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Task Force "Characterisation"- Report

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1. Executive Summary

This report has been produced by the Task Force "Characterisation" as a response to the request from the EC. The report aims to reinforce the activities of the European Materials Characterisation Council (EMCC), a European initiative set up at the beginning of 2016 in order to strengthen the existing European Materials Characterisation Cluster (created at the end of 2014). The aim of the EMCC is to assist the process of developing and improving characterisation methods and techniques as core tools to support upscaling of nanomaterials and advanced materials towards industrial exploitation. The report contains suggestions for strategic steps to be taken in order to identify the number, type, geographic distribution and complementarities between the several fragmented characterisation infrastructures (excluding the large-scale ones) in Europe. This information will subsequently facilitate the European industry to access European characterisation infrastructure and competence. It also recommends actions to achieve organisational and technical targets, which will facilitate industrial production and accelerate the industrial material production from the lab to the production scale via utilisation of material characterisation methods.

The report is structured in five main sections; Background, Characterisation Landscape, Industry Needs, Focus Actions, Concluding Remarks and Suggested Strategy and an effort has been made so that it:

- is compatible with the content of the Industrial Technologies Programme.
- contains **ideas and proposals** for actions in the characterisation field within the Industrial Technologies Programme.
- suggests **mechanisms of support and coordination**, at a regional, national, and international/European level, as well as provides suggestions on how synergy can be reinforced or created.
- proposes actions in priority ranking in the form of suggested strategic steps for the fulfilment of organisational and technical targets.
- has taken into account background work done at European level by the EMCC.

The main recommendations are summarised as follows:

- Initialise national research infrastructure roadmaps in all member states aiming to establish and/or develop national infrastructures within materials characterisation covering regional and national industrial needs. These roadmaps will screen potential participants in ESFRI projects (see below), ensure regional and national relevance, force active involvement of all member states, avoid brain drain, maintain regional balance, ensure coherency and enhance technical complementarity.
- Create a European database with existing characterisation infrastructures and competence.
- Initialise one or several ESFRI projects within characterisation methods to reinforce European coordination based on networks of national infrastructures.
- Initialise national dedicated programs for method development for established and new characterisation methods. The programs should require participation of the (local) industry, experts from academia and research institutes and will include education and training (PhD programs) for generating future characterisation experts.

Industrial partners from different sectors will benefit by sharing knowledge and experience relevant to industrial scale characterisation and testing.

- Support the development of low-cost multi-functional and multi-scale characterisation methods for industrial applications
- Develop high throughput, accurate and multi-functional inline measurement methods for industrial applications
- Development of nanomaterials, new functional and/or smart materials generates new characterisation challenges. It is anticipated that in the future, next generation characterisation methods for nanomaterials and new functional materials will focus on nanosurface properties and quantum-mechanical phenomena. Examples of actions may include, development of a European Technology Roadmap for Nanocharacterisation, research funding (national and EU, eg. FET, NMBP, ERC) supporting long-term instrument and method development, development of an ESFRI based project for long-term instrument and method development.
- Develop feasible and standardised characterisation methods to validate in silico modelling and predictions of advanced material or nanomaterial performance and behaviour during the entire life cycle.
- In the course of development and upscaling of advanced materials or nanomaterials robust characterisation methods are crucial regarding implementation of regulations, regulatory preparedness and safety aspects. Forming clusters and trilateral dialogue arenas between instrumentation/method developers (academic and non-academic), manufacturers and industrial end-users facilitates knowledge transfer and, consequently, improves quality of measurements.
- Formation of characterisation clusters with adequate and complementary expertise and methods. These clusters will improve collection of reliable data about hazardous material properties, facilitate identification and specification of all potential risks and enhance safety along the entire product development value chain.
- Provide scientific evidence and guidance documents for the regulatory definition of characterisation toolboxes and frameworks for product development.

2. Background

2.1. General

A research survey conducted by the EMCC showed that 95% of EU funded projects apply metrology and characterisation techniques to support engineering and upscaling[1].

Characterisation methods are recognised as by far the most important tools for *Engineering & Upscaling*, whilst improved characterisation methods, in line metrology systems, in situ characterisation for real time process control are amongst the most important technological developments envisaged to advance engineering and upscaling[2].

The following paragraphs contain a brief overview of various characterisation types broadly divided into two categories. A third category on (nano) particle characterisation is also included due to the increased attention in this field over the last years.

2.2. Classification in categories

Characterisation methods can be divided into two broad categories; a) those used to identify the nature (structure, chemistry) of the material and b) those evaluating the material performance.

a) **Identification** via structural and chemical characterisation

This category includes the characterisation types used for material identification and embraces methods used to identify micro/nano-structural features (geometry, morphology, defects, etc. of bulk, surfaces, interfaces) as well as the chemistry and composition at nano-, micro-, macroscale (in the bulk, at surfaces, along interfaces). Several microscopy and spectroscopy/spectrometry techniques, based on the interaction of electrons, ions, x-rays with the material, fall in this category.

b) Characterisation of material **performance** at macro-, micro-, nano-scale

This category comprises:

Characterisation of mechanical properties and constants via relevant tests: tensile/yield strength, modulus of elasticity, fracture toughness, fatigue, creep,

Assessment of the environmental behaviour such as, transformation processes (e.g.: corrosion, oxidation, dissolution, homo/-heteroaggregation), colloidal stability and mobility

Measurements of mixed properties such as stress corrosion, corrosion fatigue, creep, delamination, debounding, and others.

Other functional characterisation including (but not being limited to) characterisation of optoelectronic, magnetic, thermal, biological properties, solubility (e.g. in environmental and biological media) etc.

[1] "EMCC Survey of development needs for characterisation", "Engineering & Upscaling Survey Analysis, Fantechi, Goldbeck, Boskovic)

[2] EMCC (2015). Characterisation: a central pillar for Engineering and Upscaling. A study based on Characterisation Cluster and Engineering & Upscaling Cluster surveys and workshops in 2014/15. European Materials Characterisation Council (EMCC).

c) Characterisation of nanoparticles/nanomaterials

In line with the above text, particle characterization techniques may be also divided into two broad categories; those used for identifying particle properties and those for performance evaluation.

Identification of nanoparticles and/or nanomaterials is done via a minimum set of eight properties, which are commonly used by researchers, manufacturers, developers, commercial trade, consumers, toxico- and ecotoxico-logists and data mining. These are; size and size distribution, surface area, surface charge, zeta potential (for particles in liquid media), crystallinity, aggregation/agglomeration, chemical composition. Moreover, properties such as chemical oxidation state and morphology are important with the latter being critical especially for high aspect ratio materials, which have implications on carcinogenicity / mutagenicity and genotoxicity.

The performance of nanomaterials and products containing nanomaterials is evaluated via physico-chemical properties, mechanical properties, magnetic properties, electrical properties, optical properties and thermal properties. By far particle size and particle size distribution (PSD) are of the most important physical properties of particulate samples and they have a direct influence on material properties such as:

- Reactivity or dissolution rate for e.g. catalysts, tablets
- Stability in suspension for e.g. sediments, paints
- Efficacy of delivery for e.g. asthma inhalers
- Texture and feel for e.g. food ingredients
- Appearance for e.g. powder coatings and inks
- Flow ability and handling for e.g. granules
- Magnetic behaviour e.g., storage memory and sensors
- Viscosity for e.g. nasal sprays
- Packing density and porosity for e.g. ceramics.
- Porosity e.g. biomedical devices and polymers
- Stiffness e.g. cardiovascular stents
- Shape e.g. medical devices and sensors

Nevertheless, in real life measuring particle size and understanding how it affects products and processes can be critical to the success of many manufacturing processes. Particles are 3-dimensional objects, and unless they are perfect spheres, they cannot be fully described by a single dimension such as a radius or diameter.

In order to simplify the measurement process, it is often convenient to define the particle size using the concept of equivalent spheres. In this case, the particle sizes defined by the diameter of an equivalent sphere having the same property as the actual particle such as volume or mass for example. It is important to realize that different measurement techniques use different equivalent sphere models and therefore only in very few, very well defined cases will give exactly the same result for the particle.

Many particle-sizing techniques are based on a simple 1-dimensional sphere equivalent measuring concept, and this is often perfectly adequate for the required application.

Measuring particle size in two or more dimensions can sometimes be desirable but can also present some significant measurement and data analysis challenges.

Therefore, careful consideration is advisable when choosing the most appropriate particle sizing technique for specific application. Such a careful consideration should be brought to each technique suitable and appropriate to characterize any other properties.

To conclude the characterization of nano-objects and products containing manufactured nanomaterials requires a very careful analysis and full knowledge of the expected target, as many properties are instrumental technique dependent.

3. Characterisation Landscape

3.1. General

Material characterisation is a wide field with diversity within both materials and techniques. Commercially available instruments can today be successfully used to accomplish a large variety of characterisation tasks. The price range for these instruments spans from a few hundreds to several millions euro. More specific characterisation tasks require tailor-made equipment and often industrial trouble shooting necessitates the combination of various techniques and subsequent expertise as no single technique can provide all information needed. Moreover, it is a rather common practice that new characterisation technologies are initially tried and established in the research market.

The market for characterisation and testing equipment is rather small, competitive and dominated by small companies with innovative products. Hence, it is often hard to establish a good business case. The small market size and the wide range of test parameters to be covered require development of multi-parameter and wide measurement scale instruments in order for the manufacturer to establish a successful business case. However, this is technologically challenging.

Furthermore, the development of new functional materials and nanomaterial systems often requires development and utilisation of new characterisation techniques. Techniques based on the interaction of the material with electrons and ions currently dominate over traditional techniques based on photons (light), due to the superior spatial resolution of the former, which is often required for the characterisation of novel materials/nanomaterials. As a result of high technological demands in vacuum systems, irradiation sources and detectors, high spatial resolution techniques are difficult to implement in industrial upscaling. Typical limitations account for difficulties to reduce measurement time, to provide higher throughput, to perform in-line and in-operando characterisation. In addition, this type of instrumentation requires high investment, maintenance and analysis/service cost.

At European universities and research institutes many groups are engaged with cutting edge research having too low TRL level but they nevertheless generate knowledge which may find industrial application in a long term perspective (15-20 years). These groups operate modified or tailor made equipment in these projects. This fact, considering the limitations mentioned in the paragraph above, shows that there is a significant innovation potential, which is currently not clearly realised and explored. This potential can be utilised in order to overcome technical difficulties in industrial upscaling of advanced characterisation methods.

3.2. Report restrictions

Since the characterisation field addresses a wide range of materials and applications, the present report is confined as follows:

1. The report refers to characterisation of materials from the lab to the industrial scale and not assembled multicomponent devices and products.
2. It refers to materials used in industrial activities within the Industrial Technologies Programme.

The report includes ideas and suggestions within the following classes of materials:

Lab scale synthesised inorganic (metallic, ceramic, glass), organic (synthetic and natural polymers etc.) and hybrid materials, in various forms (particles, thin films, bulk materials, nanostructured/functionalised surfaces), and formulated active pharmaceutical ingredients, eccipients and carriers.

Industrially produced/processed materials such as, semiconductor industry products (wafer and thin films substrates, logic circuitry, etc.), pharma industry products (e.g. polymers, organic vectors, nanoparticles etc.), chemical industry products (polymers, pigments, catalysts, particles, etc.), processing/manufacturing industry products (metals/alloys, oxides and ceramics, polymer and composites, natural materials, industrial minerals, etc.), biomaterials (biopolymers, scaffolds, woven fibres, excluding advanced therapeutics).

4. Industry Needs

4.1.Industrial needs for characterisation at different stages of product development.

1. Early Research and Development stage (experimental proof of concept and validation in lab, TRL:3-4): access to a wide range of characterization techniques, (in house, national and international infrastructures); characterization of critical material and product properties during the development of new or improved products (points I, II and IV below)
2. Transition stage (validation and demonstration in industrial environment, TRL: 5-7): selection and acquisition (transfer) of know-how and techniques for production. Access and availability of the key techniques identified at stage one for the verification of the product quality and properties at pilot lines during the scale-up process.
3. Production stage (TRL: 8-9): two types of needs: (a) at- and in-line monitoring, certification; failure analysis and trouble shouting (points I, II, III and IV below) where rapid and/or real time techniques are of high priority, (b) at- and/or in-line characterization techniques towards 100% production quality control which should be applicable to large production quantities in order to justify high costs. At this stage, reliability and reproducibility of measurements should be ensured and fast non - destructive testing that does not interrupt production and limits downtime should be preferred. Off-site analysis and response should be fast and proficient.

4.2.Specific industrial needs for characterisation

I. Access to characterisation infrastructure. Characterization tools available for direct access by industry users.

Industries need fast access to both standard and state of the art research infrastructure. Large-scale facilities, such as a synchrotron, are available for industry users through their access programs. Outside joined innovation or competence building projects the industry employees use the instruments on hourly basis. Many industries especially SMEs do not have the financial resources or do not prioritise purchasing of expensive characterization instruments. A network of national characterization infrastructures could provide and guarantee access to unique and costly instrumentation. It is important to provide distributed and flexible access, since industry often wishes fast and easy access for several instruments and methods offered by the characterisation infrastructure.

II. Access to characterisation competence

a. The importance of competence associated with highly sophisticated characterization tools is in general underestimated. Small and medium sized companies usually lack this competence, which could be provided through a network of skilled operators at academic and research installations.
b. The above is also valid for large enterprises when they operate outside their core competence or when they want to diversify their products by adopting novel technologies.
c. Many industrial R&D and troubleshooting challenges, require access to high technical competence in various methods along with a pool of suitable instruments

III. Access to new characterisation technologies

a. Need for having access to databases in which new characterisation technology providers are listed. Very often this is a key barrier for many companies when they seek for new techniques and even new characterization methods
b. Need for new low cost, off-line characterisation instruments on the market (e.g. table top instruments, toolbox systems with interchangeable functionalities). These instruments should preferentially provide high quality measurements, even though these measurements may be at a lower specification level than today's state of the art in research activities. Instruments with very high specification level used in research activities are often not necessary for industrial purposes.
c. Need for at and in-line systems for production control. Reliability and high throughput are the most important properties together with user-friendliness. In many cases, manufacturers rely on a certain recipe to produce a certain material, or a certain quality of a material. This does not necessarily require complicated analysis of physical properties but most likely simple instrumentation for real time monitoring of some process parameters (e.g. temperature, pressure, atmospheric composition, etc.). In some cases, this requirement is covered by portable equipment (e.g. pyrometers or thermal imaging cameras, pressure gauges, etc.) or in-line equipment (e.g. NIR reflectometers to monitor e.g. moisture). Ideally, in some cases the instruments for at-/in- line characterisation should be multi-functional (new functionalities may be required), multi-range and provide measurement of all (or most of) relevant material parameters in a single apparatus. There is also a need for in operando (in liquids/solvents or in-pressure/temperature) testing and characterization. Methods for e.g. particle or droplet sizing in various dispersion media, and for in-pressure measurements exist but they are either not widely spread, or partially difficult to handle, or not easy to find in the market.
d. Need for off-line systems with increased functionality measuring new material properties. In this context development of new measurement principles that support the product development and production process, is also important.

e. Development of sampling tools to study intermediate products of the production lines and transferring to state of the art characterization stations available in academia and/or research institutes.
f. "New characterisation technology" may be a relative concept. What is a "standard characterisation method" in e.g. inline monitoring for a specific industry may be proved to be a "novel" characterisation technique for a different industry in another sector. In this respect, establishment of communication platforms between industries from different sectors will be beneficial.

IV. Access to measurement data

a. Databases of new materials and their properties (as e.g. refractive index, heat transfer coefficient, Young's modulus, fracture mechanical properties, conductivity, and expansion coefficient) should be made available.
b. Measurement data to confirm modelling data of materials and systems should be made available and re-useable.

V. Access to calibration standards and systems.

a. Reference materials should be readily available at low cost by National and/or EU official bodies and authorities dedicated to standards and metrology.
b. Interlaboratory comparison studies to produce unified protocols and promote data integration should be conducted.

VI. Some specific technical needs

a. Particular emphasis on light scattering, light-based spectroscopy (e.g. near IR), sonar techniques
b. The need for robust porosity/surface area measurements particularly rapid analysis for large pore size ranges
c. Particle sizing is seen as a real problem – are there techniques, which can be used during reactions?
d. XRF is seen as a critical tool for rapid elemental analysis and method development should emphasise towards expanding capability.
e. Need for surface sensitive techniques (XPS, AES) and depth resolved techniques (SIMS)
f. In-line chromatography and the speed of GC and HPLC is viewed as critical for analysis of reaction mixtures in solutions
g. Molecular weight of polymers/proteins was mentioned a few times as a problem (e.g. via GPC or MALDI TOF-MS)
h. Sampling is an issue. For example, in XRD of powders is it practical to measure 10s of samples a day? High throughput XRD is available in some research laboratories. What other techniques (e.g. RAMAN?) might be used for phase determination?

4.3. Recommendations

1. Creation of national/regional knowledge hub(s), where companies can address their "non-standard" needs for characterisation competence with respect to materials and material functions of their interest. This will ensure that industry receives feedback from a wider "competence environment". Training people for acting as interfaces between the academia and the industry. These actions may vary in their details from country to country and from region to region depending on the existing operating national/regional R&D model but it is of key importance. What is missing at present in some countries/regions is a diffuse and properly working interface. In some countries the interface between academia and industry is covered to a large extend by national or independent research institutes. EU projects, such as *QualityNano*, have identified some EU research nanoanalytical centres, but there are surely many more.

2. As a continuation of (1), we suggest the creation of a network of these knowledge hubs, at European level, allowing a choice for the industry at a broader scale. Such a network could link hubs of different countries to share experiences both on practicalities and on scientific competence.

3. Creation of national/regional databases comprising (a) the instruments available, (b) the competences of the owners of the instrumentation with respect to the materials classes/types already studied/characterised and (c) a track record with industrial activities/projects. This action should not require very substantial investments and in a short time may produce a self-sustained tool. Similar actions have already been realised on national level by e.g. some university-analytical centres in England, Germany, France, and Spain. In France for example, such a database has been developed by the "Club Nanometrologie" from data collected from academia, public and private research institutes. It should be in open access once IT services upload it on the web.

4. Industrial exploitation of results from academic research is often hindered by the fact that the quantity produced at lab scale is not enough for relevant (functional and productive) tests in industrial scale. The creation of dedicated processing infrastructures to shift production of materials with interesting/promising physico-chemical properties from the gram to the kilo/kilos scale should be useful. Alternatively, funding sources should be available for successful applicants (consortia between companies and research partners) for using existing pilot scale infrastructures to produce adequate quantities and to obtain a first evaluation of more reliable production costs. There have been EU-research and industrial leadership calls especially funding this type of development. However, for quite a few of these calls only 1-2 out of 60-120 applicants received funding.

5. Provided that characterisation instrument producers see valuable market possibilities, the triangle between industrial end users, characterisation instrument producers and academic/research institutes should be activated. Direct interaction between industrial end-users, manufacturers of characterisation instruments as well as research and academic partners is required for further enhancing, calibrating, and developing the characterisation tools and methods. In many cases, the physical quantities (measurants) are estimated after applying mathematical formulas incorporated in software algorithms. The accuracy of the

results should be confirmed by independent methods whenever is possible and verified in particular in the case of novel materials. We propose opening for dedicated H2020 or similar calls at European and/or national/regional level, with strongly committed industrial participation (end-users, instrument manufacturers). Formation of continuously working triangles (end-users, instrument manufacturers, academic and research institutes) trough validate processes, methodologies and quality assurance are expected to enhance a better communication between the different stakeholders. Strong participation of industrial partners from different sectors and sharing of knowledge and experience relevant to industrial scale characterisation and testing will be beneficial.

6. Creation of big database for new material properties, as for example, the Cambridge Structural Database (CSD) (http://www.ccdc.cam.ac.uk/solutions/csd-system/components/csd/) or NIST data repository for materials. Such database should contain particular sections with specific information on safety and regulation and shall be linked with, e.g., the ECHA database. The investment level should lie essentially at a minimum for personnel, software and data-storage. Upon successful establishment and growth, the system may generate income and become financially independent (like e.g. CSD), via e.g. data provision upon a payment of small fees.

7. Associations of companies, which are active in relevant industrial sectors, should be invited at relatively early stage to advise and contribute to this effort by publication of white papers, open access documents, SOPs or association reflection papers.

8. Enhancement of dialogue with regulators, to create guidance documents characterisation toolboxes and scientific-based frameworks for compliance.

9. Establishment of supporting tools at national and/or EU level to dedicated characterisation laboratories in academic and research institutes for the characterization of novel or "classical" nanomaterials with direct industrial relevance. The support concerns traditional techniques that have to be “optimized” for these novel classes of advanced materials.

10. Provision of access to materials characterisation and database for start-ups and SMEs at a small cost as a part of (inter)national aid for innovation-driven programs.

5. Focus Actions

Surveys and workshops organised by the Characterisation Cluster as well as the Engineering & Upscaling Cluster during 2014-15 have identified several domains, with respect to characterisation research and innovation, where coordination activities could be improved at European level. The identified main domains were; **coordination, standardization, data and information management, upscaling, in-line, in-process, in-situ, multi-technique characterisation, integrated value chain** [see footnote 2 above]. In this section we elaborate on most of the above domains that are defined here as "focus actions".

5.1. Coordinating Network for Characterisation

5.1.1. Introduction

Comprehensive and extensive characterisation infrastructures exist in many European institutions and every member state. In particular, universities and research institutes offer a wide spectrum of characterisation equipment, techniques and associated competence. Many European countries have started, along with the ESFRI roadmap[3][4], to establish national roadmaps for state of the art research infrastructure.

Characterisation equipment are often expensive to purchase, operate and maintain. Sharing costs with industry users, who are able and willing to pay full costs, is an advantage for the practitioners of the research infrastructure. Nevertheless, we should emphasise the difference between large industries and SME in supporting these initiatives.

National infrastructures established under national roadmap initiatives are excellent resources to make characterisation equipment more accessible for industry owing to the following reasons:

a) National infrastructures are selected through a competitive national evaluation process. Thus, the state of the art of both equipment and competence is guaranteed.

b) National infrastructures must have open-access policy and economically balanced running models, avoiding state-aid issues by subsidising industrial use.

c) National infrastructures are already nationally coordinated and often dispersed nationally. That makes it possible to have a single (or very few) national contact point(s) in each country. Competence building of both users and characterisation experts or research engineers are important tasks within these networks.

d) National infrastructures can prepare novel generation of highly qualified researchers to be employed at the interface between academia and industry, promoting a long-term collaboration between these entities. However, this varies from country to country and it is dependent on the national R&D models. In some countries, this interface is served by qualified researchers at public and/or independent research institutes. In general the importance of this role is not yet fully perceived everywhere by governments and academic institutions. One successful example of European advanced characterisation networks is the project ESTEEM2 the Centre of Excellence in Transmission Electron Microscopy for

[3] http://www.esfri.eu/sites/default/files/20160308_ROADMAP_single_page_LIGHT.pdf
[4] http://www.esfri.eu/roadmap-2016

Materials Science (http://esteem2.eu/). ESTEEM2 offered free access to its infrastructure after a simple application and evaluation process. However, the ESTEEM2 project ends on 30th September 2016. EU-Nanomedicine Characterisation Laboratory (EU-NCL) is the most advanced infrastructure funded by the EC-INFRAIA to assist and support the characterization and development of the nanomedicine industry (http://www.euncl.eu/).

Within the ESFRI roadmap, there are only few infrastructures relevant to the materials characterisation covered in this report. Also in the Infrastructure program (INFRAIA) only a few projects have been funded with focus on characterisation (one good example is the NFFA project – www.nffa.eu; another is the EU-NCL).

On the European level, a coordinated network of characterisation infrastructures within the ESFRI program and supported by the INFRAIA Access activities could contribute to:

- A better accessibility of characterisation research infrastructures for the European industry.
- Access to characterisation infrastructures with tailored equipment and competence for the local industry.
- Unified access routines and price systems at all European characterisation facilities.
- Increased competence of both characterisation scientists and users of the characterisation infrastructure.
- Method/methodology development for existing and novel techniques and materials.
- Increased efficiency and associated cost reduction of the existing infrastructures by competence transfer between the infrastructures.

5.1.2. Challenges

- Neither all infrastructures offer open-access for industrial users nor do all of them have a clear price system.
- Although many industrial users are familiar with the characterisation task, very few have the expertise to select the most suitable(s) technique(s).
- It is often difficult to find the right equipment near the industrial end user and the associated access modalities.
- The industry users need fast access to characterisation infrastructure. Sensitive samples are difficult to transport and often industrial users should be on site when the samples are characterised, avoid time-consuming travelling.
- Running characterisation infrastructures in economical balance is challenging because there are few qualified users and research/competence building projects often lack sufficient budget to pay the instrument costs.
- Some state-aid regulations restrict in practice industrial activity to 20% of the capacity of state funded infrastructures.
- Intellectual Properties (IPs) and IPRs may increase administrative time for processing a request for infrastructure use by the industry.
- Personnel in research infrastructures working mainly with cutting edge basic research is sometimes difficult to facilitate industrial users, since the requirements of the user groups are different. In addition, in the academic system, constant personal turnovers hamper networking activities and long-term relations between academia and industry. Availability of staff with industrial conceptualisation is crucial. This is anticipated

mainly as a problem for academic organisations and less for research institutes with established competence and interfaces with industry.

- Characterisation techniques are very diverse, and a central coordination of all characterisation techniques under the same umbrella is challenging and time consuming.
- Proper support to an industrial user requires adequate competence with respect to sample preparation in addition to selecting the optimal characterisation technique.
- In the near future characterisation infrastructures will be easier accessible for industry users, following a starting trend for full-cost pricing of the infrastructure use and requirements for economically balanced cost models and open access. However, the high cost imposed by implementing full cost models may discourage the industry (especially SMEs) the use costly advanced characterisation infrastructure.

5.1.3. Recommendations

1. Creation and establishment of national research infrastructure roadmaps in all European countries. This secures long term financing of the most important characterisation infrastructures and enables the operation at a high technological and scientific level.
2. The state-aid issue needs to be resolved. Within the framework of a full cost model, if industrial users pay full cost then there is no "state aid" issue.
3. Introduce fast mechanisms for “service pay per access” to expedite access to resources.
4. Establishing processes where existing characterisation facilities can be made available to industry with accelerated MOU/MTA in order to protect IPs but also provide efficient services to industry.
5. As also mentioned in §4.3 (recommendation 2), European coordination (via e.g. CSA model) between characterisation infrastructures is necessary. In addition to establishing high-end and large-scale infrastructures, it is important to establish European networks of national infrastructures within “standard” characterisation techniques. This will contribute to build competence in many different regions of Europe and promote a more organised and effective access for industry users. Since these networks are already nationally coordinated, a European network will be easier to coordinate.
6. Establish “access centres” for different industry branches, where characterisation experts can help industry users to find the right solution for specific characterisation needs and the most suitable European characterisation infrastructures.
7. Support (e.g. via CSA) local/regional/national mapping exercises to identify characterisation add-values which will be made available to industry. Creation of a competence “virtual” centre or hub in charge of collecting and managing characterisation knowledge and examples of excellence.
8. Creation of a platform for communication and e-learning on characterisation (developed as a result of the mapping exercises) which will allow one-to-one interaction between characterisation facilities and industry.
9. Creation of a repository of case studies and “success stories” of characterisation assisted product development and industrialization.
10. Industry needs utilisation of characterisation experts who can contribute conceptually to industrial challenges. Such a pool of experts is more likely to exist at research

institutes or at project consortia. However, investments to educate highly qualified researchers operating in national/regional infrastructures at the interface with industries should be promoted. It was mentioned before that constant personal turnovers, in particular at academia level, have adverse effects regarding expertise and quality in characterision as well as sustainable relationships between universities, research institutions and industry. The formation of a cadre of characterisation experts could improve the current situation.

11. Establishment of technical training opportunities (e.g. short-term mobility programs) at regional and/or EU level for promoting updating with focus on new standards, calibration and characterisation techniques.
12. Creation of a "characterisation award" for excellence in assisting industry in their product development and market approval.
13. Initiation of dedicated programs for methodology and technology development for characterisation equipment with involvement of academic, research and industrial sectors focusing amongst others on education of PhD/Postdoctoral fellows.

5.2. Standardization of Measurement Methods and Interlaboratory Exercises

5.2.1. Requirement for Standardisation

Characterisation of materials and products consisting of them requires the application of many different measurement techniques to evaluate the structural, chemical make-up and performance of materials over their lifetime. Standards for testing and characterisation are important for several reasons:

- facilitate and improve reproducibility and comparability of measurement data,
- facilitate product quality control and hence business,
- facilitate the prediction of possible risks, the creation of safety regulations, and regulatory preparedness regarding novel and advanced materials.
- facilitate the knowledge of the environmental fate of the materials after their use.
- build the basis for any regulation.

It has to be noted that standards are “stand-alone” products but are normally produced in view of a specific application, e.g. to enable product quality control, for human hazard and exposure assessments or for environmental fate assessments. The standards become “references” or legally binding only if they are ex- or implicitly named as such in a directive or regulation, or in a corresponding national legal act.

Hence, the development of standards are sometimes mandated by a public body to enable legal acting or industry to enable production of goods.

The provision of high quality standards for materials characterisation are therefore key to the provision of a materials characterisation infrastructure which helps to increase the competitiveness of European industry, job creation, regional development and contributes to better safety, environment respect and an improved quality of life.

5.2.2. Pre-standardization

It is helpful to look at the overall process of standardization. There are several stages to this:

- Initial conception or need of a new measurement method

- Uptake by a number of pioneering laboratories
- As interest in the usefulness of the new measurement method increases literature is established on the use of the new measurement method
- Discussion and collaboration on the measurement method takes place between a number of different laboratories with refinement of the measurement method and draft agreement on a robust and validated test protocol. This phase is often called pre-standardization
- Formal adoption of the test method as a standard or part thereof through a national or international standardization committee

The pre-standardization phase is a critical part of the process of standardization as this is when the basic work on defining the detail of the test method is carried out. Some aspects of this work can be carried out in a single laboratory, but usually several laboratories need to be involved to assess aspects such as the reproducibility of test methods. It is also important to assess how aspects such as the operator, the specific test system and overall protocol that are used, the materials that are examined and their control, and indeed the place of test affect the measurement uncertainties of the new test methods.

As standardization and pre-normative research of activities regarding nanotechnologies and nanomaterials are concerned at European level, EC DG Grow f.i. awarded CEN, CENELEC and ETSI with a mandate M461. For further information, see ftp://ftp.cencenelec.eu/CEN/WhatWeDo/Fields/Nanotech/M461.pdf.

An organisation that was set up specifically to assist with the pre-standardization phase is The Versailles Project on Advanced Materials and Standards (VAMAS), which was established following an economic summit in 1982 held at Versailles by the Heads of State of the G7 group of nations and representatives from the Commission of the European Communities. The membership has expanded over the last few years.

The main objective of VAMAS is to promote world trade by innovation and adoption of advanced materials through international collaborations and mutualisation of experience and knowledge that provide the technical basis for harmonisation of measurement methods, leading to best practices and standards.

VAMAS carries out this work through Technical Working Areas (TWA), which look at a specific sector of measurement. Since the inception of VAMAS, 39 TWAs have been set up, covering a wide range of pre-standards research needs for the application of advanced materials. Over 500 individuals from many research groups including researchers from outside the original founding countries have participated in over 80 individual projects. VAMAS does not have its own funds to support this activity, but relies on funds from partners themselves or in some cases funding from EU projects and other sources.

Typically, international collaboration takes place to agree the technical basis for test method development and, using round robin inter-comparisons, the test methods are checked to ensure that consistent results are obtainable at different laboratories, and provide precision (repeatability and reproducibility) data.

For further information on VAMAS, see http://www.vamas.org/.

Other bodies such as the OECD and IEA also have working groups that are active in prestandardization. Examples are the OECD Working Party on Manufactured Nanoparticles

(WPMN) which has carried out much prestandardization work (http://www.oecd.org/env/ehs/nanosafety/publications-series-safety-manufactured-nanomaterials.htm), on NM-solubility, tests for environmental behaviour, ecotoxicology etc., specifically dedicated to the global market, and the IEA which carries out prestandardization work through, for example the implementing agreement on advanced materials for transport.

5.2.3. Standardization Process

There are many standardization organisations concerned with standardization. Most countries have at least one official National Standards Body (NSB) who organises local representation for standardization activities and appoints representatives to attend meetings of technical meetings of regional or international standardization organisations.

Within Europe, there are three regional standardization organisations. CEN, the European Committee for Standardisation, is an association that brings together the National Standardisation Bodies of 33 European countries. CEN provides a European platform for the standardisation of products, services, processes and systems across a wide range of sectors. CENELEC is the European Committee for Electrotechnical Standardisation and is responsible for standardisation in the electrotechnical engineering field. ETSI, the European Telecommunications Standards Institute, produces globally applicable standards for Information and Communications Technologies (ICT).

Internationally the main standardization committees are ISO and the IEC. ISO (International Standardization Organisation) is an independent, non-governmental international organisation with a membership of 163 national standards bodies. Through its members, it brings together experts to share knowledge and develop voluntary, consensus-based, market relevant International Standards that support innovation and provide solutions to global challenges. The International Electrotechnical Commission (IEC) is the leading global organisation that publishes consensus-based International Standards and manages conformity assessment systems for electric and electronic products, systems and services, collectively known as electrotechnology.

Other standardization organisations exist for specific sectors or specific industries. Two that are noted here are NACE International (an authority on corrosion based in the USA) which offers industry standards on corrosion testing amongst other activities. ASTM International is a USA based standardization organisation that is very active in the production of voluntary standards for measurement methods for materials. NIST through the Standard Reference Data: Materials properties.

Further information can be found here:

CEN: https://www.cen.eu/work/areas/Pages/default.aspx

CENELEC: https://www.cenelec.eu/aboutcenelec/whoweare/

ETSI: http://www.etsi.org/about

ISO: http://www.iso.org/iso/home/about.htm

IEC: http://www.iec.ch/about/activities/?ref=menu

NACE: http://www.nace.org/About-NACE/

ASTM: https://www.astm.org/ABOUT/full_overview.html

NIST: http://www.nist.gov/srd/materials.cfm

5.2.4. Key Standardization Committees for Materials Characterisation

Some key committees concerned with materials characterisation are noted here:

CEN:

CEN TC 352 Nanotechnologies

CEN TC 184 Advanced Technical Ceramics

CEN TC 240 Thermal spraying and thermally sprayed coatings

CEN TC 262 Metallic and other inorganic coatings, including for corrosion protection and corrosion testing of metals and alloys

CEN/TC 137 Assessment of workplace exposure to chemical and biological agents

CEN/TC 138 - Non-destructive testing

CEN/TC 139 - Paints and varnishes

CEN/TC 162 - Protective clothing including hand and arm protection and lifejackets

CEN/TC 195 - Air filters for general air cleaning

CEN/TC 230 - Water analysis

CEN/TC 243 - Cleanroom technology

CEN/TC 248 - Textiles and textile products

CEN/TC 292 - Characterization of waste

ISO:

ISO/TC 229 Nanotechnologies

ISO/TC 24 Particle characterization including sieving

ISO/TC 35 Paints and varnishes

ISO/TC 135 Non-destructive testing

ISO/TC 156 Corrosion of metals and alloys

ISO/TC 164 Mechanical testing of metals

ISO/TC 201 Surface chemical analysis

ISO/TC 202 Microbeam analysis

ISO/TC 206 Fine ceramics

ISO/TC 261 Additive manufacturing

ISO/TC 6 Paper, board and pulps

ISO/TC 44 Welding and allied processes

ISO/TC 45/SC 3Raw materials (including latex) for use in the rubber industry

ISO/TC 48 Laboratory equipment

ISO/TC 61 Plastics

ISO/TC 142 Cleaning equipment for air and other gases

ISO/TC 146/SC 2 Workplace atmospheres

ISO/TC 150 Implants for surgery

ISO/TC 184/SC 4 Industrial data

ISO/TC 194 Biological evaluation of medical devices

ISO/TC 207 Environmental Management

ISO/TC 209 Cleanrooms and associated controlled environments

ISO/TC 213 Dimensional and geometrical product specifications and verification

ISO/TC 217 Cosmetics

ISO/TC 256 Pigments, dyestuffs and extenders

ISO/TC 266 Biomimetics

ISO/TC 276 Biotechnology

ISO/REMCO Committee on reference materials

IEC/TC 113 Nanotechnologies

Review of achievements of the OECD Working Party on Manufactured

Nanomaterials' Testing and Assessment Programme. From exploratory

testing to test guidelines

OECD guidelines for testing of chemicals and related documents:

Series on Testing and Assessment: Testing for Environmental Fate

Series on Testing and Assessment: Ecotoxicity Testing

Series on Testing and Assessment: Testing for Human Health

Cooperative Chemicals Assessments: Profiles

Series on Testing and Assessment: Non-Testing Methods (e.g., QSAR, grouping of chemicals, AOP)

Series on Testing and Assessment: Classification and labelling

Series on Testing and Assessment: Workshop/Meeting Reports, Surveys

Series on Testing and Assessment: Emission and Exposure

Performance Standards

OECD Series on Principles of Good Laboratory Practice (GLP) and Compliance Monitoring:

OECD Principles of GLP

GLP consensus documents

Guidance Documents for Compliance Monitoring Authorities

Advisory Documents of the Working Group on GLP

5.2.5. Interlaboratory Exercises

Interlaboratory exercises are key to the successful evaluation of the uncertainty of measurements, which must always be communicated, with the values of any measurement. Uncertainties in measurement can be associated with different aspects of the measurement such as the test system that is used, the operator, and the materials under test. Other factors such as environmental conditions may also affect the results of measurements to a certain extent.

The use of a suitable reference material (see elsewhere in this report, e.g. §5.4.3) is usually recommended for interlaboratory evaluations to minimise variability stemming from the test material itself. In this way, the method intercomparibility can be judged free from test material variability. The requirement placed on reference materials are usually very stringent in terms of composition and microstructure. Once established, a reference material can be made available more widely for checking laboratory performance. In the US, NIST has created such a repository; in Europe the EC-JRC has created a repository for nanomaterials.

Interlaboratory exercises are normally carried out as a collaboration between institutes expert in a particular field of measurement. One laboratory coordinates the exercise and develops a robust procedure that must be followed by the project partners, organises that materials to be tested, and analyses the results. Key aspects of the measurement method that result from the analysis are aspects of the measurement uncertainty such as the reproducibility and the repeatability of the results.

These measures of uncertainty are fed into the statement of uncertainty that is required in standards documents.

5.2.6. Accreditation

In most countries the quality of measurements are also assured by accreditation schemes, which ensure that measurements are carried out to well-defined procedures and standards. This gives confidence to customers of the reliability of measurements and also benefits the measurement provider by giving a market advantage through the accreditation of measurement services.

Unfortunately, in the research environment of several countries the accreditation aspect is often neglected especially in academia.

5.2.7. Recommendations

1. There is a clear requirement to ensure that the appropriate level of support is available for standardization of material characterisation techniques. The development of high quality standards for material characterisation is a complex time consuming task, particularly with respect to the pre-standardization phase where collaboration between different laboratories needs to take place with the conduction of interlaboratory

exercises. Committed industrial participation must be a prerequisite in the process. However, this activity must be incentivised by different means (e.g., creation of ISO, reference materials, methodologies etc.).

Some years ago, there was an EU programme on Standards Measurements and Testing that was very successful in developing new materials characterisation techniques right through to standardization with good effective support for the pre-standardization phase including the conduction of interlaboratory exercise. An issue with this programme was that the link of the new measurement technology to industrial and societal applications was often not that clearly identified. Because of this, the programme was not renewed but an emphasis was placed within the subsequent framework and H2020 programmes to emphasise the importance of standardization, but this was only partially successful; the main reasons were the EU project financing rules and the different timeframe of development between research and standardization processes.

2. Specific actions may be launched to promote and support those characterisation laboratories who wish to be accredited in order to facilitate their interaction with industries. Industries use ISO standards as a reference for their quality in contrast to academics who use different scientific benchmarks.

5.3. Spatially localised techniques

5.3.1. Introduction

A large range of techniques is now available to examine the variation in structural, physical and chemical properties of materials from point to point. The availability of these spatially localised techniques enables point-to-point variations (local detections) in properties to be examined so that an understanding of the response of the materials to external stimuli and its dependence on local variations can be developed and modelled. These techniques all have different lateral (point to point) and height or depth resolutions, which should be considered when choosing the most appropriate techniques to apply. This is particularly important when results from more than one technique are employed.

5.3.2. Classification of the spatially localised techniques

This section classifies the spatially localised techniques according to the technical information they provide.

Surface topography, internal morphology and tomography:

- Optical techniques such as white light interferometry, focus variation microscopy and laser confocal microscopy allow topographical reconstructions with sub-micrometre lateral resolution and few 10s of nm resolution in height. These techniques are non-destructive
- Atomic force microscopy (AFM) provides surface contour information in the nano-to-few-micrometre range and it can be coupled with other detections modes giving access to different local properties of the surface of a material.
- Digital Holographic Microscopy (DHM) allows static and dynamic 3D characterization in materials and life science applications. It enables measurement with nanometre height resolution, but with Abbe diffraction limited lateral resolution.
- Scanning electron microscopy (SEM) uses different electron signals to form images of surfaces, which have nanometric lateral resolution. There is a topographical

element to the contrast, but it is not straightforward to achieve measurements of surface topography from these images due to the mechanisms of electron scattering and compositional effects. In some limited cases 3D stereography where several images acquired at different angles of inclination to the electron beam are analysed to provide topographical maps. The internal morphology can be assessed if a cross section through the surface is prepared, but this is a destructive process.

- Transmission electron microscopy (TEM) and scanning transmission electron microscopy (STEM) provide morphological information down to atomic level, but preparation of the electron transparent samples necessary is still not always easy despite the advent of FIB preparation techniques. However, dispersions of nanoparticles or powders are amongst the easiest type samples in terms of TEM sample preparation.
- SEM in combination with focused ion beam (FIB) can be used to perform tomographic 3D reconstructions of the local structure of materials, but this is a destructive process.
- A range of X-ray Computer Tomography (XCT) systems can be used to give 3D tomographic evaluation for objects ranging in size from 100s of cms down to about 0.1 mm and with corresponding resolutions from mms to a few 10s of nm. These measurements are non-destructive, but the limited size of samples for the highest resolution systems is a major issue.
- Latest developments in electron microscopy allow tomographic evaluations at the atomic level.
- Different large-scale facility based techniques using X-rays or neutrons are under continuous development that give information of internal morphology of materials. Modern systems can give sub micrometre spatial resolution in 3D. An issue with these techniques is access to the facilities. Atom Probe Tomography (APT) allows destructive analysis of needle samples (possibly made by FIB) providing imaging and chemical analysis down to the atomic scale.
- Not strictly spatially localized techniques but important to mention are optical methods to determine particle size, shape and structure, particle size distribution and particle zeta potential: Small Angle X-ray Scattering (SAXS) provides particle size, size distribution and shape, and structure information in the lower nanometer regime for solid samples, powders, dispersions and emulsions. Dynamic Light Scattering (DLS) and Electrophoretic Light Scattering (ELS) provide particle size, size distribution and particle zeta potential in the nanometer to lower micrometer regime for dispersions and emulsions. Static Light Scattering (SLS) aka Laser Diffraction provides particle size and size distribution in the higher nanometer to micrometer regime for powders, aerosols, dispersions and emulsions. Static and Dynamic Image Analysis (SIA/DIA) provides particle size, size distribution and particle shape in the micrometer regime for powders, dispersions and emulsions.

Crystallography:

- Electron backscattered diffraction ESBD yield local crystallographic information, such as crystallographic texture and grain boundary orientation, with a lateral resolution of a few 10s of nanometres.
- When combined with FIB-tomography EBSD can be used to generate 3D datasets of the crystal structure of materials. The sample size is limited to about a 50-micrometre cube for gallium ion beam instruments and a few hundred micrometre sized cubes for more recent plasma ion instruments.

- S/TEM coupled with electron diffraction (ED) provide crystallographic information at the atomic level
- Different large-scale facility based techniques using X-rays or neutrons are under continuous development that give information of internal crystallographic of materials. Modern systems can give sub micrometre spatial resolution in 3D. An issue with these techniques is access to the facilities.

Chemical composition:

- IR microscopy (IRM) allows the identification and quantification of molecular structures, functional groups and crystallographic phases at a lateral resolution of 1-10 µm.
- Raman microscopy (RM) allows the identification of molecular structures, functional groups and crystallographic phases at a lateral resolution of down to 1 µm or even slightly lower.
- Confocal Raman spectroscopy coupled with scanning near-field optical microscopy (SNOM) offers hyperspectral image generation with a complete Raman spectrum at every image pixel. The lateral resolution is beyond the Abbe diffraction limit (~100 nm). In addition, 3D maps of complex samples can be generated.
- Nano-scale IR Spectroscopy and Tip Enhanced Raman Spectroscopy (TERS) use SPM technology to provide chemical information with a lateral resolution in the tens of nanometres regime
- SEM or TEM coupled with energy or wavelength dispersive X-ray spectroscopy (EDS or WDS, respectively) provide composition information down to the micro/nanoscale. The former spectroscopy is faster but with lower sensitivity and spectral resolution than the latter. The lateral and depth resolution are limited by the interaction volume of electrons with the sample, which is dependent on the accelerating voltage used, but is typically about 0.5 micrometre for an accelerating voltage of 30 kV. Coupling to EDS and energy loss spectroscopy (EELS) allows elemental analysis down to the atomic scale. The latter spectroscopic method is also able to provide finer chemical information.
- When combined with FIB-tomography EDS can be used to generate 3D datasets of the crystal structure of materials. The sample size is limited to about a 50-micrometre cube for gallium ion beam instruments and a few hundred micrometre sized cubes for more recent plasma ion instruments.
- Time of flight secondary ion mass spectroscopy (ToF-SIMS) allows high mass spectrometry/ mapping down to the sub-micron scale as well as depth profiling characterizations.
- X-ray photoelectron spectroscopy (XPS) and Auger electron spectroscopy (AES), can give surface composition and chemistry information down to the micro- and nanoscales respectively. Additionally depth-profiling characterizations are feasible.
- Different large-scale facility based techniques using X-rays or neutrons are under continuous development that give information on the chemical composition of materials. Modern systems can give sub micrometre spatial resolution in 3D. An issue with these techniques is access to the facilities.
- Laser induced breakdown spectroscopy (LIBS) allows like SIMS a surface selective chemical analysis of nanomaterials. The principle is based on the excitation of vaporised elements / molecules in a plasma and subsequent atomic emission

spectroscopic analysis. Surface specific chemical analysis can be also provided by APT.
- Chemical/compositional analysis via in situ/in operando methods (e.g. in-situ XPS, Raman, other x-ray techniques) are important in catalysis and other areas.

Electrical, electrochemical and optoelectronic properties:

- STM techniques based on electron tunnelling allow studying electrical properties of materials down to the atomic scale.
- Kelvin probe force microscopy (KPFM), also known as surface potential microscopy, is a noncontact type of SPM technique providing the work function of surfaces at atomic or molecular scales. The work function relates to many surface phenomena, including catalytic activity catalytic activity, reconstruction of surfaces, doping and band bending of semiconductors, charge trapping in dielectrics dielectrics and corrosion. The map of the work function produced by KPFM gives information about the composition and electronic state of the local structures on the surface of a solid at the nm scale.
- Electrostatic force microscopy (EFM), a similar SPM technique, is able to map surface charges by measuring with long-range electrostatic forces at the nm scale.
- In situ electrochemical and corrosion studies can be carried out with environmental or low-vacuum SEMs and TEMs.
- Cathode luminescence coupled with SEM and TEM can determine local optoelectronic properties related to the electronic band structure at, respectively, the micrometre and nanometre scales.
- EELS can provide information on local plasmon excitations as well as inter and intra band transitions (spatial resolution is limited by the delocalization of the phenomena)
- Scanning electrochemical microscopy (SECM) involves scanning near the surface of interest with a micro or nano electrode, with both the sample and the electrode being immersed in liquid. The tip current is measured; focus of the evaluation is the local reactivity of the surface.
- Electrochemical impedance spectroscopy (EIS, often in conjunction with SECM), is a tool for the exploration of electrode heterogeneity. EIS is used as a characterization technique for many material systems and applications (corrosion, plating, batteries, fuel cells, etc.)
- Ultrafast fibre-optic UV-VIS-IR spectroscopy is a new approach to optical inspection of large surface areas at a micrometre scale that combines the new technology of array and CCD detectors with under 5ms integration time per spectrum in conjunction with a deuterium/halogen light source in both transmission and reflection geometries, over the optical spectral range between 320 nm and 1500nm.

Mechanical and thermo-mechanical properties:

- Nano-Indenters provide localized surface hardness, elasticity and more in corresponding maps with lateral resolutions in the sub-micrometre range. Scratching modes allow the investigation of surface rigidity and delamination of coatings. There are now instruments available that can be used in situ within SEMs or indeed TEMs to enable visualisation of material deformation/failure as mechanical loads are imposed.

- Special AFM methods provide tens of nanometres resolved surface mechanical and thermo-mechanical properties. Lateral force microscopy (LFM) and force spectroscopy (FS) provide tens of nanometres resolved surface mechanical and thermo-mechanical properties at the pN level. Namely, FS can be employed to determine the mechanical strength of single molecules, binder-receptor adhesion forces and protein conformation configurations.
- In-situ mechanical tests for degradation mechanism studies at different temperatures ranging from -60°C to +900°C can be performed in situ with SEM and TEM providing details at nanometre and atomic scale, respectively.
- Thermal imaging (FLIR technology) in conjunction with optical microscopes for micrometre-size assessment of thermo-mechanical transformations of shape memory alloys for instance, or to study heat transfer in electronic devices and sensors at a microscopic scale.

5.3.3. Recommendations

1. Incorporation and registration of spatially localised techniques in existing or newly generated regional/national centres/hubs.
2. They should form/participate in networks in order to exchange expertise, provide calibration standards where such do not exist and perform inter-laboratory tests to establish metrological specifications for calibration standards.
3. Such regional centres should be preferably located in the vicinity of industrial premises or they should cover geographic regions easily accessible by industry. They should be affiliated with local universities or RTOs.
4. They should be sufficiently independent and legally fully competent to process industry orders for analytical services in a professional way.
5. Apart from that, they should also engage in educating students and industry members in the assessment, establishment, use and interpretation of such methods and techniques.
6. A permanent organization could be perhaps formed which coordinates the regional centres and represents them at the European Commission.

5.4. Data management, data provenance, databases in relation with material properties and reference materials

5.4.1. Introduction and definitions

“Data” are qualitative or quantitative values attributed to certain quantities or variables. “Data” are produced in different ways, for example as results of some experiments or as results of a computer program. According to Cambridge Dictionary, data is: “information, especially facts or numbers, collected to be examined and considered and used to help decision-making or information in an electronic form that can be stored and used by a computer”.

It results that data are important pieces of information that are collected or produced during experiments, statistics, observation, calculations, etc. Further, data can be stored, processed, analysed, compared, reported, and corrected. In any case, data can be used as inputs for models and simulations, or as arguments for justifying decisions. Therefore, data manipulation and security is very important to avoid errors that may have serious consequences on the human safety and on the quality of life. Moreover, ethical rules must be followed as in any aspects of scientific activities. Following ethical lines is important for a fruitful interaction between characterisation experts, industrial and societal end-users.

Characterisation specialists and researchers trust that the equipment manufacturers guarantee the reliability of their equipment, industry expect that researchers provide reliable characterisation services, and the consumer faiths that industry do their best to protect and ensure product quality. In relation to “data” manipulation, several aspects are of greater importance. These are:

a) Data management: describes all the procedures used to manipulate the data (how the data are stored, how can be accessed and used, who is allowed to access the data, etc.). One has to note that Horizon 2020 projects have to present a plan for data management during the project and after its termination. This action is in line with the Commission efforts to extend the “open access” policy to as many research results as possible. It must be noted that, one of the EMCC working groups is dedicated to “characterization data and information management”, underlying the importance of data management in the case of advanced materials.
b) Data provenance: known also as “data lineage”, refers to data history, meaning how the data were obtained, how they were stored, processed, used, etc. Data provenance is very important in establishing their validity and correctness. During data provenance investigations, identified errors can be removed if their cause is accurately established. Otherwise, data are compromised and a new set of data has to be generated using appropriate procedures.
c) Databases: this is an organised collection of data. In the specific case of materials, databases can refer to (and not only): material properties (e.g. structure, density, chemical formula, different electronic, thermal, mechanical properties, etc.); material processing (specific parameters for methods used to produce a material); material toxicity and safety measures, etc.
d) Type of data: in principle, this refers to original (raw) data and secondary data. The raw data are the data obtained directly from experiment or observation, without any processing. Secondary data can be considered all the results of analysis or simulations performed by various methods, eventually using the raw data as inputs.
e) Material properties: the set of data defining the basic structural and physical properties of a given material. These data can be used to design applications, or to model and simulate processes taking place in the given material. One has to take into account that intrinsic material properties apply only to those materials that are free of extrinsic contributions related to defects, impurities or parasitic phases (e.g. elemental materials, certain classes of crystalline materials for which high quality single crystals can be obtained, possible organic compounds with well-defined composition and structure). “Material properties” cannot be defined as unique properties of a material if they are strongly dependent on microstructure (e.g. ceramics, composites, glasses, etc.). In this case, we refer to a "range of material properties" or "sample properties".
f) Reference materials: these are materials used as references for calibrating characterisation methods on one hand, or materials used as references for measuring/defining intrinsic material properties on the other hand.

5.4.2. Databases

There are several databases of material properties. One of the widely known is published by Springer (see http://materials.springer.com/). Even from the starting page it is mentioned that access is offered to” numerical and graphical data on the properties of materials”. This database is updated every 3 months, with last time being April 2016. The Nature publishing

group have launched a new journal, "Scientific Data" (http://www.nature.com/sdata), dedicated to data repository archiving and sharing. There are also a large number of handbooks covering properties of different type of materials:

- Handbook on Physical Properties of Semiconductors (published by Springer)
- Handbook of Low and High Dielectric Constant Materials and Their Applications (published by Elsevier)
- Physical Properties of Polymers Handbook (published by Springer)
- Handbook of Chemistry & Physics Online (published by CRC)

There are also many on-line databases, such as:

- MatWeb (http://www.matweb.com/)
- MatDat (http://www.matdat.com/)
- NIST Standard Reference Data: Materials properties (http://www.nist.gov/srd/materials.cfm)
- JRC Nanomaterials Repository (https://ec.europa.eu/jrc/en/scientific-tool/jrc-nanomaterials-repository)

Some of the material producers also provide some information on material properties.

Except few fragmented cases (e.g. projects funded by the EC with the involvement of EC-JRC) a central database with materials properties and with full traceability of recorded data does not exist at the moment.

A relevant database should include information such as:

- Value of specific material property.
- Method used to obtain the value (if it is a “raw” value, the experimental method used for acquiring the value should be described; if it is a “secondary” value derived from a simulation or a model, then the algorithm used for calculation should be described); the used standard (procedure) should be mentioned, if any.
- Value spread, if there are more values attributed to the same material property.
- Full set of references (articles, books, etc.).
- Location of laboratories where the values where acquired; mention if inter-laboratory check was performed on the type of samples.
- Description of the sample: method used to produce the material with full set of parameters allowing reproducibility of the sample; accurate description of the process steps necessary to prepare similar sample ready for experimental measurement used to acquire the value.
- Existence of reference sample: location; storage conditions; possible alterations that can affect the accuracy of the value recorded in the database. Several funded projects, which generated data and accumulated information in the safety area can be used as guides. "NANOREG" developed a guidance document for the characterisation of nanomaterials for industrial use, whilst within JRC three comprehensive reports on characterisation and definition of nanomaterials have been published.
- Sample history from the moment when the sample was produced up to the moment when the relevant value was acquired (e.g. sample can be produced in a laboratory and the measurement can be performed in other laboratories).

Complete information regarding the values recorded in the database is necessary. If the information is not complete, then the values may be not fully reproducible. This means that someone trying to verify the value can obtain different results if the full set of parameters for producing a similar sample and extracting the value for the property of interest is not given. Uncertain values may lead to erroneous results in simulations performed to design a product or model a phenomenon. This can have serious consequences on human safety in the case of products in direct contact with the human being (e.g. erroneous prescription of pharmaceuticals; erroneous functioning of alarm systems; faults in buildings; etc.). There is a direct link between the accuracy of the values recorded in databases and the validity of the models and simulations using those values.

5.4.3. Reference materials

a. Reference materials as "standards" for material properties.

The accuracy of the values recorded in databases is directly related to reference materials. In other words, to be sure that the values given for the material properties are reliable and are obtained on a high quality sample of the irrespective material.

However, obtaining a reference material can be a very challenging task. The entire history of Si can be used as an example. Decades of intense efforts were required to obtain high quality Si single crystals. This allowed subsequent engineering of the physical properties in a highly controlled way. In general, the properties of elemental materials are not a problem as these materials exist or can be produced in high purity crystalline form. Problems start to arise when one refers to multi-component materials, as for example oxides or polymers. In these cases, it is essential to have reference materials in order to obtain reliable values for material properties, values that can be uploaded then in material databases.

Reference materials should accompany standardization of the measurement methods and inter-laboratory exercises, and should be pre-requisites to build up reliable and verified databases on material properties. Considering the fact that one can obtain a reference material, then this has to be characterised at least in a few laboratories, with standardized measurement methods, in order to extract correct material properties (see §5.2).

The following challenges exist:

- How to produce reference materials?
- How to store the reference materials?
- How many samples are needed for inter-laboratory comparison (probably minimum 5 for a decent statistics)
- Are there enough characterization laboratories able to perform complete set of investigation of material properties? (Maybe is better to focus only on those properties of interest for the applications targeted by the reference material and not on all physical properties)
- Is there need for reference material for all the materials used in industry or should focus only on those with relevant production quantity (in terms of requirements from industry)?

A possible efficient way is to start from specific applications (those of mass production), to identify the important materials and to start producing the reference samples and subsequently characterise them. The results will be inputs for databases.

After identifying the needed reference material, the next step would be to identify who can produce the reference samples and who can characterise them.

Reference materials are the basis of characterisation credibility. Often one can see results of a few research groups that cannot be reproduced by other groups. One of the hot examples is the perovskite solar cells. Only two or three groups reported efficiency around 20 %. All the other groups working in the field report anything between 3 % and 15 % although many of them use the same materials and preparation methods as the leading groups.

b. Reference materials as "calibrators" for measurement equipment and methods

This type of reference materials are used to calibrate measurement equipment and measurement methods. Some examples include: samples for calibrating AFM machines, having well defined features with precisely known dimensions; samples to calibrate equipment used for chemical analysis, especially those designed to detect traces down to ppm or ppb (ICP type techniques); samples used as standards and calibrators in industries like food and beverages, pharma and life sciences, petrochemicals, etc.

There are several producers for this type of reference materials:

- Joint Research Centre (JRC, site https://ec.europa.eu/jrc/en/knowledge/reference-measurement)-The JRC currently provides nearly 800 different reference materials under the BCR®, IRMM and ERM® brands in the fields of food and feed analysis, environmental analysis, engineering and health applications.
  All these materials come with clear traceability statements on their certificate.
  Inside JRC, there is an Institute for Reference Materials and Measurements (IRMM), located in Belgium. It provides reference materials to calibrate the laboratory equipment used to test food, environment, construction materials, etc.
- European Reference Materials (ERM, site http://www.erm-crm.org/)-this is a consortium of three entities: IRMM, BAM (Germany) and LGC (UK)
- Inorganic Ventures (site: http://www.erm-crm.org/)-reference material for ICP, ICP-MS, IC, atomic absorption, wet chemistry, and QC applications
- Sigma Aldrich (site: http://www.sigmaaldrich.com/analytical-chromatography/analytical-standards/certified-reference.html) - Sigma Aldrich offers a wide range of certified reference materials. With Cerilliant, RTC and Supelco, Sigma-Aldrich offers three in-house manufactured high quality CRM brands all produced under ISO/IEC 17025 and ISO Guide 34 double accreditation. In addition, they distribute certified reference materials from internationally recognized CRM producers such as IRMM, Paragon Scientific or Whitehouse Scientific.

All these providers of "reference materials" have to be certified according to some specific standards, as mentioned above for Sigma Aldrich.

5.4.4. Data management

Data management procedures are necessary to manipulate values inside a database. Below we present some possible scenarios:

1. A certain industry decides to develop a new product and needs research involving modelling and simulation. For this purpose, they ask the help of a research organisation or the help of their own research department. The researchers develop the algorithm for simulation and they need values as input parameters. There are two

possibilities, either to use values from literature (not certified in most cases) or to use values from a certified database. In the last case, they can purchase the needed values with the entire certified information regarding provenance, reference sample, etc. This scenario is preferable because ensures the validity of the data that will be further used in theoretical models producing the results for the industry.

2. There is a demand for data missing from the database, because either it concerns a new material or it is a material property that, previously, was not of interest in applications. The action is to complete the database with the required information. This action can be accomplished following some steps such as:

    a) identify the material and the properties of interest for the industry;
    b) find a company or laboratory able to produce reference samples;
    c) distribute the reference samples to laboratories able to extract reliable values for the properties of interest;
    d) collect and compare the results;
    e) verify if the results are reproducible;
    f) introduce the verified and certified values in the database.

Procedures can be installed for both cases presented above, ensuring full traceability of the data.

Databases and data management may require specific infrastructures in term of storing the reference samples, the information regarding the material properties and all the documents involved in accurate data traceability. All information regarding material properties can be stored in digital form, with all the necessary protocols for access, avoiding any possible misuse or intentional alteration of the recorded data. However, the storage of reference samples may require specific measures and storing conditions (temperature, humidity, light, atmosphere, etc.).

The graph below illustrates possible inter-relations between reference materials or samples, acquiring the values of interest for material properties, databases, data provenance, and data management.

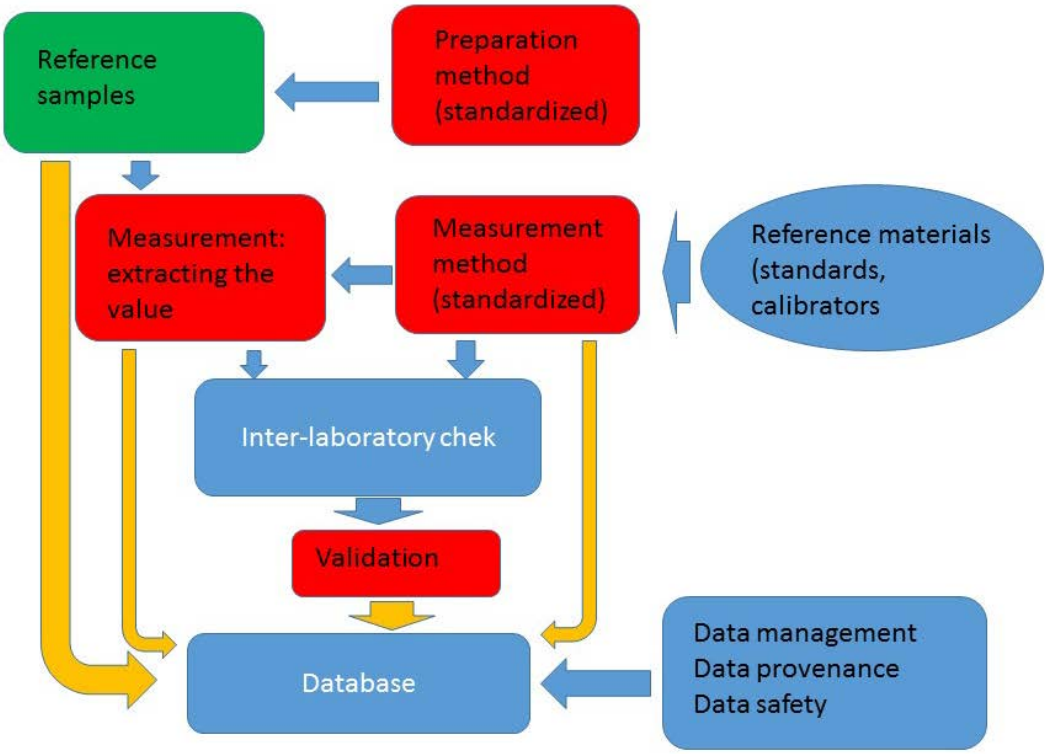


Figure 1: Inter-relations between reference materials acquiring values of interest for material properties, databases, data provenance, and data management. Red coloured areas show the critical steps and orange arrows show those data that should be included in a database.

5.4.5. Recommendations

1. Identification of materials of industrial interest. In addition to materials of substantial production and/or consumption, having significant impact on life safety and quality, also novel materials with industrial potential should be included. This action should be coordinated with similar actions at national level, EU level (e.g. JRC, ECA/REACH, EFSA) and take into account similar actions outside Europe (e.g. EPA).

2. Identification of the material properties that are of interest for industry

3. Analysis on the existing data: collecting the information; checking the provenance and traceability

4. Identification of the missing data

5. Decision on how the data will be acquired:

   a. identification and decision on who will manufacture the reference sample
   b. identification and decision on who will measure the samples and produce the values of interest (at least three different laboratories)
   c. -validation of data

6. Decision on the material database: will it be a central database or a distributed one? Where will it be located; access and procedures (open-access?)

The above-proposed actions can be included in a special program for material characterisation. Some of the actions require a significant amount of work, especially 1 and 3. Action 1 and 2 will require direct contact with relevant industries, based on inquiries regarding the materials of interest and the relevant properties for applications. Action 3 is a datamining type of action, requiring consultation of a large amount of literature in order to extract the relevant information and references. Just a simple search on “material properties” generates 528,000 results on ISI Web of Knowledge (Thomson Reuters) only from 1990 to date. Special search protocols and machines will have to be designed to extract the values for material properties, together with all the information regarding the procedure and instruments used to obtain those values. Collaboration with relevant databases for literature will be necessary for this action (Web of Knowledge, Scopus, etc.).

There are classes of materials for which generation of reliable data will be very difficult: ceramics, composites, polymers, organic formulations used in pharma and life sciences, etc. In many cases, an insignificant alteration of the parameters during preparation phase can lead to very different properties, with possible dangerous effects on humans and environment. Databases could contain also information about these observed alterations.

Therefore, it will be very important to identify the critical materials and to establish precise procedures for collecting their material properties.

5.5. Information Management

5.5.1. Introduction

Information management refers to various concepts of management concerning planning, organising, structuring, processing, controlling, evaluation and reporting of information activities closed related to production, assessment and validation of products with specific manufacturing requirements for various applications.

Information management is an important investment among modern companies and it has the role to deliver meaningful results on data, systems, technology and processes in order to provide successful decision making according to the organisational strategy. In order to achieve that, companies often rely on the DIKAR model (i.e., Data » Information » Knowledge » Actions » Results), which is a chain decision-making plan:

1. Data storage on IT infrastructure to be randomly accessed at any time for interpretation in order to render information;
2. Information has to be understood in order to provide knowledge;
3. Knowledge should be the basis for taking effective decisions;
4. Effective decisions should lead to appropriate actions;
5. Actions are expected to deliver meaningful results.

When dealing with large amounts of information, companies seek solutions to organise the information by using statistical means associated with large repositories created according to the big-data management concept: "*It’s important to remember that the primary value from big data comes not from the data in its raw form, but from the processing and analysis of it and the insights, products, and services that emerge from analysis. The sweeping changes in big data technologies and management approaches need to be accompanied by similarly*

dramatic shifts in how data supports decisions and product/service innovation." - Thomas H. Davenport in "Big Data in Big Companies".

Although the term “big data” is relatively new, the act of gathering and storing large amounts of information for future analysis is old. The concept gained momentum in the early 2000s when industry analyst Doug Laney articulated the now-mainstream definition of big data, in terms of:

- **Volume.** Organisations collect data from a variety of sources, including business transactions, social media and information from sensor or machine-to-machine data.
- **Velocity.** Data streams in at an unprecedented speed and must be dealt with in a timely manner. For instance, sensors and smart metering are driving the need to deal with torrents of data in near-real time.
- **Variety.** Data comes in all types of formats – from structured, numeric data in traditional databases to unstructured text documents (emails) and media files (video and audio).
- **Variability.** In addition to the increasing velocities and varieties of data, data flows can be highly inconsistent with periodic peaks. This is typical for unstructured data, associated with process cycling and non-periodic tests or occasional assessments.
- **Complexity.** Today's data comes from multiple sources, which makes it difficult to link, match, cleanse and transform data across systems. However, it is necessary to connect and correlate relationships, hierarchies and multiple data linkages or your data can quickly spiral out of control.

The importance of big data does not rely on the amount of data, but in the way, it is grouped for future interpretation to provide valuable information that enables time and cost reduction, new product development and performance optimisation in order to assure smart decision-making. When combined with powerful analysis tools, the big data management offers the possibility to determine root causes of failures, issues and defects in near-real time as well as to establish an entire new risk assessment scheme associated to the in-line/at-line production and characterisation in matter of minutes.

Big data management affects organisations across practically every industry, such as banking, government, manufacturing, education, health care and retail. For instance, based on the insight provided by big data, manufacturers can boost quality and output while minimizing waste in order to be highly competitive on today's market. More and more manufacturers are working in an analytics-based culture, which means they can solve problems faster and make more successful business decisions. On the other hand, in the educational sector, big data management can have a significant impact on school systems, students and curriculums. By analysing big data, educators can identify students at risk and support their progress along the learning process by implementing better evaluation systems, which are beneficial for both teachers and students.

Before discovering how big data works for a certain business or educational sector, one should first understand where it comes from. There are three major sources for big data:

1. *near-real time or sequential data streaming*, which are large sets of data and collections of results obtained upon in-line or local characterisation associated with production lines in manufacturing companies or scientific studies in universities and research institutes. At this point, one may decide on whether the streamed data is

important to be used immediately or to be kept for future analysis, whereas erroneous data sets are discarded;
2. *data from social interactions*, associated with marketing, sales and support functions, which is often unstructured or semi-structured and comes in various formats that is not always suitable for analysis;
3. *data sheets and information upon request*, as a result of engine search via networks, on-line journals / magazines and from access of large databases such as European Union Open Data Portal. The returned information is sorted according to a search key but it may contain extra information that is not relevant.

After identifying the potential sources for data, one should establish the harnessing level of relevant information. In the process, there are three possible ways to manage big data:

1. *data storage*, which has been a problem few decades ago, is now relying on low-cost - large storage capability hard disks and portable devices.
2. *analysing options*, that is interlinked with the high-performance technologies and dedicated software available nowadays, such as grid computing and in-memory analytics, which allows to take into account large amounts of data, without discarding the less relevant one. This is an important issue since *all* the obtained data are part of a *grand statistical scheme* that accounts for various parameters and conditions that influence the overall physical properties of the specimen under investigation, from controllable factors (e.g., temperature, pressure, humidity, porosity, particle-size distribution, etc.) to inherent ones (e.g., sample and precursor history, contamination, instrumentation, calibration, set-up design and not ultimately, human error).
3. *uncover important features and relations between output parameters*, often referred in literature as *factorial design*, has the purpose of studying the relation between manufacturing conditions in order to optimise the process parameters by maintaining the product quality high and keeping the capital cost low. As an example, maximising the density of BZYO proton conducting ceramics for SOFCs may be achieved by combining precursors with specific particle-size distribution compacted in pellets under a given pressure value, followed by a sintering process with a well-established thermal treatment profile that accounts for certain heating/cooling rates and dwell time at optimum temperature. Any slight deviation in the making process results in specimens with poor proton conductivity, unreliable for use with the SOFCs technology.

The final step in making big data valuable for a given purpose is to seek the technologies that help to structure the data in a logical manner to be fed directly to data analysis systems, without making use of intermediate steps. The results need to be highly structured and compacted into logical hierarchies that can be easily accessed and deconstructed into specific components / parameters / values upon request. For instance, this is a common feature of the Apache Hadoop software that facilitates distributed processing of large data sets across computing machines by using simple programming models for parallel processing, cloud and cluster allocation in large grid environments, high connectivity and high throughputs.

5.5.2. Big data streaming from local characterisation

Nowadays, trends in small and large-scale characterisation involve various methods and techniques that combine the latest technology in ultra-fast sensing elements and data acquisition systems in order to 3D characterise specimens in near real time. Thus, it is now

possible to look in more detail onto various time dependent processes, such as the sintering of nano-powders upon prolonged thermal treatment. To some extent, such an experimental approach may be regarded as a reference guide for manufacturing companies designing advanced technologies that aim at providing more insight into the realistic conditions in which materials are used. A typical example for that is the use of x-ray computed tomography in order to assess Li-ion battery performance by 3D mapping with micron-scale resolution of the structural, thermal and electrical transformations and responses occurring at anode and cathode upon charging and discharging. When combined with different time-dependent experimental methods and techniques, such as thermal analysis by using FLIR technology, one may explore key issues related to battery failure mechanisms occurring across multiple length scales and over different periods of time.

Alternatively, by using 2D ellipsometry mapping with micrometer size lateral resolution of composition gradient films obtained by co-sputtering of elementals onto large wafers, one may obtain information onto composition dependent optical constants and local thickness upon the growth process. The mapping of the optical properties of large panels turns out to be valuable in manufacturing of photovoltaic cells for instance, since both composition and thickness have critical influence onto cell performance under illumination. Not ultimately, the possibility to grow composition gradient films to form binary and ternary metallic alloys that would exhibit e.g. a metal-to-semiconductor transition upon exposure to hydrogen gas, has attracted a lot of interest lately. This is because the physics of hydrogen absorption process can be directly investigated by local optical measurements from which hydrogen concentration in the films can be determined univocally, without the need for characterisation of large batches of samples, each with predefined (constant) composition.

Experimental designs involving 2D and 3D imaging generate large amounts of data in near real-time. They consist of characterisation of surfaces together with in-depth profiles with sub-micron scale resolution. A good example for that is confocal Raman microscopy, which provides in-volume information on sample chemistry with a lateral resolution beyond Abbé diffraction limit (~230nm for the 532nm laser line). In such a way, there are thousands of spectra acquired, which carry a wealth of information on the material at the position where each spectrum is recorded. From each of the obtained spectra, information can be extracted in order to determine various phases within the sample, as well as the degree of stress/strain between them. For such purpose, the spectra have to be processed (e.g., cosmic ray removal, background subtraction and smoothing) before the relevant information is extracted by using filters and algorithms. The resulted information can then be visualised as an image (2D, 3D, 4D) and exported to an appropriate format for publishing or presentations. 4D imaging, with time being the 4^{th} dimension, is very important for dynamic studies both in lab and in real industrial environments.

The ideal case of Raman imaging is recording the basis spectra corresponding to the pure specimens in the sample. This is not always the case and the de-convolution of over imposed basis spectra is not straightforward. To that, the experimental design and settings play an important role, particularly when samples with non-uniform interfaces are investigated. An additional point is whether the pure component is affected by laser intensity or not, resulting in formation of new components upon direct investigation. One way to overcome that is to set the measurement in such a way that the overall spectrum has a relatively good signal-to-noise ratio, even at low laser intensity and short integration time. This is made possible with help

from the latest technology in electron-multiplying CCDs (EMCCDs) with 2.5MHz readout speed, based on the shot noise principle of the signal. Nevertheless, the Raman software and hardware integrators respond to customer problems and present diverse solutions consisting of protocols that enable self-controlled *z*-axis adjustments during scans and laser intensity tuning in a feedback loop with thermo or photo elements mounted on the microscope.

State-of-the-art CCD cameras such as EMCCDs can acquire single spectra, and images for dynamic processes or materials that damage under irradiation, in extremely short time (i.e., 0.76ms has already been demonstrated). This corresponds to more than 1300 spectra per second. The software must therefore be capable to handle the data at a speed of 1300 spectra/s × 6400 bytes/spectrum ~ 7.9 MB/s. This is not an easy task since the processor also has to carry out many other tasks, including data management as well as automated control of microscope table movement and sample positioning, grating system, etc. At this point, for a high resolution Raman image consisting of 512 × 521 spectra, the amount of data generated per layer is as high as 512 × 512 × 6400 bytes/spectrum = 1.56 GB. For an in-depth profile, a ten layer scan amounts 15.6GB for instance and the numbers diverge rapidly with increasing the in-depth profile scans so as the data corresponding to one single experiment may easily occupy an entire hard-disk. This turns out to be more problematic for XRF - computed tomography experiments where surfaces and volumes are investigated with sub-micron scale resolution in matter of seconds. It becomes then obvious that data streaming / management may become an issue when investigating large samples over given periods.

The obtained data sets are built-up in a logical manner. They consist of *X*, *Y* and *Z* coordinates with a given spatial resolution to which a spectrum (Raman or radiography) is associated. The spectrum contains information onto the amount of recorded intensity (count per second, for instance) at a given spectral point (e.g., cm^{-1} for Raman spectra). Additionally, for time-dependent characterisations, time stamp may also be recorded. All the information is then structured into the so-called *hyper-spectral data set,* which is a 6-dimensional vector in this case. In a real experiment, this multiplies with the data points per scan, so as a typical set-up with 256 data points per line scan represents the information of 256 × 256 = 65 536 individual spectra for a 2D surface scan and 16 777 216 spectra for 3D - volume scans. Although the detector records 2D information, the data can be used to reconstruct 3D images, revealing valuable information on the internal structure and chemical properties of the investigated specimens. From that, either different species present within the sample can be identified and quantified by using the main custom designed software or more advanced image analysis packages. Although this is easily amenable with the nowadays high computing power, large data sets require interconnected virtual stations to resolve the spectra.

Choosing the experiment parameters (resolution, point per line scan, detector integration time, etc.) is essential when investigating large surface areas of volumes. That is for the measurement time allocated per one single experiment could easily escalate from hours to days if, for instance, the acquisition time of the detector is not correctly set. Although a simple 2D scan can take from minutes to an hour, a 3D scan could take as long as a day and a half or more if detector/sample pre-alignment procedures are needed between scans to correct from drifts. Nevertheless, dedicated instrument technicians from parent companies give valuable advice onto the best set of experimental parameters to be used. However, the end user takes the final decision in using them, according with the sample specification under investigation. An example for that is the time allocated for recording 16 777 216 Raman

spectra for a 3D - volume scan at a resolution of 256 data points (i.e., spectra) per line scan. Although the experiment would take less than a half an hour for an "ideal" integration time of 0.7ms/spectrum, in reality, good signal-to-noise data can be acquired for an integration time of 50ms/spectrum, which means a complete characterisation will require 9 days. Luckily, the spatial resolution is not always important when studying, for instance, biological samples with features exhibited at micrometre-size scale, making it possible to reduce the measurement time to less than 30 hours for 150 data points per scan, for instance. Even so, the *hyper-spectral data set* associated with a low-resolution measurement could be as large as 54GB.

5.5.3. Big data clustering for further computational analyses

Experimental results forming the *hyper-spectral data set* have to be visualized first in order to choose branches and bound algorithms for efficient computational analyses of spectra. For that, software engineers design rendering codes that allow to look in detail at any record of the data set in order to set multiple spectral domains/filters of interest and to perform basis analyses on each spectra, such as background subtraction, smoothing and averaging, without altering spectral information. Even so, there are several induced artefacts that user should take into account when processing the spectra. They are related to both the filtering procedure used as well as on the intrinsic nature of the sample:

- poor background subtraction resulting in peak shouldering;
- excessive smoothing leads to information altering;
- peak absolute intensity and broadening vary with sample local density;
- similar structures yield similar features in a very narrow spectral range;
- direction dependent de-polarization factors influences peak intensity.

In order to avoid that, it is highly desirable that the rendering software allows having a preview of the residual data. This is a key issue for efficient data analysis, which assures a correct de-convolution of spectra with minimum filters and parameters involved.

There is a series of typical filters used to smooth the spectral data. These are:

- *Moving average*: defined as a "moving" window of data at left and the right position with respect to the current point whose value is replaced by the average. This is suitable for very slow changing signals, particularly for noise reduction;
- *Weighted average*: compared to the moving average, this filter also takes into account some binomial weighting factor or a Gaussian distribution for each value. The resulted values are much closer to the original values and is more suited to rapidly changing data points;
- *Median*: to remove un-correlated data point from spectrum, such as spikes;
- *Savitzky-Golay*: uses the neighbouring data values in a weighted way to fit a polynomial between the point and returns a "fit" value at the current position.
- *Wavelet transformation*: is a mathematical technique somewhat similar to Fourier transformation which maintains both time and frequency information. Wavelets are basic functions used to model a signal. Each level of wavelet decomposition returns an approximation and a detail result. The approximation is used as starting point for the next decomposition and the procedure can be repeated until the detail falls under a given threshold. The spectral information can be then reconstructed, without noise and background;

- *Maximum entropy filter*: is more related to the instrument characteristics in which neighbouring pixels are no longer statistically independent and therefore they have certain weighted values given by instrument functions, which are used to smooth the measured spectra.

With these given, one is able to reconstruct the general image of the *hyper-spectral data set*. There are two ways to do that. One way is based on taking into account each spectrum subjected to the filtering procedures described above to render one image point (2D or 3D) per spectrum, without taking into account the correlation degree between neighbouring spectra. This is the easiest way to look at the data, although important information concerning the interaction between domains may be lost. In order to avoid that, one often makes use of multivariate image generation, in which the correlation between the spectral data points among adjacent image pixels is consider throughout the entire hyper-spectral data set. For that, one may imply multivariate data analysis methods, such as Principal Component Analysis (PCA), Cluster Analysis (CA) or Vortex Component Analysis (VCA). PCA is not only used to render images but also to reduce the data size using distinct sample features based on the principal components. CA is mainly used for image generation and average calculations for further data analysis based on spectra similarities, whereas VCA is more suited to identify the most dissimilar spectra in the hyper-spectral data set.

5.5.4. Principal Component Analysis (PCA) - a powerful tool to cluster information into databases

Principal Component Analysis (PCA) was first proposed in 1901 by Karl Pearson. The method is the most common used among the other multivariate ones since the main purpose of it is to drastically reduce many-fold varieties to a small number of components, which are orthogonal on each other. For instance, the information contained in a 3D Raman scan consisting of thousands similar spectra can be reduced to 4-6 principal components, since all the other features in the spectra are linear combinations of pure principal components or basis elements. Based on PCA, one can extract a variety of results, allowing the user to:

- *reduce the data set* - as mentioned, one can refer now to only few principal components that contain the main information out of thousands of spectra;
- *weight the principal components*, in order to describe the degree of mixing between principal components, particularly for composition dependent phases;
- *reconstruct each spectrum back from principal components*, to render complex 2D/3D images containing intrinsic information onto phase segregations;
- *Cross-correlate different principal components*, particularly important when referring to spectra measured near-grain boundary where the information is intermixed within the lateral resolution limit.

Principal component analysis offers the possibility to sort out the main information contained in very large data sets and map the result as an average of thousands of spectra onto 2- or 3-dimensional real images. In such a way, one may directly select (or mask) specific domains within the sample and study their correlation and evolution in time, for instance. Although the method is automated and objective oriented, data clustering based on principal components may easily demand extra computing power and time. However, one has to take into account that poor signal-to-noise spectra are basically impossible to be analysed and therefore the

experimental conditioning (such as signal integration time, scan speed, etc.) is critical to obtain valuable results.

Based on principal components, clusters can be hierarchically grouped and mixed to obtain the big picture that mimics in great detail the real sample. Technically speaking, component analysis of measured spectra can be done in two ways:

- *starting from measured spectra* to identify the principal components, which are used to cluster the data. This might be problematic for samples with unknown chemistry and high degree of mixing, such as salt dissolved in water. However, specimens with well-defined domains (i.e.; spatially segregated, such as oil and water) and given chemistry can be analysed with high spatial resolution;
- *starting from basis spectra of each component* to reconstruct the chemical mixtures based on weighted averages over imposed onto each other to reproduce the partial contribution of each chemical specie in part. From that, the overall features exhibited by composite samples can be reconstructed from micro- to macro-scale.

Both procedures described above involve a set of well-defined basis components that the user may add to his library for later use and data analysis. Although software developers offers additional modules related to data built up in large repositories, there is a lack of compatibility between them, as software developers have personalized protocols for structuring the library components, such as the way data is saved, stored and accessed at a later time. Even so, one can easily imagine that the repository size may escalate exponentially, depending on the data storage preference of the user. For this reason, accessing any particular information may become a problem for data compatibility often requires format conversion and transfer of multi-GB sized files, which demands time and hardware support. Either way, building up large libraries containing the core features obtained from principal component analysis is not always straight-forward since the process involves a series of extra steps to be taken in order to provide the "*knowledge discovery in databases*", such as: data pre-processing and clustering, establishing metrics among clusters and components, user interfacing and modelling, enabled structure discovery from post-processing, visualization and on-line updating. These aspects of database handling are often referred as "*data mining*", which is a computational process whose purpose is to discover patterns in large data sets involving statistical methods, artificial intelligence and database management. This step in data analysis is essential to identify bad data sets and anomalies, normally associated with system failure, as well as dependencies that enables near real-time product quality control, results validation and automated process adjustment.

5.5.5. Bridging the gap between academic research and industry production

The possibility to analyse in near real-time large amounts of data offers the unique possibility to make critical decisions onto optimising process parameters, which is an important issue mainly for industry sectors to maintain the product quality high by keeping the capital costs low. For that, the industry sectors make use of dedicated software analyses to investigate the relation between statistically structured groups of data with similar or dissimilar characteristics. This process is based on statistical algorithms to correlate data into clusters that exhibit similar patterns, based on principal component analysis (PCA). Although the method is objective oriented, analysing large streams of data in near real-time makes it

possible to create large repositories of data, which can be used at a later time for further analyses.

Unlike industrial strategy, the academia research aims at producing meaningful scientific results to validate existing models or to test new theories. The obtained results are often large sets of data, which need to be interpreted in order to draw conclusions. In the process, however, it is only the high impact results that are selected to be published or patented, whereas the less meaningful ones are discarded or not considered for future reference. This should be avoided since *all* the obtained results are part of a *grand statistical scheme* that provides knowledge. To some extent, this is sometimes visible among published materials, which are mainly focused on novelty matters, whereas poorly correlated results lack in interpretation. Here it is the industry that has a strong point since faulty matters in production chains have to be addressed immediately in order to maintain the quality high by keeping production risks low.

On the other hand, academic and research institutes as well as parts of the industry have strong knowledge of characterisation methods and techniques, although the academic research is highly resourceful in designing and integrating various experimental set-ups for property assessment of new materials intended for specific applications. A typical example in this case is the *co-sputtering of composition gradient thin films* in conjunction with in-situ/ex-situ structural, magnetic, electrical and optical characterisations in order to seek and find new superconducting materials with high critical temperature, reinforced proton conducting polymers with high mechanical and thermal stability for water electrolysis, composite metal-hydride phases for hydrogen storage purposes and multi-layered thin film architectures for photovoltaic elements with enhanced solar energy conversion efficiency. Although many combinatorial characterisation methods are patented, industry does not make use of resources to implement them due to a high degree of risk associated with pure exploratory work.

The industrial, research institute and university research sectors meet somewhere in between when considering *"lab on a chip"* technology. This is specific to a whole class of sensors and actuators that are patterned on millimetre size substrates in a *"ready-to-use"* form. The final product has to be, however, integrated with an electronic platform consisting of power supply, interconnecting wires and electronics, display modules and command interfaces. Although this stage of development and prototyping can be easily carried out within university electronic departments, it is the industry R&D expertise involved in compacting product size and lowering the production costs in order to make the product feasible on market. Besides that, industry has the capability and resources to assess the impact of a new product on the market by addressing specific issues targeted towards customers in order to draw the so-called "*learning curve*" of the product, which is product value projection in time for various application sectors as well as for future product development and commercialisation.

One nice example of how research at universities and independent research institutes can generate valuable input to industry sectors is the deployment of *spin-off* companies, highly oriented towards narrow production fields. Typical examples in this sense are small companies that deal with powder processing and production by mechanical alloying by ball-milling and chemical combustion methods. In the process, there is limited infrastructure involved comprising planetary milling machines, bench-top XRD systems for fast structural

characterization and SEM/EDS/TEM for microscopy analysis, eventually. Once the production protocol is established, powders with given particle size (and shape) can be obtained without the need of using complex characterisation techniques, such as SEM or TEM. The obtained powders can then be transferred to pilot facilities for electrode casting and assembling lines to produce super-capacitive cells and batteries. The difference between research performed at universities and/or research institutes and industry production in the field of nano-structured electrodes is that the former is restricted to studying electrodes with small sizes (i.e., less than $1cm^2$ for electrochemical assessment, most probably due to limited budgets), whereas typical 18650 Li-ion batteries obtained from pilot assembling lines contain electrodes with surfaces that are three orders of magnitude higher in size (i.e., ~700 cm^2). Additionally, university research is constantly focused on finding new solutions to, for instance, increase electrode porosity by using 3D carbon nano-tube decorated materials (i.e., up to 3 wt% per cm^2) in order to enhance charge-discharge capacity and battery lifetime. This is unlikely to be directly transferred to large surface area production lines for scaling up electrode size by a factor 1000 in large batches requires good control of several process parameters such ink viscosity, humidity, thickness and homogeneity, which drastically influence the battery performance. In a feed-back loop with the pilot assembling lines, large size electrodes can be sampled in well-defined sizes and shapes and submitted to university and/or research institute centres to conduct small scale characterisations, from structure and morphology analysis to electronic characterisations upon many charge-discharge cycles. In the process, data is transferred between both sides, such as sample ID, files associated with the characterisation methods and techniques involved, data correlation involving PCA and data clustering, which rapidly builds up into large databases. The sum of activities and decisions taken so far are consistent with a technology readiness level (TRL) of 2 or 3 at most.

Bridging the gap between research at universities and/or research institutes and industry production requires taking a concept proof, from TRL 3 to TRL 5 or even 6, when considering pilot battery assembling lines. This involves a different approach to experiment conditioning, data structuring, analysis and mining to render *the big statistical picture* that describes the critical influence of manufacturing parameters onto the performance of the final product. This part is the most demanding in terms of time, costs and work force, not mentioning the exponential growth of information and knowledge generated. Without going much into detail, let one assume that the industry is interested in producing a new battery with specific capacity and lifetime. For that, industry undergoes a series of procedures in order to optimise the battery performance based on a statistical assessment whose role is to determine which parameters in the production line are the most influential and which ones have less impact. This procedure is referred in literature as "*factorial design*". The input data in *the big statistical scheme* is based on *common knowledge* (as a result of experience) associated with university/institute research and the results obtained so far by industry, according to their integration protocols. The industry integration protocols for batteries involve a series of steps, from electrode foil pre-treatment, slurries mixing containing binders and dispersants in certain proportions, casting, cold or hot pressing, electrode dehydration and winding including the polymer separator, contact welding, cell crimping for atmosphere controlled sealing and addition of electrolyte. Although many of these protocols are trivial, some of them demand extensive studies to assure quality control. For instance, the amount of binder and dispersant used together with the active Li-based material as well as the cathode

load influences both the battery capacity and the lifetime performance. Additionally, electrode compacting upon pressing influences sticking onto the metallic collectors, which may result in a premature battery failure. Above all that, inhomogeneous electrodes with pin-point defects resulted from casting is critical since there is only one defect point on a 700cm^2 electrode to compromise the battery performance. In order to circumvent that, industry makes use of statistical algorithms that account for successful rates for battery manufacturing. The method resembles to a large extent to identifying critical components in an orthogonal space group by using the minimum amount of experiments to explore that. Simply, considering that electrode homogeneity, thickness and compacting conditions are critical parameters, assessing a multi-variable 3D matrix of elements in a space group with 3 variables (i.e., such as low, mid and high levels) demands roughly $3^2x3^2x3^2 \sim 730$ experimental combinations, whereas a diagonal form based on a linear combination of orthogonal matrix elements requires only 9 experiments plus 1 which is a replicate of any of the 9 experiments, eventually. Even so, a poor conditioning of the input parameters in factorial designs may result in lack of information. However, more complex dependencies blocks may be constructed at a later stage to involve other dependent parameters in a way that even poorly correlated data may become important at a later time in information assessment in order to provide knowledge.

It is nevertheless important to specify the missing link between research at university and research institutes and the industry sector related to data management. There is not only one missing link but several ones, which are mainly objective oriented, and work force dependent. It is true that industry makes use of R&D departments to structure information in a way that makes it easier to interpret and use it at a later time. Universities, however, make use of unlimited resources when it comes to data management. A simple way to understand that is to consider the amount of work carried out by master and PhD students, which is more related to optimising experimental design, managing big data sets as a result of complex interfacing with multiple instruments to characterise large batches of samples, as well as the effort spent to program multi-language codes to sort, analyse, fit, plot and present data for publishing and at conferences. The truth about this issue is that this part of student work is never acknowledged and even though robust data analysis is carried out by each student in part, their programming codes are not always passed on since new students come with new ideas onto structuring and analysing data. One other important issue concerning data management at university level is that the master and PhD programs are highly focused on producing valuable knowledge that is quantified into published manuscripts, attendance at conferences and writing a thesis. Since there are no margins for failure during the training period, students are often compelled to discard data and results mainly due to lack of time to correlate them, to understand faulty issues related to their experimental design or data interpretation and even to write a paper or a new chapter in their thesis. In many cases, this part of student work, which is lost, is quantified up to 30% of the student time spent for training. Therefore, it is imperative that new approaches to maximize students outcome should be considered, perhaps with more involvement from the IT divisions within universities and by improving self-managerial skills of the students with help from company personnel with expertise in the field. A strong link between universities and research institutes is always beneficial as the latter can guarantee continuity in the scientific process owing to the permanent nature of employment of the research scientists.

5.5.6. Recommendations

1. Universities should be financially supported with EU frameworks to create dedicated IT environments (i.e., hardware, software and personnel) for data management, meaning data streaming, clustering into databases, data mining, rendering and modelling. One can imagine that multi-GB data files are constantly generated in near real-time when involving high resolution imaging techniques and methods, which are improper to be accommodated even on ONE high capacity HD that comes with the process system. Due to the complexity of data, the experimental results do not have to be interpreted immediately but it may take days or weeks to de-convolute them into principal components, basis spectra, etc. Therefore, a robust back-up networking is needed.
2. IT departments and small companies should be more involved in data management from complex experiments carried out by natural science departments involving large data sets, which have to be structured in a logical manner. Accordingly, science departments designing complex data acquisition interfaces should work in a feedback loop with IT departments or small companies in the field to make it easier to manage large data sets into libraries for further statistical analysis that generates knowledge. Therefore, EU may consider elaborating new strategies and programs to have IT departments or small companies included in research programs as a valuable asset that guarantees proper data management, minimal data loss and high knowledge output;
3. EU should initiate programs to maximize student training programs within universities in a way that encourages young code-writers and software developers to start a *spin-off* company that would be a great input for universities and macro-companies as well, particularly in their field of expertise;

5.6. Multi-technique characterisation methods

5.6.1. Introduction

Multitechnique characterization methods (MCMs) are important for the industry to characterise new materials originated from R&D efforts as well as to control quality and functionality of materials in production. MCMs offer complementarity in measuring different properties and assessing performances and can facilitate the validation of material and their production routes. In industrial upscaling processes, reliability and reproducibility of material synthesis developed at lab scale are some of the main challenges. In addition, non-destructive testing routines must be establish to ensure product quality, without interrupting the production process. Once the production stage of a material is reached, industries do not normally use "academic" laboratories for characterisation and testing unless deep investigations of unexpected problems or material improvements are required. At the production stage, industries favour use of in-line and real time characterisation tools (see also §5.5). However, suitable combinations of multitechnique tools at research laboratories may reduce the number of steps of the tests to be performed approaching thus the rapid or real time techniques preferred by companies. A number of companies require materials characterisation under harsh production/processing conditions, such as in liquid, under high-pressure, in vacuum or in a controlled atmosphere. In these cases, single and/or multitechniques tools based on light (or other easy to handle types of radiation) are more suited as it is often possible to investigate the products without removing them from the in-line production stream.

Increased interest in specific material types and applications have set up strong requests for developing dedicated multitechnique characterisation tools for assessing the properties of these materials with respect to given applications. In this context, there is for example a marked exigence for developing multitechnique tools for characterising rapidly porosity/surface area of materials with large pore size ranges. Other examples include, rapid measurement/assessment of molecular weight of polymers which is important in synthetic processes as well as in the field of protein-derivate products; in-line chromatography for characterising products and by-products in a production line, pushing GC, HPLC and mass spectrometry to higher speed of shorter analysis time.

In general, the speed of analysis is considered as one of the key performance parameters to be improved. The difficulty for some commonly used techniques to achieve a faster operation is challenging. This is indeed the case for the already widely diffuse XRD and XRF systems. Moreover, many of these techniques are often available in academic laboratories rather than in industrial plants, owing to their high cost and the need of specialised operating personnel. Nevertheless, concrete advances have been achieved in this direction, as it can be seen e.g. for electron microscopy (EM), another very versatile and popular multitechnique toolbox. In EM, several modifications and additional operation modes were introduced during the last decade to face some of the issues mentioned before. As a result, low-vacuum SEM is now used for sizing and characterisation of outgassing non-conducting samples. Tabletop SEMs work also at low-vacuum and can even offer sub-micron spatial resolution. Avoiding sample conducting coatings, via use of low-vacuum SEM, provides non-destructive analysis and the sample could in practice be returned to the processing line. In liquid environmental SEM (ESEM) is less time-consuming than environmental TEM (ETEM) and provides solutions in characterisation tasks requiring inferior (than ETEM) spatial resolutions (tens of nanometre). In-air-SEMs may be combined with in-line processing for characterization of native samples. It is worth of mentioning that semiconductor industry already utilises on-line inspection SEMs, which work under automatic modes and are tailored-made to meet specific processes requirements. These developments could be adopted in a broader group of materials applications. At the moment, the choices for the industry in terms of EM vary from regular academic EM systems, bench EM to automatic EM. On the basis of low budget and non-destructive inspection, it seems likely that industry will be moving towards bench-type and low-vacuum EM solutions. This type instrumentation is expected to be further developed in various applications and combined to operate automatically under materials processing/production.

Table 1 below summarises different techniques commonly used for material identification and property characterisation at different steps of material development, ranging from first laboratory trials to final mass production. Each cell can be considered a multiple technique toolbox. The Table shows a reduction of the multitechnique toolbox size when we move from the lab scale/pilot scale, i.e. where the analysis time is not that important, towards the production stage where a material flow is generated and the tests should be performed rapidly in real timer. It is therefore evident that there is a potential of development of multi-technique toolboxes in industrial production. Some of these aspects are also discussed in other sections of the report (e.g. §5.7).

Table 2 below shows another example of the importance of multitechnique approaches, in characterising nanomaterials in complex environmental samples. It should be emphasised that efforts are still needed for instrumentation developments and grouping of techniques in unique platforms, not only for industry needs but also for environmental monitoring as well

as regulation, health and safety. Important documentary standards still under drafting will be of great interest for the industries focused on research or product manufacturing. Two of these are:

CEN/TS 17010 Nanotechnologies - Guidance on measurands for characterising nano-objects and materials that contain them (to be published by the end of 2016)

ISO/TR 12885:201x Nanotechnologies – Health and safety practices in occupational settings (to be published by the end of 2017/ early 2018)

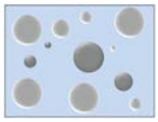
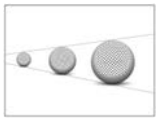
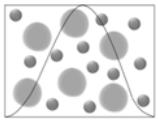
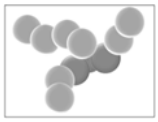
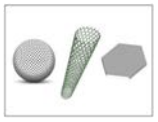
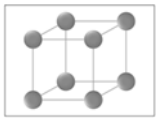
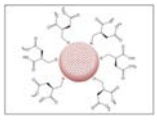
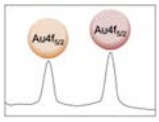
Table 2 also includes techniques for aerosol measurements that allow emission monitoring of airborne colloidal particles and nanomaterials (down to PM2.5 and below).

Table 1. Multi-technique toolboxes and associated acronyms for specific characterisation types

Information extracted	Material Development Stage →		
	Initial trials (+ modelling) at the lab. level, synthesis-proved and validated (*at the bench scale*)	Validation and demonstration in industrial environment (*at the pilot scale*)	Industrial production and market uptake
Composition/chemistry	XRD, XRF, EDS/WDS , FTIR, Raman, SERS, TERS, PIXE, AES, ICP-MS, MALDI, SIMS, XPS, XAS, EXAFS	XRD , EDS/WDS, FTIR, AES, ICP-MS, SERS, XPS	XRD, EDS/WDS, FTIR, AES
Geometry (size, morphology, etc.)	Optical microscopy, DLS, SEM, TEM, HRTEM, NTA, BET, SMLS, NIR, XAS, XRD, XRT, FBR, SFT, SFU, ORM	Optical microscopy, DLS, SEM, NTA, BET, SMLS, NIR, XAS, XRD, XRT, FBR, SFT, SFU, ORM	Optical microscopy, DLS, SEM, NTA, BET, SMLS, NIR, XRD, FBR, SFT, SFU, ORM
Crystallography	TEM, FEG-STEM, XRD	XRD	XRD
Spatial sensitivity	TEM, SEM, AFM	SEM, AFM	SEM, AFM
Surface sensitivity/catalytic activity	XPS, AFM, AES, LEIS, UVPS, TOF –SIMS, LIBS, XAS, ATR FT-IR, CA, GD-OES	XPS, AFM, AES, TOF-SIMS, ATR FT-IR, CA, GD-OES	AFM, CA
Optical properties	UV-vis absorption spectroscopy, CD	UV-vis absorption spectroscopy, CD	UV-vis absorption spectroscopy, CD
Electrical properties	ESPM, STM, SCM, SMM, KPFM, SSRM, Transport measurements	ESPM, SCM, SMM, KPFM, SSRM, Transport measurements	Transport measurements
Mechanical properties	AFM, macro- and micro-nanoindentation, macro-micro-nano-tensile, compressive, flexural and torsional tests, fracture toughness, Fatigue, Creep, XRT, adhesion tests for coatings (scratch, tensile, pull-off), DMA, TMA	AFM (Peak-Force, macro- and micro-nanoindentation, XRT, adhesion tests for coatings (scratch, tensile, pull-off), DMA, TMA	Charpy/Izod tests, macro-tensile/compressive, flexural and torsional tests, macro- and micro-nanoindentation, DMA
Magnetic properties	AC and DC susceptibility, MFM, SHPM, MOKE, XMCD, VSM, SQUID Magnetometry, Magnetotransport measurements, EPR, FMR	AC and DC susceptibility, MOKE, Magnetotransport measurements, EPR, FMR	AC and DC susceptibility, low field magnetization measurements.
Thermal properties	SThM, TGA, DSC, DTA, Thermal diffusivity/conductivity measurements (e.g. Laser flash), dilatometry and thermal expansion measurements	SThM, TGA, DSC, DTA,Thermal diffusivity/conductivity measurements (e.g. Laser flash), dilatometry and thermal expansion measurements	TGA
Viscosity	Rheometry/Microrehometry, Diffusion-Quarz crystal microbalance	Rheometry/Microrehometry, Diffusion-Quarz crystal microbalance	Rheometry
Electrochemical properties	Potentiodynamic polarisation methods, LPR, EIS, EN	Potentiodynamic polarisation methods, LPR, EIS, EN, Salt Spray/Fog	Salt Spray/Fog

AC and DC susceptibility: susceptibility in Alternate Current or in Direct Current AES: Auger electron spectroscopy ATR-FTIR: Attenuated Total Reflectance FTIR BET: Brunauer, Emmett, Teller surface area measurement CA: Static and dynamic Contact Angle CD: Circular Dichroism DMA: Dynamic Mechanical Analysis DSC: Differential Scanning Calorimetry DTA: Differential Thermal Analysis EIS: Electrochemical Impedance Spectroscopy EN: Electrochemical noise EPR: Electron Paramagnetic Spectroscopy ESPM : Electrical Scanning Probe Microscopy EXAFS: Extended X-ray Absorption Fine Structure FBR: focussed beam reflectance FEG-STEM: field emission gun scanning transmission electron microscope FFF (AFFF/CFFF): Field Flow Fractionation FMR: Ferromagnetic Resonance FTIR: Fourier Transform Infrared Spectroscopy GD-OES: Glow Discharge - Optical Emission Spectroscopy HRTEM: High Resolution TEM KPFM: Kelvin Probe Force Microscopy (work function) ICP-MS: Inductively Coupled Plasma – Mass Spectrometry LEIS: Low Energy Ion Scattering	LIBS: Laser Induced Breakdown Spectroscopy LPR: Linear polarization resistance MALDI: Matrix-Assisted Laser Desorption/Ionization MFM: Magnetic Force Microscopy MOKE: Magneto Optic Kerr Effect ORM: 3D optical reflectance measurements NTA: Nanoparticle Tracking Analysis PIXE: Proton-Induced X-Ray Emission SFT: spatial filtering technique SMLS: Static Multiple Light Scattering SCM: Scanning Capacitance Microscopy SERS: Surface Enhanced Raman Spectroscopy SFU: single frequency ultrasound SHPM: Scanning Hall Probe Microscopy SIMS: Secondary Ion Mass Spectrometry SMLS: Static Multiple Light Scattering SMM: Scanning Microwave Microscopy SSRM: Scanning Spread Resistance Microscopy SThM: Scanning Thermal Microscopy TERS: Tip Enhanced Raman Spectroscopy TMA: Thermomechanical analysis TOF-SIMS: Time-of-Flight Secondary Ion Mass Spectrometry UVPS: Ultraviolet Photoelectron Spectroscopy WDS: Wavelenght Dispersion Spectroscopy XAS: X-Ray Absorption Spectroscopy XMCD: X-ray Magnetic Circular Dicroism XRD: X-Ray Diffraction XRF: X-Ray Fluorescence XRT: X-ray micro-Tomography

Table 2: Overview of nanomaterial characterising parameters and corresponding analytical techniques (from Part et al., see also: http://dx.doi.org/10.1016/j.wasman.2015.05.035)

Nanomaterial characterising parameter		Analytical techniques
Concentration related to particle number or mass		FS, GC-MS, MALS, ICP-MS, SP-ICP-MS, UV/vis
Elemental composition		EDS, GC-MS, ICP-MS, SP-ICP-MS, XPS, AES
Particle size		AFM, APS*, CE, CLSM, CPC*, DMA*, DLS, ELPI*, FFF, FMPS*, FS, HDC, NTA, MALS, SAXS, SEC, SEM, SMPS*, SP-ICP-MS, TEM, XRD
Particle size distribution		AFM, APS*, CE, CLSM, CPC*, DMA*, DLS, ELPI*, FFF, FMPS*, FS, HDC, NTA, MALS, SAXS, SEC, SEM, SMPS*, SP-ICP-MS, TEM, XRD
Agglomeration aggregation state		AFM, DLS, CLSM, FFF, FS, NTA, SEM, SP-ICP-MS, TEM
Shape		AFM, CLSM, FFF, SEM, TEM, XRT, DLS, SAXS
Structure / crystallinity		HR-TEM, SAED, SAXS, XRD, XAS
Surface area		AFM, BET, SEM, TEM, XPS
Surface charge		AFM, BET, zeta potential by DLS, XPS
Surface functionality		EELS, FTIR, Raman, XPS, ToF-SIMS, XAS
Surface speciation		AFM, Fluorescence labelling,ToF- SIMS, STM, XPS, XAS

* Only for aerosol measurements

AAS: Atomic absorption spectrometry AES: Atomic emission spectrometry AF4: Asymmetric flow field flow fractionation *APS: Aerodynamic particle sizer BET: Molecular gas adsorption according to Brunauer–Emmett–Teller Theory CE: Capillary electrophoresis CLSM: Confocal laser scanning microscopy *CPC: Condensation particle counter DLS: Dynamic light scattering *EDB: Electronic diffusion battery *ELPI: Electrical low pressure impactor *FMPS: Fast mobility particle sizer FS: Fluorescence spectroscopy GC-MS: Gas chromatography – mass spectrometry HAADF-STEM: Scanning transmission electron microscopy with a high-angle annular dark field detector	HDC: Hydrodynamic chromatography HLPC: High-performance liquid chromatography ICP-AES: Inductively coupled plasma atomic emission spectroscopy MALS: Multi-angle light scattering *(Nano)DMA: (Nano) differential mobility analyser SAED: Selected area electron diffraction SAXS: Small-angle X-ray scattering SEC: Size exclusion chromatography *SMPS: Scanning mobility particle sizer SP-ICP-MS: Single particle ICP-MS ToF-SIMS: Time of light secondary ion mass spectrometry XAS: X-Ray absorption spectroscopy XRT: X-Ray micro-tomography

5.6.2. Recommendations

1 Upon evidence of lack at regional and/or national level, EC should promote and support the creation of **novel** multitechnique platforms in collaboration with national/regional funding agencies/bodies and with manufacturers and industries suitable for the characterisation and for the explorative production of innovative materials.
2 Support technical upgrades of pre-existing platforms.
3 Establishment of multitechnique experts able to interact with the instrument manufacturers as well as with industrial users.
4 EC should promote standardization of several instrumental parts in these platforms e.g. mounting stages, sample holders, sample transport under controlled atmosphere etc. to guarantee complementarity among different platforms.
5 EC should promote networking activities between the different platforms

5.7. Process Analytical Techniques (*In-situ* and *In-line* Characterisation)

5.7.1. Terminology:

There is a confusion regarding the terms used to describe analytics applied to the materials manufacturing industry and definition is required here. The field of analysis when applied to an industrial process is in general governed by the term **process analytical techniques (PATs)** and is defined very strictly below. It governs the application of analysis methods to the measurement or understanding of a process. PAT overlaps with the general concept of **advanced process control (APC)** which is centred on using process measurement to control the process. ***In-situ*** techniques refer to property and/or spectroscopic measurements and/or imaging that can be applied to a reactor process or a suitable model system to provide fundamental understanding. We use the term **in-line** (there is very little consensus in the use of these terms) to describe analytical measurements that are carried out during the process (strictly should be described as on-line) or products at speeds consistent with production rate.

5.7.2. Background:

The scale-up of a laboratory process into a full-scale manufacturing process is challenging. It requires careful design and several stages of quantity magnification moving from micro-reactors, macro-reactors, pilot scale, side-stream and then full production. Very often, scale-up will involve different materials (e.g. moving from glassware to stainless steel), changes in

pressure, reactor design (simple stirred pot to continuous reactor bed), changes in solvent (e.g. to solvents of low health and environmental impact) and, of course, the challenges of moving from grams of materials through to kg and tonnes. The design of industrial reactors must be consistent with high energy, environmental and material efficiency and very often require starting material recycle and product separation from mixed exit streams. Scale-up will also involve both environmental legislation conformance, as well as industry/product defined regulation/standardization.

Scale-up itself is often loosely used and is a very general term. It involves developments such as:

a) The scale-up of a laboratory process to full-scale production. As described above it is extremely challenging (and expensive) and it requires multiple inputs from scientific personnel (chemists, physicists, biotechnologists etc.), equipment designers, engineers (chemical, electrical, mechanical, metallurgical etc.), software designers, health and safety experts and numerous ancillary supports.
b) Process intensification – where a process is modified to allow greater yield or greater rate of production. This might include larger reactors, use of high conversion temperatures, higher pressures etc. This might also demand changes from batch reactors to continuous flow-through reactors.
c) 'Lean' production demands where reactors, conditions and materials are developed to maximise yields, minimize waste and deliver environmentally benign processes.

In order to scale a process, several layers of characterisation are required. The first of these is raw material characterisation and confirmation of specification in agreement with supplier and user. The second is characterisation of the product in terms of the customer specifications and industry regulation. The material characterisation required here is dealt with in preceding sections and requires the usual material properties of composition, morphology, size, crystal structure, mechanical properties, thermal properties etc. These analyses are often off-line and carried out remotely from the reactors at internal or external quality control laboratories.

More challenging is the choice of the right characterisation type that will deliver a comprehensive understanding of the reaction and the process during manufacturing. The metrologies available can be described in two broad terms:

In-situ* methods:** These are techniques that can study a reaction/process as it progresses. **Remote *in-situ methods follow reactions in model reactors or environments that mimic industrial environments. **True *in-situ*** techniques can be applied to actual reactors. Clearly, for scale-up, the development and use of techniques that are at true reaction conditions (true in-situ techniques) provide the maximum value but other *in-situ* analysis techniques (remote in-situ methods) can provide fundamental knowledge of the process.

In-line characterisation: This is also a loosely used term but specifically here means techniques that can be used to monitor production. **At-line** is sometimes used to describe techniques that are used at the reactor or process equipment. **Real-time** techniques have a meaning in the industrial sector. These are analyses carried out in a period shorter than that when changes might occur to the product. In-line analysis can include these methods but it mainly refers to any characterisation method that is used and which allows for the process or

product to be monitored in order to maintain process and/or product specification. The aim of in-line methods is to allow the process to be run so that reliability and reproducibility are ensured and be non-destructive (to both the samples and the continuation of the process) so that any testing does not interrupt runs. It must be recognised that owing to the fact that industrial production occurs at large scale, meaningful analysis needs to be carried out on multiple lots and multiple times. There is also a need to develop in-line methods that allow rapid **'screening'** of products and which are consistent with assessing the reliability and reproducibility of the process through production.

5.7.3. *In-situ* techniques

For convenience, these will be divided into laboratory or remote based methods that mimic process conditions and true *in-situ* tools that can be applied to production equipment. It should be noted that the tools required would differ from sector to sector. For example, semiconductor fabrication can involve high vacuum and ultra-high vacuum techniques. Heterogeneous catalysis can involve gas pressures from 1 bar to 100's of bar. Liquid phase techniques can include a range of methods around homogeneous synthesis, particle precipitation and film formation at substrates. Each of these will require specialised equipment sets. A challenge that should be noted is the need to develop equipment that is generic in nature and can be used in multiple sectors or multiple material products.

5.7.3.1. Remote in-situ techniques:

These techniques are either too expensive or too complex to be used within an industrial environment. They can be used to quantify important parameters such as phase changes, defect formation, thin film growth and quality, morphological, compositional, chemical state and property changes etc. Some of these can be used as real *in-situ* techniques such as RHEED (reflection high-energy electron diffraction) used to monitor film fabrication in some semiconductor technologies.

Electron microscopy (both scanning EM and transmission EM) is becoming an important tool for *in-situ* characterisation. The advances in low-vacuum electron microscopy allow structural and morphological assessment of materials in real or close to real conditions. For example, it is now possible to look at film formation from polymer-solvent solutions and study effects such as phase separation. These low-vacuum techniques can also neglect the need for coating and allows non-destructive testing of samples. Bench top instruments that allow this form of analysis are now becoming available and coupled to software advances that allow automatic sampling and analysis (e.g. for particle size and distribution determination). A number of cells have been developed for both SEM and TEM that allow (a) *In-situ* micro/nano-mechanical methods (tensile/compression, indentation tests) for nano/micro mechanical properties, (b) In-situ heating for annealing/reaction using metals, polymers, semiconductors etc., (c) In-situ growth/self-assembly/reaction in liquid/gas environment usually for nano-material fabrication, modification, growth and manipulation and (f) In-situ wetting/condensation for characterisation of hydrophilic/hydrophobic surfaces, low dimensional materials, heat transfer applications etc. However, it is true to say that most of the in-situ methods are still at the early research and development stage and have not moved yet towards the industrial stage. It is also important to recognise the importance of scanning probe techniques and atomic force microscopy, which can operate at high pressures and in liquids for the study of materials in real environments. These have been applied to biological technologies but like electron-based methods, have yet to be truly developed for

industrial use. The challenges of any microscopy-based tool is the accuracy of sample representation. Complete statistical representation can require analysis of many samples and with vacuum-based techniques or methods involving complex sample preparation, true statistical compliance may not be possible.

Various spectroscopic techniques have emerged in recent years as a way of probing chemistry and processes in conditions akin to those used industrially. Electron-based processes (where either the incident probe at the sample and/or the exit, reflected or scattered, beam) are particularly challenging for *in-situ* because of a number of factors. Principle amongst these are the limited path length of electrons through non-vacuum environments because of the strong interactions of electrons with matter. This can also result in strong signals from the environment and separation of signal from the atoms of the sample and e.g. the gas phase atoms in high pressures can be complex. However, the design of instruments with short path lengths between the source-sample-detector coupled to differential pumping methods that allow relatively high pressures or liquid phases within a vacuum chamber can allow various forms of electron spectroscopies to be carried out. These techniques are also under development for electron microscopy as mentioned above. This type of developments have allowed advances at *in-situ* x-ray photoelectron spectroscopy (XPS). XPS has been a critical method in surface science since the early 1970's but in principle as an ultra-high vacuum (UHV) method. The ability to investigate samples in close to real world conditions (e.g. low vacuum, ambient and/or high pressures) will be of real importance to understanding the mechanism of catalytic reactions and processing/modification of surfaces.

Spectroscopic analysis performed simultaneously with a reaction/process is described as '**operando spectroscopy'** and although very limited in application to real industrial processes, is a developing field of research. The earliest operando methods were built around gas and liquid sampling (e.g. by mass spectrometry, gas chromatography, high-pressure-liquid chromatography etc.). This allows reaction yields, equilibrium and reaction performance (yield, selectivity) to be directly monitored. These techniques can and are used to monitor real world processes of course. The speed of modern analysis by techniques such as Fourier transform infrared (FTIR) allows almost real-time analysis of reactor performance. Spectroscopies such as FTIR, UV-Vis, Raman etc. can also be used to study reactions and not only quantify performance but reaction intermediates. In this context, the role of surfaces and reaction conditions can also be investigated. More specialist techniques such as surface enhanced Raman spectroscopy (SERS) can also offer great insight to reaction mechanisms and surface chemistry in real conditions. However, it is worth emphasising that considerable effort must be applied to the design of cells for model studies. In theory, careful design of reactor side streams by inclusion of windows and sample holders could allow these studies on industrial scale equipment. However, ensuring the equivalence of side streams to the main reactor (bearing in mind pressure and flow changes, pressure drops, thermal gradients etc.) is a very significant challenge for process engineers.

X-ray-based methods are of particular relevance. The weak interaction of x-rays with matter alleviate the problems of e.g. electron-based analysis methods since x-rays have relatively large path lengths through matter and interact little with gas phase molecules and atoms. They have been applied to study surfaces in liquid and high-pressure environments. The last 30 years has seen a rapid development of x-ray based techniques. X-ray diffraction (XRD), x-ray fluorescence spectroscopy (XRF), small x-ray scattering (SAXS) have become well

established. The development of new detectors now allows very rapid collection of XRD diffractograms (decreased from hours to minutes or even seconds). XRF has been revolutionised by new detectors and software development that allows quantitative elemental analysis. Software developments have also spurred XRD through phase identification and composition analysis. New developments such as background analysis may allow XRF to become a means of identifying atom environments but this work is relatively recent. These techniques can be made surface sensitive by grazing incidence studies. Here, surface sensitivity is imposed when incident light is below the critical angle for total external reflection and a standing wave is formed at the surface of the sample. Total external reflection XRF and grazing incidence SAXS are examples of these methods. Synchrotron radiation also underpins many of these techniques allowing rapid analysis and the development of techniques such as extended x-ray absorption fine structure (EXAFS) and x-ray absorption near edge spectroscopy (XANES) which would be otherwise impossible. Whilst these techniques have been developed, their application to manufacturing processes is limited. Cost of high power x-ray sources, detectors and specialist personal limits their development and it is more practical for model studies on carefully designed cells. A number of commercial suppliers now build and supply such cells.

Other techniques can be used but are very specialised due to complexity, cost and availability of equipment or the challenging nature of the work. Mossbauer spectroscopy, positron emission tomography and positron annihilation, neutron scattering, nuclear magnetic resonance are examples of techniques, which are limited to specialist laboratories. However, all of these methods can provide the understanding that underpins successful process development.

5.7.3.2. True in-situ techniques

There is clearly a strong overlap between this section and the following sections that describe in-line methods. Whilst the techniques used may be the same, the difference is that methods described here could be used to study reaction mechanism and reactant changes rather than simple reaction monitoring.

Scanning electron microscopy advances from high vacuum, through low vacuum and environmental SEM (ESEM) could allow on-line process monitoring. Liquid – ESEM at wet interfaces can provide image resolution from <100 nm and "air-SEM" for characterization of native samples could be adapted to specific on-line processes. Automatic operation modes through software instrument control allows the development of rapid inspection tools for many industries. It might be expected that, with the right support, a significant number of companies could move to simple, automatic, bench top systems that would allow materials processing and production to be monitored and controlled.

In a similar way, it might be imagined that low cost, bench top XRD and XRF systems coupled to software that allows sample collection, sampling and analysis could provide continuous, on-line monitoring of processes. These sort of instruments are widely used in the pharmaceutical industry where phase analysis is critical and the development of low-cost detectors capable of ultra-fast analysis would allow the instrument to move towards continuous use.

The key differentiation of these instruments is the number of samples that can be collected and analysed. Whilst simple periodic sampling allows monitoring of materials for quality and

specification purposes there is not enough statistical accuracy to allow process operators to 'tune' conditions to maximize yield or quality. Very often, considerable variation occurs in processes due to environmental and process control drift (temperature, pressure, humidity, flow-rates etc.). Thus, understanding effects based on complex parameter relationships can be an enormous challenge requiring analysis of very many samples. In this way, these experimental techniques must be linked to development of 'big data' software that allows parameter independences to be assessed accurately.

5.7.4. In-line Characterisation

In-line characterization and analysis is not new and is well established. In the simplest case, this concerns mainly environmental monitoring. These approaches can be described under the general heading of process analytical techniques (PATs) where the analytical technique is used to qualify the process through measurement of yield and/or critical material parameters. The FDA describes PAT as 'a mechanism to design, analyse and control pharmaceutical manufacturing processes through the measurement of (critical) process parameters that affect the quality attributes of the product'.

Simple PATs include e.g. infrared-based techniques allowing real time monitoring of simple gases. Simple sensor systems can be used e.g. to continuously monitor the efficiency of combustion processes. Perhaps the simplest form of in-line characterisation is temperature measurement, which can be used to estimate an exotherm and therefore the reaction progress. Even simple reactor mass measurements can be used to monitor the progress of reactions such as evaporation and distillation.

However, in-line techniques that can quantitatively relate a measurement to the desired physiochemical properties of a material are of particular interest since they allow reaction conditions to be optimized to provide a precisely defined product. Such techniques have emerged relatively recently and there is a verifiable need to develop these and other emerging techniques to allow maximum production efficiency. They have a particular role to play in scale-up and translation of laboratory research because conditions can vary considerably from small-scale lab equipment.

Here we centre on liquid phase reactions. Gas phase reactions, such as in heterogeneous catalysis, are well served by techniques such as in-line mass spectrometry and infrared that allow quantification of reactants and products. Solid phase reactions in e.g. metallurgy and solid phase transformations are in general slow and off-line analysis is a practical solution. Liquid phase reactions and liquid-solid reactions (e.g. precipitation, phase separation, emulsification etc.) are more challenging to monitor because of the density of the reaction phase and what can be aggressive (temperature, pressure, pH, etc.) conditions.

Viscosity measurements can be critical to many types of process including biological production, polymer synthesis, emulsification and precipitation. Traditional methods of measuring viscosity and other rheological properties can be slow or indirect. However, techniques such as photon density wave spectroscopy have been developed that allow on-line or in-line use. Here modulated light from a laser is passed through the fluid via an optical fibre into a second optical fibre that allows detection at a photo diode. It is a light scattering technique that allows rheological and particle size changes to be monitored. Sonar based methods are also extremely useful in measuring the rheology of fluids and particle suspensions, emulsion etc. Here, ultrasound is used to interrogate fluids and the Doppler

Effect used to create velocity profiles. These techniques are used remotely and can be applied through steel pipes and vessels. The sensitivity and application of these type of methods is becoming more sophisticated and may become a critical technology in analysing process performance.

Electrochemical measurements can provide a simple method of measuring both reaction progress as well as product evolution and properties. Even simple redox potential techniques can provide rich information.

In-line spectroscopic methods have been briefly reviewed above. Raman, UV and IR spectroscopies can all be used. Challenges for reactor design include the choice of windows, which may not be compatible with reactors. These techniques can also be expensive but have the advantage of being molecule or species specific. Near-IR (NIR) methods are becoming used in industrial environments. They are relatively low cost and simple to use. The development of optical fibre, Fourier transform NIR has led to the development of robust, low-cost equipment that can be used for process information in real-time and have found use in the petrochemical refining industry and the fermentation sector amongst others. The drawback of NIR techniques is the overlapping of bands that requires use of computational techniques such principal component analysis (see §5.5.4) to provide quantifiable data.

Particle size analysis is critical across a wide range of industries central to the European manufacturing sector. Pharmaceutical synthesis is an obvious case but metal and oxide particle synthesis, chromatographic material production are also typical examples. The mining and food industries are also highly reliant on good particle size and size dispersion measurements. There is a host of techniques for off-line analysis including light scattering, various microscopies, sieve analysis and laser diffraction. Backlight imaging and direct imaging methods are now emerging that allow very rapid measurements to be made. Direct imaging is a technique where particles are illuminated and imaged from the same side. Complex image analysis algorithms are needed to quantify sizes and to facilitate morphological data to be estimated. Stream scanning methods (i.e. analysis of one particle at a time) can be used for in-line analysis and one example is the focussed beam reflectance (FBR) technique that is based around reflection of laser light from particles. FBR analyses particles from around 500 nm to greater than 1000 µm and allows both in-line and real time measurements. The spatial filtering technique (SFT) is another example, which holds significant promise for analysis of particle suspensions. Here, the velocity of an object is determined as it passes through a spatial filter in front of a detector and can be used to determine size and velocity simultaneously. However, the minimum particle size that can be analysed is 10’s of a micron. Some useful tools are being developed based on sonar methods. Ultrasonic extinction is very promising, as highly robust, generally applicable instrumentation has been released onto the market. Compared to light based techniques, very dense liquids containing up to 70% solid, can be studied. The apparatus consist of an RF generator and detector across which ultrasonic waves are generated. The extinction of the waves is calculated from the ratio of the signal amplitudes of the generator and detector.

In-line crystal phase measurements are of critical importance to e.g. the pharmaceutical and ceramic powder industries. Techniques such as rapid XRD, Raman and NIR might be used both *in-situ* and off-line to assess materials, however, true inline techniques are less common. However, examples of industrial focused tools are emerging and one of these is the FBR

method described above. Two of the more promising methods are single frequency ultrasound (SFU) and 3D optical reflectance measurements (ORM). SFU is based on the attenuation and speed of an ultrasound frequency (around 2MHz so as not to cause cavitation) through the medium. ORM is related to techniques described above and based on characterisation of back scattered pulsed laser light. This is dependent on the exposed surface area of the particulates and is sensitive to habit, roughness and refractive index. The powerful element of this technique is that it can be carried out on selected particle sizes and shapes.

Surface area, pore size and pore size distribution are other key elements of solid analysis. This is critical to the effectiveness of catalysts, chromatography materials, battery materials, pharmaceuticals and a range of other materials. Despite the importance of these measurements, the number of techniques that can be used to measure these important parameters is very limited and we would stress the need to accelerate the delivery of new rapid and in-line analysis methods. Techniques such as BET (nitrogen and other gas adsorption studies) and mercury porosimetry can give precise answers but are slow and cannot be used in-line. Further, the cost of equipment, time needed and dedicated staff make this a very resource limited analysis. Detailed and accurate pore size distribution analysis can take a few hours by these techniques. However, new analytical methods are being developed based on successful research programmes. The frequency response method is based on the different polarization behaviour of materials in alternating electric fields. The permittivity and dielectric loss are strongly influenced by porosity. This technique has been used for rapid analysis of ceramic powder slurries. One of the most promising methods for particle size analysis is ultrasonic extinction, which can be used for solids, liquids and slurries. The equipment is mechanically, chemically and thermally robust and is being adopted in e.g. the mining industry. However, a new type of equipment based on electroacoustics has emerged where very high frequency conductivity measurements allow for the rapid determination of mean pore size and pore size in membranes and powders. This metrology does not need mercury, vacuum or pressurized gases. Further, this technique also provides the zeta potential of the surface inside the pore structure, which is important for surface functionalization. Samples have to be prepared in wetting solutions. Therefore, this is not a true inline technique but nevertheless allows for very rapid screening during production and both data collection and analysis can be software controlled allowing proper statistical analysis of production materials.

Finally, an area of concern for industrialists has been the in-line analysis of film thickness. Optical methods are making a strong contribution to this field and a host of methods are now available. Laser interferometry is becoming widely used. One variation consists of an LED to create surface reflections, which are then analysed using a laser to define thickness and surface profiles. Various forms of this technique can now be used to look at membranes and to detect defects. There has also been various developments of novel tools for analysis of films and coatings. One example is quantum cascade laser infrared spectroscopy which can analyse coatings remotely and at speeds approaching real time and through challenging environments.

5.7.5. Recommendations

In-situ, in-/at-line and in operando characterisation methods are important for the industry but their development and implementation at both laboratory and industrial scale are challenging. We therefore propose EU and/or national calls within the following indicative areas.

1 Translation of laboratory processes into full production through specific calls.
2 Calls targeting to developing tools that allow characterisation in large-scale manufacturing environments (process analytical techniques) that allow rapid analysis of reaction progress and products.
3 Development of focus calls that allow software development aimed at analysis of large and complex data sets so that accurate parameter dependences can be ascertained in complex processes.
4 Calls focused on the development of *in-situ* analysis techniques for a range of industry sectors. These *in-situ* methods include development of laboratory equipment that allows the industrial environment to be mimicked as well as techniques that can be applied directly to the equipment being used in production. Funding for the development of 'operando methods' is emphasised. Also stressed is the need to fund work in the development of specialist cells that allow reactions to be probed.
5 Specialist calls that allow centres with existing specialised in-situ equipment to be funded for collaborative work programmes with industry partners.
6 Calls focused on the development of in-line analysis for process development. We stress in particular the need for the rapid development of practical and rapid methods to measure surface area, pore size and pores size distribution in porous materials.
7 Calls scoped towards development of rapid 'screening' techniques that allow product material to be characterised at rates appropriate to production.
8 Calls focused on the development of ultra-fast characterisation techniques through development of new sources, detectors and analysis software.
9 Specific calls targeted towards different sectors of the industry recognising the different tool-sets and methodologies needed.
10 Calls requiring a mandatory participation of end-product company (or several companies in order to facilitate development of generic characterisation tools), instrument producers/suppliers and research/academic partners for the development and testing of metrology equipment.

5.8. Regulation, Toxicology and Safety

5.8.1. Introduction

Introducing new products into markets involves considerable risks and high levels of uncertainty. In particular, before novel materials and products will be placed on the European market it is crucial to minimise potential risks regarding development costs as well as, regulatory needs and environmental concerns (health and safety aspects). It is noted that in the European Union and in terms of the precautionary principle it is crucial to identify and minimise potential risks at early stages while considering the life cycle and entire value chain of a product (from production to recycling / disposal). On the one hand, robust characterisation methods are needed towards emission monitoring. On the other hand, characterisation methods are crucial towards testing of novel, advanced materials that is required prior to approval and introduction on the market. On the example of nanomaterials, responsible authorities and organisations (i.e. ECHA, EFSA, OECD etc.) have recognised

that “conventional”, hazardous material properties, such as chemical composition, inflammable or explosive, are insufficient to prove that such novel materials are harmless or not. It was proposed that other material properties, such as size, size distribution, shape or surface charge, need to be consider in addition in order to assess the environmental impacts of advanced materials – in particular, of nanomaterials. Moreover, introduction of novel materials may lead to re-assessment of environmental exposure. As a consequence, it is an ongoing process to adapt and, lastly, standardise methods for material testing as well as for exposure assessment. It has been highlighted by the corresponding Task Force "Safety” that characterisation method protocols, including sample preparation, permanently need to be adapted, as material characterisation plays a key role regarding risk assessment, management and monitoring of advanced products and materials.

It has been indicated that the risks of nano-object containing materials should be assessed on a case-by-case basis (e.g., SCENIHR 2009 [2], EFSA scientific committee 2011 [3]), with particular emphasis on medical devices (SCENIHR 2015 [4]). It is also recognized that a lot of physical effort, financial resources and animal tests are required in order to obtain physicochemical, exposure and hazard data for all relevant exposure scenarios and endpoints for each individual nano-component with specific size, shape, surface chemistry, etc. characteristics. Many initiatives have therefore been taken to explore ways that enable a risk assessment of nanomaterials without demanding to test each individual nanoform in a full test battery. Important aspects of these new approaches include amending tools like (quantitative) structure-activity relationships ((Q)SARs), grouping, read-across and high-throughput screening for assessing batteries of advanced materials. For successful applicability of such new approaches, it is crucial that sufficient nanospecific information becomes available ([5]; [6]).

In particular, the identification of standard calibration and reference materials are therefore crucial for the identification and comparison of exposure scenarios and risks for both human health and the environment. Therefore, prioritisation on the material property characterisation is fundamental for risk identification and categorisation. Furthermore, aspects of exposure, kinetics or hazard assessment are also influenced by the specific properties of the advanced material(s) under assessment. Results, obtained from toxicity assays for material testing, need to be brought into context with such material properties and therefore, reliability, reproducibility and accuracy of characterisation methods are crucial.

Considerable effort has been invested into developing approaches that will guide the developers (e.g. research laboratories and/or industry), producers (industry) users (e.g., consumers, association, stakeholders) and indirect recipient (e.g., environment) towards the assessment of those properties of a specific material that are most likely to cause human health risks during all life stages of the material in different applications [7].

In most areas of research and development where the fast pace on scientific discoveries and materials-based innovation is advancing, there is not sufficient baseline knowledge for defining benchmarks, cut-off values, validation and subsequent regulatory acceptance of specific applications of (quantitative) structure-activity relationships ((Q)SARs), grouping and read across tools.

Thorough characterisation of the physicochemical properties provides sufficient knowledge to indicate the most important risk assessment aspects that are likely to be influenced by

material specific properties. Thus, one aspect to develop is a feasible and regulatory acceptable frameworks and toolboxes to point towards the generation of acceptable data needed for regulatory acceptance.

For instance in the nanomaterials field which, is by far the most attractive from an industrialisation perspective, there is no indication that nanomaterials will lead to other toxicological endpoints than those known for non-nanomaterials [8,9,10]. For this reason, current regulatory frameworks, such as the regulatory framework for chemicals REACH (Registration, Evaluation, Authorisation and restriction of Chemicals [11], are generally considered suitable to address the risks of nanomaterials [12, 13, 14]. Guidance is being modified to explain this, whereas there is a call to adapt the legal text, especially with regard to the information requirements on physicochemical properties. Some (European) legislation has recently been adapted to set rules for the identification of nano-enabled applications (e.g. Cosmetics Regulation EC No 1223/2009 (EU, 2009) and Biocidal Product Regulation 528/2012 (EU 2012)).

In parallel to the regulatory discussion, there is a scientific challenge to provide further insights in the specific properties that are key in the behaviour and toxicology of nanomaterials. These insights can aid in performing a proper and efficient risk assessment for nanomaterials in the future, preferably in a way that accelerates the rate in which the information needed for risk assessment can be generated to assist product introduction in the market.

This has also created a growing awareness amongst stakeholders that responsible innovation is required which is directly oriented towards social and environmental needs. In many countries, responsible innovation is supported by state-led initiatives, in a quest to ensure the safety, desirability and usefulness of emerging innovations for both society as a whole and the environment on which we depend. While regulation plays an ongoing important role for ensuring product safety, within the approach of responsible innovation, considerations of safety questions are also moved further up in the innovation chain. They therefore become integrated into the research and development process itself that have to be assessed [15].

The identification of the following points are of outmost importance:

a) applications of advanced materials with the highest potential to cause human health risks (due to high exposure and/or toxicity)
b) aspects of exposure, kinetics or hazard that address in the risk assessment of the materials,
c) the type of information needed for the regulatory acceptance
d) industrial cases where the use of specific characterisation or grouping, read across and (Q)SARS is likely to become feasible and potentially regulatory acceptable in the future.

Thus, future effort will have to be put into the use of grouping and read-across methods, which will be applicable to safe innovation approaches during the development of new materials in the research and development phase. Examples for nanomaterials already exist [16].

Finally, alignment has to be established between the industrialisation of advanced materials and its safe use. Feasible and standardised characterisation methods are often needed for

experimental studies and for calibrating computerised prediction-making models or models for release, fate and exposure to nanomaterials or advanced materials, as proposed by the Task Force "Safety".

Thus prior to market introduction and penetration, characterisation and detection methods are a prerequisite to determine key material properties, such as size distribution, surface charge or surface density and others, which are critical for product introduction in the market.

Currently a proposed risk assessment strategy has been suggested by Dekker et al, within WP5 in the NANOREG project, which is based on the assessment of six critical elements [17] (see also figure 2). These can be used to prioritise those nanomaterial applications that may lead to high risks for human health. Different phases have to be addressed within the risk assessment, depending on the specific, nano or not, material application, life cycle stage and exposure situation. Furthermore, the suggested approach can also be used to identify those cases where the use of nano-, or not, specific grouping, read across and (Q)SAR tools is likely to become feasible in the future. The approach may also point towards the generation of the type of data that is needed for scientific justification, which may lead to regulatory acceptance of nano-specific applications of these tools.

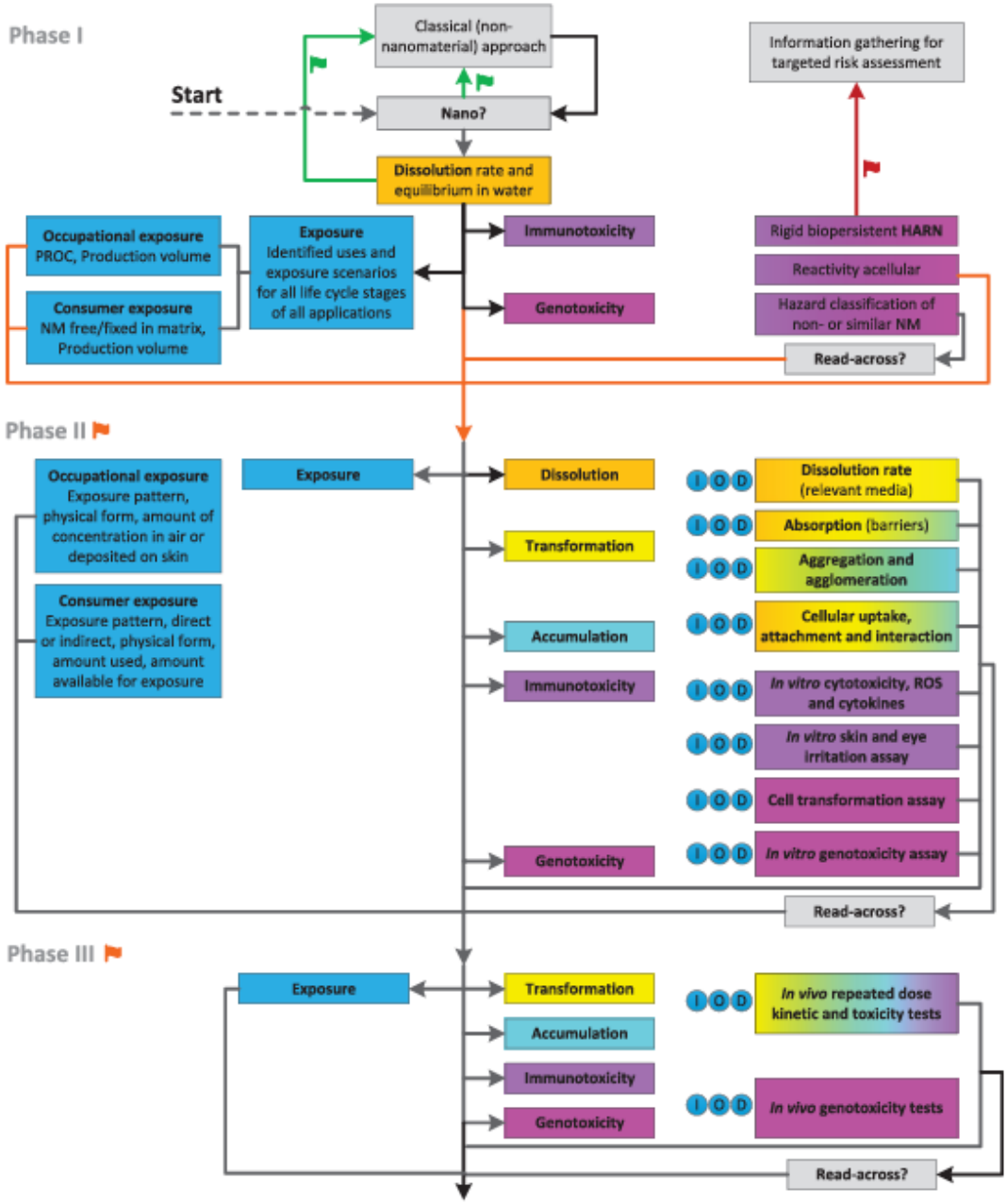


Figure 2. Overview of the different phases of the flow chart (adapted from Dekker et al, 2016). The flow chart can be navigated by following the different colours of the arrows, as described in details in the footnote[5].

[5] Green arrows: the material is no nanomaterial or has such a high dissolution rate in water that it falls apart into its molecular or ionic form before it reaches its target .> the classical (non-nanomaterial) risk assessment approach can be performed. Red arrow: the material is a **"**rigid and biopersistent High Aspect Ratio Nanomaterial (HARN)**".**> substitution or information gathering for targeted risk assessment to evaluated the potential to cause mesothelioma is needed. Orange arrows: the material does not meet the criteria for classical (non-nanomaterial) risk assessment or targeted risk assessment to evaluate the potential to cause mesothelioma **.**> use information of phase I for prioritisation and/or further evaluation following the proposed elements related to the kinetics, toxicity and exposure in phase II, III and further. Black arrows: evaluation of the nanomaterial following the proposed elements related to the kinetics, toxicity and exposure in phase I, II, III and further.

REFERENCES

1. OECD (2007-2016). Testing programme of manufactured nanomaterials http://www.oecd.org/chemicalsafety/nanosafety/overview-testing-programme-manufactured-nanomaterials.htm
2. SCENIHR, 2009. Risk assessment of products of nanotechnologies, 19 January 2009.
3. EFSA Scientific Committee, 2011. Scientific opinion on guidance on the risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain. EFSA Journal 9: 2140
4. SCENHIR, 2015 Guidance on the Determination of Potential Health Effects of Nanomaterials Used in Medical Devices, 6 January 2015
5. OECD (2014). Environment, Health and Safety Publications. Guidance on grouping of chemicals, second edition. Series on Testing & Assessment No. 194, ENV/JM/MONO (2014)4.
6. Tantra R, Bouwmeester H, Bolea E, Rey-Castro C, David CA, Dogné JM, Jarman J, Laborda F, Laloy J, Robinson KN, Undas AK, van der Zande M. Suitability of analytical methods to measure solubility for the purpose of nanoregulation. Nanotoxicology. 2015 May 22:1-12.
7. Collins et al., High throughput screening methods applied to the study of toxicity of nanomaterials, WIREs Nanomed Nanobiotechnol 2016. doi: 10.1002/wnan.1413.
8. Nel, A.; Xia, T.; Meng, H.; Wang, X.; Lin, S.; Ji, Z.; Zhang, H. (2014) Nanomaterial toxicity testing in the 21st century: Use of a predictive toxicological approach and high-throughput screening. Accounts Chem. Res. 2013, 46, 607–621.
9. Donaldson, K.; Poland, C.A. Nanotoxicity: Challenging the myth of nano-specific toxicity. Curr. Opin. Biotech. 2013, 24, 724–734.
10. Gebel, T.; Foth, H.; Damm, G.; Freyberger, A.; Kramer, P.J.; Lilienblum, W.; Rohl, C.; Schupp, T.; Weiss, C.; Wollin, K.M.; et al. Manufactured nanomaterials: Categorization and approaches to hazard assessment. Arch. Toxicol. 2014, 88, 2191–2211.
11. Schwirn et al.: Why are nanomaterials different and how can they be appropriately regulated under REACH? Environmental Sciences Europe 2014 26:4. doi:10.1186/2190-4715-26-4
12. EC, 2012 Second review http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52012DC0572&from=EN ;
13. EC, 2013 REACH review
14. ECHA (2013) Grouping of substances and read-across approach Part 1: Introductory note and Part 2: Read-across illustrative example (Analogue approach: similarity based on breakdown products). Accessible via https://echa.europa.eu/support/grouping-of-substances-and-read-across.
15. NANOREG WP6 Discussion on toxicity testing between Drug development and Manufactured NanoMaterials safety testing [Deliverable 6.3, CONFIDENTIAL]
16. Sips AJAM, Noorlander CW, Lehman HC, Hoehener C. (2015) NANoREG Safe-by-design (SbD) concept. Available at: http://www.nanoreg.eu/images/20150530_SbD_Working_Draft_EU_US_and_ProSafe.pdf
17. Dekkers, S., Oomen, A.G., Bleeker, E.A.J., Vandebriel, R.J., Micheletti, C., Cabellos, J., Janer, G., Fuentes, N., Vázquez-Campos, S., Borges, T., Silva, M.J., Prina-Mello, A., Movia, D., Nesslany, F., Ribeiro, A., Leite, P.E., Groenewold, M., Cassee, F.R., Sips, A.J.A.M., Dijkzeul, A., van Teunenbroek, T., Wijnhoven, S.W.P., Towards a nanospecific approach for risk assessment, Regulatory Toxicology and Pharmacology 80 (2016) 46-59,

5.9. Value Chain Integration and risk management

To enhance value chain integration of all stakeholders regarding material characterisation and up-scaling, existing (national) clusters need to be connected as well as ongoing projects – at

PROC. process and operational conditions. I: inhalation route of exposure. O: oral route of exposure. D: dermal route of exposure.

different stages along the value chain – need to be clustered. In the EMCC[6] survey it was stated that "a characterisation cluster will be ideally placed for both establishing and strengthening such value chain in Europe". In summary, such clusters would facilitate networking and would strengthen the triangular communication between instrumentation/method developers (academic and non-academic), manufacturers and industrial end-users. In particular, such clusters would bring diverse European SMEs together (as depicted in Figure 3). It is noted and highlighted again that robust characterisation methods are crucial towards regulation and approval of novel, advanced materials. For this, projects about method and material standardisation should be promoted, where as many relevant enabling stakeholders as possible should be involved along the entire value chain.

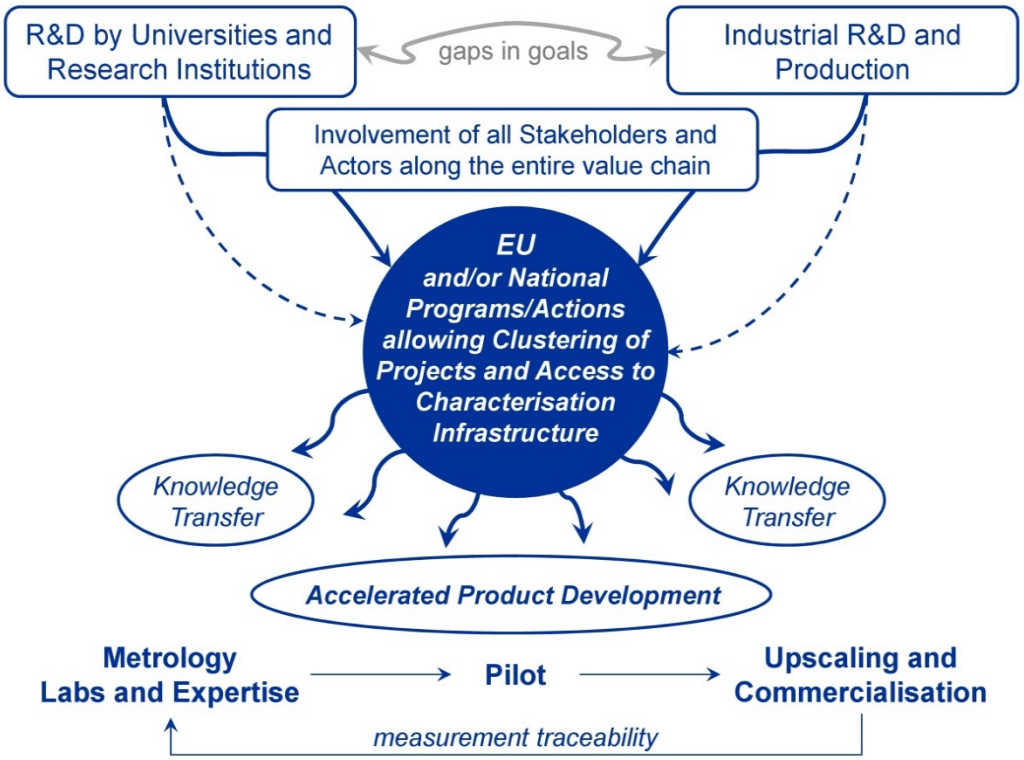


Figure 3. *Proposed EU and/or national programs/actions on material characterisation that allow clustering of projects, networking between stakeholder, access to infrastructure (in particular for SMEs) to accelerate product development*

On the example on engineered nanomaterials and according to the CTTM[7], the value chain from an idea to market very much depends on the technology readiness levels (TRLs): from research, prove of feasibility, development of a pilot, to industrial scale-up and commercialisation. In general, it is challenging to get an overview of all relevant guidance documents about material use and handling (e.g. from SCCS, ECHA, REACH, OECD, SCENHIR etc.) as well as, relevant regulations that highly depend on the respective sectors and business cases. To increase bankability of safety and consumer / costumer's confidence the CTTM propose that the (nano)safety dimension shall be integrated in a business plan as

[6] EMCC (2015). Characterisation: a central pillar for Engineering and Upscaling. A study based on Characterisation Cluster and Engineering & Upscaling Cluster surveys and workshops in 2014/15. European Materials Characterisation Council (EMCC).

[7] Falk et al. (2016). Research roadmap for nanosafety Part III: Closer to the market (CTTM). http://www.nanosafetycluster.eu/news/189/66/Closer-to-the-market-Roadmap-CTTM.html

soon as possible (at low TRLs). For example, in the case of industrial innovation projects of nano-enabled products the so-called Safe-by-Design (SbD) concept by NANoREG[8], expanded as case studies in PROSAFE project, may be used to identify and minimise uncertainties and potential risks at the earliest possible and/or feasible stage of development. This SbD concept and similar risk management tools aims at the integration of different industrial management processes and at showing risk management options together with their associated costs (e.g., in form of precautionary measures and safety dossiers). It is noted that in the course of an innovation project, it is important to consider the entire life cycle of a product and its entire value chain (see figure 4 below).

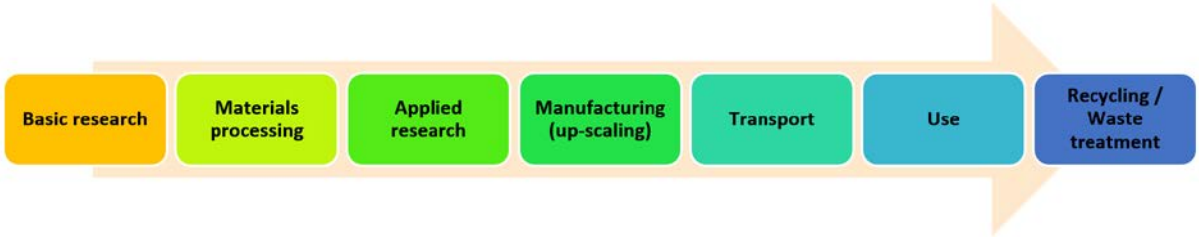


Figure 4: An example of value chain for advanced materials life cycle (Source: NANoREG project)

Figure 4 shows the entire value chain of advanced materials and in each step, the material characterisation plays a key role regarding regulatory preparedness. In addition, advanced materials may (unintentionally) release to the environment, where robust characterisation methods are crucial to assess and monitor potential emissions.

To consider the entire value chain of new products and advanced materials, a lot of effort has been spent in developing decision-making risk management tools that can be standardised, as presented in the previous section. For example, the so-called SbD concept was especially developed for nanomaterials and is in principle based upon industrially adopted stage-gate innovation model. Briefly summarised, the product description – as starting point –passes "gate 1", a business-concept phase can be started at "stage 1" to pass to "gate 2". If then the full product reach the production (described as "stage 5"), the innovation model lead into a market launch. The SbD concept may be then applied to an innovation project to identify risks regarding safety and regulations on a step-by-step basis ("from gate to gate"). Such approach aims at facilitating up-scaling and manufacturing as well as enabling "safer" products and regulatory preparedness.

In addition, to identify and careful assess and weigh all potential risks of advanced products, reliable data about material properties and qualities either have to be available or have to be provided by characterisation clusters having relevant expertise and methods. In addition, it would be beneficial to involve all stakeholders and relevant organisations, who may have different understanding of risk potential associated with the material under characterisation. For example, this could take the form of open discussion and reflection processes, conducted for each stage and gate along the entire value chain. In terms of long-term future vision and sustainability, it is important that "successful industrial product development stories" are

[8] Sips et al. (2015). NANoREG Safe-by-Design (SbD) Concept. © RIVM and TEMAS AG 2016 http://www.nanoreg.eu/images/20150530_SbD_Working_Draft_EU_US_and_ProSafe.pdf

disseminated in their entireness. One example could be the "PACITA" FP7-project[9]. This implies that stakeholders, research and NGO organisations, policy makers as well as consumers, should be kept informed on the ongoing projects, which are at different stages of the value chain. Several reports[10] summarised that stakeholder integration is a key factor in engineering as well as up scaling. The survey by the EMCC[11] highlighted that it is crucial to present the entire value chain. For example, material suppliers may need to adapt their production lines, when they are dealing with new technologies and, consequently, may need novel in-line characterisation techniques. As a result, sub-suppliers or even instrumentation developers may make use of this knowledge to other applications and this may lead to the establishment of future markets. It would be therefore interesting to test the applicability of a product or novel instrumentations to new markets or processes, respectively.

As an example, the NANOfutures[12] initiatives and roadmap focused on several value chains, identifying technical and non-technical actions to be performed at short, medium or long term in order to achieve the final target, i.e. the commercialisation of sustainable and safe nano-enabled products. Such or similar documents may be used to identify gaps which hinder the development and commercialisation of advanced materials, where again robust characterisation methods have a key role.

[9] Parliaments and civil society in Technology Assessment (PACITA). See also: http://www.pacitaproject.eu/

[10] European Science Foundation. Materials Science and Engineering Expert Committee: http://www.esf.org/fileadmin/Public_documents/Publications/ExpCttee_matseec.pdf

[11] EMCC (2015). Characterisation: a central pillar for Engineering and Upscaling. A study based on Characterisation Cluster and Engineering & Upscaling Cluster surveys and workshops in 2014/15. European Materials Characterisation Council (EMCC).

[12] http://www.nanofutures.eu/sites/default/files/VALUE4NANO%20Implementation%20roadmap.pdf

6. Concluding remarks and suggested strategy for materials characterisation in industrial upscaling

6.1. General

This section summarises the most important conclusions in terms of current status and future target and makes suggestions of the subsequent steps to achieve the target (see fig. 5 below)

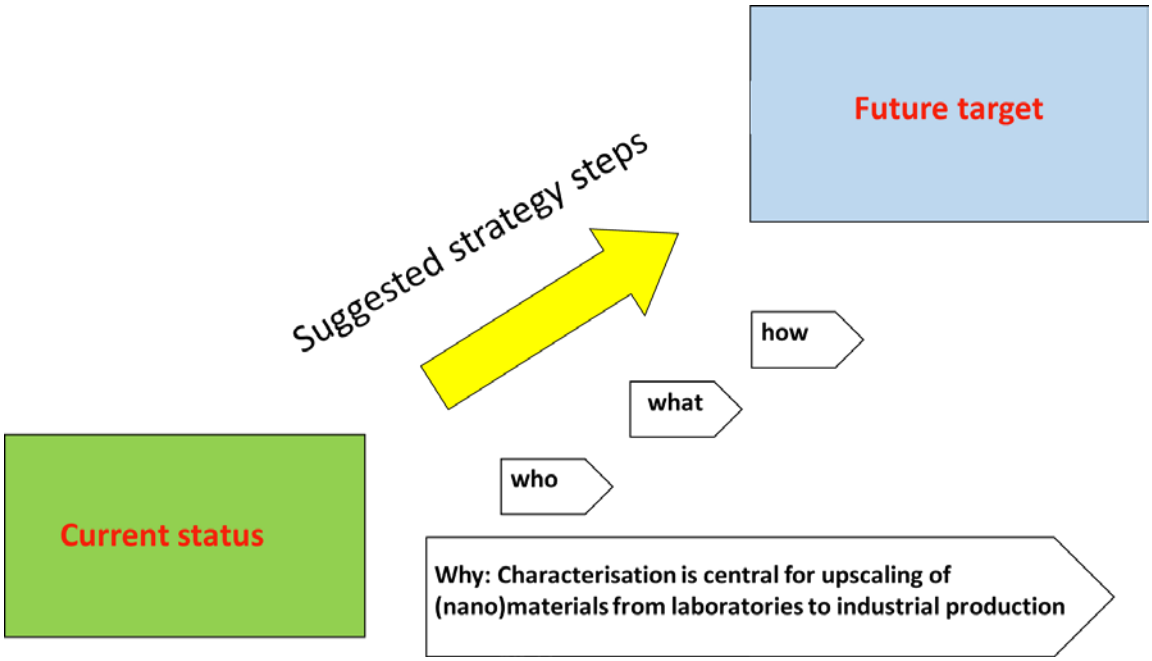


Figure 5: Schematic of suggested strategy. The description of current status and future target is given in the paragraphs below. Suggested strategy steps are summarised in Table 1 in §6.3

The starting point is that the “current status” is based on main conclusions as presented in sections §4 and 5. Whereas the “future targets” are defined as the fulfilment of the identified industry needs based on industry requests as well as, the experience, technical expertise and subsequent assessments of the task force members.

The key elements in the description of the "current status" are classified into organisational and technical aspects.

6.2. Current status

Organisational aspects:

1. Besides the known major analytical facilities, there is a large number of characterisation facilities, mostly fragmented and dispersed regionally and nationally. These infrastructures and the associated competence are not mapped. Few exceptions are some characterisation infrastructure projects in the ESFRI roadmap, which have nevertheless limited industrial applicability, or projects such as ESTEEM2 terminating in 2016 or new infrastructure projects such as EU-NCL. However, the big picture is still missing.

2. National characterisation infrastructures and roadmaps are established in some European countries but not in all.
3. Lack of coordination networking of national characterisation infrastructures at regional and/or European level.
4. Lack of dedicated researchers acting as permanent interfaces between academic characterisation laboratories and industries. This is a real gap in countries and regions with no research institutes or organisations providing an interface.
5. Not uniform access and pricing models in the various infrastructures. There is the "state aid" issue for the use of nationally funded infrastructures by the industry. High costs for industry (especially SMEs) to access advanced characterisation if the characterisation facilities operate at a full cost model.
6. Lack of coordination among instrument producers-industry end users- characterisation scientific experts at national/regional/EU level

Technical aspects:

1. Large diversity of characterisation techniques
2. Wide expertise in standard and tailor-made characterisation methods and methodologies at various groups in European academic and research institutes
3. Advanced characterisation techniques (e.g. spatially localised, multitechnique toolboxes) provide important information especially to nanomaterials and new materials but are difficult to use in- operando, at-/in-line due to technical challenges. However, there is a potential for future development
4. Limited number of in-/at-line, in-situ, in-operando, rapid screening, ultra-fast, low cost techniques and even more limited use at industrial scale.
5. Characterisation to tackle industrial problems often requires multi-technique, multi-competence approaches and industrial conceptualisation by the characterisation experts. These requirements are met today only at a few large research/academic institutions.
6. Lack of large databases with new materials and properties.
7. Lack of reference materials and calibration standards especially for new materials.
8. Absence of calls at national, regional EU level dedicated to characterisation method development.
9. Lack of in silico modelling to predict the material behaviour and performance during the life cycle.
10. Lack of comprehensive scientific evidence and guidance documents for the regulatory definition of characterisation toolboxes and frameworks for product development.
11. Lack of identification and decision making properties to enhance safety along the entire product value chain

6.3. Future targets and suggested steps to reach them

In order to mirror the structure of "current status" we also divide the targets in organisational and technical aspects. The suggested actions/steps to achieve the future targets are described in the Table below where they are prioritised as follows:

Blue cells identify steps with highest priority
Green cells identify actions with medium priority
Yellow cells refer to steps with lower priority

Organisational Targets	**Suggested Steps/Actions**
Allow fast and effective access to infrastructure and fast and effective access to existing competence	**What:** Creation of an effective European access instrument that makes infrastructure and competence available for industrial users, resolving high-cost and the state-aid issue. **How:** (1) One or several ESFRI network(s) of national characterisation infrastructures aiming to (a) map characterisation hubs, (b) create new hubs if needed, (c) enable coordination and networking of hubs to offer complementarity, circumvent lack of capacity, (d) increase competence and enable method development (e) assist ease of access or utilisation for industry users (2) Creation of national roadmaps for research infrastructure (in particular characterisation infrastructure) in all member states These will: • prequalify potential participants in ESFRI projects • ensure regional and national relevance • force active involvement of all member states • avoid brain drain • achieve capacity • maintain regional balance • ensure coherency • pave the way for hub mapping/generation/networking **Who:** (1) Regional hubs targeting local industry requirements, (2) National roadmaps and selection of national infrastructures, (3) National/transnational programs dedicated to characterisation methods development including training of future experts (PhD studentships), (4) EU coordination using the ESFRI and INFRA IA instruments to support coordination and method development.

Fast and professional provision of service	**What:** Interface industrial needs with characterisation (academic) expertise **How**: (1) Accreditation of academic and research labs, (2) well trained characterisation experts at characterisation hubs/centres, (3) availability of hubs in the vicinity of industry and/or effective networking **Who:** National/EU level
Health, Safety, Responsible Research and innovation	**What:** Method development for industrial upscaling should confine with environmental health and safety policies **How:** Involvement of regulators **Who:** National/EU level
Increase data availability, awareness of characterisation methods/principles	**What:** Creation of platforms for communication and e-learning **How**: EU funding **Who**: Transnational characterisation consortia
Technical Targets	**Suggested Steps/Actions**
Next generation characterisation methods for nanomaterials and new type of functional materials (e.g. characterisation of nanosurface properties and quantum-mechanical phenomena)	**What:** Development of disruptive characterisation methods and instruments **How:** (1) Development of a European Technology Roadmap for Nanocharacterisation, (2) Research funding (national and EU, e.g. NMBP) support long term instrument and method development (3) Development of an ESFRI based project for long-term instrument and method development **Who:** National: long-term research programs for characterisation of nanomaterials European Commission: ESFRI, ERC, FET and NMBP funding for instrument and method development for characterisation of nanomaterials

Development and implementation of low cost multifunctional, multiscale and high throughput characterisation methods	**What:** Strengthening of triangle among characterisation instrument producers-industrial end-users-characterisation research experts **How:** Invitation of industry associations, preparation of white papers. Launching dedicated National/Regional/EU calls **Who:** National/EU funding bodies
Access to calibration standards and systems	**What:** develop, store, register high quality standards **How:** Interlaboratory exercise via dedicated EU calls **Who**: Accredited labs, specialist labs
Access to databases for existing and new materials and properties	**What:** creation of big databases for existing new materials and properties. Creation of an efficient automatic updating system for the created databases. **How**: EU calls **Who:** Consortia with adequate complementarity
Development and implementation of in situ, in-/at-line, in operando characterisation, sampling tools, rapid screening, ultra-fast analysis	**What:** Strengthening of triangle among characterisation instrument producers-industrial end-users-characterisation research experts **How:** Invitation of industry associations, preparation of white papers. Launching dedicated National/Regional/EU calls **Who:** National/Regional/EU funding bodies
Development and implementation of off-line (and) tailor-made characterisation methods for new materials	**What:** Strengthening of triangle among characterisation instrument producers-industrial end-users-characterisation research experts **How:** Launching dedicated National/Regional/EU calls **Who:** National/Regional/EU funding bodies

Characterisation and testing of upscaled material production	**What:** Characterise amount/volume of materials relevant to industrial production **How:** Collaboration with and subsequent fund allocation to newly created or existing processing infrastructures (pilot scale) that can process larger quantities of new materials (from a few grams in lab to few kilos in the pilot line) via networking of projects **Who:** Interdisciplinary consortia via national/EU calls
Value Chain, full life cycle assessment and safety	**What:** Strengthening of quadrangle between characterisation instrument producers-industrial end-users-characterisation research experts and regulatory bodies **How:** Invitation of Industry associations, Regulatory and notified bodies to the Preparation of white papers and reflection papers on shortages and limitation in current status characterisation. Launching dedicated National/Regional/EU calls **Who:** National/Regional/EU funding bodies/International Regulatory bodies

Table 3: Suggested targets and strategy steps in priority order, high priority (blue cells), medium priority (green cells), lower priority (yellow cells).

APPENDIX 1: Task Force "Characterisation"-aims

Contact: Sophia Fantechi (Sophia.Fantechi@ec.europa.eu)

The European Materials Characterisation Council (EMMC) is a European initiative set up at the beginning of 2016, based on and strengthening the existing European Materials Characterisation Cluster (created at the end of 2014).

The aim of the EMCC, with the support of the Member States and Regions, is to support the process of developing and improving characterisation tools to bring the development of nanomaterials and advanced materials in Europe into end products more successfully.

Coordination between European, national, regional initiatives and Member State support and contribution will be essential to reach full impact of the EMCC.

The Task Force could intervene in/work with one or more working groups of the European Materials Characterisation Council (EMMC).

Working groups of EMCC include: Instrumentation and Metrology, Reference materials and measurements for standardisation, Characterisation Data and Information Management, Regulation, toxicology and safety, Networking Activities, SMEs & Industrial Needs, Policy and Dissemination.

The Task Force should identify strengths and complementarities and give recommendations to increase input from the Member States and regions into strategic programming and policy development. At the same time, by knowing the MS and regions' interests, policy options can be more effectively defined.

The Task Force is called to concretely contribute to and reinforce the activities undertaken at European level by the EMCC. The focus must be put on characterisation as a core tool to support upscaling and industrial exploitation of research results and hence affect the European economy.

The Task Force should identify regional and national mechanisms to support commercialisation and regulation through the provision of characterisation tools, and seek interaction with regional and national activities.

Meeting date: 18 May 2016

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