identified 667 accidents. The great majority of these occurred at fixed facilities (454) and a smaller number during transport (147), followed by pipelines (37) and offshore (9). According to the study, OECD countries accounted for nearly two-thirds of the events (421 out of 667), but barely one-third of the deaths (201 out of 579).[8]

The EHS' Chemical Accidents Programme ensures cost savings across countries by avoiding duplication of efforts to identify adequate methods for prevention, preparedness and response, and thus by reducing economic losses caused by chemical accidents. The programme has developed some of the EHS Programme's most widely used documents; the *OECD Guiding Principles for Chemical Accident Prevention, Preparedness and Response* is one example (OECD, 2003), which provides general and specific guidance for the safe planning, construction, management, operation and review of the safety performance of hazardous installations. The Guiding Principles form the basis of the 2004 *Recommendation of the Council concerning Chemical Accident Prevention, Preparedness and Response* (OECD, 2004) and are accompanied by the OECD *Guidance on Developing*

Safety Performance Indicators Related to Chemical Accident Prevention, Preparedness and Response (OECD, 2008).

3.9. Advancing harmonisation of biocides regulation

Since its establishment in 2003, the OECD Biocide Programme has sought to ensure a high level of protection for users, the public at large and the environment, and to remove non-tariff barriers to trade in biocides.[9] The programme provides a global platform for making progress in regulating, registering and placing biocidal products on the market, as well as for the exchange of best practices on the sustainable use of biocides, offering benefits to regulators as well as to industry.

Notably, the programme yields benefits to governmental authorities related to the risk assessment and evaluation of biocide products and their active substances. Harmonising essential parts of authorisation procedures enables governments to assess the risks of biocides in a quicker, more thorough and harmonised manner. The workload of countries is greatly reduced by agreeing on common evaluation methodologies and by sharing the burden of evaluation. The Biocides Programme facilitates the exchange of study evaluations between authorities, through, among other things, a new initiative known as Review Sharing of Acute Studies (see Box 1.2). This reduces the resources needed for evaluating dossiers.

As there are a wide variety of applications for biocides, estimating potential releases of these products can be very complex. As a result, the OECD has developed a number of Emission Scenario Documents (ESDs) on biocides, including on insecticides, anti-fouling products and wood preservatives. This not only reduces the need for any one government to develop such ESDs independently, it also promotes the harmonisation of release estimations across regulatory agencies. Further, the OECD has developed test methods specifically aimed at biocides (on release estimations for treated wood, efficacy for disinfectants, storage stability, insecticides and treated articles), as well as harmonised templates to report tests in a structured format. These and other OECD harmonised data and test method requirements create direct benefits for industry, by avoiding the duplication of testing in the various countries in which they operate and hence reducing the costs of testing.

3.10. Reducing repeat testing for new pharmaceuticals

Similar to companies from the industries surveyed for this report, pharmaceutical companies also conduct a number of non-clinical tests using OECD Test Guidelines and following the OECD Good Laboratory Practice Principles. Hence, significant potential benefits could accrue to this industry as a result of the MAD system. In 2016, the average number of new pharmaceutical active ingredients registered by OECD governments was 34,[10] and the cost of non-clinical testing of such substances is likely to be several million euros. Assuming that pharmaceutical companies market their products in as many regions as biocides, pesticides and industrial chemicals companies do, the savings to governments and industry resulting from the reduction in duplicative testing, due to MAD, would be substantial.

3.11. Counteracting the illegal trade of pesticides

In order to ensure food security and safety while protecting human health and the environment, the pesticides market is highly regulated. Pesticide producers face large expenses due to long-term research and development efforts, significant testing, regulatory approval and other associated development costs for new products. Production costs of pesticides are, however, relatively low. This creates opportunities for illegal traders wishing to benefit from inserting cheaper, untested and thus possibly dangerous, illegal products onto the market. In some countries, the share of illegal pesticides on the regular market is reportedly as high as 20%. Over the period 2009-14, direct and knock-on economic effects from illegal pesticides sales amounted to EUR 2.8 billion annually in the European Union alone, as a result of lost sales, subsequent employment loss and loss of government revenues (EUIPO, 2017). This is on top of the costs due to crop loss and impacts on human health and the environment caused by the use of illegal pesticides.

Since 2010, the OECD has been co-ordinating activities to counteract the illegal trade of pesticides, so that:

- countries and consumers can rely on the risk assessment and risk management policies that are in place to protect human health and the environment, and that markets are not impacted by illegal pesticides
- efforts and investments by pesticide producers when registering pesticides are not undermined by rogue traders.

For instance, the OECD has developed a Rapid Alert System, which allows regulatory authorities in OECD countries and other invited countries to rapidly exchange information on suspicious or rejected shipments of pesticides via a protected website, thereby reducing the risk of illegal pesticides entering a market. This enables countries to prevent possible damages to crops, human health and the environment resulting from the use of illegal pesticides.

Within the OECD Network on Illegal Trade of Pesticides, member countries exchange experiences and best practices in the identification of illegal pesticides and methodologies to counteract them. This has resulted in the development of a Best Practice Guidance publication (OECD, 2018c) and a draft OECD Council Recommendation for identifying and tackling illegal pesticides throughout the complete lifecycle of a pesticide (i.e. from manufacture through formulation, trade and use to final disposal). It is anticipated that the Recommendation will be adopted in early 2019. The OECD Network on Illegal Trade of Pesticides also exchanges information with the United Nations Interregional Crime and Justice Research Institute, EUROPOL, the World Customs Organisation, INTERPOL, industry and various other organisations, and informs the Strategic Approach to International Chemicals Management on a regular basis to create better policies against the illegal trade in pesticides.

Notes

1. eChemPortal, available at: www.oecd.org/env/ehs/risk-assessment/echemportalglobalportaltoinformationonchemicalsubstances.htm.
2. See: www.oecd.org/ehs/templates.
3. Test Guideline 318: Dispersion Stability of Nanomaterials in Simulated Environmental Media; Test Guideline 412: 28-Day (Subacute) Inhalation Toxicity Study; and Test Guideline 413: 90-Day (Subchronic) Inhalation Toxicity Study.
4. See the OECD webpage on the Series on "Harmonisation of Regulatory Oversight in Biotechnology": https://doi.org/10.1787/23114622.
5. *OECD BioTrack Product Database* available at: https://biotrackproductdatabase.oecd.org.
6. See: www.oecd.org/environment/genome-editing-agriculture.
7. See the OECD webpage on the "OECD Council Acts Related to the Mutual Acceptance of Data (MAD)": www.oecd.org/chemicalsafety/testing/council-acts-on-mutual-acceptance-of-data.htm.
8. It is noted that media reports do not represent all incidents that occur, since many events are not reported in (mainly EU) languages used for searching and some are not reported at all. The data generally over-represent English-speaking sources, countries with strong media sectors and those that have a strong awareness of chemical hazards.
9. "Biocides" are a diverse group of products including disinfectants used in homes and hospitals; products to preserve wood; products to prevent fouling on boats; and products to control insects, mice or rats in homes and industries.
10. Thirty-four is the average of the number of registrations of new active substances noted in the European Medical Agency's *Human Medicines Highlights* for 2015, 2016 and 2017. See: www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/document_listing/document_listing_000256.jsp&mid=WC0b01ac0580099fbb). The same figure can be found in CIRS (2017).

References

CIRS (2017), "New drug approvals in six major authorities – 2007-2016: Focus on the internationalisation of medicines", *R&D Briefing*, No. 65, Centre for Innovation in Regulatory Science, London, www.cirsci.org/wp-content/uploads/2017/11/CIRS-RD-Briefing-65-20112017.pdf.

EUIPO (2017), "The economic cost of IPR infringement in the pesticides sector", EU Intellectual Property Office, Alicante, Spain, https://euipo.europa.eu/tunnel-web/secure/webdav/guest/document_library/observatory/resources/research-and-studies/ip_infringement/study10/pesticides_sector_en.pdf.

European Commission (2018), "Commission Regulation (EU) 2018/605 of 19 April 2018 amending Annex II to Regulation (EC) No. 1107/2009 by setting out scientific criteria for the determination of endocrine disrupting properties", *Official Journal of the European Union*, L101/33-36, Publications

Office of the European Union, Brussles, https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32018R0605.

Government of Argentina (2018), *Resolución 26/2018: Procedimiento de Autorización Comercial a los Organismos Genéticamente Modificados (OGM)*, Buenos Aires, *https://www.erreius.com/Legislacion/documento/20180518075705968*.

OECD (2018a), *Decision-Recommendation of the Council on the Co-operative Investigation and Risk Reduction of Chemicals*, OECD, Paris, https://legalinstruments.oecd.org/en/instruments/OECD-LEGAL-0441.

OECD (2018b), *Revised Guidance Document 150 on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption*, OECD Series on Testing and Assessment, No. 150, OECD Publishing, Paris, https://doi.org/10.1787/9789264304741-en.

OECD (2018c), "Best Practice Guide to Identify Illegal Trade of Pesticides", *Series on Pesticides*, No. 99, ENV/JM/MONO(2018)35, OECD Publishing, Paris, www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2018)35&doclanguage=en.

OECD (2013), *Recommendation of the Council on the Safety Testing and Assessment of Manufactured Nanomaterials*, OECD, Paris, https://legalinstruments.oecd.org/en/instruments/298.

OECD (2012), "Guidance document on standardised test guidelines for evaluating chemicals for endocrine disruption", *Series on Testing and Assessment*, No. 150, ENV/JM/MONO(2012)22, OECD Publishing, Paris, www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2012)22&doclanguage=en.

OECD (2008), *Guidance on Developing Safety Performance Indicators Related to Chemical Accident Prevention, Preparedness and Response,* OECD, Paris, www.oecd-ilibrary.org/environment/guidance-on-developing-safety-performance-indicators-for-public-authorities-and-communities-public_9789264221734-en;jsessionid=YbEFm-nVFFQcna_qyc-5JhJw.ip-10-240-5-76.

OECD (2004), "OECD principles for the validation, for regulatory purposes, of (Quantitative) Structure-Activity Relationship Models", http://www.oecd.org/env/ehs/risk-assessment/37849783.pdf

OECD (2003), *OECD Guiding Principles for Chemical Accident Prevention, Preparedness and Response: Guidance for Industry (Including management and Labour), Public Authorities, Communities and Other Stakeholders*, OECD, Paris, www.oecd.org/env/ehs/chemical-accidents/Guiding-principles-chemical-accident.pdf.

OECD (1989), *Decision-Recommendation of the Council on Compliance with Principles of Good Laboratory Practice*, OECD/LEGAL/0252, OECD, Paris, https://legalinstruments.oecd.org/en/instruments/58.

Stanton, K. and F.H. Kruszewski (2016), "Quantifying the benefits of using read-across and in silico techniques to fulfil hazard data requirements for chemical categories", *Regulatory Toxicology and Pharmacology*, Vol. 81, pp. 250-259, https://doi.org/10.1016/j.yrtph.2016.09.004.

US EPA (2013), "Attachment F: Calculations for paperwork burden and costs for data generation activities (as of April 3, 2013)", EDSP ICR Addendum (EDSP ICR Addendum, Attachment F. EPA ICR #2488.01; OMB # 2070-[new]), United States Environmental Protection Agency, Washington, DC, https://www.regulations.gov/document?D=EPA-HQ-OPPT-2013-0275-0017.

Wood, M. (2017), "Incidents in the media – 1 October 2016 to 30 September 2017", European Commission Joint Research Centre, presentation to the 2017 Annual Meeting of the OECD Working Group on Chemical Accidents.