High Accuracy printed electronics down to µm size, for Organic Large Area Electronics (OLAE) Thin Film Transistor (TFT) and Display Applications

H2020- DT-NMBP-18-2019

EC Grant Agreement Number: 862410

Deliverable Report: D5.4
Nanosafety assessment of front-plane display materials

Submission Date: 13.10.2023

Delivery Date: 10.10.2023

Prepared by: Susanne Resch, Clemens Wolf & Matiss Reinfelds (BNN)

Type: PU

This project has received funding from the *European Union's Horizon 2020 research and innovation programme* under grant agreement No 862410.

Dissemination level		
PU	Public	**X**
CO	Confidential, only for members of the consortium (including the Commission Services)	

1 ACKNOWLEDGEMENTS

This report was supported by previous work performed within the scope of **Hi-Response**[1] ("Innovative High Resolution Electro-Static printing of Multifunctional Materials", H2020 NMP-PILOTS-Programme) and **INSPIRED**[2] ("INdustrial Scale Production of Innovative nanomateRials for printEd Devices", H2020 NMP-PILOTS-Programme). Further consultation with colleagues from the project **Gov4Nano**[3] ("Implementation of Risk Governance: meeting the needs of nanotechnology", H2020 NMBP-Programme) and the **European NanoSafety Cluster**[4] **(NSC)**, including its different Working Groups, enhanced interdisciplinary and international collaboration in the field of nanosafety and Safe-by-Design. WP5 leader IAP provided project-specific technical specifications and practical insights into all project-relevant processes during an on-site company visit. Alexander Graff, expert at ÖSBS, conducted workplace measurements for potential exposure assessment and supported in the results evaluation.

[1] https://cordis.europa.eu/project/id/646296
[2] https://cordis.europa.eu/project/id/646155/de
[3] https://cordis.europa.eu/project/id/814401/
[4] https://www.nanosafetycluster.eu/

2 DOCUMENT CONTROL

Document Version	Change Made	Reason for Change	Date of Change	Changed By
v1.0	Document creation	N.a.	09.12.2022	BNN
v1.1	Elaboration of chapter 6 (Safe and Sustainable QD Production)	Evaluation of on-site company visit at IAP	03.04.2023	BNN
v1.2	Revision and refinement of overall content	State-of-the-Art Literature review	05.09.2023	BNN
v1.3	Final version for approval by Consortium	Minor corrections and proof-reading	10.10.2023	BNN
v1.4	Modification on confidential information	Minor corrections and proof-reading	12.10.2023	IAP

3 EXECUTIVE SUMMARY

This report is built as an orientation document for small and medium enterprises (SMEs) which are planning to incorporate work with quantum dots in their production. To that end, basic concepts of good manufacturing practices, risk assessment tools and EU regulations which could become relevant, are provided. This is followed by a methodology which can be used to ensure safety and sustainability of nanomanufacturing pipelines, as well as examples of the ways how HI-ACCURACY partners are implementing safe work procedures in research and development laboratories. Readers of the document are provided with further recommended materials which could turn out to be helpful in designing safe and sustainable quantum dot (and other manufactured nanomaterial) production lines.

4 CONTENTS

5 INTRODUCTION

The central part of the QLED display front-plane comprises the light-emitting materials known as quantum dots (in the name QLED, the "Q" stands for quantum dots). Quantum dots are manufactured nanomaterials renowned for their exceptional light-emitting properties. They are based on elements such as cadmium, selenium, or indium. Especially important is the possibility of tuning of the emitted light's wavelength by doing chemical modifications. As a result, quantum dots are widely used in display technology to enhance the color accuracy and brightness of screens.

In the WP5 of the HI-ACCURACY project, front-plane display materials have been investigated. Within this safety assessment the main emphasis will be given to the activities undertaken in the task 5.1, naming, quantum dot synthesis. Reason for that is the other tasks within this work package (from nano-safety perspective) are similar to WP2 and WP4, thus, the relevant safety evaluations have been performed within those WP.

6 SAFE AND SUSTAINABLE QUANTOM DOTS PRODUCTION

6.1 GOOD MANUFACTURING PRACTICES

Good manufacturing practices (GMP) is a quality-oriented approach to ensure that produced goods are safe and meeting the quality needs for their intended use. Originally introduced by the World Health Organisation in 1968 for pharmaceutical products, various “good practice” (GxP) guidelines (and regulations) have emerged ever since. There are five key principles of GMP: people, process, procedure, premises and equipment, and products (Figure 1).

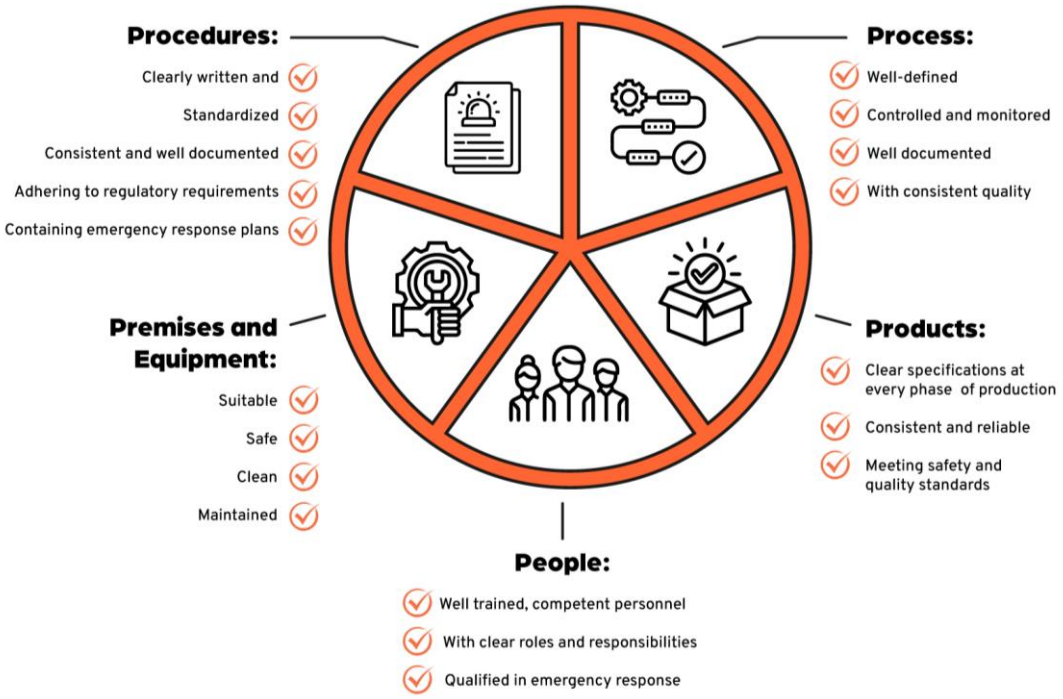


Figure 1: Five key principles of good manufacturing practice.

The GMP principle 'People' emphasizes the significance of well-trained and competent personnel to uphold product quality and safety. Well-defined, controlled, and monitored production processes play a crucial role in ensuring consistent product quality. The 'Procedure' principle underscores the critical role of well-documented and standardized processes, serving as a roadmap for consistent manufacturing, quality control, and regulatory compliance. This ensures that every step of product production and distribution adheres to predefined guidelines, resulting in safe and effective products for consumers. 'Premises and Equipment' in GMP refer to maintaining clean, suitable facilities and well-maintained equipment to guarantee product quality and safety. Finally, the 'Products' principle encapsulates the fundamental objective of any manufacturing process, which is to consistently deliver high-quality goods meeting defined standards. Rigorous quality control, adherence to specifications, and meticulous attention to detail throughout production are essential to ensure the reliability and satisfaction of end-users. Despite GMP being initially developed for medical products, their principles can be adopted to chemical manufacturing in broader sense as well.

In the following chapters it will be elaborated how SMEs can adopt GMP principles in their work with nanomaterials (including, but not limited to quantum dots), with focus on safety and regulatory compliance.

6.2 CHEMICAL RISK ASSESSMENT

The logical first step for development of safe work procedures is understanding what are the potential risks associated with the chemicals used in the production. The basis of a classical chemical risk assessment is the paradigm “Risk = exposure x hazard” (Figure 2).

Figure 2: Risk = Hazard x Exposure.

To prepare a comprehensive **exposure** assessment, it is necessary to map all possible exposure scenarios: (i) occupational exposure, (ii) environmental exposure, and (iii) consumer exposure. Within the framework of this project, the first two are most relevant. For (occupational) human exposure, different possible routes of exposure need to be considered, e.g., inhalation and dermal exposure. Regarding environmental exposure, the three main environmental compartments air, water and soil need to be considered.

To evaluate **hazard**, it is important to collect all the available, relevant information which might assist on the identification of hazardous properties. This information can be categorized as follows:

- Substance identity/chemical category
- Physicochemical properties
- (Eco-)toxicological outcomes (mammalian toxicity, ecotoxicity, toxicokinetic)
- Occupational and environmental benchmark/threshold limits

Research chemicals which are purchased from commercial vendors would usually be supplied together with relevant, reliable and adequate information about above-described categories. Materials produced during research can be already well known, thus obtaining information about hazardous properties is possible using information databases and similar sources (internet search engines, material safety data sheets, published scientific literature, etc.). Meanwhile, the situation is different with novel materials. In this case, read-across and grouping approaches can be used to make estimates about hazards of the novel substance. This is particularly relevant for nanomaterials, including quantum dots.

Like all nanotechnologies, quantum dots raise concerns about their safety and sustainability (see more, chapter 6.5). Even though a lot of research has been done, an overall harmonized approach on how to deal with potential risks caused from using nanomaterials (NMs) along the entire value chain is missing (1), despites nanotechnologies already being used in consumer goods. For example, there are often no exposure limit values for NMs available due to limited scientific data provided on them. Thus, only qualitative and semi-quantitative risk assessments without full quantitative determination can be conducted (1).

Hence, the importance of Safe-by-Design (SbD) principles is increasingly paramount. SbD actions prioritize hazard and risk avoidance during the design or planning stage, which is often a more cost-effective and simpler approach than addressing these issues later when they transform into tangible risks. Furthermore, within the SbD approach, compliance is sought not only with current regulations, but also with those expected in the future (see also, Figure 3).

Figure 3: Risk assessment according to SbD princple (adopted from D1.4).

Project partners were familiarized with the SbD concept in a consortium-internal meeting during the month 6 of the project (24.09.2020) and it was described in the deliverable report D1.4 “Safe-by-Design concept report that will serve as basis for further safety assessments and Safe-by-Design actions” (20.10.2022, not public). The Joint Research Centre from the European Commission has since published a cornerstone framework on “Safe and sustainable by design chemicals and materials” (2), which will be briefly introduced in the “Final safety assessment report for general public & consortium members” (D8.9).

6.3 POLICY CONTEXT

Within the EU, the most important horizontal legislations (which apply across all industries) on chemicals are REACH, TMR and CLP. Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) is EU regulation with the aim of protecting human health and the environment from risks that can be posed by chemicals. Test Methods Regulation (TMR) lays down test methods pursuant to REACH. While Classification and Labelling (CLP) regulation ensures that the hazards presented by chemicals are clearly communicated to workers and

consumers in the EU through classification and labelling of chemicals. The responsible for the administration of REACH and CLP in the EU is European Chemicals Agency (ECHA). To facilitate the implementation of these and various other regulations or directives, EACH is preparing guidance documents in which good practice on how to fulfil the obligations are described. These guidance documents are available in the ECHA website and are highly advisable as starting point for SMEs interested in a particular topic under the domains of REACH. Table 1 provides a non-exhaustive overview of these and other legislative documents which might be relevant to small and medium-sized enterprises.

The safety of nanomaterials in the EU is regulated by various legislations, since the concerns and priorities differ from one sector to another. It is worth noting that various legislations define nanomaterials differently. Partly this is due to historical reason (as some documents predates the EC recommended nanomaterial definition). But another reason is that different legislations have different boundaries for what they address. Among examples of legislations, which address nanomaterials, can be named the biocidal products regulation (EU) No 528/2012, and the medical devices regulation (EU) 2017/745. There are regulations also for food, food packaging, and cosmetics, but all these are outside of the scope of this report. Recently, the recommendation of the definition of nanomaterials (Figure 4) was updated by the European Commission (2022/C 229/01).

'Nanomaterial' means a natural, incidental or manufactured material consisting of solid particles that are present, either on their own or as identifiable constituent particles in aggregates or agglomerates, and where 50 % or more of these particles in the number-based size distribution fulfil at least one of the following conditions:

(a) one or more external dimensions of the particle are in the size range 1 nm to 100 nm;

(b) the particle has an elongated shape, such as a rod, fibre or tube, where two external dimensions are smaller than 1 nm and the other dimension is larger than 100 nm;

(c) the particle has a plate-like shape, where one external dimension is smaller than 1 nm and the other dimensions are larger than 100 nm.

In the determination of the particle number-based size distribution, particles with at least two orthogonal external dimensions larger than 100 µm need not be considered.

However, a material with a specific surface area by volume of < 6 m^2/cm^3 shall not be considered a nanomaterial.

Figure 4: Definition of "nanomaterials" as given in EC Recommendation 2022/C 229/01

For legal purposes, REACH has a slight modification of this definition of nanomaterials (or nanoforms, see Annex VI of the REACH regulation).

Table 1. Overview of EU legislations.

Legislation title or subject area	Abbreviation (if exists)	Purpose	Type of legal instruments	Legislation Number	ELI
Registration, Evaluation, Authorisation and Restriction of Chemicals	REACH	The main EU law to protect health and the environment against harmful chemicals.	Regulation	1907/2006	[5]
Classification and Labelling	CLP	Ensuring that hazards posed by chemicals are clearly communicated when placed on the market.	Regulation	1272/2008	[6]
Export and import of hazardous chemicals	PIC	Implement the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade. Promote shared responsibility and cooperative efforts in the international movement of hazardous chemicals in order to protect human health and the environment from potential harm; Contribute to the environmentally sound use of hazardous chemicals.	Regulation	649/2012	[7]
Test Methods Regulation	TMR	Lists the approved methods for testing chemicals.	Regulation	440/2008	[8]

[5] http://data.europa.eu/eli/reg/2006/1907/2022-12-17
[6] http://data.europa.eu/eli/reg/2008/1272/2023-07-31
[7] http://data.europa.eu/eli/reg/2012/649/2022-07-01
[8] http://data.europa.eu/eli/reg/2008/440/2023-03-26

Major-accident hazards	Seveso III	Control of major-accident hazards involving dangerous substances.	Directive	2012/18/EU	[9]
Worker protection		Introduction of measures to encourage improvements in the safety and health of workers at work.	Directive	89/391/EEC	[10]
Chemical Agents Directive	CAD	For the protection of workers from risks to their safety and health arising, or likely to arise, from the effects of chemical agents that are present at the workplace.	Directive	98/24/EC	[11]
Carcinogens, Mutagens or Reprotoxic substances Directive	CMRD	Protection of workers against risks to their health and safety arising from or likely to arise from exposure to carcinogens, mutagens or reprotoxic substances at work, including the prevention of such risks.	Directive	2004/37/EC	[12]
Waste Framework Directive	WFD	Measures to protect the environment and human health by preventing or reducing the generation of waste.	Directive	2008/98/EC	[13]
Air pollution control		Defining and establishing objectives for ambient air quality designed to avoid, prevent or reduce harmful effects on human health and the environment as a whole.	Directive	2008/50/EC	[14]
Water Framework Directive	WFD	Establishing a framework for Community action in the field of water policy.	Directive	2000/60/EC	[15]

[9] http://data.europa.eu/eli/dir/2012/18/oj
[10] http://data.europa.eu/eli/dir/1989/391/2008-12-11
[11] http://data.europa.eu/eli/dir/1998/24/2019-07-26
[12] http://data.europa.eu/eli/dir/2004/37/2014-03-25
[13] http://data.europa.eu/eli/dir/2008/98/2018-07-05
[14] http://data.europa.eu/eli/dir/2008/50/2015-09-18
[15] http://data.europa.eu/eli/dir/2000/60/2014-11-20

Persistent organic pollutants	POPs	To protect human health and the environment from POPs.	Regulation	2019/1021	[16]
Electrical and electronic equipment waste	WEEE	To protect the environment and human health by preventing or reducing the adverse impacts of the generation and management of waste from electrical and electronic equipment and by reducing overall impacts of resource use and improving the efficiency of such use, thereby contributing to sustainable development.	Directive	2012/19/EU	[17]

[16] http://data.europa.eu/eli/reg/2019/1021/2023-08-28
[17] http://data.europa.eu/eli/dir/2012/19/2018-07-04

The Joint Research Centre of the European Commission (JRC) has published a guidance explaining "how terms and concepts used in the European Commission's nanomaterial definition should be understood, and it reflects established technologies and measurement practices". The guidance also includes a decision tree which can be used as a help with identifying nanomaterials (Figure 5).

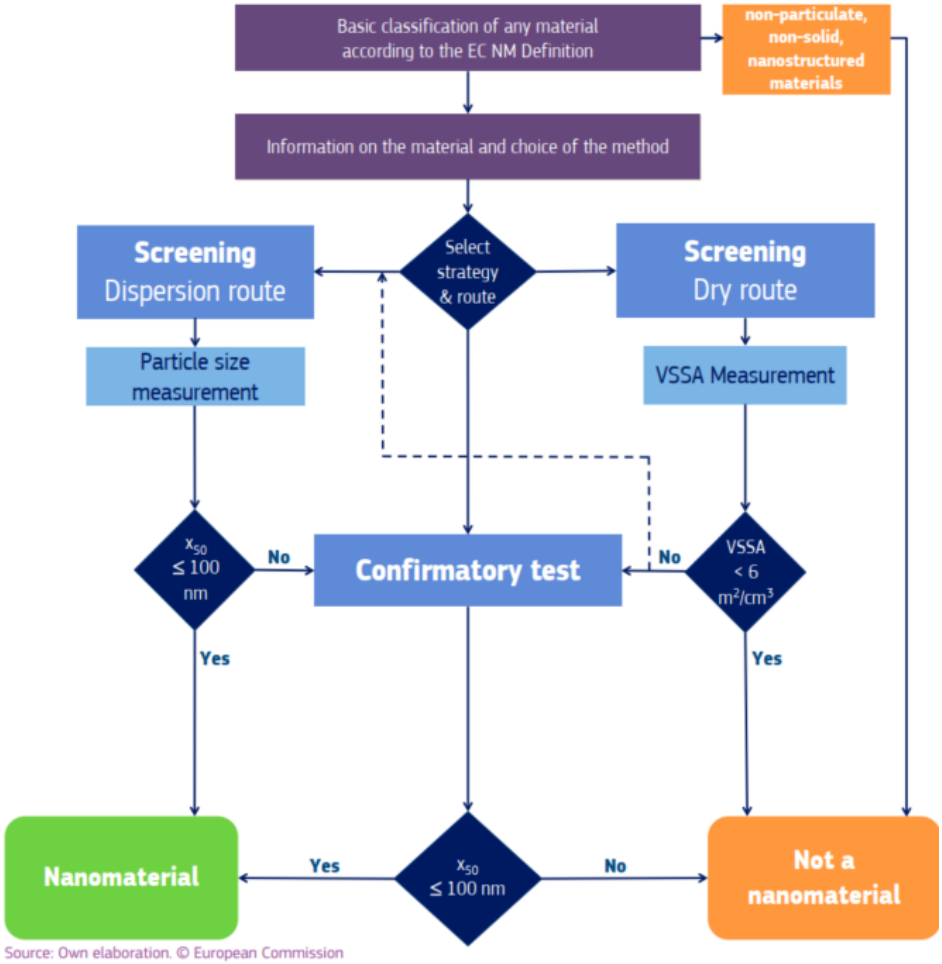


Figure 5: A decision tree helping to identify nanomaterials according to EC classification. Reproduced from Rauscher et al. (3) according to CC BY 4.0 Deed licence.

6.4 SUSTAINABILITY IN NANOMANUFACTURING

To help enterprises with implementing sustainability requirements early on in nanomanufacturing pilot lines, the European Committee for standardization (CEN) has published a workshop agreement CWA17935(4). It describes the sustainable nanomanufacturing framework (SNF) based on the traditional sustainability areas – the social, environmental and economical dimension (Table 2).

Table 2: The three dimensions of sustainable development adjusted to sustainable nanomanufacturing framework (adapted from CWA17935), copyright CEN-CENELEC.

Social dimension	- Nano occupational health & safety
Environmental dimension	- Nanomaterials and nanoproducts - Nano air emissions - Nano wastewaters - Nano wastes - Energy
Economic dimension	- Economic performance - Quality - Digitalization

With the help of this model, diagnosis of pilot lines can be performed. The obtained results should allow to develop a sustainability plan.

The operational procedure for the preparation of a full diagnosis and improvement plan is summarized in Table 3. These steps are supposed to help manufacturers to implement the “plan–do–check–act”-cycle (Figure 6). Using the model, presented in the workshop document, diagnosis and planning can be performed.

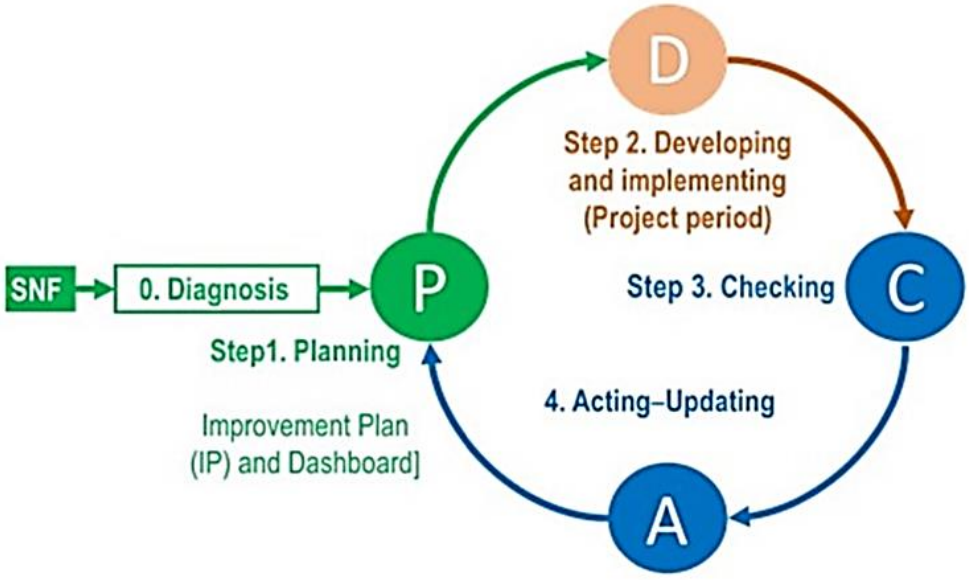


Figure 6: Plan–do–check–act cycle, reproduced from CWA17935, © CEN-CENELEC.

Table 3: Diagnosis development procedure (adapted from CWA17935), © CEN-CENELEC.

	Step	Result
	1. Enter basic information of the Pilot Line (PL) and select the scope of the diagnosis	Diagnosis customized
Sustainability management assessment	2. Assess Sustainability Management (SM)	SM-Scored questionnaires
	3. Generate results of the Sustainability Management diagnosis	SM-Current Baseline
	4. Establish the improvement baseline for Sustainability Management	SM-Target Baseline
	5. Visualize Sustainability Management (current and target baselines)	SM-Dashboard (Radar diagram)
Sustainability results assessment	6. Select and parameterize the most appropriate Key Performance Indicators (KPIs) to monitor Sustainability Results (SR)	SR-Current Baseline
	7. Establish the baseline for improving Sustainability Results (KPIs)	SR-Target Baseline
	8. Visualize Sustainability Results (current and target baselines)	SR-Dashboard (Radar diagram)
	9. Elaborate the Improvement Plan for sustainability	Improvement Plan
	10. Diagnosis and Improvement Plan Accepted by the Pilot Line (PL)	Pilot Line-Signature

6.5 QUANTUM DOTS - A SHORT INTRODUCTION

The term “quantum dot” was first introduced in the 1980s to describe zero-dimensional semiconductor structures (5). Per definition, quantum dots are engineered nanoparticles. To be precise they are metallic and non-metallic semiconductor nanocrystals with fluorescent properties (6). The efficiency of quantum dots is determined by the quantum yield, which is their ability to emit light after light absorption. A higher quantum yield (more photons emitted per those absorbed) indicates more useful quantum dots for display manufacturing processes, which comprise more than 70% of the applications using quantum dots. Other applications include LED lighting, biomedical applications, counterfeit-security and solar technique (7).

6.6 EXPOSURE TO QUANTUM DOTS

Exposure for workers and the environment to quantum dots can occur at multiple steps in the life cycle (see Figure 7). This includes synthesis, processing, application and end of life (7, 8). Environmental concentrations are expected to rise with increasing usage of quantum dots in modern applications. Estimates range from 0.057 to 1.14 tons of quantum dots released into the environment each year during the production phase, of which the largest part is released into waste water and the atmosphere (7, 8), however this is based on typical estimates of nanoparticle release as precise measurement data are lacking. Regarding loss of material to the environment during use, the risk is considered rather low as typically quantum dots are securely embedded in the respective products (9) and enclosed behind layers of glass and

plastic (10), especially for quantum dots used in electronics (7). At the end of life the majority of quantum dots will be moved to landfills, incinerated or recycled (11), which leads to the potential deposition of quantum dots in the environment. Nonetheless, even in landfill simulations, quantum dots have been shown to exhibit low spread of metals into environment due to the strong encapsulation (7). Regarding incineration, levels of hazardous metals were higher here in resulting ashes as the majority of material deposited there (12). While recycling products containing quantum dots reduces the environmental exposure (10), workers involved in these processes typically face higher exposure levels. Data on improper disposal of quantum dots is mostly absent from current literature, therefore the possibility of deposition in the environment via this path cannot be fully excluded (7).

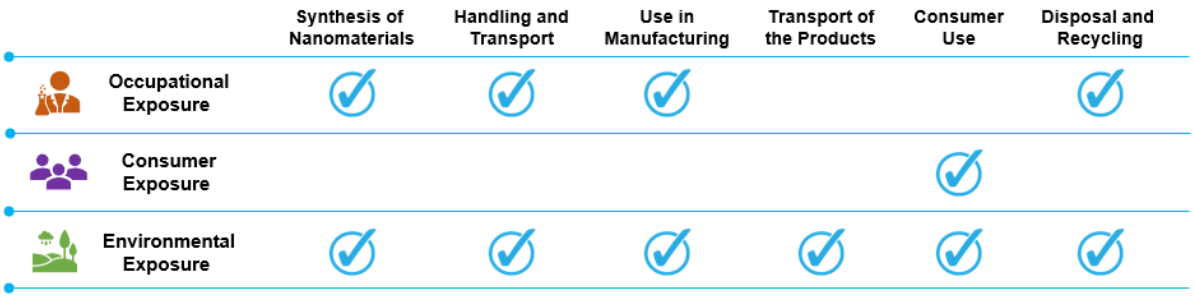


Figure 7: Overview of the exposure to manufactured nanomaterials along the life-cycle.

6.7 SAFETY AND SUSTAINABILITY OF QUANTUM DOTS: FOCUS ON CADMIUM-BASED VERSUS CADMIUM-FREE QUANTUM DOTS

Especially Cd-based quantum dots have received considerable attention as they present with high-level properties. However, following the boom in usage reporting on potential cytotoxicity increased, labelling them as target for substitution was done (13). Multiple *in vitro* studies using a variety of model organisms (including plants, microorganisms and human cell models) using Cd-based quantum dots (comprehensively reviewed in (7, 8)) showed potential adverse effects on both terrestrial and aquatic organisms. This included elevated production of oxidative stress and impaired immunological response (14), increased genotoxicity (15), cytotoxicity and changes in metabolism (16), among an excessive list of other impairments. Although also the physicochemical properties are altered if the basis of quantum dots is changed, safety concerns should be of highest priorities. HI-ACCURACY therefore relied on the synthesis of Cd-free quantum dots based on InP, GaP, ZnSe, ZnS and ZnSeS. However, data availability for these alternatives is still in its early phase and comprehensive safety assessment is warranted. First reports of pristine quantum dots composed of InP and Zns have been evidently shown to be non-cytotoxic. However, adverse effects for aged and weathered quantum dots based on InP and ZnS are reported in the form of increased mortality of human skin cells (17). This highlights the importance of strategies to reduce the exposure and to close knowledge gaps.

6.8 QUANTUM DOTS PRODUCTION AND USE IN HI-ACCURACY: CASE STUDY OF SAFE WORK PROCEDURE IMPLEMENTATION AND MONITORING

In the HI-ACCURACY project, synthesis of quantum dots are done by Fraunhofer IAP. BNN, in close collaboration with IAP, performed a risk assessment of the synthesis, characterization and successive application of the quantum dots. To help discovering the potential exposure situations, a questionnaire was prepared (Annex 1). The answers which are relevant to this particular case study are summarized in the Table 4.

Table 4: Questions and answers to topics relevant for quantum-dot synthesis and handling.

Question	Answer
Which of your processes within the HI-ACCURACY project include the use of nanoparticles/nanomaterials?	Synthesis of quantum dots, ESJET printing of QLED devices
Are these processes open or closed systems?	Both
Please specify open system processes:	Syntheses and ESJET printing are partially open processes[a]
Is there any kind of known occupational exposure to nanoparticles/nanomaterials? (Workplace safety issues)	There is no known direct exposure since the processes are done under the general safety regulations in chemical lab. However, potential exposure can happen during the processing
Is there any kind of known environmental nanoparticle/nanomaterial exposure? (E.g., rinsing processes, cleaning, etc.)	No
For each nano-relevant process: What are the tasks involved?	QD Synthesis: T1 Synthesis steps to provide blue, green and red QD T2 Purification of QDs T3 Characterization of QDs: quantum yield, UV-VIS spectroscopy, TGA, TEM, UPS, T4 Ink formulation ESJET printing of QD devices (QDs, ZnO): T1 ESJET printing and curing of active layers T2 device characterization: AFM, profilometry, fluorescence microscopy, ILV characteristic
For each task of the process: What are the quantities of nanoparticles/nanomaterials normally used? (E.g., grams, kilos)	all processes less than one gram, QD and ZnO inks usually have 10 mg/ml
For each task of the process: What is the physical form of the nanomaterial?	Powder; Dispersed in a liquid

	QDs are in powder form after synthesis and purification, processing is always done with nanoparticles dispersed in a liquid
Is there any risk management measure implemented? (E.g., specific procedures for safe handling of nano-powders during its transferring)	QDs can be monitored using UV light
Do you have any quantitative/qualitative measure of worker exposure to nanomaterials?	No
Can you present any certificates, review, validation, inspection, etc. for your product (produced according to guidelines like GMP, GLP, ISO, etc.)?	No
Do you have any EHS data regarding consumer use of your product?	No
Do you have data on the release of nanoparticles from your final product/application to the final consumer (Life Cycle Assessment - from raw material extraction and conversion; to manufacture and distribution; through use, re-use, and recycling; to ultimate disposal)?	No
Where do you see possible issues regarding occupational/environmental safety within your process?	During the purification steps of quantum dots, the weighting of components for ink formulation, and the cleaning of used tools in open environment
Where in the process do you think is a lot of potential for improvement, and where might be technological limitations?	All processes are done in a lab environment with the limitations of research labs. Potential of improvement is the transfer of critical steps into closed systems

a - underlined are key identified risk factors

This questionnaire allowed a fast identification of critical steps within the quantum dots production and application: quantum dot synthesis, purification and characterization are partly done with a powdered material form. Consequently, increased likeness for inhalation and dermal exposure is present. However, the small scale (regarding material weight, less than 1g) these processes are performed, speaks in favor to a minimal danger of exposure (18). Furthermore, the photochemical properties of these materials (strong luminescence), allows to monitor possible contamination of surfaces using UV light (for example, around laboratory balance, around physicochemical properties determination setups etc.). That way, accidental dermal exposure can be limited by a regular inspection of the laboratory and cleaning if necessary.

Precursors for the synthesis of quantum dots are common chemicals (not nanomaterials), thus regular chemical lab safety procedures can be applied. An example of good practice

implemented by IAP is the documentation sheet which contains a full list of the key chemicals used in for the synthesis of quantum dots; experimental apparatus; and standard working procedures (see Annex 2). Where possible, work on quantum dot synthesis (as well as waste management) is done in a closed (glovebox, Schlenk line) or well ventilated (fume hoods) environment (see Annex 3).

In small chemical research and development laboratories, implementing uniform safety measures presents a significant challenge due to the dynamic and non-standard nature of the work conducted within. These research labs operate in an environment where processes continually evolve from one project to the next, making it difficult to establish rigid safety protocols that fit all scenarios. As indicated by Basinas et al., effectiveness of some local exposure control measures is higher in larger (or industrial) production, with possible reasons being more adapted equipment and workers to some specific activity (19). The ever-shifting experimental landscape in research and development laboratories demands a flexible approach to safety, where adaptability and constant vigilance become paramount. Generally, global safety measures should take precedence over local (personal) protection measures. But in cases where implementing collective protection measures is not feasible, particularly great attention should be given personal protective measures at least.

The manufactured quantum dots are utilized for ink production and the final ink formulations are then used in printing processes, such as, ESJET. An on-site company visit and exposure measurements were performed in another project partner - Johanneum Research. The printing setup is located in fume hood (Figure 8).

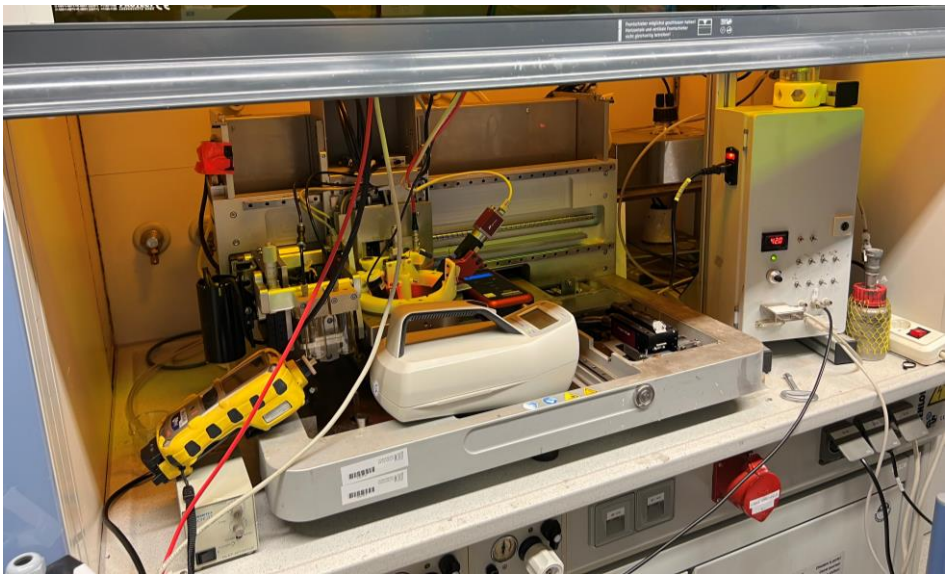


Figure 8: ESJET printing setup in Johanneum Research during exposure measurements (measurement devices are visible in the photo).

Measurements were performed by the “Österreichische Staubbekämpfungsstelle” (ÖSBS, Austrian Dust Control Agency). Results relevant for the ESJET printing are summarized in Table 5). Measurements indicate that during the printing process a minimal increase of nano-sized particles can be observed. These specific measurements were performed for printing

process with silver nanoparticle ink, however, can be used as an estimation also for quantum dot-based inks, since exposure is more process and operational conditions than nanomaterial dependent (19).

Table 5: ÖSBS measurement of particle concentration/size at different locations in the chemical laboratory of Johanneum Research (Weiz 2) in Weiz, Austria.

Location	Background/ active process	Vent in fume hood (on/off)	Sampling time	Particle Number Concentration (CPC 3007) N/cm^3	Particle Number Concentration (DiSCmini) N/cm^3	Size (DiSCmini) nm
laboratory	Background	-	09:55 – 10:05	560	1100	60
fume hood	Background	off	10:06 – 10:16	610	1030	67
fume hood	ESJET	on	10:16 – 10:31	820	1340	66
fume hood	ESJET	off	10:32 – 10:47	530	780	84
fume hood	no process	off	10:47 – 10:55	450	550	101
fume hood	no process	on	10:55 – 11:00	590	700	87

These results are placed within literature context for nanoparticle exposure during various printing processes in the Deliverable Report: D2.5 “Nanosafety assessment of conductors, dielectrics and OSCs”.

7 RECOMENDATIONS AND SOURCES OF FURTHER INFORMATION

1. To ensure the safe production of nanomaterials, it is recommended to establish a robust safety culture within the company. This can be achieved by leveraging good manufacturing practices (GMP) guidelines as the foundation. It involves the comprehensive training and competence development of personnel who are responsible for nanomaterial production. Furthermore, it entails the diligent execution of processes in accordance with well-documented procedures and strict adherence to safety standards. This proactive approach to safety not only minimizes risks but also contributes to the overall efficiency and quality of nanomaterial production.

2. Safety regulations and directives are in place to safeguard both individuals and the environment, emphasizing protection rather than punitive measures against manufacturers. It is crucial to acquaint yourself with the relevant legislation during the initial stages of manufacturing planning. Take advantage of available resources, such as ECHA guideline documents, consultations, and similar forms of support. This proactive approach not only ensures compliance but also fosters a safer and more responsible manufacturing

3. Existing manufacturing pipelines can also be enhanced to be more sustainable and secure. In this regard, the European Committee for Standardization (CEN) Workshop Agreement CWA17935 can be a valuable resource. Additionally, implementing straightforward measures such as safety questionnaires, similar to those utilized in this project, and conducting exposure measurements during laboratory work, can yield significant improvements. It's essential to collaborate closely with individuals directly engaged in the practical aspects of the work, as they possess the most pertinent insights into potential risks that may arise in specific areas.

Recommended literature and sources:

In the following, we provide SMEs with a list of further information sources, which are not explicitly reviewed in this report, but nevertheless are relevant:

- Joint Research Centre (European Commission) framework on **"Safe and sustainable by design chemicals and materials**" (2). This report includes a methodology for the definition of possible SSbD criteria and implementation mechanisms. Permanent link: https://op.europa.eu/s/y1TP (accessed on 05.10.2023).

- The European Union Observatory for Nanomaterials (EUON), hosted by ECHA: https://euon.echa.europa.eu/ (accessed on 05.10.2023) which, quoting the webpage: "**provides information about existing nanomaterials on the EU market**. Whether you are developing policies in the area, a consumer or representing industry or a green NGO, the information on the EUON offers interesting reading about the safety, innovation, research and uses of nanomaterials."

- **European Agency for Safety and Health at Work** webpage on the topic of **nanomaterials**, including multiple useful further information references https://oshwiki.osha.europa.eu/en/themes/nanomaterials (accessed on 05.10.2023).

- European Commission, Directorate-General for Employment, Social Affairs and Inclusion, **Working safely with manufactured nanomaterials – Non-binding guide for workers**, Publications Office, 2019, https://data.europa.eu/doi/10.2767/28405 (accessed on 05.10.2023).

- "E-fact 72: **Tools for the management of nanomaterials in the workplace and prevention measures**", published in 2013 by European Agency for Safety and Health at Work. Available online: https://osha.europa.eu/en/publications/e-fact-72-tools-management-nanomaterials-workplace-and-prevention-measures (accessed on 05.10.2023)

- "**General Safe Practices for Working with Engineered Nanomaterials in Research Laboratories**" published by The National Institute for Occupational Safety and Health (NIOSH) based in Ohio (USA). Publication No. 2012–147, available online https://www.cdc.gov/niosh/docs/2012-147/ (accessed on 05.10.2023)

- "**Engineered Nanoparticles – Health and Safety Considerations**", published by Employment and Social Development Canada, Labour Program, c2016. ISBN 978-0-660-06748-3, PDF available for download https://publications.gc.ca/site/eng/9.827163/publication.html (accessed on 05.10.2023)

8 REFERENCES & BIBLIOGRAPHY

1. Schimpel C, Resch S, Flament G, Carlander D, Vaquero C, Bustero I, et al. A methodology on how to create a real-life relevant risk profile for a given nanomaterial. Journal of Chemical Health & Safety. 2018;25(1):12-23. doi:https://doi.org/10.1016/j.jchas.2017.06.002.

2. Caldeira C, Farcal R, Garmendia AI, Mancini L, Tosches D, Amelio A, et al. Safe and sustainable by design chemicals and materials-Framework for the definition of criteria and evaluation procedure for chemicals and materials. Luxembourg: Publications Office of the European Union; 2022. Available from: https://publications.jrc.ec.europa.eu/repository/handle/JRC128591.

3. European C, Joint Research C, Rauscher H, Rasmussen K, Linsinger T, Stefaniak E, et al. Guidance on the implementation of the Commission Recommendation 2022/C 229/01 on the definition of nanomaterial. 2023. doi:https://doi.org/10.2760/143118.

4. López de Ipiña J, Steck, J, Friedrichs, S., Batsouli, D., Koutsoukis, G., Vavouliotis, A., Resch, S., Wolf. C., Clavaguera, S., Girardot, C., Schug, B., Le Dantec, M., Laranjeira, J., Matos, C., Favre, G., Masouras, A., Hoxha, D., Viviente, J. L., Duralek, P., Kosmider, P., Machicado, F., Martínez Egido, R., Klee Morán, R. O., Sánchez, M. L., Sánchez, P., Toledo Murcia, L., Tsantzalis , S., Kostopoulos, V., Gomendiourrutia, P. . Sustainable Nanomanufacturing Framework (CWA 17935:2022). Brussels: CEN-CENELEC Management Centre; 2022.

5. Reed MA, Randall JN, Aggarwal RJ, Matyi RJ, Moore TM, Wetsel AE. Observation of discrete electronic states in a zero-dimensional semiconductor nanostructure. Phys Rev Lett. 1988;60(6):535-7. doi:https://doi.org/10.1103/PhysRevLett.60.535.

6. Park H, Shin DJ, Yu J. Categorization of Quantum Dots, Clusters, Nanoclusters, and Nanodots. Journal of Chemical Education. 2021;98(3):703-9. doi:https://doi.org/10.1021/acs.jchemed.0c01403.

7. Giroux M, Zahra Z, Salawu OA, Burgess RM, Ho KT, Adeleye AS. Assessing the Environmental Effects Related to Quantum Dot Structure, Function, Synthesis and Exposure. Environ Sci Nano. 2022;9(3):867-910. doi:https://doi.org/10.1039/d1en00712b.

8. Liu Q, Ding X, Pang Y, Cao Y, Lei J, Wu J, et al. New insights into the safety assessment of quantum dots: potential release pathways, environmental transformations, and health risks. Environmental Science: Nano. 2022;9(9):3277-311. doi:https://doi.org/10.1039/D2EN00252C.

9. Wang Y, Nowack B. Dynamic probabilistic material flow analysis of nano-SiO(2), nano iron oxides, nano-CeO(2), nano-Al(2)O(3), and quantum dots in seven European regions. Environ Pollut. 2018;235:589-601. doi:https://doi.org/10.1016/j.envpol.2018.01.004.

10. Brown FC, Bi Y, Chopra SS, Hristovski KD, Westerhoff P, Theis TL. End-of-Life Heavy Metal Releases from Photovoltaic Panels and Quantum Dot Films: Hazardous Waste Concerns or Not? ACS Sustainable Chemistry & Engineering. 2018;6(7):9369-74. doi:https://doi.org/10.1021/acssuschemeng.8b01705.

11. Wang T, Wagner A, Gehwolf R, Yan W, Passini FS, Thien C, et al. Load-induced regulation of tendon homeostasis by SPARC, a genetic predisposition factor for tendon and ligament injuries. Science Translational Medicine. 2021;13(582):eabe5738. doi:https://doi.org/10.1126/scitranslmed.abe5738.

12. Vejerano EP, Leon EC, Holder AL, Marr LC. Characterization of particle emissions and fate of nanomaterials during incineration. Environmental Science: Nano. 2014;1(2):133-43. doi:https://doi.org/10.1039/C3EN00080J.

13. Chen N, He Y, Su Y, Li X, Huang Q, Wang H, et al. The cytotoxicity of cadmium-based quantum dots. Biomaterials. 2012;33(5):1238-44. doi:https://doi.org/10.1016/j.biomaterials.2011.10.070.

14. Katsumiti A, Gilliland D, Arostegui I, Cajaraville MP. Cytotoxicity and cellular mechanisms involved in the toxicity of CdS quantum dots in hemocytes and gill cells of the mussel Mytilus galloprovincialis. Aquat Toxicol. 2014;153:39-52. doi:https://doi.org/10.1016/j.aquatox.2014.02.003.

15. Munari M, Sturve J, Frenzilli G, Sanders MB, Christian P, Nigro M, et al. Genotoxic effects of Ag2S and CdS nanoparticles in blue mussel (Mytilus edulis) haemocytes. Chemistry and Ecology. 2014;30(8):719-25. doi:https://doi.org/10.1080/02757540.2014.894989.

16. Majumdar S, Pagano L, Wohlschlegel JA, Villani M, Zappettini A, White JC, et al. Proteomic, gene and metabolite characterization reveal the uptake and toxicity mechanisms of cadmium sulfide quantum dots in soybean plants. Environmental Science: Nano. 2019;6(10):3010-26. doi:https://doi.org/10.1039/C9EN00599D.

17. Tarantini A, Wegner KD, Dussert F, Sarret G, Beal D, Mattera L, et al. Physicochemical alterations and toxicity of InP alloyed quantum dots aged in environmental conditions: A safer by design evaluation. NanoImpact. 2019;14:100168. doi:https://doi.org/10.1016/j.impact.2019.100168.

18. Bekker C, Kuijpers E, Brouwer DH, Vermeulen R, Fransman W. Occupational Exposure to Nano-Objects and Their Agglomerates and Aggregates Across Various Life Cycle Stages; A Broad-Scale Exposure Study. The Annals of Occupational Hygiene. 2015;59(6):681-704. doi:https://doi.org/10.1093/annhyg/mev023.

19. Basinas I, Jiménez AS, Galea KS, Tongeren Mv, Hurley F. A Systematic Review of the Routes and Forms of Exposure to Engineered Nanomaterials. Annals of Work Exposures and Health. 2018;62(6):639-62. doi:https://doi.org/10.1093/annweh/wxy048.

9 APPENDICES

9.1 ANNEX 1

The full safety questionnaire contained the following questions:

1. Please enter your name, organization and email address

2. Which nanoparticles/nanomaterials are you using? (Please provide information on registration numbers, article numbers, suppliers, reference codes of the materials, etc.)

3. What kind of characterization data is available for these nanoparticles/nanomaterials? (Please provide characterization data, e.g., agglomeration/aggregation, crystalline phase, crystallite size, dustiness, TEM, particle size distribution, specific surface area/charge, etc.)

4. What kind of safety data are available for these nanoparticles/nanomaterials? (Please provide Material Safety Data Sheets (MSDS), exposure scenarios, toxicity screenings, etc.)

5. Which of your processes within the HI-ACCURACY project include the use of nanoparticles/nanomaterials?

6. Are these processes open or closed systems?

7. Is there any kind of known occupational exposure to nanoparticles/nanomaterials? (Workplace safety issues)

8. Is there any kind of known environmental nanoparticle/nanomaterial exposure? (E.g., rinsing processes, cleaning, etc.)

9. For each nano-relevant process: What are the tasks involved?

10. For each task of the process: What are the quantities of nanoparticles/nanomaterials normally used? (E.g., grams, kilos)

11. For each task of the process: What is the physical form of the nanomaterial?

12. Is there any risk management measure implemented? (E.g., specific procedures for safe handling of nano-powders during its transferring)

13. Do you have any quantitative/qualitative measure of worker exposure to nanomaterials?

14. If yes, which guidelines/procedure do you use to do the measurements?

15. Is your product an end-product or will it be further processed (intermediate product(s) further used in the production process)?

16. Is your product an application (e.g., machinery, touchscreen, LCD display, etc.)?

17. If yes, what kind of application is your product?

18. What kind of intermediate product to you produce?

19. What kind of nano-property improves the quality of the product?

20. Does your product feature/show nanostructures?

21. If yes, which kind of nanostructures?

22. What kind of nano-relevant characterization data is available for the end-product? (Please provide characterization data, etc.)

23. What kind of nano-relevant safety data is available for the end-product? (Please provide Material Safety Data Sheets, User Manuals, Guidance Documents, etc.)

24. If you produce end-products/applications, who are the customers for your end-products?

25. If you produce an intermediary product (e.g., inks) who are the users and downstream users?

26. Can you present any certificates, review, validation, inspection, etc. for your product (produced according to guidelines like GMP, GLP, ISO, etc.)?

27. Do you have any EHS data regarding consumer use of your product?

28. Do you have data on the release of nanoparticles from your final product/application to the final consumer?

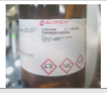
29. Where do you see possible issues regarding occupational/environmental safety within your process?

30. Where in the process do you think is a lot of potential for improvement, and where might be technological limitations?

9.2 ANNEX 2

Example of the documentation sheets as implemented by Fraunhofer IAP, containing the chemical used (Figure A1), apparatus (Figure A2) and synthesis description (Figure A3) documentation sheets.

Synthetic reagents in colloidal InP/ZnSe/ZnS nanoparticles

no	Part	name	CAS	purity	Distributor	Photo	article. no
1	core	Indium(III) acetate	25114-58-3	99.99% trace metals basis	Sigma-aldrich		510270
		Zinc acetate	557-05-1	purum, 10-12% Zn basis	Sigma-aldrich		26423
		1-octanethiol	111-88-6	≥98.5%	Sigma-aldrich		471836
		Tris(trimethylsilyl) phosphine	15573-38-3	96.00%	VeZerf Laborsynthesen GmbH		WA20111801
		Trioctylamine	1116-76-3	98%	Sigma-aldrich		T81000
		1-Octadecene	112-88-9	technical grade, 90%	Sigma-aldrich		O806
3	midshell	Selenium	7782-49-2	powder, −100 mesh, 99.99% trace metals basis	Sigma-aldrich		229865
		Sulfur	7704-34-9	powder, ≥99.0%	Sigma-aldrich		13825-1KG-R
		Trioctylphosphine	4731-53-7	97%	Sigma-aldrich		718165

1. Reagent | 2. Apparatus and equipment | 3. Experimental detail | ⊕

Figure A1: Example for documentation chemical inventory used for the synthesis of quantum dots.

Apparatus & synthetic equipment					
	name	spec.	photo	Manufacturer	article no.
3	Three-necked round flask	Three-necked round-bottom flasks side necks, bevelled, 50 ml, 14/23, 14/23		Roth	KY18.1
	Air condensor	Extension piece, 14/23, 14/23, 120 mm		Roth	TK08.1
	Transitioin cock	Transition piece with core and stop cock Curved tubing olive, 14/23		Roth	CC28.1
	Schlenkline, mit 5 Patenthähnen	Umbau Schlenk line 134030100 modified with 2x hose connector left side		Gebr. Rettberg GmbH https://www.rettberg.biz/en/	134030100
	Silicon line (for vacuum)	No. S5 5*9mm (10m/1box)		Roth	9742.1
	Vacuum grease	1. Melting point: > +200 °C 2. Steam pressure: <1 x 10-5 torr 3. Application temperature up to: 180 °C		APIEZON (Roth)	C987.1
	Magnetic bars	Ø: 10 mm, 20 mm		Roth	NK68.1
					

1. Reagent | 2. Apparatus and equipment | 3. Experimental detail

Figure A2: Example for documentation for lab inventory used for the synthesis of quantum dots.

General synthesis process in colloidal InP/ZnSe/ZnS nanoparticles _ J. Kim et al., Small 2022, 18, 2203093				
No.	Class	Process	Experimental detail	Annex.
0		Material	Indium acetate (In(Ac)3), zinc acetate (Zn(Ac)2) tri-n-octylphosphine (TOP), 1-octanoic acid (OA), 1-octadecene (ODE), zinc stearate (ZnSA), 1-octanethiol (OTT), selenium (Se), sulfur (S), acetone (AC), toluene, ethanol (EtOH), Tri(trimethylsilyl) phosphine (TMSP), Zinc octanoate (ZnOA), tri-octylphosphine selenide (TOP–Se), and tri-octylphosphine sulfide (TOP–S)	
1	Stock solution	Preparation of ZnOA	Zn(Ac)2 (3.70g, 20 mmol) and OA (6.40 ml, 40.4 mmol) were placed in a 100ml three-neck round bottom flask connected to a reflux condenser and equipped with rubber septa and thermocouple. The mixture was heated to 120°C and degassed under reduced pressure (<150 mTorr) for 10 h with vigorous stirring to remove water and acetic acid species. After backfilling the reactor with N2 atmosphere, reaction flask cooled down to 80°C, the reaction mixture of which are poured into 250 ml of acetone for crystallization and filtered by Buchner funnel under low pressure to eliminate unreacted OA and acetone (<50 Torr). After filtration of mixture, ZnOA powder was dried at 80°C for 24 h.	
		Preparation of 2M TOP–Se	Se powder (1.58 g, 20 mmol) and TOP (10 ml) were placed in 50ml two-neck round flask with rubber septa and thermocouple. The mixture was heated to 80°C for 2 h under reduced pressure (<150 mTorr). Se powder was dissolved in TOP and became a clear solution, 2M TOP–Se. After backfilling the reactor with N2 atmosphere, the flask was cooled down to room temperature.	
		Preparation of TOP–S	S powder (0.64 g, 20 mmol) and TOP (10 ml) were placed in 50ml two-neck round flask with rubber septa and thermocouple. The mixture was heated to 80°C for 2 h under reduced pressure (<150 mTorr). Se powder was dissolved in TOP and became a clear solution, 2M TOP–S. After backfilling the reactor with N2 atmosphere, the flask was cooled down to room temperature.	
		1N TMSP in ODE solution	The 1-octadecene solvent is prepared after degassing at 120°C for 2 hours. This process should be allowed to perform in the glove box with Nitrogen and oxygen of under 0.5 ppm. The 1-octadecene solvent is prepared after degassing at 120°C for 2 hours. In the glove box, 2.902 ml (10 mmol) of TMSP was diluted with 10 ml of ODE in the sample vial and capped under Nitrogen conditions.	
2	Core	Synthesis of InP QDs	In(Ac)3 (584 mg, 2mmol), ZnSA (1.26 g, 2mmol), and 10ml of ODE were added into a 50ml three-neck round bottom flask connected to a reflux condenser and equipped with rubber septa and thermocouple. The mixture was heated to 150°C and degassed under reduced pressure (<150 mTorr) for 10 hours with vigorous stirring to remove water and oxygen species. After backfilling the reactor with N2 atmosphere, 1 mmol of 1M TMSP dissolved in ODE was rapidly injected into the flask at 150°C and the solution was heated up to 300°C (5 min / °C) for 3 min with vigorous stirring, and the growth solution cooled down to room temperature.	
		Synthesis of	All synthesis processes, including ZnSe and ZnS shelling on InP QDs, were continuously performed without purification. For ZnSe shelling on the surface of InP QD, ZnOA powder (2.11 g, 6 mmol) was introduced to the reaction flask, heated to 130 °C, and degassed under reduced pressure (<150 mTorr) for 30 min with vigorous stirring to remove water and oxygen species. After backfilling the reactor with N2 atmosphere, the mixture was heated to 280°C and maintained for 10 min. 2M TOP–Se (3 mL, 6 mmol) was injected to reaction flask at 280°C and the injection temperature	

1. Reagent | 2. Apparatus and equipment | **3. Experimental detail** ⊕

Figure A3: Example for documentation of the quantum dot synthesis procedure.

9.3 ANNEX 3

Overview for the synthesis setup (fume hood and glove box), as well as waste management in Fraunhofer IAP.

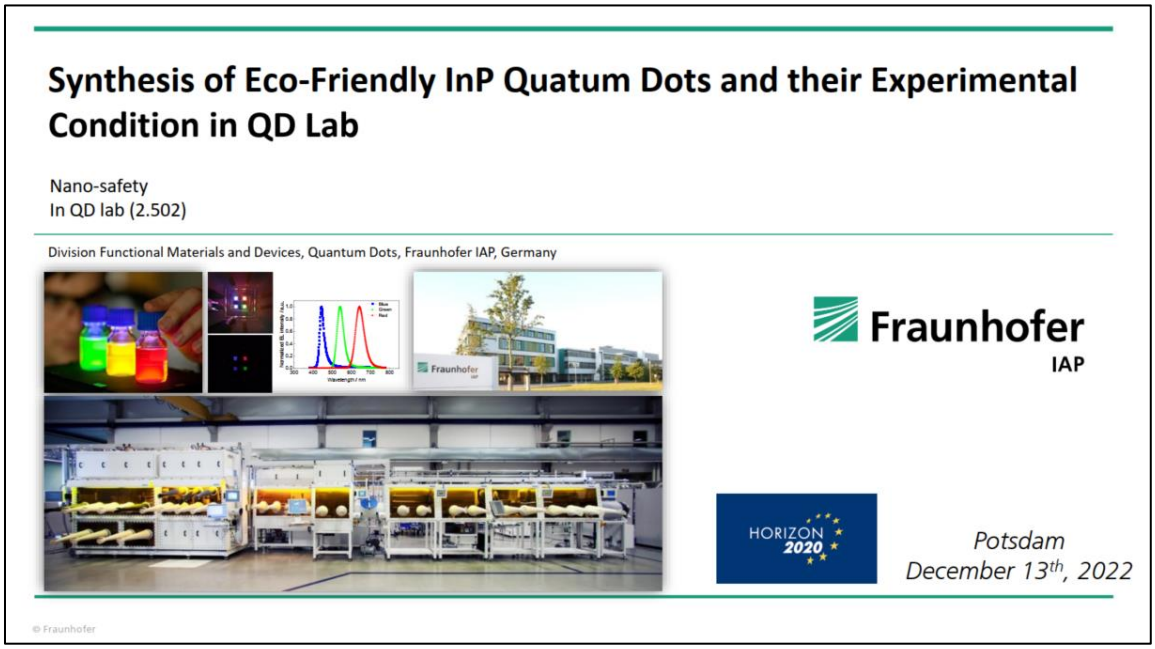


Figure A4: Presentation of experimental conditions in QD Lab, presented during BNN on site visit to Fraunhofer IAP.

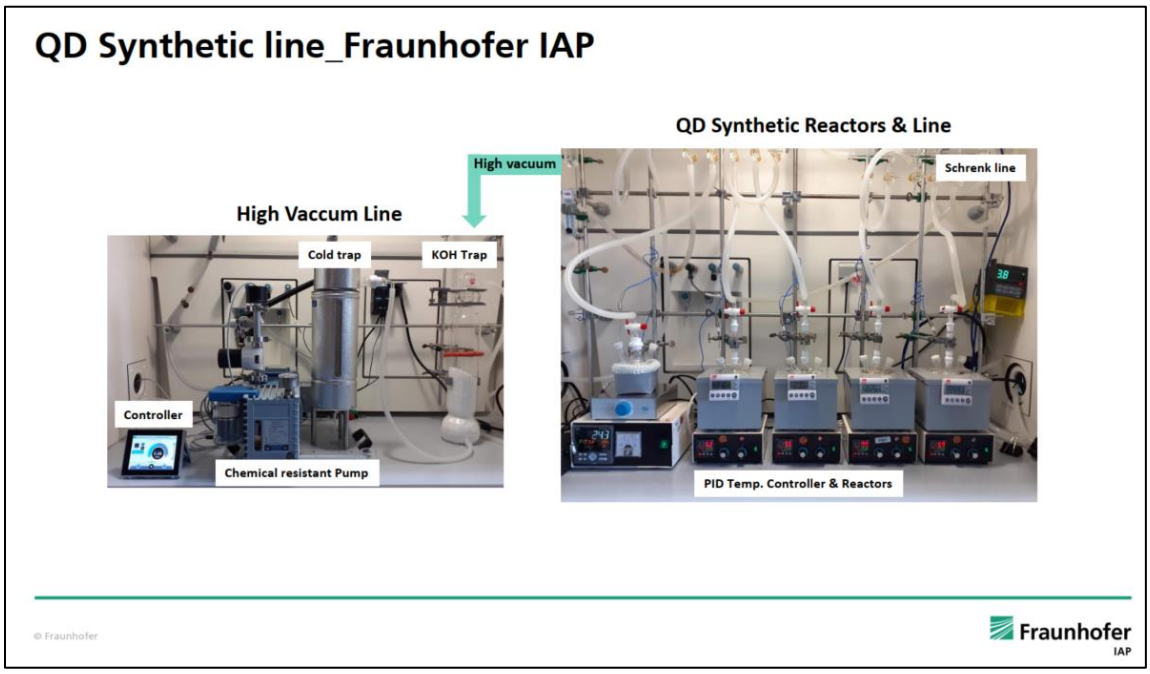


Figure A5: QD synthesis setup in fume hood.

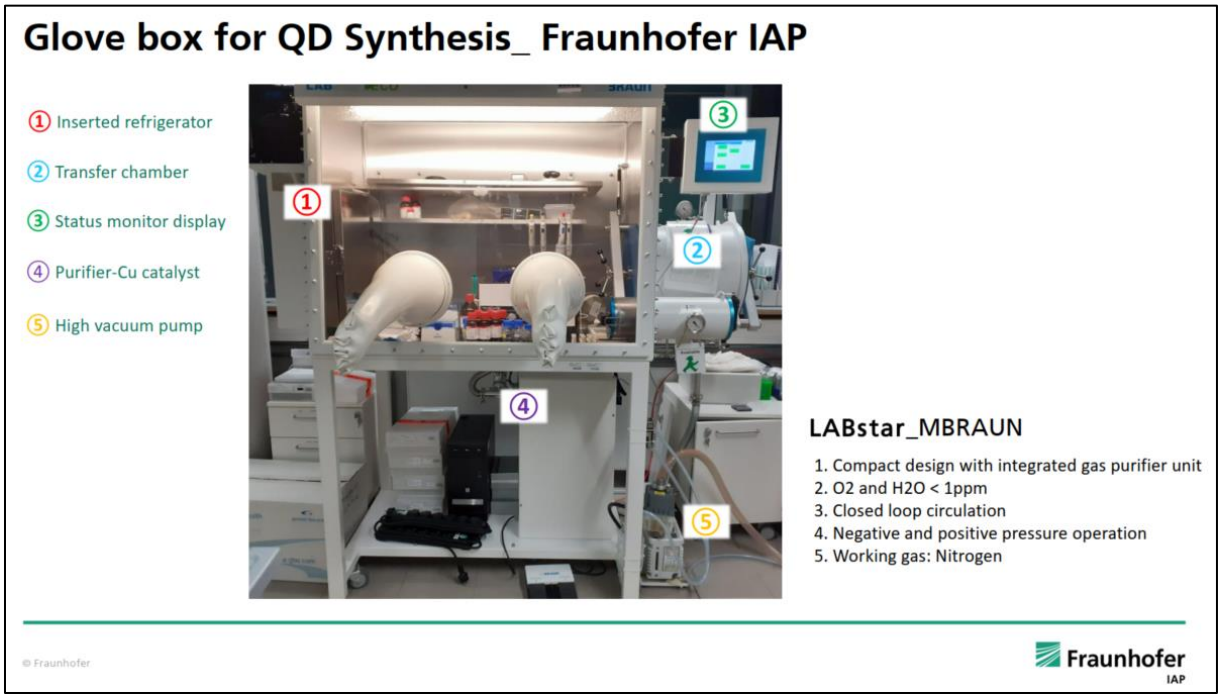


Figure A6: Glove box system used for preparing the precursor and the purification process.

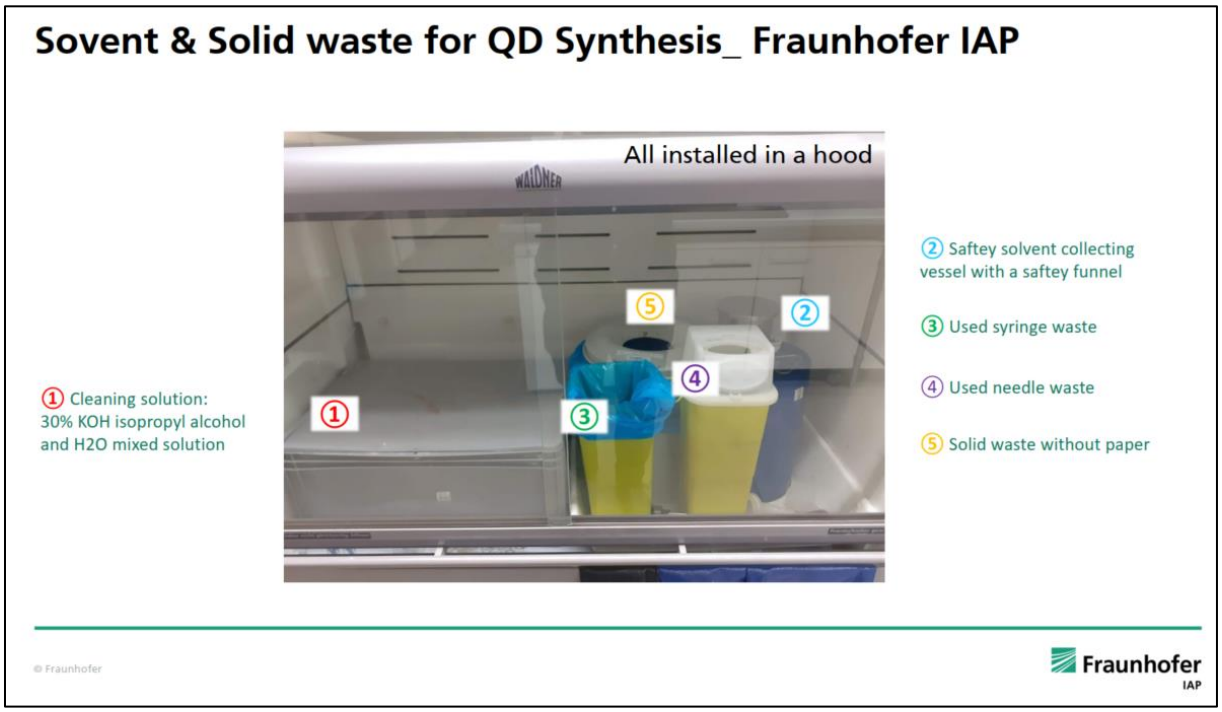


Figure A7: QD synthesis laboratory waste management.