



Questions and answers  
on measurement  
implications of REACH  
and CLP

Second edition

LGC/R/2011/187  
December 2011

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*Setting standards  
in analytical science*

# **Questions and answers on measurement implications of REACH and CLP**

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A handwritten signature in black ink, appearing to be 'M. Selby', written over a horizontal line.

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**Date:**

**26 January 2012**

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# 1. Introduction

## 1.1 Intended readership

This advice is mainly intended for businesses of all kinds, and particularly SMEs, that are required to comply with the REACH Regulation<sup>1</sup>. It also aims to help those obliged to notify classification and labelling for a wider range of substances under the CLP Regulation<sup>2</sup>. Moreover, scientists, SIEFs<sup>3</sup> and consortia, trade associations, regulators, consultants and some general enquirers may find it useful to consider the measurement implications of these Regulations.

We continue to welcome feedback, corrections, additional topics to be covered and other suggestions for improvement for future editions.

## 1.2 Scope

The first REACH registration deadline for phase-in substances<sup>4</sup> - 30 November 2010<sup>5</sup> - has now passed. Many more companies will now face the obligation to register in 2013 and 2018. This Q&A document continues to foster awareness that correct substance identity is pivotal for successful registration, and addresses key practical requirements.

Experience to date shows that the European Chemicals Agency (ECHA) attaches the highest significance to correct substance identity, which forms the foundation of most REACH processes, including decisions about hazard testing as well as enforcement. It is clear that this emphasis will continue, being the only way to ensure that other REACH actions are well-defined. Thus over the coming three years ECHA aims to 'Ensure to the extent possible that the substance identity of the submitted dossiers is correct so that information and regulatory action on substances is targeted and well understood by industry and authorities'<sup>6</sup>.

The CLP Regulation, which gives effect in the European Union (EU) to the United Nations Globally Harmonised System of Classification and Labelling of Chemicals (GHS), is closely aligned with REACH. We are mindful that measurements may have been needed to underpin the CLP classification of many substances due to be notified to ECHA by 3 January 2011, even if they are not subject to REACH registration. In the light of data gathered during the pre-registration phase of REACH, ECHA recognises that the first version of the public classification and labelling inventory may contain many entries with insufficient substance identity, but will be seeking to rectify this by 2013.

In places, this document goes beyond REACH registration issues in seeking to share understanding of wider measurement requirements arising under REACH and CLP. Developing a picture of the overall role of measurement science should help compliance and enforcement activities to be planned cost-effectively.

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<sup>1</sup> Regulation (EC) No 1907/2006 *concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)* as amended. Current consolidated text: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:2006R1907:20090627:EN:PDF>

<sup>2</sup> Regulation (EC) No 1272/2008 *on classification, labelling and packaging (CLP) of substances and mixtures* as amended. Original act: <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2008:353:0001:1355:EN:PDF>

<sup>3</sup> Substance information exchange fora (REACH Regulation, Article 29)

<sup>4</sup> As defined by REACH Article 3(20). In general terms, substances that the previous regulatory framework treated as 'existing', which are now coming under detailed scrutiny for the first time

<sup>5</sup> This deadline applies to high-tonnage and certain high-hazard substances, as detailed in Article 23(1) of the REACH Regulation

<sup>6</sup> ECHA, *Draft multi-annual work programme 2011-2013*. 12 March 2010: [http://echa.europa.eu/documents/10162/17096/pr\\_10\\_04\\_maw\\_2011\\_2013\\_20100312\\_en.pdf](http://echa.europa.eu/documents/10162/17096/pr_10_04_maw_2011_2013_20100312_en.pdf)

However, as time and resources are limited, a number of topics likely to have measurement implications are either not covered or discussed only briefly in this version. Examples include polymers, nanomaterials, crystalline forms, substances in articles, strictly controlled conditions for intermediates, and requirements for analysis to support hazard and exposure assessment. We may extend coverage in future if there is demand. We have not covered the legislation and guidance on REACH restrictions because we believe it is relatively clear<sup>7</sup>, but here, as elsewhere, feedback on any measurement-related issues is very welcome.

### 1.3 How we developed this document

In the UK, the Government Chemist<sup>8</sup> has a long-standing duty to provide advice on the analytical science implications of policy, standards and regulation. The Government Chemist function is funded by the UK Department for Business, Innovation and Skills through the National Measurement Office.

Over the last year, feedback from stakeholders, including questions raised at our open event in November 2010<sup>9</sup>, continued to suggest that there are significant uncertainties about the measurement implications of REACH. We therefore undertook to develop further advice based on case studies with industry. Furthermore, we intend to hold further open events with stakeholders.

As before<sup>10,11,12</sup>, we appointed an independent consultant<sup>13</sup> to profile measurement issues relating to REACH compliance for several industrial chemical products, in conjunction with companies involved in their supply. Broadly, we considered three further cases as follows:

- An inorganic mineral that disperses and degrades in water
- An unstable multi-constituent organic substance
- An aqueous extract of a plant material.

This document utilises the consultant's findings, together with our own experience arising from involvement with REACH since the early days of policy development. To safeguard confidentiality, we discuss lessons learnt from the industry case studies only in the broadest terms - in fact, only as far as is necessary to derive, validate or illustrate advice.

The measurement implications of REACH are ultimately determined by the legislation, supported by official technical guidance documents<sup>14</sup>; in addition, the ECHA Substance Identity Workshop<sup>15</sup> provided valuable context. We consulted the EU and ECHA sources extensively whilst preparing this document.

This second edition incorporates further research, taking account of developments in REACH implementation and interpretation, as well as feedback on the original version which in the authors' judgement reflects acceptable practice. The authors would like to acknowledge the valuable input from staff at ECHA to this document.

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<sup>7</sup> ECHA, Existing restrictions webpage: [List of Restrictions - ECHA](#)

<sup>8</sup> The Government Chemist: <http://www.governmentchemist.org.uk/>

<sup>9</sup> *Science for REACH and CLP compliance*. Held in partnership with the Chemical Hazards Communication Society (CHCS), Teddington, 4 November 2010: <http://www.governmentchemist.org.uk/Events.aspx?m=93&amid=830>

<sup>10</sup> Francis J, Scott R and Selby M, Analytical issues relating to chemical substance identity under REACH (March 2008, LGC/GC/2007/016): <http://www.governmentchemist.org.uk/Publications.aspx?m=77&amid=474>

<sup>11</sup> Francis J, Scott R and Selby M, Analytical issues relating to chemical substance definition under REACH (March 2009, LGC/RT/2009/015): <http://www.governmentchemist.org.uk/Generic.aspx?m=77&amid=730>

<sup>12</sup> Francis J, Analytical issues relating to chemical substance definition under REACH: supplement on dyes (March 2009, LGC/RT/2009/016): <http://www.governmentchemist.org.uk/Generic.aspx?m=77&amid=731>

<sup>13</sup> Denehurst Chemical Safety Ltd

<sup>14</sup> ECHA, Guidance documents: [Guidance on REACH and CLP implementation - ECHA](#)

<sup>15</sup> Held in Helsinki, 1 December 2009: [News - ECHA](#)

We cannot guarantee that our advice will meet existing or future regulatory requirements. Readers should consult the legal texts, the technical guidance documents published by ECHA and, if appropriate, seek their own specific advice.

## 2. Questions and answers on measurement implications of REACH and CLP

### 2.1 General

#### 2.1.1 How should I find out about REACH measurement requirements?

The primary sources are the REACH Regulation as amended<sup>16</sup>, and ECHA guidance - particularly the guidance document on identification and naming<sup>17</sup>. Authoritative advice may be obtained from the UK Competent Authority helpdesk<sup>18</sup>, or from ECHA<sup>19</sup>. A series of summary guidance documents, aimed at SMEs, from ECHA also make for useful reading<sup>20,21,22</sup>. The Substance Identity Workshop held in December 2009 is a useful source of advice provided directly by ECHA on some of the key measurement requirements.

Intermediaries, including trade associations and reputable independent consultants, are helping to interpret the specific implications of REACH. The UK Government Chemist's role is limited to impartial scientific advice on the analytical measurement implications, and stems from a generic responsibility to provide advice within our field of expertise rather than from a specific mandate under REACH.

A document published by the UK Analytical Partnership (UKAP) in 2002 entitled "Guidance Document on Regulatory Physico-Chemical Testing in the United Kingdom"<sup>23</sup> also provides some useful information which is still relevant today.

#### 2.1.2 What are the main areas of analytical requirement?

We have been evaluating this question throughout the development of REACH. The legislation depends on analytical measurement in so many ways that we still cannot provide an exhaustive answer, but key areas include:

1. Primarily, establishing substance identity for the purposes of a REACH registration, or another regulatory submission such as a PPORD notification<sup>24</sup> or an inquiry<sup>25</sup>. Substance identity requirements apply both for substances of well defined composition and UVCBs<sup>26</sup>.

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<sup>16</sup> ECHA, REACH legislation: [Legislation - ECHA](#)

<sup>17</sup> ECHA, Identification and naming of substances under REACH and CLP, Version 1.1, November 2011: [http://echa.europa.eu/documents/10162/17235/substance\\_id\\_en.pdf](http://echa.europa.eu/documents/10162/17235/substance_id_en.pdf)

<sup>18</sup> HSE, UK REACH Competent Authority: <http://www.hse.gov.uk/reach/compauth.htm>

<sup>19</sup> ECHA, ECHA helpdesk: [ECHA Helpdesk - ECHA](#)

<sup>20</sup> Guidance in a Nutshell Requirements for Substances in Articles; [http://echa.europa.eu/documents/10162/17224/nutshell\\_guidance\\_articles2\\_en.pdf](http://echa.europa.eu/documents/10162/17224/nutshell_guidance_articles2_en.pdf)

<sup>21</sup> Guidance in a nutshell: Registration data and dossier handling: [http://echa.europa.eu/documents/10162/17224/nutshell\\_guidance\\_registration\\_en.pdf](http://echa.europa.eu/documents/10162/17224/nutshell_guidance_registration_en.pdf)

<sup>22</sup> Guidance in a Nutshell on Identification and naming of substances under REACH and CLP: [http://echa.europa.eu/documents/10162/17235/nutshell\\_guidance\\_substance\\_en.pdf](http://echa.europa.eu/documents/10162/17235/nutshell_guidance_substance_en.pdf)

<sup>23</sup> UKAP "Guidance Document on Regulatory Physico-Chemical Testing in the United Kingdom": <http://www.ecotoxchem.co.uk/downloads/physico.pdf>

<sup>24</sup> ECHA, Guidance on Scientific Research and Development (SR&D) and Product and Process Oriented Research and Development (PPORD), February 2008: [http://echa.europa.eu/documents/10162/17224/ppord\\_en.pdf](http://echa.europa.eu/documents/10162/17224/ppord_en.pdf)

<sup>25</sup> Where required prior to registration in accordance with Article 26 of the REACH Regulation

<sup>26</sup> UVCB substances: substances of unknown or variable composition, complex reaction products or biological materials (ECHA, Guidance for identification and naming of substances under REACH, page 10)

2. Demonstrating whether substances from different sources are the same to allow for data-sharing and joint registration.
3. Providing evidence of structural similarity between substances, to support the read-across of valuable data on physicochemical, toxicological and ecotoxicological properties<sup>27</sup>
4. Deciding which substances qualify as polymers
5. Deciding whether a product is chemically identical to a substance found in nature, as certain substances found in nature are exempt from registration under REACH
6. Process and pre-release quality control to check that substances, mixtures and articles comply with restrictions, limits on SVHC<sup>28</sup>, and potentially authorisation conditions
7. Checking that a variable product continues to meet the specification for a single substance
8. Filling gaps in supply chain data, such as for imported materials - for example, establishing whether they are products of a chemical reaction or deliberate mixtures, before proceeding to substance identity and the question of whether different suppliers actually deliver the same substance
9. In hazard studies - particularly innovative alternatives to in vivo testing - measuring the dose (identity and stability of the test material) and response (substance transformation and effect)
10. To support toxicokinetic studies as required, for example to improve the robustness of a read-across hypothesis<sup>29</sup>; and in research on the fundamental mechanisms of toxicity (toxicodynamics)
11. Validation and improvement of exposure models by measuring real datasets, typically using environmental or biological samples taken under carefully chosen conditions
12. Regular monitoring of emissions and cumulative chemical burdens, for example to build an exposure assessment<sup>30</sup>, or provide evidence of compliance with the strictly controlled conditions required for the manufacture and use of intermediates
13. Enforcement, such as testing whether a substance is really what it is claimed to be, checking the nature and concentrations of substances in mixtures and articles, and policing restrictions.

### 2.1.3 How can I gauge the level of effort required?

Experience shows that:

- ECHA expects to see certain basic analytical data (spectra, chromatograms). Substance identity needs to be reported in enough detail for the reader to replicate the analysis
- Sufficient work needs to be performed to enable possible discussions about the sameness of substances, or read-across with similar ones
- The behaviour of a substance in water and biotic conditions needs to be known, to allow environmental fate and toxicokinetic assessments to be made (the exact requirements may depend on tonnage).

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<sup>27</sup> Read-across is about predicting hazard properties from chemical structure or reactivity, rather than inferring substance identity or sameness from physicochemical properties (cf. REACH Annex XI section 1.5)

<sup>28</sup> Substances of very high concern, as defined in Title VII of the REACH Regulation

<sup>29</sup> Cf. ECHA, Evaluation under REACH - progress report 2009. ECHA-10-R-001-EN, 25 February 2010, chapter 3.1.2.4: [http://echa.europa.eu/documents/10162/17221/progress\\_report\\_2009\\_en.pdf](http://echa.europa.eu/documents/10162/17221/progress_report_2009_en.pdf)

<sup>30</sup> An exposure assessment may be needed to justify the waiving of ecotoxicity tests - cf. ECHA, Waiving information requirements. Webinar, 10 December 2009 - slide 29: [http://echa.europa.eu/documents/10162/17242/waiving\\_information\\_requirements\\_wim\\_de\\_coen\\_echa\\_en.pdf](http://echa.europa.eu/documents/10162/17242/waiving_information_requirements_wim_de_coen_echa_en.pdf)



## 2.1.4 How do measurement and modelling support one another?

- Studies have shown that there is a dearth of exposure data for many exposure scenarios and inadequate information on which to base reliable and accurate exposure estimates
- Exposure assessment modelling tools are designed to ensure that exposures are not underestimated and could lead to the need for improved and potentially costly risk management measures (RMM)
- The only certain way of determining workplace exposures is to undertake a properly designed measurement survey. The combination of good measurement data with the use of a modelling tool enables a realistic exposure assessment to be made leading to a proper assessment of the risk characterisation ratio.

## 2.1.5 How can analytical science help counteract compliance costs?

Analytical measurement can offer benefits over and above bare compliance with the law. It can:

- Provide evidence that a substance is exempt from registration
- Show that certain hazard tests are not required
- Be a crucial component of alternatives to costly and undesirable animal testing
- Show that a product is suitable for specialised, high value uses, or has wider market potential.

A planned approach to the analytical work is advisable to:

- Minimise costly replication, by optimising the experimental design and relative timing of studies
- Avoid paying urgency premiums, and potential enforcement penalties.

## 2.1.6 What about quality assurance?

Compliance with good laboratory practice (GLP) is not a legal requirement for the analytical work to establish the identity of a substance subject to REACH/CLP. ECHA intends to accept appropriate data generated by in-house laboratories. The level and form of quality assurance that ECHA does expect will become clearer as industry gains more experience with submitting dossiers. Meanwhile we recommend that analytical work conforms to GLP principles, such as internal checking, sign-off by responsible persons and record-keeping. In any event, for ecotoxicological and toxicological analyses, GLP principles should be observed.<sup>31</sup>

Although not explicitly required by ECHA, we suggest that confidence in the analytical data could be underpinned by explaining arrangements for the accreditation of laboratory work, staff qualifications and training, how methods were validated, use of appropriate certified or matrix-matched reference materials, the nature and meaning of control experiments, and the handling of measurement uncertainty. Evidence of accreditation assessments, internal audits, method validation studies and other peer review procedures would be beneficial in this regard.

## 2.1.7 Will REACH be enforced in relation to specific substances and mixtures?

The evidence so far is that enforcement in the UK will be highly specific and targeted. Enforcement regimes may differ across the EU, but member states have a commitment to share best practice.

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<sup>31</sup> REACH Regulation, Article 13(4)

The first joint REACH project co-ordinated by ECHA's Forum for Exchange of Information on Enforcement finished at the end of 2009. It focused on checking for the registration or pre-registration of phase-in substances; safety data sheets (SDS) were also inspected. Preliminary data showed that 850 inspections were delivered across 28 countries. The next joint enforcement project focuses on formulators of mixtures, and is due to conclude at the end of June 2012. This is conceived as a logical extension of enforcement focused on manufacturers and importers (which is ongoing). Most mixtures are sold on to article producers, but others are consumer products, e.g. detergents, paints, personal care. On-site inspections are being carried out throughout 2011<sup>32</sup> and will continue in 2012.

The UK REACH Competent Authority is launching intelligence-led, substance-specific inspection campaigns. These focus on the duty to register - the 'no data, no market' principle - but are likely to extend to checking compliance with other REACH duties.<sup>33</sup> REACH restrictions are also being enforced in a substance-specific, risk-based manner, and early examples have been publicised.<sup>34</sup> A new Strategy and Guidance document on REACH enforcement was published in April 2010.<sup>35</sup>

### 2.1.8 How can science-based disputes be resolved?

Under REACH, there is no officially prescribed referee function<sup>36</sup> devoted to disputes about analytical measurement, whether these arise within industry or between businesses and the enforcement authorities. The Manual of Decisions<sup>37</sup> compiled under the former Notification of New Substances (NONS) legislation may help to resolve some technical points, e.g. as to what spectral and chromatographic details need to be reported.

ECHA has provided information concerning procedural disputes over data sharing.<sup>38</sup> Related guidance suggests that consortium agreements could contain clauses covering dispute resolution.<sup>39</sup> New guidance on data sharing will be issued by ECHA in April 2012.<sup>40</sup> This includes a new sub-section covering data sharing disputes according to articles 30(2) and 30(3), and on available legal remedies against ECHA decisions which is included in a new section 3 on data sharing within SIEFs.

Dispute resolution in relation to SIEFs has been addressed by an independent legal group<sup>41</sup>. A general finding was that parties will need to deploy imagination and common sense in resolving disputes over REACH implementation.

In the UK, the REACH Enforcement Regulations 2008 point to an arbitration mechanism for determining compensation, or a formal appeals process, in certain circumstances.<sup>42</sup>

<sup>32</sup> ECHA, Forum decides on checking how formulators comply with REACH. News alert ECHA/NA/09/34, 14 December 2009: [http://echa.europa.eu/documents/10162/17095/na\\_09\\_34\\_forum\\_20091214\\_en.pdf](http://echa.europa.eu/documents/10162/17095/na_09_34_forum_20091214_en.pdf)

<sup>33</sup> HSE, Enforcement activities of the UK REACH Competent Authority: <http://www.hse.gov.uk/reach/ourwork.htm>

<sup>34</sup> UK REACH Competent Authority (Environment Agency), Environmental aspects of the enforcement of REACH in the UK: [http://www.governmentchemist.org.uk/dm\\_documents/091123RichardHawkins\\_XdQCE.pdf](http://www.governmentchemist.org.uk/dm_documents/091123RichardHawkins_XdQCE.pdf)

<sup>35</sup> Health & Safety Executive: Strategy and Guidance for Enforcement of REACH in the UK: <http://www.hse.gov.uk/reach/resources/enforcementstrategy.pdf>

<sup>36</sup> Along the lines of the functions fulfilled by the Government Chemist under national legislation to improve safety and protect the public, such as the Food Safety Act 1990, the Agriculture Act 1970 and the Medicines Act 1968

<sup>37</sup> European Commission Joint Research Centre - Institute for Health and Consumer Protection - former European Chemicals Bureau, Manual of decisions for implementation of the sixth and seventh amendments to Directive 67/548/EEC on dangerous substances (Directives 79/831/EEC and 92/32/EEC) - non-confidential version, EUR 22311 EN, July 2006: [http://ecb.jrc.ec.europa.eu/DOCUMENTS/New-Chemicals/Manual\\_of\\_decisions.pdf](http://ecb.jrc.ec.europa.eu/DOCUMENTS/New-Chemicals/Manual_of_decisions.pdf)

<sup>38</sup> ECHA website, Data sharing. 18 May 2010:

[http://echa.europa.eu/documents/10162/17095/na\\_10\\_24\\_datasaharing\\_20100430\\_en.pdf](http://echa.europa.eu/documents/10162/17095/na_10_24_datasaharing_20100430_en.pdf)

<sup>39</sup> ECHA, Guidance on data sharing, September 2007, section 10.7:

[http://echa.europa.eu/documents/10162/17223/guidance\\_on\\_data\\_sharing\\_en.pdf](http://echa.europa.eu/documents/10162/17223/guidance_on_data_sharing_en.pdf)

<sup>40</sup> ECHA, Draft Guidance on data sharing, due for publication April 2012:

[http://echa.europa.eu/documents/10162/17235/guidance\\_dsh\\_peg\\_comments\\_implemented\\_en.pdf](http://echa.europa.eu/documents/10162/17235/guidance_dsh_peg_comments_implemented_en.pdf)

<sup>41</sup> NautaDutilh, SIEFs and dispute resolution, May 2009, reference 9000001 1 P 467324 / 13 (55049):

<http://chemicalwatch.com/downloads/NautaDutilh%20SIEFs%20and%20dispute%20resolutions.pdf>

<sup>42</sup> Statutory Instrument 2008 No. 2852: [http://www.opsi.gov.uk/si/si2008/pdf/uksi\\_20082852\\_en.pdf](http://www.opsi.gov.uk/si/si2008/pdf/uksi_20082852_en.pdf)

Parties are of course free to seek the opinion of an independent expert. The resolution of some questions, such as around substance sameness, may hinge on an impartial review of analytical data, or on definitive measurement. Recourse to an independent expert may work best if the parties can agree in advance how they will respond to the opinion.

### 2.1.9 Can REACH support science-based innovation and growth?

The potential for product and process innovation has been widely debated, but the broad chemical scope and extensive data requirements of REACH will also place new demands on measurement science. In this field, experience suggests that much of the demand-driven innovation is likely to be transferable, and therefore capable of delivering economic impact across a wide front.

ECHA expects to see spectra and chromatograms resulting from the more routine, readily interpretable measurement techniques, which is unsurprising given the scope and timetable for REACH implementation. This does not exclude the submission of data derived from innovative techniques. Indeed, substance identity requirements will need to be met using whatever techniques and data are scientifically suitable.

The ECHA guidance on mono-constituent and multi-constituent substances does state that 'Spectroscopic and analytical methods are subject to continuous change. Therefore, it is the responsibility of the registrant to present appropriate spectral and analytical data.'<sup>43</sup> For substances of unknown or variable composition, complex reaction products or biological materials (UVCB substances), the guidance highlights the part played by developing insight into how to use methods.<sup>44</sup>

We should not forget that sample preparation is a major factor in determining the validity of spectroscopic and chromatographic techniques, as well as in their smooth running, ease of interpretation and clarity of reporting. Sample preparation continues to offer a great deal of scope for innovation - for example, through novel solvents, optimised chemistries, bio-based and affinity separations, and robust automation. Equally, analytical instrument manufacturers can play a key part in growing capability to tackle complex measurement issues, as well as in enabling the generation of valid data more cost-effectively.

## 2.2 Specific

### 2.2.1 What is a REACH substance?

REACH assumes that a substance is not a pure element or compound. Unless a substance is in the natural state, it is effectively whatever results from the manufacturing process, including both (wanted) constituents and (unintended) impurities. The legal definition takes this understanding into account:

'substance: means a chemical element and its compounds in the natural state or obtained by any manufacturing process, including any additive necessary to preserve its stability and any impurity deriving from the process used, but excluding any solvent which may be separated without affecting the stability of the substance or changing its composition'<sup>45</sup>.

As implied by this definition, additives and solvents (including water) should be removed as far as practical when establishing substance identity, unless needed to stabilise the substance.

<sup>43</sup> ECHA, Guidance for identification and naming of substances under REACH and CLP, pages 20 and 22

<sup>44</sup> ECHA, Guidance for identification and naming of substances under REACH and CLP, pages 30 and 31

<sup>45</sup> REACH Regulation, Article 3(1)

Substances, including those that result from a chemical reaction, are distinct from mixtures. There is no intentional chemical reaction when a mixture is made.

## 2.2.2 How are substances grouped - and does it matter?

Substances are either 'well defined' by chemical composition, or 'of unknown or variable composition, complex reaction products or biological materials' (UVCB)<sup>46</sup>.

Well defined substances include those that are:

- Mono-constituent: A mono-constituent substance is 'As a general rule, a substance, defined by its composition, in which one main constituent is present to at least 80 % (w/w)'<sup>47</sup>
- Multi-constituent: 'As a general rule, a substance, defined by its composition, in which more than one main constituent is present in a concentration  $\geq 10$  % (w/w) and  $< 80$  % (w/w)'<sup>47</sup>
- Defined by more than the chemical composition (e.g. some crystalline forms).

These groups and subgroups are important in that they affect the naming of the substance, and the mechanics of submitting data to ECHA via the dedicated software (IUCLID). The 10 % and 80 % limits in the above definitions are flexible under some circumstances, provided that the registrant justifies the course taken.

## 2.2.3 Are natural products exempt?

Substances covered by certain entries in Annex V of the REACH Regulation, and meeting all the conditions laid down there, may be exempt from registration provided that they are not chemically modified. Certain substances which occur in nature or are obtained from natural sources may qualify.<sup>48</sup> Measurement may be needed to determine whether any allowable<sup>49</sup> processing leads to chemical changes (see case study 1).

### Case study 1

In one of the cases we encountered, a plant material is heated to obtain a water extract that contains valuable organic fragrance compounds. There was a view that the extract might qualify under the Annex V entry 8 exemption from REACH registration for certain substances which occur in nature. To qualify, the extract has to be a 'not chemically modified substance'<sup>50</sup>. The analytical work required to show that a substance is not chemically modified was much like that needed to provide identity data for registration, so could usefully be taken forward without deciding whether other conditions for the exemption were met. (Among those other conditions, the implications of the actual processing undertaken remained in doubt, and may depend on a conjoint interpretation of 'steam distillation' and 'heating solely to remove water'.<sup>51</sup>)

The extract cannot be dried without losing valuable constituents, so the solvent (water) can be regarded as part of the REACH substance. This extract is a UVCB substance containing a

<sup>46</sup> ECHA, Guidance for identification and naming of substances under REACH, Chapter 4.1

<sup>47</sup> ECHA, Guidance for identification and naming of substances under REACH, Chapter 2.2

<sup>48</sup> ECHA, Guidance for Annex V - Exemptions from the obligation to register. Version 1, ECHA-10-G-02-EN, 31 March 2010 - pages 18-36: [http://echa.europa.eu/documents/10162/17224/annex\\_v\\_en.pdf](http://echa.europa.eu/documents/10162/17224/annex_v_en.pdf)

<sup>49</sup> Cf. REACH Regulation, Article 3(39)

<sup>50</sup> REACH Regulation, Article 3(40).

<sup>51</sup> REACH Regulation, Article 3(39); cf. ECHA, Guidance for Annex V, page 19.

wide variety of other constituents, including sugars and complex carbohydrates, amino acids, low molecular weight alkyl acids, and inorganic salts. Many of these can support microbial growth, so analytical samples were prepared under sterile conditions.

IR was performed on the plant extract and the crushed plant source material. In both cases, complex spectra were obtained. However, after using the instrument software to subtract the IR signal of water, the spectra appeared the same, suggesting that the extraction process does not chemically modify the natural constituents.

HPLC and GC methods were developed for some of the key constituents, including the main fragrance compound. These constituents can be regarded as measurable indicators of any chemical change that occurs during extraction. In addition, the concentrations of various metals, which are typically present in plant material as counter-ions, were compared by inductively coupled plasma atomic emission spectroscopy (ICP-AES); evidence that no new metals are present after extraction could provide a further indication of identity with the plant source material.

The exemption for substances which occur in nature does not extend to synthetic versions. However, a synthetic form of the main fragrance compound is commercially available, and has been used in medicinal products. On the strength of analytical work (in this case GC-MS) to establish the extent and nature of similarities between the two forms, hazard data already available for the synthetic molecule could help to justify waiving some test requirements if the plant extract does have to be registered.

#### 2.2.4 How detailed does the analysis need to be?

All constituents and impurities<sup>52</sup> (including isomers and by-products) which are known to make up 1 % or more of a substance should be identified and quantified. In addition, impurities should be identified and quantified wherever the product owner is aware that they pose a potential risk - even below 1 % - where they affect the hazard classification and/or PBT<sup>53</sup> assessment of the substance. It is also important to highlight the total number and concentration range of unknown impurities. Ideally, sensitivity to 0.1 % is needed to identify sub-components and impurities.

Additives - substances that have been intentionally added to stabilise the substance<sup>54</sup>, such as stabilising agents or inhibitors - should be identified, and their concentrations indicated, typically in ppm or % units<sup>55</sup>. We believe that it may be scientifically justifiable, on a case-by-case basis, to identify and indicate the concentration of an additive based on the amount added to the substance, rather than on measurement.

For REACH, quantification means providing the typical concentration, together with the upper and lower limits. The unit of concentration (typically w/w) needs to be selected in IUCLID<sup>56</sup>, so laboratories should be made aware before planning the analysis that they are constrained in this respect by the software options available.

At least 99 %, and ideally 100 %, of a well-defined substance should be accounted for. Any unknown impurities need to be listed, with their concentration ranges, in order to complete the mass balance. In practice, we find that it is generally feasible to establish the purities of relatively refined chemicals in the range of 99-100 % with uncertainties in the region of 0.5 % or below. For the avoidance of later doubt, we suggest that laboratories could record and

<sup>52</sup> An impurity, or unintended constituent, typically makes up less than 10 % (w/w) of the bulk.

<sup>53</sup> Persistent, bioaccumulative and toxic

<sup>54</sup> ECHA, Guidance for identification and naming of substances under REACH and CLP, Chapter 2.2

<sup>55</sup> REACH Regulation, Annex VI, section 2.3.4

<sup>56</sup> International Uniform Chemical Information Database - the software platform that enables REACH and other regulatory dossiers to be prepared: <http://iuclid.echa.europa.eu/>

retain evidence (such as extract and residue weights) showing that all fractions of the sample have been analysed so as to give a mass balance of the entire substance.

## 2.2.5 What are the core measurements required by the regulator?

The requirements listed in Annex VI Section 2 of the REACH Regulation must be met unless a science-based justification is provided. Most have been carried forward from earlier EU chemicals legislation. The central requirement is for sufficient information to allow the substance to be identified.

ECHA guidance<sup>57</sup> points in particular to:

- Ultraviolet-visible absorption (UV-Vis) spectra (at pH range of 4-9 if water soluble<sup>58</sup>)
- Infrared (IR) spectra
- Nuclear magnetic resonance (NMR) spectra and/or<sup>59</sup> mass spectrometry (MS) data
- Gas chromatography (GC) and/or high-performance<sup>60</sup> liquid chromatography (HPLC).

The spectral data are intended to confirm structure, and the chromatographic methods to confirm composition, of the substance. Although more sophisticated techniques may be needed to meet substance identity requirements, it is proving important to show ECHA that UV-Vis, IR, proton (or possibly carbon-13) NMR and appropriate chromatographic methods have at least been attempted. We recognise that it is scientifically valid to challenge any requirement for unnecessary data. Indeed, the REACH Regulation permits registrants to provide a justification where it does not appear scientifically necessary to give information of this kind<sup>61</sup>. However, if any of the above spectra or chromatographic data cannot be provided, there must be a scientific reason. There are few valid reasons not to supply the spectra - lack of access, or suggesting that they are meaningless, has not proven acceptable. Existing data may be unfit for purpose or subject to ownership issues, but, unless otherwise shown, regulators are likely to assume that the registrant can generate their own directly relevant data using the core measurement techniques.

## 2.2.6 Are there specific information requirements for each technique?

ECHA expects to receive certain details about each of the standard techniques:

- For UV-Vis, the concentration of the test substance, cuvette path length, solvent
- For IR, details of sample preparation
- For NMR, operating frequency, nucleus, concentration of test substance, solvent, internal standard, range (which must be suitable - typically 15 ppm for proton NMR), chemical shift integrals
- For GC or LC, the specific method for the substance in hand, including the experimental set-up, preparation of solutions and identity of standards. The details should include the column type, length and diameter; injection volume; mobile phase/carrier gas; GC temperature programme; flow rate; concentrations of HPLC standard solutions; detection technique; and run time.

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<sup>57</sup> ECHA, Guidance for identification and naming of substances under REACH and CLP, pages 20, 22, 25, 30 and 31

<sup>58</sup> Requirement to investigate pH range established through experience with regulatory submissions

<sup>59</sup> Cf. REACH Regulation, Annex VI, section 2.3.5. At present, NMR is generally viewed as definitive by ECHA, but the use of MS could be justified on a case-by-case basis

<sup>60</sup> The REACH Regulation itself (Annex VI, section 2.3.6) specifies a high-pressure liquid chromatogram. We believe the terms to be interchangeable for REACH purposes

<sup>61</sup> Annex VI, note 1 and section 2

- Any output chromatograph should include solvent / mobile phase fronts and ideally a solvent blank control. The chromatograph should also show a period of at least 2 minutes following the last retained peak.

Quantitation procedures should be fully reported. For example, a table of data could show the assignment of constituents to chromatographic peaks, and the use of peak areas, standards and calibration curves.

### 2.2.7 What other data may be needed?

Depending on circumstances, including the chemistry of the constituents, and particularly if the core techniques listed in Annex VI section 2 of the REACH Regulation are unsuitable, ECHA will look for complementary data which help to confirm structure and define the whole substance, for example:

- NMR based on other elements present, e.g. carbon, phosphorus or fluorine. For example,  $^{13}\text{C}$  NMR may indicate the ratio of positional isomers present in a multi-constituent substance. ECHA has recognised the value in making good use of information-rich NMR spectra<sup>62</sup>, and of more advanced experiments such as DEPT<sup>63</sup> in contributing to molecular structure determination
- Valid constituent separation techniques other than GC and HPLC to confirm the composition
- For inorganic substances, elemental analysis such as atomic absorption spectroscopy (AAS) or X-ray fluorescence (XRF). Also crystallographic techniques, such as powder X-ray diffraction (XRD), which will usually be needed to confirm the name of a mineral
- Measurement of metals and other counter-ions, e.g. by potentiometric titration
- Karl Fischer determination for water
- Thermal analysis, for example thermogravimetric analysis (TGA) or differential scanning calorimetry (DSC).

However, registrants do not have to develop specialised analytical techniques which would require additional investment. From ECHA's point of view, industry is responsible for selecting appropriate methods and showing that they are suitable; justification should be provided for non-standard techniques. The details provided should be sufficient for the method to be reproduced, including, for example, sample preparation, instrument operating characteristics, calibration of the method, and quantification of results.

### 2.2.8 Should I measure isomers?

The concentrations of isomers should be submitted, whether they occur in a characteristic ratio within a multi-constituent substance, or are present as impurities.

For optical isomers, see question 2.2.16.

### 2.2.9 Do ionic substances present special problems?

ECHA expects all parts of a substance, including the inorganic counter-ions of organic moieties, to be identified and quantified. The identity of ions needs to be chemically specific - for example, chloride or another specific halide should be named, rather than simply reported as X<sup>-</sup>. Ionic structures can be complex to describe and quantify, but presentable data may be gathered by combining a range of available techniques (see case study 2a).

<sup>62</sup> ECHA, Substance identity webinar for Lead Registrants, 25 January 2010:

[http://echa.europa.eu/documents/10162/17242/general\\_information\\_on\\_clp\\_gabriele\\_schoening\\_echa\\_en.pdf](http://echa.europa.eu/documents/10162/17242/general_information_on_clp_gabriele_schoening_echa_en.pdf)

<sup>63</sup> Distortionless enhancement by polarisation transfer in  $^{13}\text{C}$  NMR

### Case study 2a (continued under Question 2.2.18)

A silicate substance - essentially a mineral material - is used as a flocculant and clarity enhancer for personal care and domestic products. It contains sparingly soluble particles, so the exchange of internal counter-ions with water may be restricted. This could bias some measurement methods. Best efforts are required to establish the identity of the substance, with appropriate use of data on the particle structure itself or the composition in pure water<sup>64</sup>.

A destructive elemental analysis technique such as AAS can be used to establish the empirical formula, but does not specifically confirm the arrangement of the atoms and ions in the intact substance. XRD provided basic fingerprint data, suitable for discussing sameness between commercial products in the context of SIEF formation. More information was obtained by employing dialysis to drive the dissociation of the substance toward completion; the ionic composition of the dilute dialysate was then determined by highly sensitive inductively coupled plasma mass spectrometry (ICP-MS).

Beyond substance identity, the potential bioavailability of the counter-ion may have implications for biota or environmental systems. Bioavailability of the bulk of the substance could also be affected by structural changes resulting from ion exchange with the wide range of charged species potentially present in natural media. Further studies of the substance, including its behaviour in hard and soft waters, acidic and alkaline media, may therefore depend on the analytical monitoring of ionic concentrations and exchange trends over time.

#### 2.2.10 Can I rely on traditional methods, low resolution data, 'fingerprinting'?

We believe that all these data sources can play a valuable part in REACH compliance, but in many cases they are unlikely to provide enough information to complete and submit a dossier successfully.

Some traditional methods are highly sensitive and specific. Provided that they are appropriately validated, in our view they could be scientifically justifiable if they can be applied to hazardous constituents or impurities which may occur in a substance at levels of concern.

Low resolution data and 'fingerprint' patterns derived from any applicable technique could be used to evaluate the sameness of substances from different companies, and thus contribute to SIEF formation. This would limit the initial disclosure of compositional detail - or at least, its assignment to chemical structure - with the advantage that pre-SIEF discussions could progress while collaborators build trust, or participating competitors develop suitable data protection arrangements. However, pattern-matching approaches are often based on libraries of spectra built up over many years, and caution in their use is appropriate when it comes to decision making. We recommend validation of the primary reference underlying any significant library match.

'Broad brush' data could also help provide a shared profile of the substance for the joint registration dossier. Low resolution profiling may give clear-cut evidence as to the presence or absence of a key constituent that would affect the EC Inventory name and number of the substance. Likewise, having just enough data to quantify a key impurity may facilitate the sharing of hazard testing data, or help determine the CLP classification.

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<sup>64</sup> A substance as defined by Article 3(1) of the REACH Regulation excludes 'any solvent which may be separated without affecting the stability of the substance or changing its composition'. Nevertheless, making measurements on a dissolved substance may be scientifically appropriate to provide data about its solvent-free composition.



### 2.2.11 What substance identity data must each individual registrant provide?

For a well-defined substance, the identities of the main constituents, which contribute to the name, are usually the same for all members of a SIEF, but their concentration ranges may differ. Registrations may cover products derived from a variety of starting materials and processes, so the impurity profiles may differ in nature as well as concentration.

The layout of the IUCLID sections for submitting substance identity data is the same for individual and joint registrations.<sup>65</sup> Each individual registrant's dossier needs to include data on their substance, as manufactured, including:

- As far as possible, the main constituents, and their typical concentrations along with upper and lower limits
- Purity, based on the concentrations of the main constituents
- Impurities. We recommend that particular attention is paid to describing and quantifying any impurities which might be less clearly summarised in the joint submission. For example, one company in a SIEF may have experience with a group of impurities sharing a distinctive molecular structural motif. These could arise from the choice of starting materials, reaction conditions and equipment, or from non-attributed process variability or the environment. The individual registrant might already know that low concentrations of similar impurities are hazardous, and may need to carry out more detailed identification and quantification which cannot be fully presented in the joint dossier for reasons of complexity, confidentiality or timing. The individual submission should help to ensure that any potential risks are duly considered.

The individual specification should be within the scope of the material used for hazard tests on the substance. Registrants will be aware that the impurity profile can provide clues to production methods, including the starting materials, solvents, catalysts and other processing aids, and may choose to flag certain details of the submission as confidential.

### 2.2.12 ECHA looks for consistent substance identity data. What does this mean?

ECHA may consider a submission non-compliant unless the data entered in the substance identity fields (1.1, 1.2 and 1.4) of the IUCLID dossier preparation software are consistent, and enable the substance composition to be verified. For example, the substance name (IUCLID section 1.1) needs to take account of the number and concentration of identified constituents (IUCLID section 1.2). If reported techniques yield different types of compositional data, for example on counter-ions or certain groups of constituents, this should be explained.

The Agency looks for consistent substance identity data. What does this mean, in practice? There is a logical link between the name of a substance, its chemical composition and the analytical data. When an inconsistency is noted between these three elements of substance identification, ECHA may be in a situation where the exact identity of the substance can not be established.

### 2.2.13 How to report variability in the substance specification?

In real life, the concentrations of all constituents will be subject to some degree of variability. The concentration ranges of the constituents should be provided. Also, more than one composition can be reported, for example to reflect different grades of a single substance, or manufacturing sites.<sup>66</sup>

<sup>65</sup> Cf. ECHA, IUCLID 5 end-user manual. 2010, chapter E.1.1 to E.1.5:

[http://iuclid.echa.europa.eu/download/documents/usermanual/iuclid5\\_usermanual\\_2010-02-12\\_en.pdf](http://iuclid.echa.europa.eu/download/documents/usermanual/iuclid5_usermanual_2010-02-12_en.pdf) (NB large file)

<sup>66</sup> ECHA, Data submission manual - Part 18 - How to report the substance identity in IUCLID 5 for registration under REACH. ECHA-10-B-27-EN, June 2010, chapter 2.3.Q&A8: [News - ECHA](#)

It is not usually necessary to prove variability by submitting multiple chromatograms. However, if the same substance is obtained from different suppliers, any differences in the impurity profiles should at least be described.

### 2.2.14 How to establish the identity of a UVCB substance?

In this case, there is no hard and fast distinction between main constituents and impurities. Registrants are expected to carry out the usual spectroscopic and chromatographic analyses, and to provide whatever evidence they can about the make-up of each constituent, aiming to report its identity, typical concentration and range. This is expected for constituents amounting to 10 % or more of the substance. All constituents that affect classification and/or PBT assessment should also be identified. Unknown constituents should be described generically - for example, in groups based on clear features of the analytical data (e.g. by chain length, functional group, or double bonding pattern).

### 2.2.15 How can substance stability issues be tackled?

Instability can 'move the goalposts' during substance identity studies, and is likely to be even more of a problem during hazard testing under a range of environmental and biological conditions. Precautions will be needed throughout sampling, transportation, storage, sample preparation and measurement to preserve the 'dossier substance'<sup>67</sup> both qualitatively and quantitatively. Breakdown products are likely to complicate the analytical data, and may need to be considered when assessing the fate and consequent risk associated with the dossier substance. Destructive methods of analysis will be of limited value in this situation because they will tend to blur the distinction between a substance and its breakdown products.

Part of the analytical chemist's skill lies in knowing which sources of uncertainty in the measurement process may be significant for a particular substance, and how to control them. Experienced scientists will be able to recognise and control the potential effect of variables such as timing, temperature, pH, moisture, air, dilution, the sample container, interactions between constituents and impurities, and stabilising additives. Laboratory procedures can often be carried out under cryogenic, desiccative or anoxic conditions. Control experiments can be performed to monitor and compensate for substance breakdown. For a practical example, see case study 3.

#### Case study 3

One of the substances we studied was manufactured by reacting several starting materials in a particular order, as is often done to produce functional organic structures that perform specific tasks in mixtures such as lubricants, paints and adhesives. This complex structure was unstable in water and damp air, reverting back to starting materials including amines and alcohols. Results from the standard substance identification techniques - UV-Vis, IR, NMR and chromatography - were difficult to interpret (although HPLC was of some use to confirm the partition coefficient and adsorption coefficient range). Performing UV-Vis over a range of pH values established that the substance was more stable under alkaline conditions. HPLC-MS was subsequently performed at pH 8 in 20:80 (v/v) water:acetonitrile. The results provided evidence for the theoretical structure and degradation pathways of the substance, but it remained challenging to make a distinction between peaks that belong to the substance and those that belong to the starting materials and breakdown products.

For toxicological and environmental assessment, HPLC studies were refocused on breakdown products, including alkylamines and water-soluble alcohols. The data provided sufficient

<sup>67</sup> i.e. a substance which is subject to registration through a SIEF, or where applicable to the inquiry procedure or a PPORD notification.

evidence that the substance would break down rapidly in water. Thus the results of hazard tests performed on the breakdown products (as well as the starting materials for the synthesis, which are of similar structure) could be read across<sup>68</sup> to the substance, and only a few additional procedures are required, such as *in vitro* irritation and *Daphnia* immobilisation. Bacterial sludge inhibition and biodegradation tests, which are easy and inexpensive, will also be carried out to confirm that read-across is appropriate.

### 2.2.16 Should I determine optical isomers?

If different optical isomers exist, yes - they count as separate constituents of the substance<sup>69</sup>. IUCLID includes an 'Optical activity' field which prompts for an overview, while further data can be given as part of the description of analytical methods. The format of the reported data may depend on the number of chiral centres in the substance and on the measurement techniques. Modern techniques are often based on the interaction of the constituents with chiral media, e.g. chiral chromatography.

If polarimetry is used, we suggest that laboratories could record the magnitude and sign of the optical rotation for the substance, and provide an interpretation in terms of the proportions of stereoisomers. Measurements on fractions of the substance may be needed to complete the breakdown of its optical activity. Accompanying data would include the measurement conditions - optical wavelength (particularly if not 589 nm), optical path length, concentration of the measured sample, solvent, temperature - and other details of the method, e.g. instrument, sample preparation, blanks, standards and controls, replication, concentration dependence.

### 2.2.17 Should I generate data on surface chemistry?

New requirements for safety data sheets, which amend REACH Annex II, state that appropriate and available safety information on surface chemistry should be indicated.<sup>70</sup> We would welcome views on the need to develop advice about suitable analytical approaches.

### 2.2.18 Are there special requirements for substances in the nanoform?

In 2007, ECHA guidance stated: 'The current developments in nano-technology and insights in related hazard effects may cause the need for additional information on size of the substances in the future. The current state of development is not mature enough to include guidance on the identification of substances in the nanoform in this guidance document.'<sup>71</sup>

Clearly the situation is evolving, and seems likely to continue doing so. One issue will be the clear definition of substances within scope (see case study 2b).

#### Case study 2b (continued from Question 2.2.9)

At concentrations below 1 000 mg L<sup>-1</sup>, mixtures of a certain silicate substance with water are clear, but could be described as nano-suspensions because the substance does not fully dissociate into the dissolved state. A side-effect of this colloidal character is that chromatography cannot be performed; the value of UV-Vis, IR and NMR is also questionable, as meaningful interpretation may prove challenging. At present we are unsure whether such a substance might be considered a nanomaterial.

<sup>68</sup> Read-across is the inference of properties using information from structurally related substances (REACH Regulation, Article 13; Annex XI section 1.5; and *passim*)

<sup>69</sup> ECHA, Data submission manual - Part 18 - How to report the substance identity in IUCLID 5 for registration under REACH. Chapter 2.3.Q&A4

<sup>70</sup> Regulation (EU) No 453/2010 amending Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), Section 3 (pages 7 and 27): <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2010:133:0001:0043:EN:PDF>

<sup>71</sup> ECHA, Guidance for identification and naming of substances under REACH, page 24

ECHA has published guidance on data submission procedures for nanomaterials.<sup>72</sup> A nanomaterial can be registered in its own right, or as a form of a more widely defined substance. This question of substance sameness is for registrants to decide, perhaps with the aid of comparative measurement; the decision affects data entry procedures in IUCLID.

There are still no specific information requirements for nanomaterials, but 'registrants are encouraged to include any information they consider relevant to better describe the substance and to demonstrate its safe use'.<sup>73</sup> By way of example, ECHA refers to OECD guidance.<sup>74</sup> The analytical information should, as usual, be sufficient to enable the substance to be identified, and any methods that fulfil this requirement may be used - for example, those listed by OECD.<sup>75</sup> The formula entered for a nanomaterial should be descriptive of the composition and bonding.<sup>76</sup> There is also space to submit a free text description of the main constituent of the nanoform.<sup>77</sup>

Nanomaterials are a chemically and structurally diverse category. Moreover, the risks they pose may depend not only on molecular, but also nanoscale and (through aggregation) microscale structure. Along with mainstream analytical techniques such as those mentioned at 2.2.5 and 2.2.7 above, advanced (electron) microscopies and particle size analysis are likely to feature in characterisation work. In conjunction with high performance analysers such as ICP-MS, specialised separation techniques like field flow fractionation (FFF) could be used to refine understanding of the relationship between chemistry and particle size. Low-capital approaches to the sizing step, such as nanofiltration, may also be worth exploring.

The IUCLID software provides for the form of a substance subjected to hazard testing to be clearly specified, even if there is more than one nanoform. It can be categorised as 'nanomaterial', further described (for example as 'fibre'), and linked by means of a user-defined text label to the appropriate block of compositional data.<sup>78</sup> It may be that the text label could be incorporated within explanatory wording if the substance identity differs slightly from, but is justified as representing, the form subjected to hazard testing. In any case, the exact details should be made clear by appropriately describing each batch of material used in hazard testing, including its 'identity, batch number, purity, composition, concentrations, or other defining characteristics (e.g. nanomaterial size distribution)'.<sup>79</sup> This batch-by-batch data requirement is based on GLP<sup>80</sup>.

For nanomaterials, certain physicochemical endpoints such as Particle size distribution (Granulometry) may require particular attention.<sup>81</sup> Registrants may report on additional properties, such as those covered by OECD guidance, for example: specific surface area, zeta potential, porosity, surface chemistry, agglomeration/aggregation, crystalline phase, photocatalytic activity, pour density, and aspect ratio/shape.<sup>82</sup>

<sup>72</sup> ECHA, IUCLID 5 guidance and support - Nanomaterials in IUCLID 5.2. Version 1.0, 1 June 2010:

[http://iuclid.echa.europa.eu/index.php?fuseaction=home\\_documentation#reachmanual](http://iuclid.echa.europa.eu/index.php?fuseaction=home_documentation#reachmanual)

<sup>73</sup> ECHA, Nanomaterials in IUCLID 5.2, page 4

<sup>74</sup> Organisation for Economic Co-operation and Development - Environment Directorate, Publications in the series on the safety of manufactured nanomaterials:

[http://www.oecd.org/document/53/0,3343,en\\_2649\\_370153404\\_37760309\\_1\\_1\\_1\\_1,00.html](http://www.oecd.org/document/53/0,3343,en_2649_370153404_37760309_1_1_1_1,00.html). Note particularly that the following update on testing has become available since the ECHA reference was published: Guidance manual for the testing of manufactured nanomaterials: OECD's sponsorship programme. First revision, 2 June 2010, OECD Series on the Safety of Manufactured Nanomaterials No. 25, ENV/JM/MONO(2009)20/REV:

[http://www.oecd.org/officialdocuments/displaydocumentpdf/?cote=env/jm/mono\(2009\)20/rev&doclanguage=en](http://www.oecd.org/officialdocuments/displaydocumentpdf/?cote=env/jm/mono(2009)20/rev&doclanguage=en)

<sup>75</sup> ECHA, Nanomaterials in IUCLID 5.2, pages 10-11

<sup>76</sup> ECHA, Nanomaterials in IUCLID 5.2, page 16

<sup>77</sup> ECHA, Nanomaterials in IUCLID 5.2, page 15

<sup>78</sup> ECHA, Nanomaterials in IUCLID 5.2, pages 8-9

<sup>79</sup> ECHA, Nanomaterials in IUCLID 5.2, page 22

<sup>80</sup> Specifically, testing should be performed in accordance with the requirements of Directive 2004/10/EC on the harmonisation of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances

<sup>81</sup> Cf. ECHA, Nanomaterials in IUCLID 5.2, pages 19-20

<sup>82</sup> ECHA, Nanomaterials in IUCLID 5.2, pages 20-21

The European Commission may propose changes to the REACH Regulation concerning nanomaterials in 2011.<sup>83</sup> The Commission have also now agreed a definition of a nanomaterial.<sup>84</sup>

## 2.2.19 Have you any practical tips on submitting analytical reports?

Based on current experience, we recommend:

- Use the same sample for all analytical work if possible. Otherwise, establish sameness by analysing all available samples at the same time (under identical measurement conditions)
- Record the substance name (consistent with the nomenclature to be used for registration), a batch number or laboratory code with dates, identity of the facility where the analysis took place, and details of equipment, sample preparation, and methods. A certificate of analysis format could be used to structure the information
- ECHA is liable to question dossiers unless they contain all the standard spectra, and as much detail as is necessary to replicate the measurements - particularly for quantitative procedures such as chromatography. The biggest cause of failure for Inquiries is the quality of the analysis.
- Write analytical reports as if they were intended for the sales manager - they need to be legible, relatively easy to understand, and show that they relate to the material actually being supplied; structures and reaction mechanisms are also good as they will help provide a picture of the substance and possible by-products
- Try to get all the spectra into one report to attach to the IUCLID file. Although it is possible to create repeat blocks to add separate files, in practice a single spectra report is the best way. The chromatography and other analysis should again be condensed into a single report and attached to the IUCLID section asking for these details.

## 2.2.20 What measurement is required for a CLP notification?

The CLP obligation to notify classification and labelling to ECHA applies to a wider range of substances than REACH.<sup>85</sup> Companies must classify substances based on the available hazard data.<sup>86</sup> To make a meaningful classification, a clear substance identity is needed. The identity data that actually need to be submitted are a subset of the REACH requirements, as they are specified by section 2.1 to 2.3.4 of REACH Annex VI.<sup>87</sup> The notification must include at least one entry defining a composition (i.e. listing constituents, impurities and additives) for the whole substance. The underlying evidence base, consisting of spectra, chromatograms and a self-sufficient description of the analytical methods, does not need to be submitted. However, we suggest that laboratories do record and retain all the underlying details, in case the authorities ask to inspect them.

The whole substance should be accounted for by the composition data. The upper and lower bounds of the concentration range for each constituent should, as far as possible, be provided.<sup>88</sup> If applicable, provide information on the optical activity and typical ratio of (stereo)isomers.<sup>89</sup>

<sup>83</sup> Council of the European Union, 2009 Environment policy review. SEC(2010) 975, 13 August 2010 - page 19:

<http://register.consilium.europa.eu/pdf/en/10/st12/st12830.en10.pdf>

<sup>84</sup> European Commission, DG Environment, nanomaterial Definition: [European Commission - Environment - Chemicals](http://ec.europa.eu/environment/chemicals/nanomaterial_definition.htm)

<sup>85</sup> ECHA, Practical guide 7: How to notify substances in the Classification and Labelling Inventory. ECHA-10-B-01-EN, 19 May 2010 - chapter 2.2: [http://echa.europa.eu/documents/10162/17235/pg\\_7\\_clp\\_notif\\_en.pdf](http://echa.europa.eu/documents/10162/17235/pg_7_clp_notif_en.pdf)

<sup>86</sup> CLP Regulation, Article 5

<sup>87</sup> ECHA, Introductory guidance on the CLP Regulation. ECHA-09-G-01-EN, 25 August 2009 - page 78:

[http://echa.europa.eu/documents/10162/17217/clp\\_introductory\\_en.pdf](http://echa.europa.eu/documents/10162/17217/clp_introductory_en.pdf)

<sup>88</sup> ECHA, Practical guide 7, chapter 4.3

<sup>89</sup> ECHA, Data submission manual - Part 12, chapter 5.6

Preparations for a classification and labelling notification may involve some hazard testing, particularly for physicochemical properties. If so, it may also be necessary to measure and record data showing that the test material is representative of the notified substance.

If different classifications are submitted for the same substance, the reasons should be given.<sup>87</sup> The justification may hinge on data concerning impurities that are relevant for the classification.

### 3. Glossary of Terms

CLP	Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures, as amended
DEPT	Distortionless Enhancement by Polarization Transfer, allows the determination of the multiplicity of carbon atom substitution with hydrogens in NMR
GLP	Good Laboratory Practice; Accreditation scheme
ECHA	European Chemicals Agency
IUCLID	International Uniform Chemical Information Database, a software application to capture, store, maintain and exchange data on intrinsic and hazard properties of chemical substances
OECD	Organisation for Economic Co-operation and Development
PBT	REACH substances which are Persistent, Bio-accumulative and Toxic
PPORD	Product and Process Oriented Research and Development
REACH	Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals, as amended
SIEF	REACH Substance Information Exchange Forum
SME	Small or Medium-sized Enterprise (<250 employees)
SVHC	REACH Substance of Very High Concern
UVCB	substances of Unknown or Variable composition, Complex reaction products or Biological materials

## 4. Request for feedback

We hope this advice is a useful starting point. Please be aware that any decision to update and improve the document may depend on your feedback. Amendments and comments of all kinds would be most welcome. Please contact:

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We would particularly like to hear about any measurement-related topics and issues that you would like to see addressed in further editions.