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TRACE ELEMENTS AND
NANOMATERIALS

OVEREENKOMST 2018 ter uitvoering van een studie “Nalevingscontrole en inhoudelijke evaluatie van de registratie van stoffen geproduceerd in nanoparticulaire toestand volgens KB 27 mei 2014”

“NanoRegister Evaluation”

1/11/2018 – 30/10/2020

ANNUAL REPORT
PHASE 2-TRADE YEAR 2018

OCTOBER 2020

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WHO WE ARE

SCIENSANO can count on more than 700 staff members who commit themselves, day after day, to achieving our motto: Healthy all life long. As our name suggests, science and health are central to our mission. Sciensano's strength and uniqueness lie within the holistic and multidisciplinary approach to health. More particularly we focus on the close and indissoluble interconnection between human and animal health and their environment (the "One health" concept). By combining different research perspectives within this framework, Sciensano contributes in a unique way to everybody's health.

For this, Sciensano builds on the more than 100 years of scientific expertise of the former Veterinary and Agrochemical Research Centre (CODA-CERVA) and the ex-Scientific Institute of Public Health (WIV-ISP).

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LIST OF ABBREVIATIONS

Symbol	Signification
AFM	Atomic Force Microscopy
BET	Brunauer–Emmett–Teller
CAS	Chemical Abstracts Service
DLS	Dynamic Light Scattering
EC	European Commission
EC	Enzyme Commission
EM	Electron Microscopy
EU	European Union
FESEM	Field Emission Scanning Electron Microscopy
GC	Gas Chromatography
HPLC	High-Performance Liquid Chromatography
ICP-MS	Inductively Coupled Plasma - Mass Spectrometry
ICP-OES	Inductively Coupled Plasma - Optical Emission Spectroscopy
NM	Nanomaterial
NP	Nanoparticle
REACH	Registration, Evaluation, Authorization and Restriction of Chemicals
SD	Standard Deviation
SEM	Scanning Electron Microscopy
STEM	Scanning Transmission Electron Microscopy
TEM	Transmission Electron Microscopy
XRD	X-Ray powder Diffraction

EXECUTIVE SUMMARY

This project evaluates the registration of materials produced in a nanoparticulate state according to the KB of May 27th 2014. The Royal Decree concerning the placing on the market of substances manufactured in nanoparticulate state was signed on May 27th, 2014, published on September 24th, 2014, and modified on December 22nd, 2017. According to this Royal Decree, the deadlines for registration of substances and mixtures manufactured in a nanoparticulate state were January 1st, 2016 and January 1st, 2018, respectively. The registration software was launched on September 15th, 2015. Phase 1 of the project included the evaluation of the registrations of the trade year 2017 and was successfully completed and reported previously. Phase 2 of the project included the evaluation of the registrations of the trade year 2018 and is reported in this document.

For the trade year 2018, the completion of obligatory fields within the registration dossiers ("compliance check") and the quality of the content of selected parameters of the submitted dossiers were assessed. For the complete registrations, the compliance check assessed if all obligatory fields were completed by the applicants for each dossier. For the simplified registrations it was checked if the declaration of honour was added to the dossier. For the limited registrations, a derived, "compliance" database was constructed and a statistical analysis of the data in the "compliance" database was done.
The content of the register was evaluated per parameter, and included listing and evaluating the methods used for measuring each registered parameter, and the number of different materials and their quantity. For the complete dossiers, it was assessed per parameter if the reported physicochemical data are in accordance with the current technical possibilities.
The results of the assessment and a list of recommendations for further optimization of the nanoregister based on this assessment are reported in this document.

The main results for the trade year 2018 are summarized as:

- During the trade year 2018, 540 registrations were submitted including 100 complete, 424 limited, and 16 simplified registrations.
- Evaluation of the complete registrations showed that most of the applicants provided the requested information for the materials they registered, and the declaration of honour for the simplified registrations was mostly undersigned (94%).
- In the complete registrations, most of the information was present, as indicated from the compliance check, although specific parameters, as for instance the uncertainties of size measurements, were systematically missing (12%). A decreased compliance was also observed for the REACH registration numbers (71%) and for the parameters "shape of agglomerates" (42%), "shapes of aggregates" (80%), "determination method of impurities" (80%), "surface charge ionic strength" (80%) and "sector of use of the material" (71%). Interestingly, the low compliance of these parameters was also observed previously in the compliance evaluation of the trade year 2017, suggesting difficulties of the applicants to register the specific information.

- In 98% of the limited registrations the applicants provided the previous registration numbers (92% for the trade year 2017) and the compliance check revealed that the physicochemical characteristics of the substances were mostly present (≥93%). Only two parameters showed decreased compliance, the parameter of the median size of dimension 1 (88%) and the standard deviation (80%).
- Evaluation of the determination methods used to characterize the physicochemical characteristics of the nanoparticulate materials in the complete registrations showed that the applicants employed well established methods, such as EM for the characterization of the constituent particle size (72%) and of the aggregates size (74%), and BET (88%) for the calculation of the mean specific surface area.
- For the limited registrations the applicants also used EM methods (87%) to characterize the size of the constituent particles.
- In total 190 different materials (chemical substances) were identified that are presented in the Annex. The chemical identification makes no distinction between the possible differences in the physicochemical properties of these substances.
- The total quantity of substances in the nanoparticulate state, which was introduced on the Belgian market during the trade year 2018 was 120734587.2 kg (120734.5872 tons) based on the recorded data, decreased by 40% compared to the quantities of 2017 (201429.5336 tons).
- The substances that were introduced on the Belgian market during the trade year 2018 in a total quantity that is larger than 1000 tons were diiron trioxide, calcium carbonate, silicon dioxide, precipited calcium carbonate and carbon black.
- In most of the registrations (77%), the applicants declared quantities that range from 10 to 100000 kg.
- About 51% (187 registrations) of the submitted registrations reported quantities below 1 ton and would therefore be considered to be out of the scope of the current REACH-regulation.

THE BELGIAN REGISTER OF NANOMATERIALS

1. Objectives

The Royal Decree concerning the placing of substances produced in nanoparticulate state on the market was signed on the 27th May 2014 [1]. This Royal Decree is based on the one hand on the law of the 21st December 1998 on product standards to promote sustainable production and consumption patterns and on the protection of the environment, public health and workers, and on the other hand on the law of the 4th August 1996 on the well-being of workers in the execution of their works. The creation of the register aims at the following objectives [2]:

- ensuring that the evolution of this innovative technology proceeds in harmony with the protection of human health;
- acquiring better knowledge of the market, the characteristics of the nanomaterials, the potential risk of human exposure to these substances, and of the speed and extent of the evolution towards more complex nanomaterials;
- guaranteeing transparency and strengthening the trust of the public and employees with regard to these substances;
- guaranteeing traceability and therefore offering the government the possibility to intervene in case of a risk for the public health or for the safety of employees;
- introducing a knowledge base that might be necessary for the future regulatory evolution at national and European level with regard to these substances.

Specifically, the register will in particular make it possible to guarantee the traceability of products containing substances produced in nanoparticulate state. The register will:

- make efficient intervention possible if a type of nanomaterial turns out to be dangerous to public health;
- provide the public authorities competent for the safety of employees with the relevant information in order to be able to carry out their duties concerning information, regulation and control in a targeted manner;
- assure, if necessary, that the collected data (non-confidential data or aggregated data) can be made public to inform the public about the increasing presence of nanomaterials on the market, and to avoid misunderstandings and confusion.

Additionally, the register should offer the government the possibility to collect key information about the substances produced in nanoparticulate state that are present on the Belgian market in order to:

- have a basis for scientific research on the possible toxicity of the various types of substances produced in a nanoparticulate state and,

if necessary, be able to focus on the regulations that may be needed to protect public or workers' health from certain types of substances produced in a nanoparticulate state.

2. Key concepts and definitions

2.1. DEFINITION OF A SUBSTANCE IN A NANOPARTICULATE STATE

The definition for a nanoparticulate substance is included in the Royal Decree of the 27th May 2014. This definition is largely based on the European Commission's recommendation for the definition of nanomaterial (Recommendation 2011/696 /EU) [3], but excludes naturally formed nanomaterials and nanomaterials formed as a by-product of human activities.

A substance produced in a nanoparticulate state is considered therefore as "a substance that contains particles either in the unbound state or as an aggregate or agglomerate and of which at least 50% of the particles in the quantified size distribution have one or more external dimensions within the range of one nanometer (1 nm) to one hundred nanometers (100 nm), with the exception of natural, non-chemically modified substances, and substances whose fraction between one nanometer and one hundred nanometers is a by-product of human activities. Fullerenes, graphene flakes and single-walled carbon nanotubes with one or more external dimensions below one nanometer are considered equal to substances produced in the nanoparticulate state.

2.2. EXEMPTED FROM REGISTRATION

In the Royal Decree 27th May 2014, substances produced in a nanoparticulate state are exempt from registration if these substances fall within the scope of another legislation. More specifically, it concerns:

1. The biocides and treated articles that fall within the scope of Regulation (EU) No 528/2012 of the European Parliament and of the Council of 22 May 2012 concerning the market introduction and application of biocides, and the biocides that were registered or for which an authorization has been granted in accordance with the provisions of the Royal Decree of 22 May 2003 concerning the placing on the market and use of biocides.
2. Medicinal products falling within the scope of Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31st March 2004 establishing Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency.
3. Medicinal products for human and veterinary use falling within the scope of the Royal Decree of 14th December 2006 on medicinal products for human and veterinary use.
4. Food, articles and substances intended to come into contact with food, referred to in Article 1, 1° and 2° of the Law of 24th January 1977 on the protection of users' health with regard to food and other products.
5. Feed, as defined in Article 3 of Regulation (EC) No 178/2002 of the European Parliament and of the Council of 28th January 2002 laying down the general principles and requirements of food law, establishing a European Food Safety Authority and establishing procedures for food safety matters.
6. Medicines and medicated feed that fall within the scope of the Act of 21st June 1983 on medicated feed.

7. Processing aids and other products, which may be used for the processing of biologically produced ingredients of agricultural origin, as referred to in Part B of Annex VIII of Commission Regulation (EC) No 889/2008 of 5th September 2008 laying down provisions for implementing Council Regulation (EC) No 834/2007 on organic production and labeling of organic products, with regard to organic production, labeling and control.
8. Pigments, if they are placed on the market in a mixture, an item or a composite item.

2.3. DEADLINES FOR REGISTRATION

The Royal Decree of 27 May 2014 makes a distinction between substances produced in the nanoparticulate state, marketed as:

- substances
- incorporated in a mixture
- integrated into an object or composite object.

Nanoparticulate substances, placed on the market as substances and already available on the market, had to be registered before 1st January 2016.
In the first quarter following 2016, i.e. before the 1st April 2017, the estimates had to be replaced by the current data for the 2016 trading year. This annual update must be carried out in the first three months of the following calendar year.
For substances produced in a nanoparticulate state, placed on the market and processed in a mixture, the same principle is applied, but then one year later.
No deadline has yet been set for substances produced in a nanoparticulate state, integrated into an object or composite object.
Nanoparticulate substances that are placed on the market after the deadlines set in the Royal Decree of 27th May 2014 must be registered before they are effectively placed on the market.

2.4. TYPES OF REGISTRANTS

In the software of the Belgian register, the registrant creates his own account and manages his username and password. The account allows the registrant access to the software and can use one or more submit registrations.
In the registry's software, the applicant can choose between different account types, which are:

- Declarant: according to the provisions of the Royal Decree of 27 May 2014, this is required to register the products that the declarant places on the market. This obligation follows from the fact that the registrant himself places his products on the Belgian market, or from the fact that he acts as a representative for another company. These two types are always considered together in the further report.

- Foreign Supplier: according to the provisions of the Royal Decree of 27 May 2014, this supplier is not obliged to register, because he does not market his products on the Belgian market himself. He has the possibility to register his products in the register, whereby in addition to the identification of his company, he only records the physical and chemical characteristics of the nanomaterial, as laid down in section 2 of annex 1 to the Royal Decree of 27 May 2014. A foreign supplier does not register quantities, customs, trade names or professional users of its products. The Foreign Supplier can then pass a number of his registrations to his (submitted to registration) customers. They can then register their products using a "limited" registration. In this way, these customers do not have to repeat the physicochemical characteristics of the substances produced in the nanoparticulate state. The term "foreign" mentioned with this type of account indicates that the supplier does not market his products in Belgium (but does market abroad), and does not necessarily have anything to do with the nationality of the company.

2.5. TYPES OF REGISTRATIONS

Different types of registrations can be submitted in the register by the applicants. In addition to a complete registration, an applicant can register two other types including:

- A limited registration: this concerns the registration of a substance for which the data has already been registered, by another Declarant or by a Foreign Supplier. In this type of registration, the registrant can replace the physicochemical characteristics of the substance in the nanoparticulate state, as laid down in Section 2 of Annex 1 to the Royal Decree of 27 May 2014, by entering the registration number of the registration submitted earlier.
- A simplified registration: this type of registration is used for substances in the nanoparticulate state that are exclusively intended for scientific research and development or for research and development focused on products and processes. In addition to the identification of the Declarant, this type of registration only requires the chemical identification of the substances produced in the nanoparticulate state and a declaration that the substance in question will not be placed on the market for commercial purposes.

The "Foreign Supplier" account type cannot perform simplified registrations.

2.6. DEFINITION OF ROLES IN THE SUPPLY CHAIN

When the Declarant states how much (quantity) of a certain substance is placed on the market in a nanoparticulate state, it can also indicate what role it plays in the supply chain.
The different roles in the supply chain are:

- Producer: produces a substance in the nanoparticulate state, as such or contained in a mixture and places it on the market.
- Distributor: stores substances produced in a nanoparticulate state, as such or contained in a mixture, and places them on the market for third parties.
- Importer: is responsible for the physical introduction on the market of the substance produced in nanoparticulate state, as such or contained in a mixture.

- Formulator: produces mixtures and generally supplies them further in the supply chain or directly to consumers. It mixes the substances produced in a nanoparticulate state, as such or contained in a mixture, without changing the properties of these substances. Examples of such mixtures are paints, adhesives, cosmetics, lubricants, detergents, etc.
- Refiller: brings substances produced in a nanoparticulate state, as such or contained in a mixture, from one container to another, generally during repackaging or to change brand.
- Other: to be specified.

NANOREGISTER EVALUATION

1. Description of the project

The aim of this project is to evaluate the quality of the submitted registrations of substances produced in nanoparticulate state according to the Royal Decree of 27 May 2014. It must also be checked whether all mandatory fields within a registration dossier were entered correctly. The combination of all these mandatory fields corresponds to the complete physicochemical characterization of the substance. The interface of the NanoRegister platform (NANO) is divided in different topics allowing the applicant to introduce general information of the registrant, the chemical identification of the product, the primary particle size and shape, the agglomerates and aggregates size and shape, the existence of coating and its nature, the presence of impurities, the crystallographic phases of the product, the specific surface area and the surface charge. The project's goal is not to evaluate if the registered measurements are correct or not, but it is to evaluate if the methodology that was used to characterize the physicochemical properties of the substances for each topic was adequate.

2. Main Goals of the project

The goal of the project is to evaluate the registration of substances in nanoparticulate state for the trade year 2017 (1^{st} phase) and for the year 2018 (2^{nd} phase), and to verify the compliance according to the Royal Decree of 27 May 2014. In particular:

- For each complete registration, it will be checked per parameter whether all requested data are present (compliance check).
- For the simplified registrations, it will be checked whether the declaration of honour (signed by the research institute, not the registrant) is present for the nanomaterials listed.
- A derived, compliance database will be set up based on the compliance check.
- The data in the compliance database will be analyzed statistically.
- The data in the NanoRegister will be evaluated evaluation of per parameter by listing the different methods used for meeting each parameter in the NanoRegister.
- The different methods used from the applicants for meeting each parameter in the NanoRegister will be evaluated based on literature data and on the results of research projects such as NanoDefine, NANoREG and To2DeNano projects.
- For registrations using a previous registration number (limited registrations), it will be checked whether the used "previous registration number" is valid and that it contains the data that also apply to the registration concerned.
- For the complete dossiers, it will be evaluated per parameter whether the physicochemical data reported are in accordance with what is currently technically possible.

- A derived, "quality" database will be created based on T2.3 and T2.4 and the data will be analyzed statistically.
- A report of the results will be prepared.
- Recommendations for further optimization of the Belgian NanoRegister based on the evaluation and reporting will be given.

3. Scope of the present report

The present report gives an overview of the registrations of the trade year 2018 (second phase of the project) and aims to contribute to a better understanding of the situation of nanomaterials on the Belgian market. The results are structured as follows:

- Qualitative analysis of a subset of the database and
- Quantitative analysis of the registered data of the trade year 2018, when feasible.

The quantitative analysis of the data is done after filtering to extract the relevant information.

RESULTS

1. Qualitative analysis

An important step was to assure access to the Nano platform, such that the data could be analyzed qualitatively and quantitative. The qualitative examination of the data showed that there are several problematics, as was also observed in the first phase of the project. Most of the problematics were common in the two phases. Some of them are summarized as follows:

i. Multiple registrations with the same number are present related to updates and adaptations of the data over time.

ii. Overall, the registrations were done in several languages making the comparison and statistics analysis difficult.

iii. For the same registration, completed fields can be found both in French and in English.

iv. Within the same parameter the applicants utilized no harmonized wording.

v. Many of the required parameters leave room for interpretation by the applicants.

vi. Many measurands are asked for and many fields are not completed.

vii. There are no standardized descriptors for size and shape measurands.

viii. The input should be better defined. It cannot be determined whether the absence of information "-" means a negative answer or absence of answer.

ix. Annexes are missing making interpretation of the provided information difficult (no metadata).

x. It is impossible, also for experts, to interpret many of the inputs provided for many parameters e.g. "Setting microscoop 1:44:000".

xi. Certain characterization methods are not suitable and the arguments given to justify these methods are wrong.

xii. In most cases and for most parameters no measurements uncertainties are indicated.

2. Quantitative analysis

2.1. DATA EXTRACTION

The access to the NANO platform database allowed us to extract the data of the registrations. A specific dataset was extracted, built for Sciensano earlier by DG5, under the name “Reporting/aanpassingen Sciensano”. This new dataset contains the limited and complete registrations from 15/09/2015 to 20/05/2020. The date of extraction was 25/05/2020. The qualitative analysis of the extracted data showed that a filtering step was necessary for evaluation . The developed algorithm, which was previously used for filtering the data of the phase 1 to extract relevant information from this original dataset (Figure 1), was also successfully applied here. This algorithm applies an iterative approach to extract relevant data sorted by category (substance/mixture) and year and identifies unique registrations, resulting in a new dataset useful for statistical analysis.

The original data under the tab “Reporting/aanpassingen Sciensano” consisted of a Table of 3725 lines, each corresponding to a registration (complete or limited) and of 163 columns, which refer to the parameters provided by the applicants. The registrations were sorted by year and only these of the trade year 2018 were kept. This first filtering resulted in a Table of 1110 registrations categorized in substances and mixtures. Then, the two categories were treated separately using the developed algorithm (Figure 1). The algorithm identifies the most recent registration automatically and previous registrations of the same substance/mixture are omitted from the dataset. If multiple registrations for the same substance/mixture were introduced on the same day, the registration with the most filled cells is kept. Even though this approach assumes that the registration with the most filled cells is the most complete, it addresses the problem having multiple registrations for the same substance/mixture.

Statistical analysis of the data is performed, when applicable, by using the python libraries pandas and matplotlib.

The simplified registrations, in which the applicants had only to undersign the declaration of honour, were manually checked.

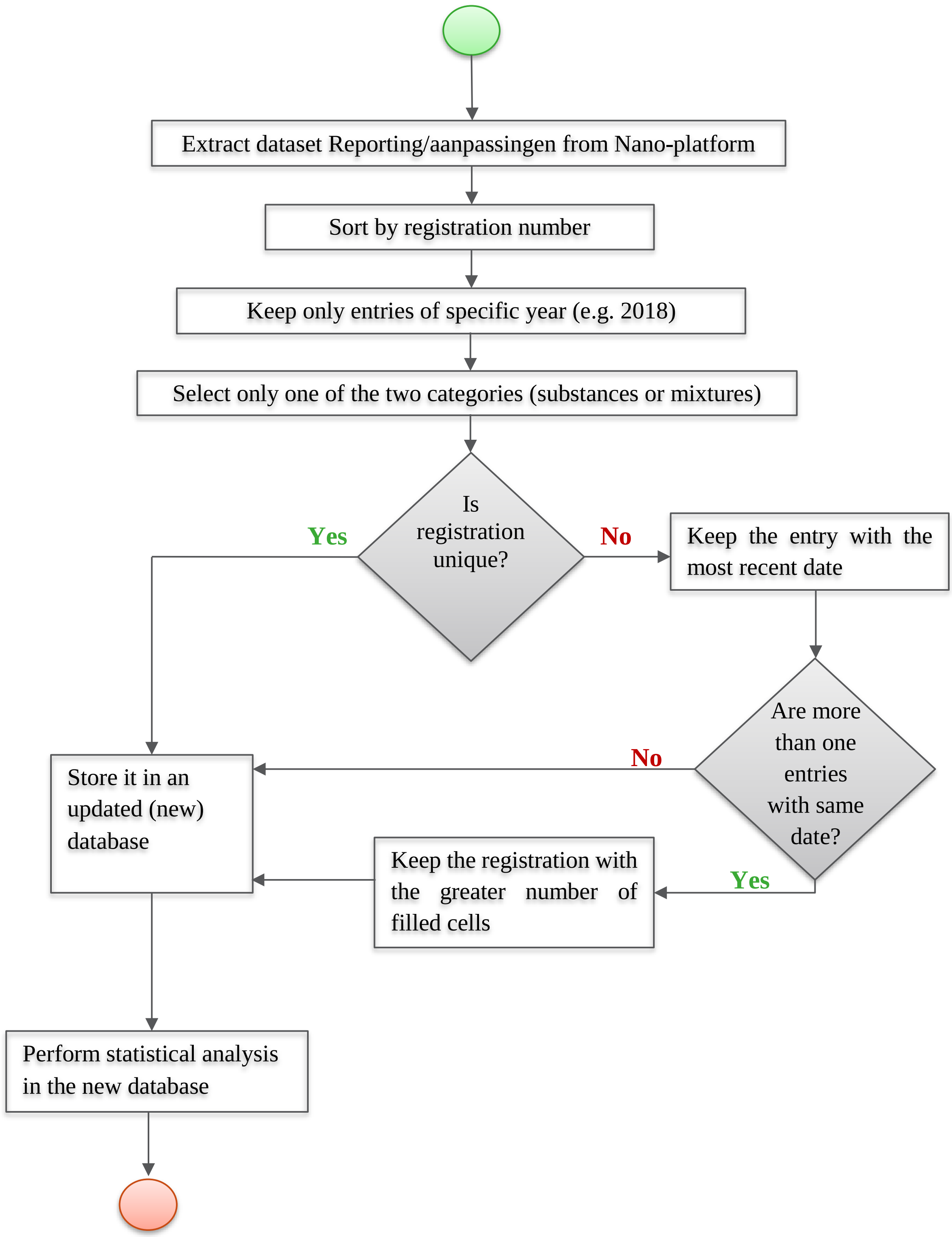

Figure 1. Flowchart of the developed algorithm used for the data filtering of the NanoRegister.

2.2. ANALYSIS OF THE DIFFERENT TYPES OF REGISTRATIONS

Application of the developed algorithm resulted in 524 registrations (from 1110) for the trade year 2018 including 424 limited registrations (7 of them did not include previous registration numbers) and 100 complete registrations. Table 1 gives an overview of the registrations.

The number of the simplified registrations for the trade year of 2018, for which only the presence of the declaration of honour was checked, was 16. To evaluate the simplified registrations another dataset from the Nano back office platform was downloaded, under the name “All registrations”.

The total number of all registrations that was evaluated (complete, limited and simplified) for the trade year 2018 are 540. This number increased with 20% compared to that of the trade year 2017 (Phase 1 of the project).

Table 1. Registrations of the trade year 2018.

Complete	Limited		Simplified
100	**424**		**16**
	With previous Reg. No.	Without previous Reg. No.	
	417	**7**	

2.3. DATA ANALYSIS

2.3.1. Complete registrations

The final number of the complete registrations for the trade year 2018 that was evaluated in detail is 100, with 18% registered as mixtures and 82% as substances.

The compliance check is performed for each file per parameter for the complete registrations in order to evaluate whether all data requested from the applicants are present. Below, the data are analyzed and discussed according to the nine main categories, namely the chemical identification, the particle size and shape, the agglomerates and aggregates, the coating, the impurities, the crystallographic structure, the surface charge, the sector of use and the quantity. The applicants introduce the relevant information when registering a material according to these categories. For each category the percentage of input of the key parameters is calculated. For the calculation, the symbol “-” in the exported and filtered database is considered as an absence of answer.

2.3.1.1. Chemical identification

In the category chemical identification, the compliance check is performed for the following subcategories: the chemical name (chemical names are presented in Annex) and chemical formula of the material, and the presence of the CAS number, the REACH number and the EC number. Figure 2 shows the percentage of the applicants registered the relevant information. Most subcategories of the chemical identification show high compliance. As in 2017 and for a yet unclear reason, a decreased percentage (71%) is only found for the REACH number registrations. The corresponding value of the trade year 2017 was 67%.

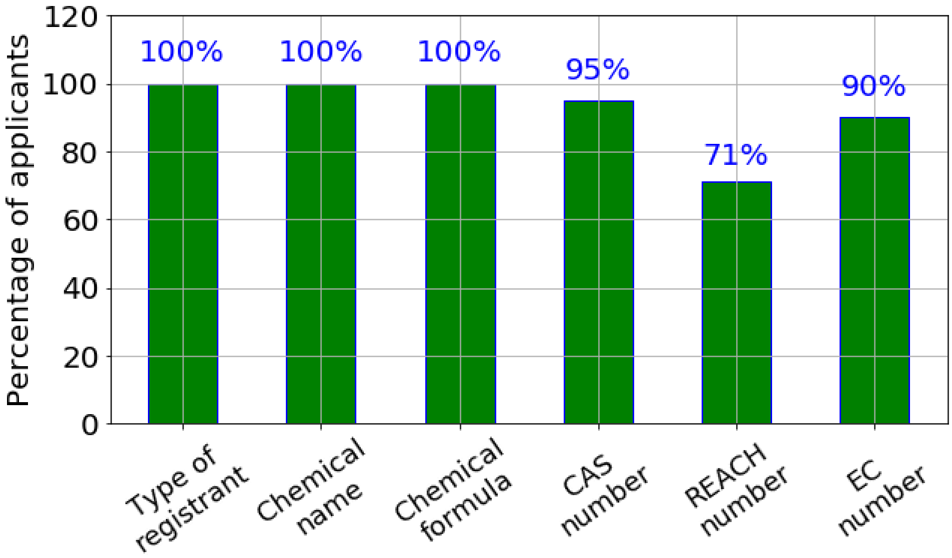

Figure 2. Compliance check for the category: chemical identification.

2.3.1.2. Particle size and shape

In the category particle size and shape, the compliance check is performed for the following subcategories: the determination method of the size and shape of the material, the shape and the number of dimensions of the material, the median and mean size of dimensions 1, 2 and 3 and the standard deviation of dimensions 1, 2 and 3. Figure 3 and Figure 4 show the percentage of the applicants that registered the relevant information. Additionally, a compliance check is performed for the method motivation, the experimental circumstances, the traceability, the measurement uncertainty, the ability to complete the requested data and the justification if data are not completed, as shown in Figure 5.

Most subcategories of the particle size and shape characteristics show high compliance (>90%) and the applicants who declared a second and/or a third dimension of their material registered the relevant information (100%). However, a limited number of applicants registered their measurements uncertainties (12%), as was also observed in the compliance check of the trade year 2017 (15%). This can be explained by the fact that completion of the specific field is not obligatory when registering a material.

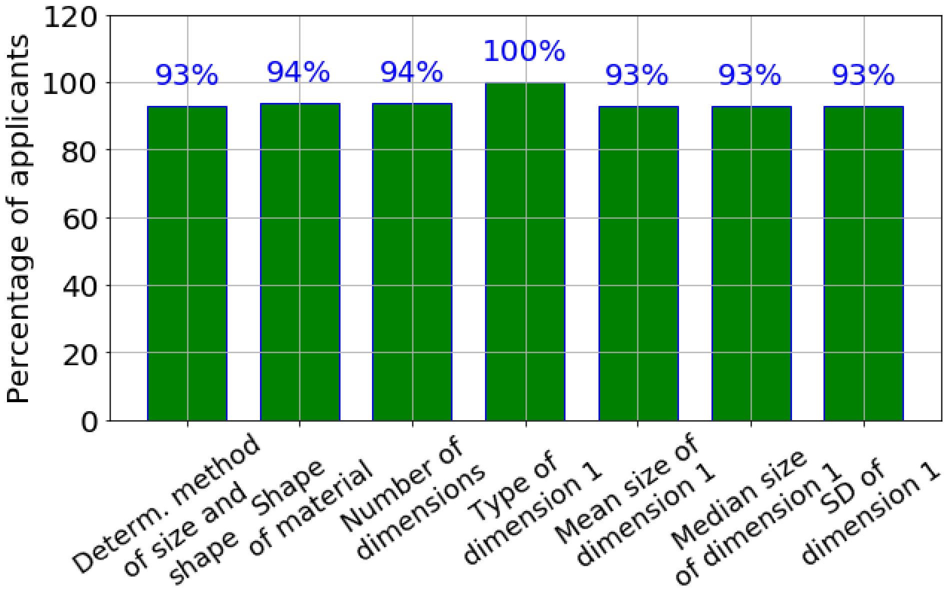

Figure 3. Compliance check for the category: particle size and shape.

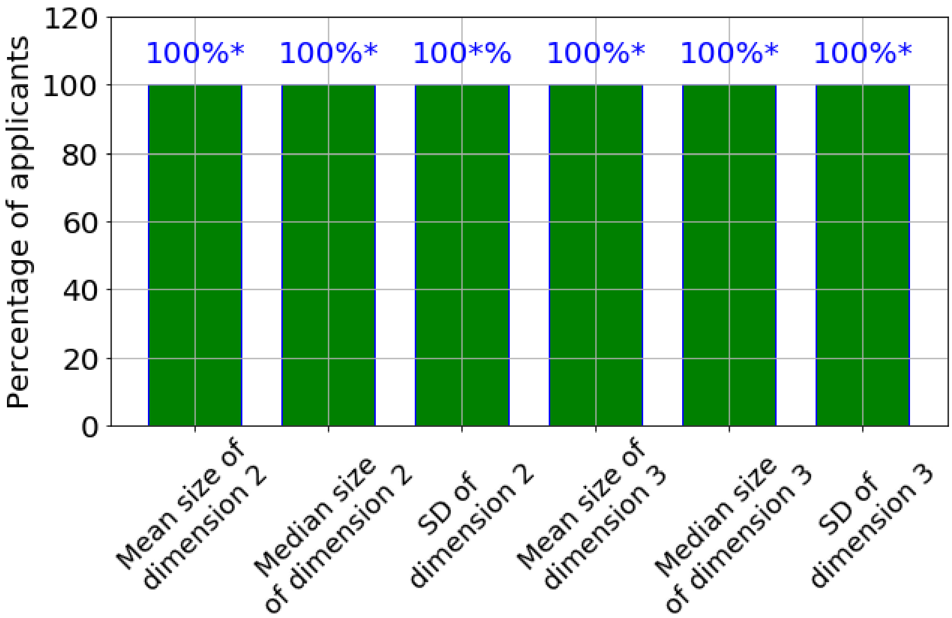

Figure 4. Compliance check for the category: particle size and shape. *Percentage of the applicants declared a corresponding second or third dimension of the material.

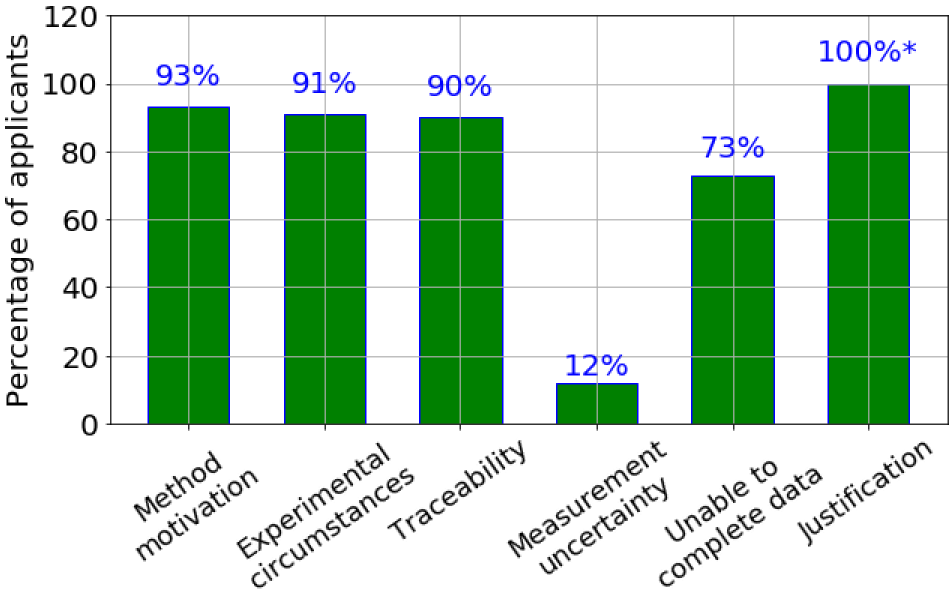

Figure 5. Compliance check for the category: particle size and shape. *From the applicants replied they were unable to complete data.

2.3.1.3. Agglomerates and aggregates

In the category agglomerates the compliance check is performed for the following subcategories: if the material is sold in form of agglomerates, the estimation method of agglomerates size, the measure type, the mean size and the standard deviation of dimension 1, the shape of agglomerates and the determination method of the agglomerates size. Additionally, compliance check is performed for the method motivation, the experimental circumstances and the traceability, as shown in Figure 6. In most subcategories, the applicants introduced the relevant information and the compliance percentage is very high (≥97%). The only parameter, which shows limited compliance, is related to the shape of agglomerates (42%). Similarly, a decreased compliance (27%) was previously found for the trade year 2017.

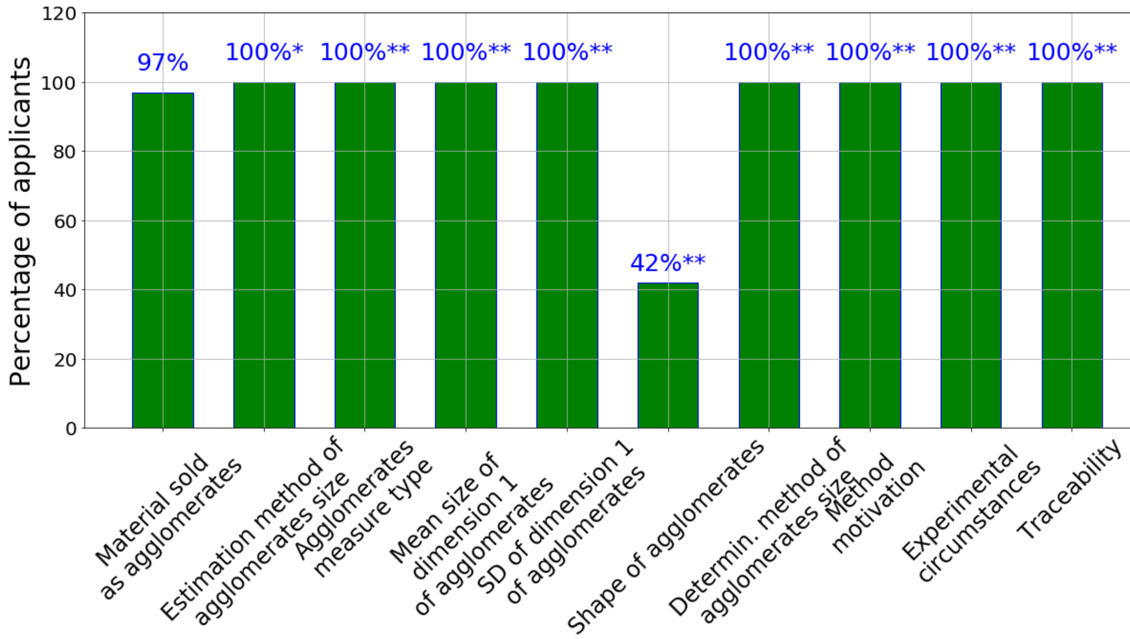

Figure 6. Compliance check for the category agglomerates. *Estimation method of agglomerates sizes could be: separate from aggregates, together with aggregates or size is not registered and percentage is given for the registrants who declared that their material is sold in form of agglomerates. **Percentage from those declared that the material is sold in form of agglomerates and the characteristics were measured separately from aggregates.

In the category aggregates the compliance check is performed for the following subcategories: if the material is sold in form of aggregates, the measure type, the mean size and the standard deviation of dimension 1, the dimension 1 interval min and max, the shape of agglomerates and the determination method of the agglomerates size. Additionally, compliance check is performed for the method motivation, the experimental circumstances and the traceability, as shown in Figure 7. In most subcategories, the applicants introduced the relevant information and the compliance percentage is very high (≥98%). A decreased percentage (80%) is only found for the aggregates shape registrations, as was similarly observed for the trade year 2017, with compliance of 73%.

Figure 6 and Figure 7 show that the applicants had difficulties to register the shapes of the agglomerates and aggregates of their materials. A possible reason for the relatively low compliance in these categories could be that the applicants employed determination methods which cannot provide shape information, such as DLS, rather than descriptive EM methods, which besides size information also gives information about the shape of the materials. Also, the NanoRegister platform lacks specific guidance for the shape categorization of aggregates/agglomerates. To categorize and describe the shape of aggregates and agglomerates, the systems proposed by Lopeze-de-Uralde et al. [4] are suggested.

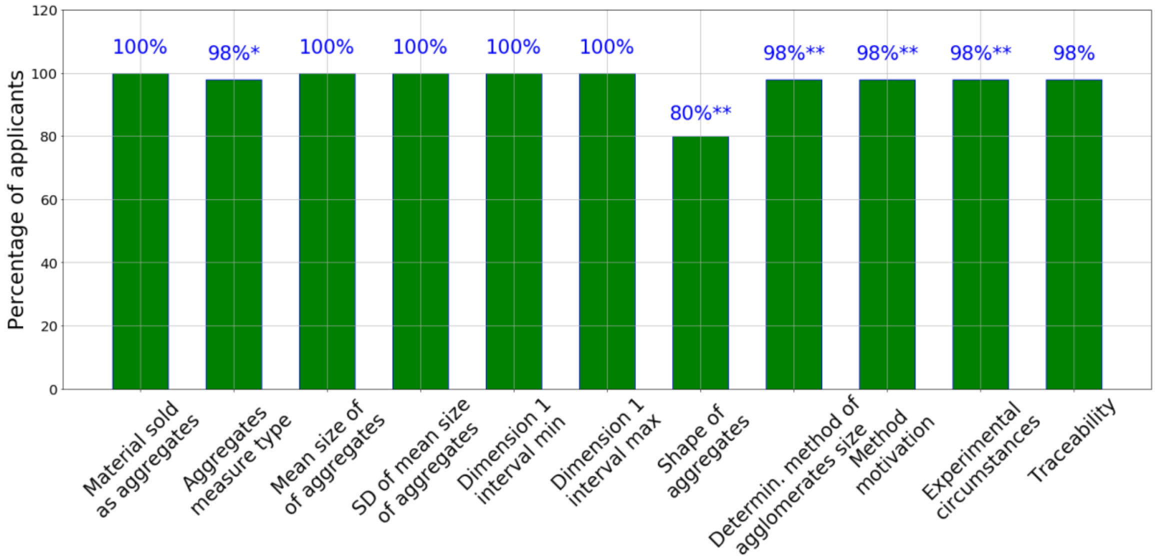

Figure 7. Compliance check for the category: aggregates. *Measure type could be: mean size or interval. **Percentage of applicants registered that the material is sold in form of aggregates.

2.3.1.4. Coating, impurities and crystallographic analysis

In the categories coating, impurities and crystallographic analysis the compliance check was performed for the following subcategories: presence of coating, type of coating, presence of impurities, impurities mass concentration, determination method of impurities, crystallographic analysis and crystallographic structure. Figure 8 shows the percentage of the applicants that registered the relevant information. In most subcategories, the applicants introduced the relevant information and the compliance percentage is very high (>93%). A decreased percentage (80%) is only found for the determination methods of impurities. For the trade year 2017 the compliance for the specific parameter was also decreased (76%).

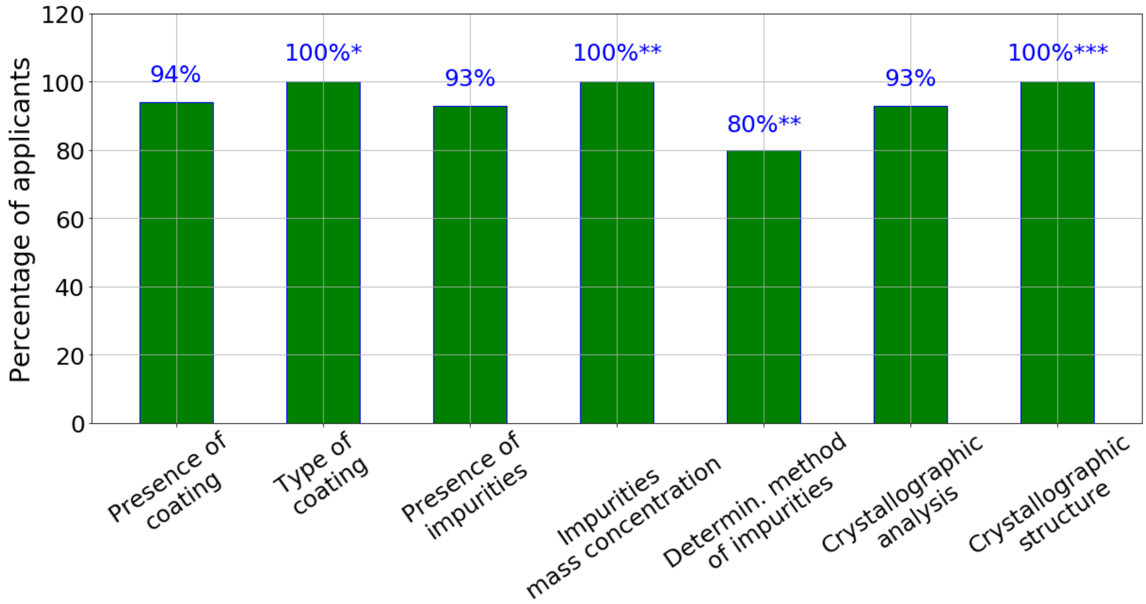

Figure 8. Compliance check for the categories: coating, impurities and crystallographic analysis. *Percentage of applicants declared that the material has a coating. **Percentage of applicants declared that the material contains impurities. ***Percentage of applicants declared crystallographic analysis.

2.3.1.5. Specific surface area and surface charge

In the category specific surface area the compliance check is performed for the following subcategories: mean specific surface area and its standard deviation, determination method of specific surface area, determination method motivation and experimental circumstances. In the category surface charge, the compliance check is performed for the following subcategories: presence of surface charge data, zeta potential, pH and ionic strength. Figure 9 shows the percentage of the applicants that registered the relevant information. In all subcategories for the specific surface area the compliance is very high (≥93%). In the subcategories for the surface charge the compliance is also high and only the compliance of the parameter “surface charge ionic strength” is limited (80%). The compliance of the specific parameter was also found decreased (62%) during the compliance evaluation of the trade year 2017.

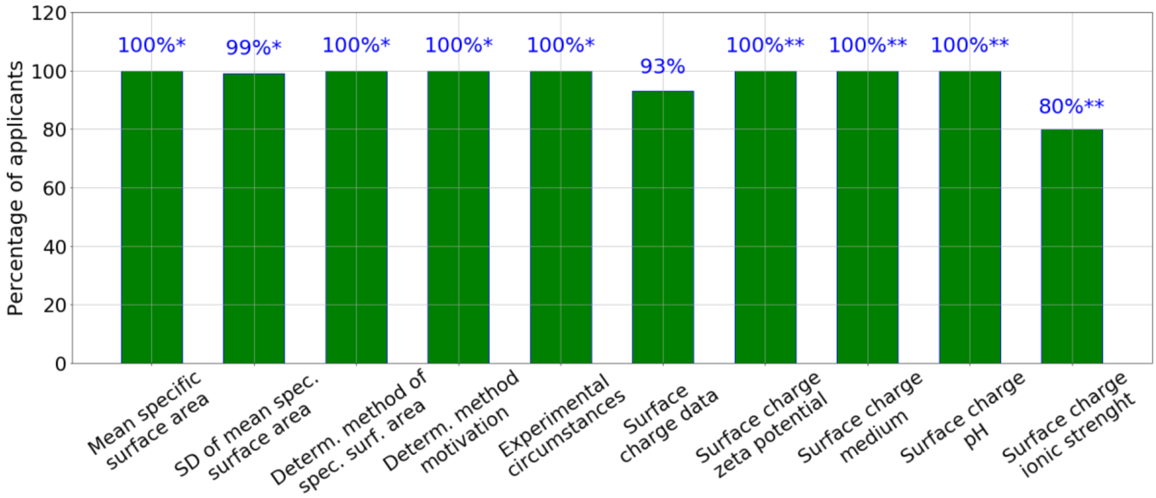

Figure 9. Compliance check for the categories: specific surface area and surface charge. *Percentage of applicants answered positively for specific surface area data. **Percentage of applicants answered positively for surface charge data.

2.3.1.6. Sector of use of the material

In the category sector of use the compliance check is performed for the following subcategories: the sector of use, if the material is used in chemical products, the category of the chemical product, if the material is used in chemical processes, if the material is used in applications where there is environmental release and in which categories, if the material is used in articles and the article’s category. Figure 10 shows the percentage of the applicants that registered the relevant information. 71% of the applicants answered if their material has a sector of use. During the trade year 2017, only 51% of the applicants provided the relevant information.

The applicants that answered positively, they also registered the relevant information in the subcategories of the sectors of use of their material reaching a compliance of 100%.

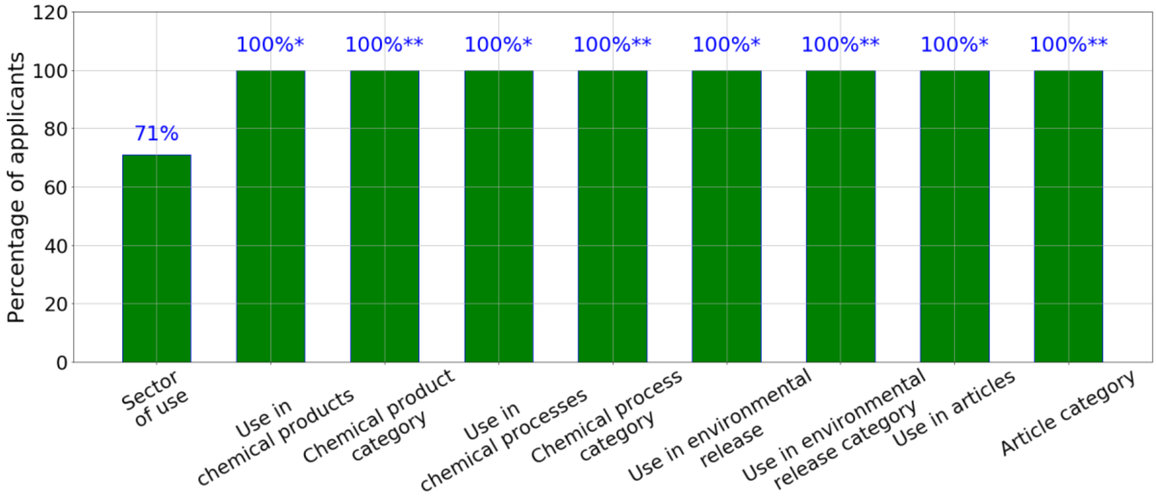

Figure 10. Compliance check for the sector of use of the materials. *Percentage of applicants who answered positively in the sector of use. **Percentage of applicants who answered positively in the corresponding sectors of use.

2.3.2. Simplified registrations

For the simplified registrations only the presence of the declaration of honour was checked. From the NanoRegister back office platform, a dataset was extracted under the tab Reporting\All registrations (accessed 20/05/2020), to find relative information for the simplified registrations. In total, 16 simplified registrations were submitted for the trade year 2018 and their files were downloaded via the platform. All files of the submitted registrations were checked, and one declaration of honour was not undersigned. For the 94% of them the declaration of honour was undersigned.

2.3.3. Statistical analysis of the compliance database

The compliance check of the complete registrations was performed for the parameters described in paragraph 2.3.1. The derived dataset is then used for the statistical analysis.

The statistical analysis is performed for relevant parameters of the different categories including: the type of shape of the material, the aggregates shape, the determination method of the size and shape of the material, the determination method of the agglomerates size, the determination method of the aggregates size and shape and the determination method of impurities mean specific surface area of the material. Additionally to the statistics, the determination methods are evaluated in 2.3.4.

Figure 11 shows the percentage of the different types of shapes of the registered materials. Among the different choices given to the applicants (sphere, sticks, capsule, flakes, etc.), the option “other” was the most selected (62%), similarly to the trade year 2017 (“other” was selected by 55% of the applicants). This creates confusion because the applicants had the choice to add new shapes, as shown in Figure 12. Most of these shapes can be attributed to one of the types presented in Figure 11. Describing particles shapes according to standardized nomenclatures as proposed by Lopez-de-Uralde [4], Krumbein and Sloss [5] and Munoz-Marmol [6] gives some guidance and avoids such confusion.

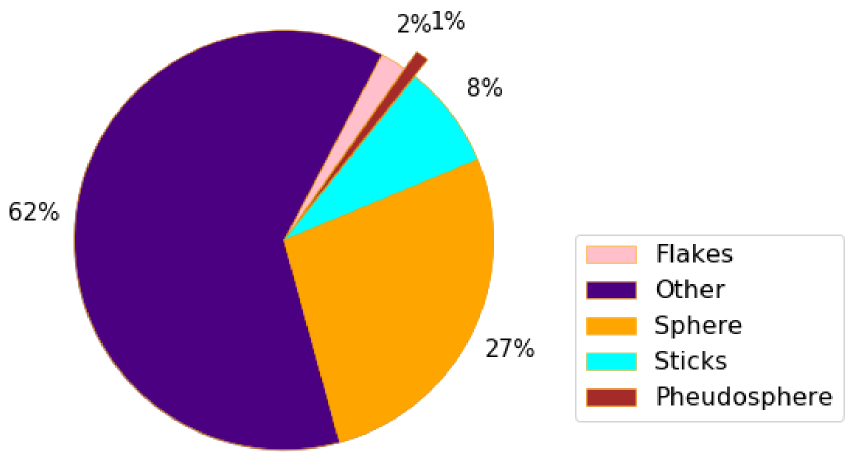

Figure 11. Types of shape of the registered materials.

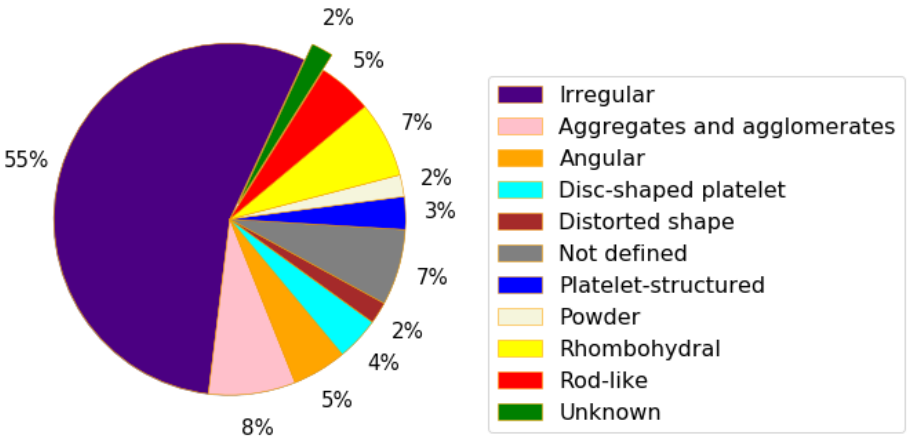

Figure 12. Other types of shape of the registered materials.

Most of the applicants declared that the shape of the aggregates in their materials is pseudo-spherical (70%) and spherical (23%), as depicted in Figure 13. Lower percentage is found for the other shapes registered. Description of the aggregates shapes using guidance for shapes categorization, as described by Lopez-de-Uralde [4], could be used to avoid confusion.

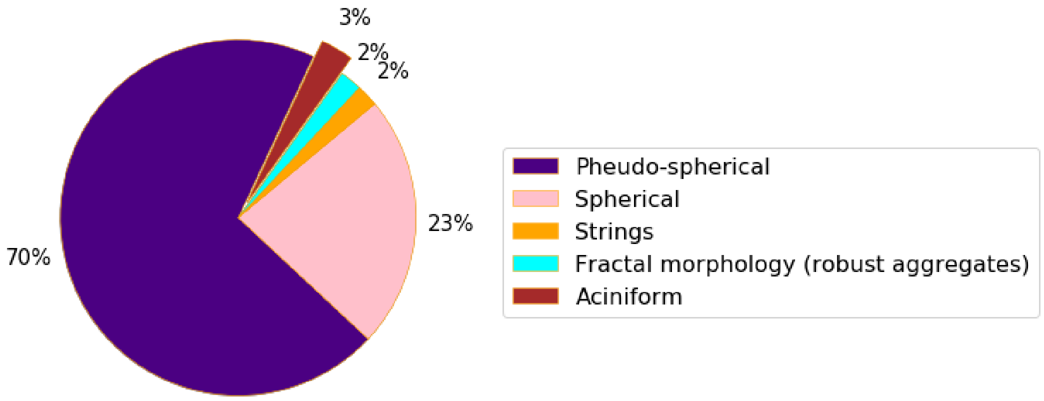

Figure 13. Shapes of aggregates.

The percentage of the used determination methods for characterizing the size and shape of the materials is presented in Figure 14. When registering a material in the NanoRegister platform, the applicant could select between three default options (TEM, SEM and AFM) or “Other”, to introduce the determination method of the size and shape of the material.

The two most used methods are EM methods including SEM (48%) and TEM (24%). During the trade year 2017, ~67% the of applicants also used EM methods. A relative low number of applicants (3%) employed two methods, while 25% of the applicants declared other methods (than the three default methods), including Supplier information (7%), DLS (7%), Surface titration (5%), Turbidity and Interference Optics (2%), Laser particle sizer (1%), Centrifuge Photosedimentometry (1%), FESEM (1%) and Dry sieving (1%).

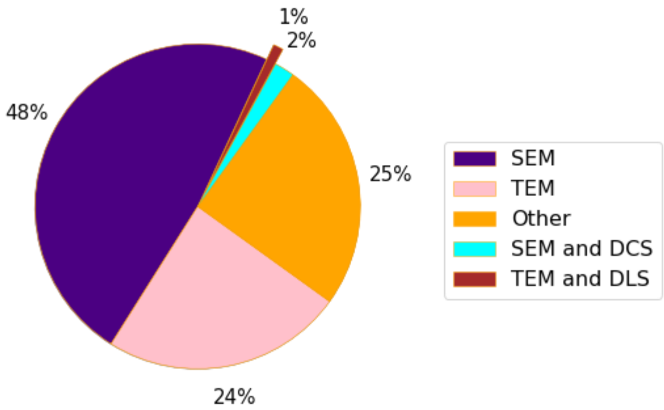

Figure 14. Determination methods used for characterizing the shape and the size of the constituent particles.

For the determination method of agglomerates, three choices were provided to the applicants, who had to choose if the agglomerates were determined together with the aggregates, if the agglomerates were determined separately from the aggregates or if the agglomerates were not at all determined.

75% of the applicants registered that the size of agglomerates were determined together with the size of aggregates, 12.5% that the size of agglomerates was not determined and 12.5% that the size of agglomerates was determined separately from the aggregates size.

For the determination methods of aggregates, the applicants were free to introduce the determination method they used (no default options were provided in the platform). Figure 15 depicts the percentage of the different methods used to determine the shape and the size of aggregates. Among them, the most used methods are SEM (~74%) and Laser diffraction (10%). During the trade year 2017, ~53% applicants used SEM and 10% DLS to determine the size and shape of the aggregates.

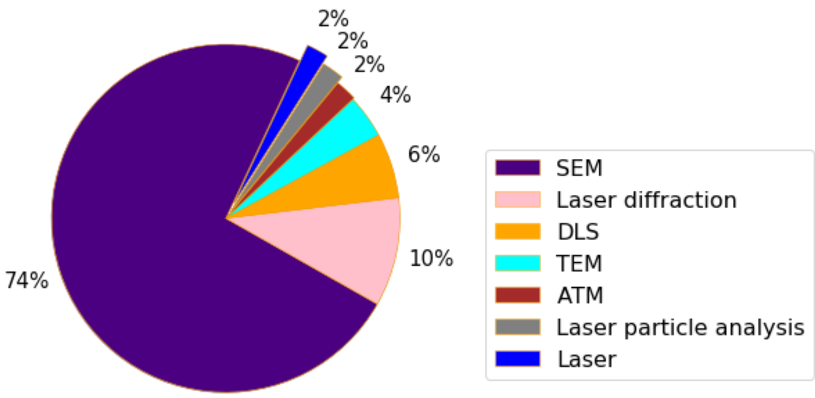

Figure 15. Determination methods used for characterizing the shape and size of aggregates.

34% of the applicants declared that the material they registered contained impurities and 27% introduced the method they used. Figure 16 depicts the methods used for determining the impurities in these materials. HPLC was the most used method with 60%, similarly to the trade year 2017 (~41%).

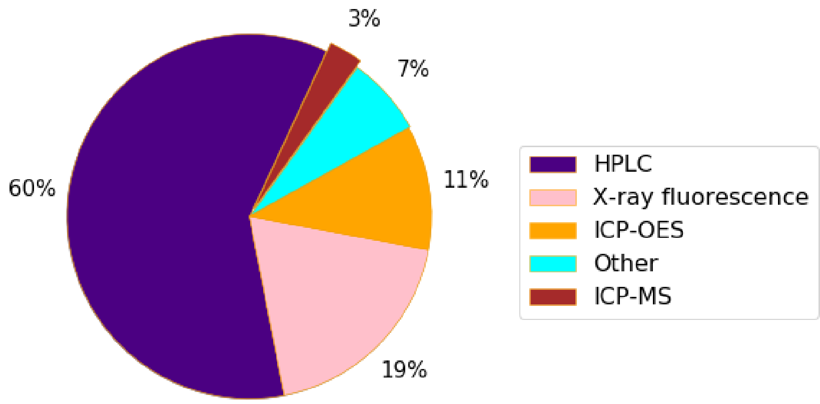

Figure 16. Determination methods of impurities of the registered materials.

73% of the applicants registered the values of the mean specific areas of their materials, with 88% of them declaring that they used the BET (94% during the trade year 2017), 11% used other methods (surface titration mostly) and 1% used TEM method.

2.3.4. Evaluation of the determination methods used in the NanoRegister.

Table 2 summarizes the different methods used for meeting the different parameters provided by the applicants in the complete registrations.

Table 2. Summary of the determination methods used by the applicants for the different parameters in the NanoRegister during the trade year 2018.

Size and shape		Impurities	Specific surface area
Constituent particles	Agglomerates/Aggregates		
SEM (48%)	SEM (74%)	HPLC (60%)	BET (88%)
TEM (24%)	Laser diffraction (10%)	X-ray Fluorescence (19%)	Other (11%)
Supplier Information (7%)	DLS (6%)	ICP-OES (11%)	TEM (1%)
DLS (7%)	TEM (4%)	Other (7%)	
Surface titration (5%)	Laser (2%)	ICP-MS (3%)	
Turbidity and Interference Optics (2%)	ATM (2%)		
SEM and DCS (2%)	Laser particle analysis (2%)		
Laser particle sizer (1%)			
Centrifuge Photosedimentometry(1%)			
FESEM (1%)			
Dry sieving (1%)			
TEM and DLS (1%)			

72% of the applicants used Electron Microscopy (EM) methods, and in particular SEM (48%) and TEM (24%) to determine the size and shape of the constituent particles and 78% of the applicants used Electron Microscopy (EM) methods to determine the size and shape of the aggregates.

TEM and SEM belong to the counting methods that allow for the determination of size and size distributions, as they measure the particle properties at the level of individual particles, and both use an electron beam for sample visualization down to the nm scale [7].

If done properly counting methods like TEM, SEM and AFM will result in a reliable number based distribution of the size of the constituent particles and they will allow identifying individual constituent particles and agglomerates/aggregates.

In very few cases measurement uncertainties and description of the parameters are reported (Figure 5), which makes assessment of the quality of the measurements difficult.

Dynamic Light Scattering (DLS) was also used for the size and shape determination of both constituent particles (7%) and aggregates (6%). DLS, which belongs in the ensemble methods (all particles in the sample are measured at the same time and the size distribution is extracted from a combined signal from all particles), is a technique for characterization of colloidal systems based on the scattering of visible light resulting from the difference in refractive index between the dispersed colloids and the dispersion medium.

Ensemble methods, such as DLS, Static light scattering and Laser Diffraction do not allow to identify constituent particles in agglomerates and aggregates and they tend to give wrongly biased results in case of polydisperse size distributions. Estimation of the constituent particles sizes by these methods is often unreliable. This is elaborated in detail in Nanodefine Methods Manual JRC technical reports [7].

Many types of impurities can be expected depending on the type of the material. Therefore, for impurities detection in the materials several methods were used, including HPLC (60%), X-ray Fluorescence (19%) and ICP-OES (11%). These methods can analyze different types of impurities.

The mean specific surface area was mostly calculating by the applicants (88%) by using the BET method. BET, is a standardized method [8] that specifies the determination of the overall specific external and internal surface area of disperse (e.g. nano-powders) or porous solids by measuring the amount of physically adsorbed gas according to the Brunauer, Emmett and Teller (BET) method. It takes account of the International Union for Pure and Applied Chemistry (IUPAC) recommendations of 1984 and 1994.

To be able to obtain reliable BET results, conditions regarding the polydispersity, the presence of impurities and the porosity should be met [7]. This information is mostly provided in (Figure 8).

2.3.5. Limited registrations

The number of limited registrations for the trade year 2018 was 424. 417 registrations had a previous registration number and 7 did not have. According to the NanoRegister and as described in section 2.5, for the limited registrations the registrant could replace the physicochemical characteristics of the nanoparticulate state substance by entering the registration number of this previous registration. Therefore, for these registrations, the physicochemical characteristics of the substances were only provided in pdf files from the previous registrations.

For these registrations using a previous registration number, it was checked whether the used "previous registration number" was valid and that it contained the data that also apply to the concerned registration .

Note that for different limited registrations the same previous registration number was given multiple times. The 417 limited registrations were corresponding to 140 previous registrations. The files of these 140 registrations were downloaded and checked one by one. From them, 66 registrations were incomplete and the applicants declared that the results of the physicochemical characterization were pending, in 8 registrations the applicants declared that they had already submitted the data in previous registrations (which were also checked), 3 registrations were associated with mixtures and did not provide physicochemical data, 2 registrations provided the same previous number as the registrations themselves and 1 registration did not exist.

The compliance check was therefore performed for the rest 68 limited registrations. The following physicochemical parameters that the applicants provided were checked: shape of the material and determination method of its size and shape, mean and median sizes of dimensions 1 and 2 their standard deviations, and the presence of answer for the existence of: agglomerates, aggregates, determination method of aggregates, coating, impurities, crystallographic phase, specific surface area, and surface charge. The results of the compliance check are presented in Figure 17 and Figure 18. As observed, in the 68 registrations, the applicants provided most of the relevant information and the compliance for most parameters is greater than 93%, with exception the parameter of median size of dimension 1 and the standard deviation of dimension 1, which are 88% and 80% respectively.

Additionally, for these 68 dossiers, it was evaluated per parameter whether the physicochemical data reported were in accordance with what is currently technically possible on the basis of literature data and of the results of research projects such as NanoDefine, NANoREG and To2DeNano projects and the data were analyzed statistically.

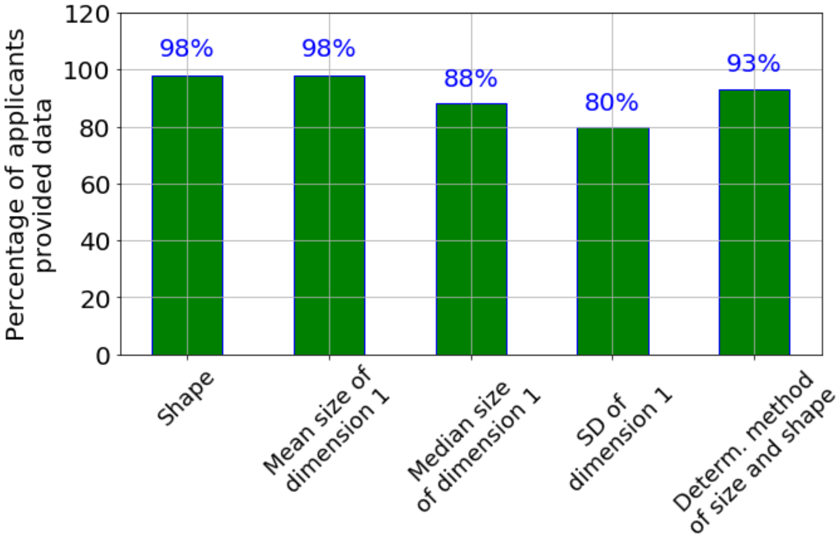

Figure 17. Compliance check for the limited registrations of the trade year 2018.

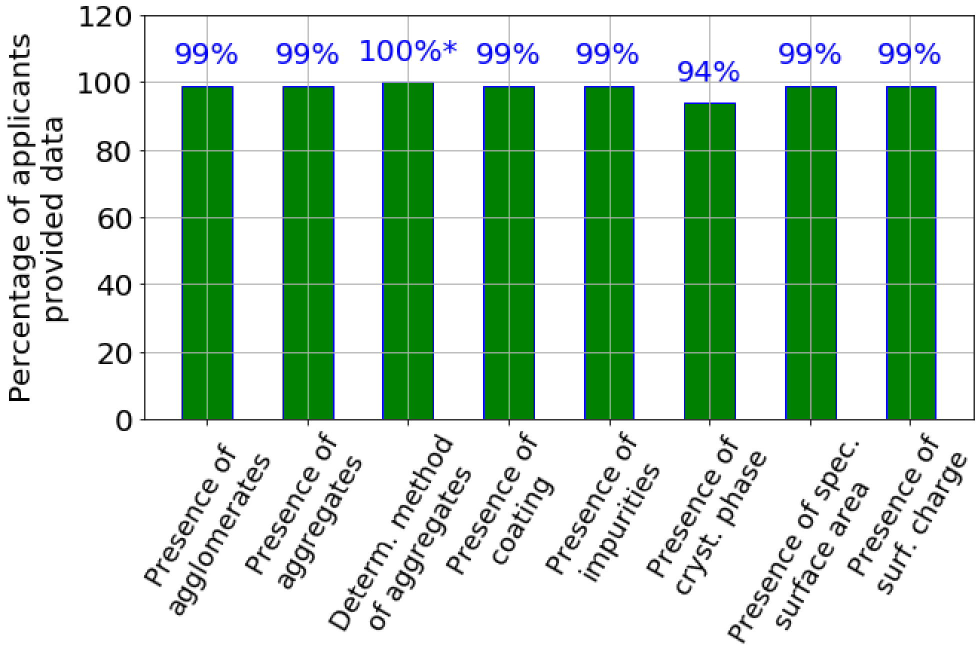

Figure 18. Compliance check for the limited registrations of the trade year 2018. *Percentage of those declaring presence of aggregates.

According to the input data of the limited registrations, for the determination method of the mean and the median size of constituent particles the applicants used six main methods, which are TEM (76%), SEM (11%), DLS (5%), turbidity optics and interference optics (5%), laser particle sizer (1.5%) and surface titration (1.5%). It is unclear what is meant with surface titration. Therefore, EM methods were mostly used (87%), similarly to the trade year 2017 (92%).

For the determination method of the size of aggregates the applicants declared that they used DLS (44%), TEM (34%), laser diffraction (13%), laser scanning (3%), laser scattering (3%) and static light scattering (3%). Figure 19 shows the summarized results.

Most of the applicants (87%) used EM methods to characterize the size of the constituent particles. EM methods can give suitable constituent particles measurements, as previously discussed for the complete registrations in paragraph 2.3.4.

For the size determination of the aggregates the applicants used mostly DLS, while in the complete registrations SEM was mostly employed method. Comparison of results obtained by different methods is very difficult: results of these methods based on different principles are method-dependent [7].

To conclude, the determination methods used for the size and shape of the constituent particles and agglomerates/aggregates in the limited registrations are similar with the ones of the complete registrations. Because results are method-dependant, only comparisons between results obtained by the same method are meaningful.

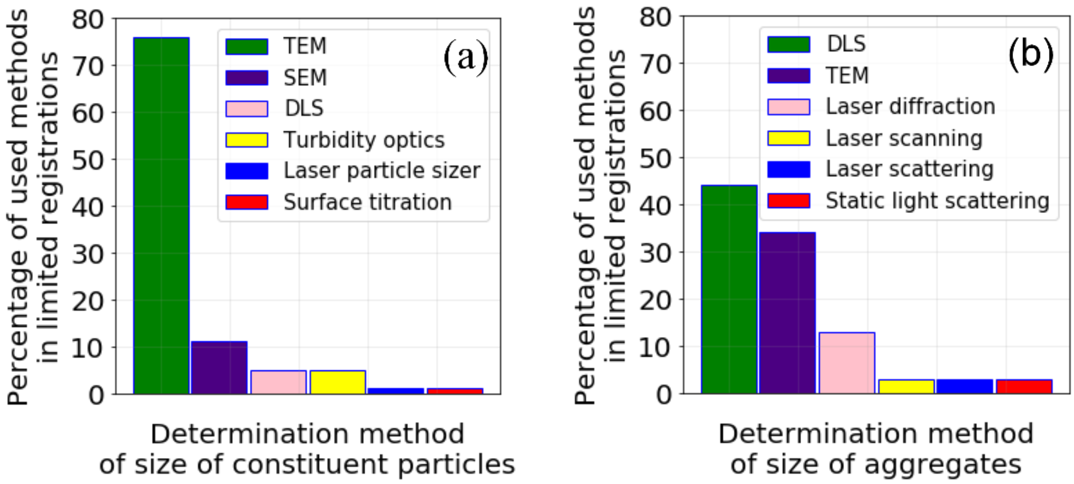

Figure 19. Characterization methods used for (a) the size determination of constituent particles and (b) the size determination of aggregates in limited registrations.

2.4. REGISTERED QUANTITIES

Only the substances used for commercial purposes are subjected to registration and are submitted by the Declarants who indicate the quantities that were placed on the Belgian market. The registrations of substances exclusively used for scientific purposes (simplified registrations) and the registrations submitted by the Foreign Supplier do not require indication of quantities.

For the trade year 2018, 812 registrations of quantity were submitted. The quantities could be registered in kilograms either as estimated quantities or as real quantities. From the 812 registrations 408 were mixtures (Enregistrement mélange) and 19 were simplified registrations (Enregistrement simplifié). Therefore, for these 427 registrations (52%) no quantities were provided.

The rest 385 registrations concerned substances, from which 17 did not indicate quantities, 60 indicated estimated quantities and 308 real quantities. The status of these 385 registrations of substances were: 321 archived (83%), 46 (12%) submitted and 18 draft (5%). Statistics were done for the grouped estimated and real quantities (368 registrations) of substances.

The total quantity of substances in the nanoparticulate state, which was introduced on the Belgian market in 2018, as calculated from the 368 substance registrations, is 120734587.2 kg (120734.5872 tons) based on the recorded data with:

- 48240.5 tons imported and,
- 72494 tons produced.

This section does not take into account the amount of substances that was distributed, since this is in fact a relocation of a product that is already on the Belgian market. The total quantity of substances in nanoparticulate state is decreased by 40% compared to the quantities registered in the trade year 2017 (201429 tons).

In particular, a decrease of 24% is recorded for the import of substances in the nanoparticulate state and a decrease of 47% for the production of substances in the nanoparticulate state.

Figure 20 shows the quantities of the substances containing nanomaterials registered during the trade year 2018. In most of the registrations (77%), the applicant declared quantities that range between 10 and 100000 kg. A significant percentage of about 51% (187 registrations) concerns quantities of less than 1 ton and therefore falls outside the scope of the REACH legislation.

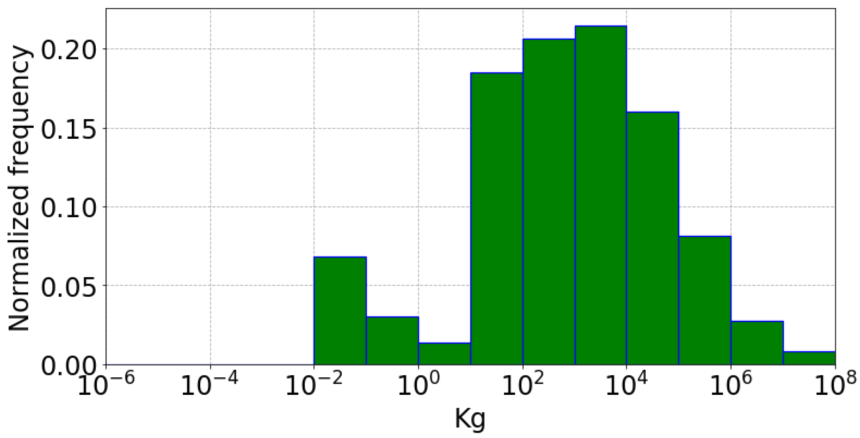

Figure 20. Normalized number of registrations per interval quantity imported or produced during the trade year 2018.

Only 13 registrations declared quantities more than 1000 tons. The list of the generic names of the substances that were introduced on the Belgian market in a total quantity that is larger than 1000 tons as indicated in the pdf files of the registrations are presented in Table 3. This amount refers to the sum of all registrations submitted under the specified generic name.

Table 3. Generic name of the nanomaterials that were produced and/or imported in quantities >1000 tons in the trade year 2018.

Chemical name of substance
Diiron trioxide
Calcium carbonate
Silicon dioxide
Precipitated calcium carbonate
Carbon black

2.5. ROLES IN SUPPLY CHAIN

During the registration of the substances in nanoparticulate state, the registrant could be assigned by different roles in the supply chain. Five choices in the NanoRegister platform give the possibility to the applicant to select his role. These choices include the “Distributor”, the “Importer”, the “Formulator”, the “Producer” and “Other”. Figure 21 shows the normalized quantity registered per role for the trade year 2018 and Figure 22 shows the distribution of the quantities per role.

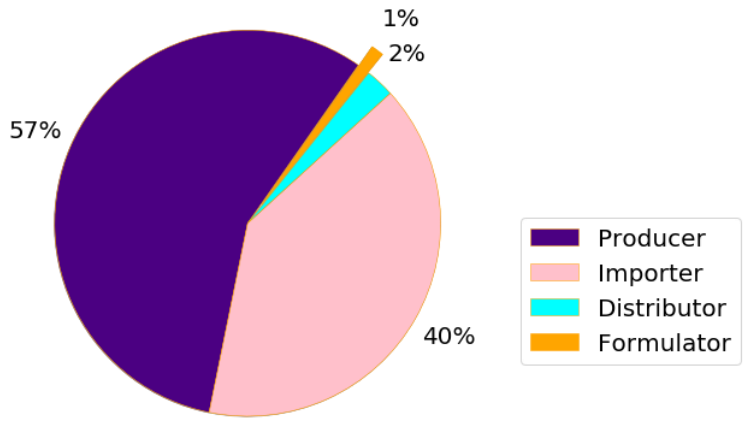

Figure 21. Quantity percentage registered from the different roles for the trade year 2018.

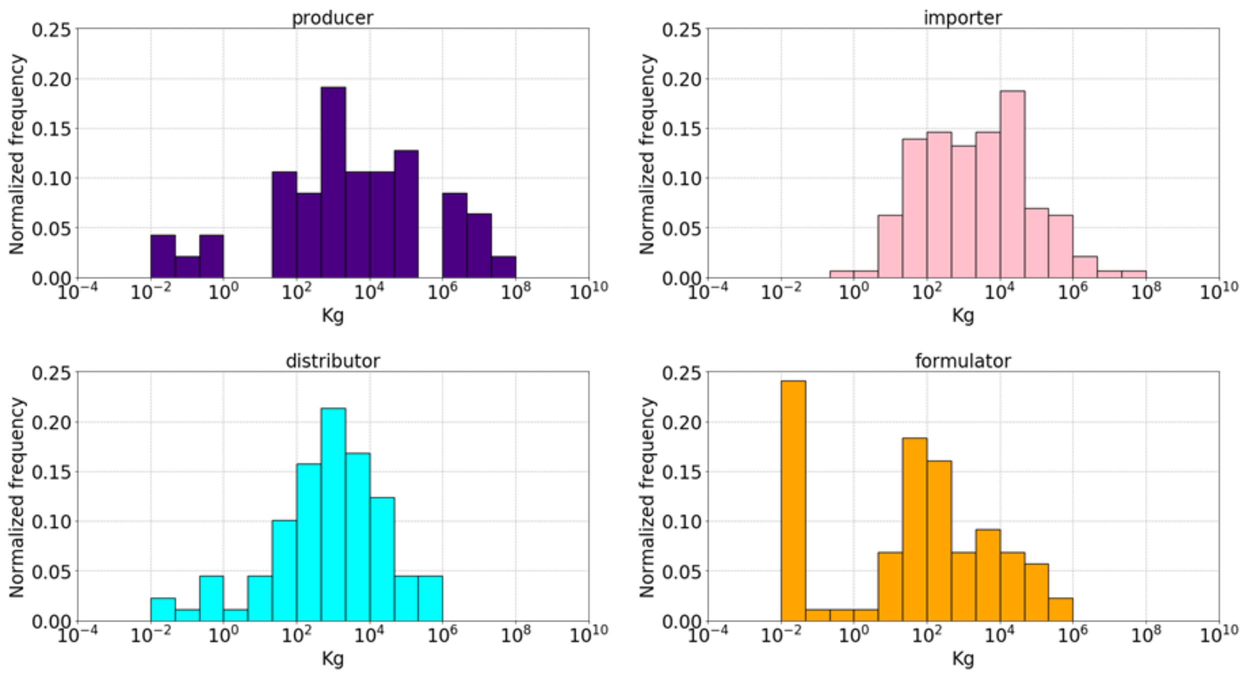

Figure 22. Normalized registrations of quantities of materials in the nanoparticulate state per role in the supply chain.

3. Suggestions and solutions

Based on the present analysis, several problems, indicated in bold were observed. Possible solutions to deal with these problems are suggested and, hereinafter indicated in blue color. The proposed adaptations for the optimization of the NanoRegister and for future data collection are indicated in black.

i. **Multiple registrations with the same number are present related to updates and adaptations of the data over time.** An algorithm was written that identifies the most recent registration automatically and allows to base the evaluation only on these recent registrations. Previous registrations of the same product/material were omitted from the new dataset. When multiple registrations for the same product/material were introduced on the same day, the registration with the most filled cells was kept. Even though this approach assumes that the registration with the most filled cells is the most complete, it addresses and solves the problem of having multiple registrations for the same product/material.

   Because this is a complex solution, in the future the system should foresee a possibility to update the data without creating a new registration number.

ii. **Overall the registrations were done in several languages making the comparison and statistics analysis difficult.**

iii. **For the same registration completed fields can be found both in French and English.** For the present evaluation, the data were translated in English and introduced in a new database.

   We suggest to adapt the user interface of the database such that only data in one language can be entered (preferably English) or to work with language independent codes.

iv. **Within the same parameter the applicants utilized no harmonized wording.** For the present evaluation the data entered in multiple terms will be grouped, when feasible, in English.

   We suggest to adapt the user interface of the database for example by foreseeing obligatory drop lists, such that generally more harmonized wording is used.

v. **The NanoRegister assumes that the applicants can distinguish the aggregates from agglomerates.** There are no standardized methods to distinguish the agglomerates from aggregates yet.

   We suggest not to make a distinction between agglomerates and aggregates for any of the parameters requested.

vi. **Many of the required parameters leave room for interpretation by the applicants.**

vii. **Many measurands are asked and for specific parameters very little information is provided.** We analyzed all data but found out that measurands with a low number of entries make interpretation of statistical analysis problematic. An example is the surface charge where information is relevant only for dispersions. This partly explains the limited data (5%) provided by the applicants for zeta potential, medium, pH value and ionic strength.

   We propose to foresee these additional information conditionally, depending on the input values e.g. no requirements for zeta potential, medium, pH value and ionic strength for powders, only for dispersions.

viii. **There are no standardized descriptors for size and shape measurands.**

ix. **The input should be better defined. It can, for example, not be determined whether the absence of information "-" means a negative answer or absence of answer.** In the new database, we interpreted the data case by case and we reformulated the input and wording, when possible.

We suggest to require standardized descriptors in obligatory drop lists.

x. **Because of missing metadata, for example medium of surface charge, the provided values cannot be interpreted. For example in the particle size and shape characteristics, the applicants are asked to describe the experimental circumstances of the used method and the motivation for the use of this method but the responses are not standardized.**

xi. **Annexes are missing making interpretation of the provided information difficult (no metadata).**

xii. **It is impossible, also for experts, to interpret many of the inputs provided for many parameters e.g. "Setting microscoop 1:44:000" for electron microscopy.** Because the predefined, method-specific metadata were not included or were difficult to access in the annexes, no in depth analysis of the quality of the reported data was possible.

Support should be provided to the applicants directing them to international standards and guidelines (ISO, OECD, CEN). These also foresee requirements for metadata and reporting.

xiii. **For critical parameters, often no measurements uncertainties are provided.** We consider this a problem. It makes proper evaluation of the data difficult because considerable variation is expected and unknown.

Provision of measurements uncertainties should be obligatory for specific parameters, in line with international standards and guidelines (ISO, OECD, CEN). Instructive sessions, presentations or webinars providing technical support on methodological issues can improve standardization and quality of the reported data and their uncertainties.

xiv. **During registration applicants can provide CAS, EC and REACH registry numbers, however, no specific format is required to enter these numbers.** We could only do a compliance check and could not check if the input information was correct.

We propose to implement a strict input format in the NanoRegister so the applicants can avoid erroneous introduction of registry numbers. For instance, a CAS registry number includes up to 10 digits which are separated into 3 groups by hyphens (xxxxxxx-yy-z).

xv. **The characteristics dimensions that the applicants are asked to provide are not always optimal and adapted to the applied methodology.** Only a compliance check could be done.

The requested parameters should be revisited and adapted in line with relevant (international) guidelines for example ISO and CEN standards and manuals like "the Nanodefine Methods Manual" [7].

CONCLUSIONS

This project evaluates the registration of materials produced in a nanoparticulate state according to the KB of May 27th 2014. The Royal Decree concerning the placing on the market of substances manufactured in nanoparticulate state was signed on May 27th, 2014, published on September 24th, 2014, and modified on December 22nd, 2017. According to this Royal Decree, the deadlines for registration of substances and mixtures manufactured in a nanoparticulate state were January 1st, 2016 and January 1st, 2018, respectively. The registration software was launched on September 15th, 2015.

Phase 1 and phase 2 of the project included the evaluation of the registrations of the trade year 2017 and 2018, respectively. Phase 1 was successfully completed and reported previously. Evaluation of the registrations of the trade year 2018 was completed and reported in this document.

For 2018, the completion of obligatory fields within the registration dossiers (“compliance check”) and the quality of the content of the submitted dossiers were assessed.
For the complete registrations, the compliance check assessed for each dossier if all obligatory fields were completed by the applicants.
For the simplified registrations it was checked if the declaration of honor was added to the dossier.
For the limited registrations a derived, “compliance” database was constructed and a statistical analysis of the data in the “compliance“ database was done.

The content of the register was evaluated per parameter, and included listing and evaluating the methods used for measuring selected registered parameter, and the number of different materials and their quantity. The reported data were evaluated at a high level: for the complete dossiers, it was assessed per parameter if the physicochemical data were reported and whether they are in accordance with the current technical possibilities. The reported data do not allow a detailed evaluation of their quality. Several, non-obligatory fields are foreseen to make such analysis possible, but these are very rarely completed. The systematic lack of the mention of the (ISO and CEN) standards followed, the lack of attachments giving detailed results and explanations (metadata) concerning the applied methods, and the absence and very rudimentary provision of measurement uncertainties suggest that there is room for improvement and possibly a need for guidance and technical support to the applicants. The results of the assessment and a list of recommendations for further optimization of the register based on this assessment are reported in this document.

THE NANOREGISTER IN NUMBERS

The main quantitative results for the trade year 2018 are summarized as follows:

- During the trade year 2018, 540 registrations were submitted including 100 complete, 424 limited, and 16 simplified registrations.
- Evaluation of the complete registrations showed that most of the applicants provided the requested information for the materials they registered, and the declaration of honour for the simplified registrations was mostly undersigned (94%).
- In the complete registrations, most of the information was present, as indicated from the compliance check, although specific parameters, as for instance the uncertainties of size measurements, were almost systematically missing (12%). A decreased compliance was also observed for the REACH registration numbers (71%) and for the parameters "shape of agglomerates" (42%), "shapes of aggregates" (80%), “determination method of impurities” (80%), “surface charge ionic strength” (80%) and “sector of use of the material” (71%). Interestingly, the low compliance of these parameters was also observed previously in the compliance evaluation of the trade year 2017, indicating the difficulties of the applicants to register the specific information.
- In 98% of the limited registrations the applicants provided the previous registration numbers (92% for the trade year 2017) and the compliance check revealed that the physicochemical characteristics of the substances were mostly present (≥93%). Only two parameters showed decreased compliance, the parameter of the median size of dimension 1 (88%) and the standard deviation (80%).
- Evaluation of the determination methods used to characterize the physicochemical characteristics of the nanoparticulate materials in the complete registrations showed that the applicants employed well established methods, such as EM for the characterization of the constituent particle size (72%) and of the aggregates size (74%), and BET (88%) for the calculation of the mean specific surface area.
- For the limited registrations the applicants also used EM methods (87%) to characterize the size of the constituent particles.
- In total 190 different materials (chemical substances) were identified that are presented in the Annex. The chemical identification makes no distinction between the possible differences in the physicochemical properties of these substances.
- The total quantity of substances in the nanoparticulate state, which was introduced on the Belgian market during the trade year 2018 was 120734587.2 kg (120734.5872 tons) based on the recorded data, decreased by 40% compared to the quantities of 2017 (201429.5336 tons).
- The substances that were introduced on the Belgian market during the trade year 2018 in a total quantity that is larger than 1000 tons were diiron trioxide, calcium carbonate, silicon dioxide, precipitated calcium carbonate and carbon black.
- In most of the registrations (77%), the applicants declared quantities that range between 10 and 100000 kg.
- About 51% (187 registrations) of the submitted registrations reported quantities below 1 ton and would therefore be considered to be out of the scope of the REACH-regulation.

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ANNEX

List of the names of the chemical substances registered during the trade year 2018.

Chemical Name of substance
[1,3-dihydroxy-5,6-bis[[(2-hydroxy-1-naphthalenyl)-metylene]amino]2H-Benzimidazole-2-onato(2-)N5,N6,O5,O6-nickel
Strontium 4-[(E)-(3-chloro-4-methyl-5-sulfophenyl)diazenyl]-3-oxidonaphthalene-2-carboxylate
(2E)-10,12-dioxa-2,3,6,8,14,16-hexaaza-11-nickelatricyclo[11.4.0.04,9]heptadeca-1(13),2,4(9)-triene-5,7,15,17-tetrone; 1,3,5-triazine-2,4,6-triamine
(3-carboxy-1,1'-(1,2-dicyanovinylenebis(nitrilomethylidyne)-2,2'-dinaphtholato)nickel(II)
,4,5,6-tetrachloro-N-[2-(4,5,6,7-tetrachloro-2,3-dihydro-1,3-dioxo-1H-inden-2-yl)-8-quinolyl]phthalimide
[1,2,3,4,8,9,10,11,15,16,17,18,22,23,25-pentadecachloro-5,26-dihydro-29H,31H-phthalocyaninato(2-)-¿2N29,N31]copper
1,4-bis(butylamino)anthracene-9,10-dione
1,4-bis(mesitylamino)anthraquinone
1,4-Bis(p-tolylamino)anthraquinone
12H-Phthaloperin-12-one
14H-Anthra(2,1,9-mna)thioxanthen-14-one
14H-benz[4,5]isoquino[2,1-a]perimidin-14-one
1-hydroxy-4-(p-toluidino)anthraquinone
2-(3-hydroxy-2-quinolyl)-1H-indene-1,3(2H)-dione
2-(3-Oxobenzo[b]thien-2(3H)-ylidene)-benzo[b]thiophene-3(2H)-one
2,2'-(1,4-phenylene)bis[4-[(4-methoxyphenyl)methylene]oxazol-5(4H)-one]
2,2'-[(2,2',5,5'-tetrachloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[N-(2,4-dimethylphenyl)-3-oxobutyramide]
2,2'-[(3,3'-dichloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[N-(2,4-dimethylphenyl)-3-oxobutyramide]
2,2'-[ethylenebis(oxyphenyl-2,1-eneazo)]bis[N-(2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)-3-oxobutyramide
2,9-bis(3,5-dimethylphenyl)anthra[2,1,9-def:6,5,10-d'e'f']diisoquinoline-1,3,8,10(2H,9H)-tetrone
2-[(4-chloro-2-nitrophenyl)azo]-N-(2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)-3-oxobutyramide
2-[[1-[[(2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)amino]carbonyl]-2-oxopropyl]azo]benzoic acid
29H,31H-phthalocyaninato(2-)-N29,N30,N31,N32 copper
2-octadecyl-1H-benzo[3,4]isothiochromeno[7,8,1-def]isoquinoline-1,3(2H)-dione
2-Propenoic acid, 2-methyl-, polymer with ethene, potassium salt
2-Propenoic acid, polymer with ethene, compd. with 2-(dimethylamino)ethanol
3,3'-[#9,10-dihydro-9,10-dioxo-1,4-anthrylene#diimino]bis[N-cyclohexyl-2,4,6-trimethylbenzenesulphonamide]
3,3'-[(2-chloro-5-methyl-p-phenylene)bis[imino(1-acetyl-2-oxoethylene)azo]]bis[4-chloro-N-(3-chloro-o-tolyl)benzamide]
3,6-Bis(4-chlorophenyl)-1H,2H,4H,5H-pyrrolo(3,4-C)pyrrole-1,4-dione
3,6-bis(4-chlorophenyl)-2,5-dihydropyrrolo[3,4-c]pyrrol-1,4-dione
4,4'-[(3,3'-dichloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[2,4-dihydro-5-methyl-2-(p-tolyl)-3H-pyrazol-3-one]
4,4'-diamino[1,1'-bianthracene]-9,9',10,10'-tetraone
4,4'-methylylidenebis(5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one)
4,5,6,7-tetrachloro-3-[[3-methyl-4-[[4-[(4,5,6,7-tetrachloro-1H-isoindol-3-yl)amino]-phenyl]azo]phenyl]amino-1-H-Isoindol-1-one4,5,6,7-tetrachloro-3-[[3-methyl-4-[[4-[(4,5,6,7-tetrachloro-1H-isoindol-3-yl)amino]-phenyl]azo]phenyl]amino-1-H-Isoindol-1-one
4-[[4-(aminocarbonyl)phenyl]azo]-N-(2-ethoxyphenyl)-3-hydroxynaphthalene-2-carboxamide
5,12-Dihydro-2,9-dimethylquino[2,3-b]acridine-7,14-dione
5,12-Dihydroquino[2,3-b]acridine-7,14-dione

5,5'-(1H-isoindole-1,3(2H)-diylidene)dibarbituric acid
8,18-dichloro-5,15-diethyl-5,15-dihydrodiindolo[3,2-b:3',2'-m]triphenodioxazine
8,9,10,11-tetrachloro-12H-phthaloperin-12-one
8,9,10,12-tetrahydro-6H-benzo[lm]diimidazo[4,5-c:1',2'-f]phenanthridine-7,11-dione
Acematt OK412
Acematt TS100
Aluminium oxide
Aluminiumhydroxide
Amorphous silica
Amorphous silicon dioxide, chemically prepared, precipitated
Amorphous sodium aluminium silicate
Barium sulfate
Benzamide, 3,3'-[(2-chloro-1,4-phenylene)bis[imino(1-acetyl-2-oxo-2,1-ethanediyl)azo]]bis[4-methyl-
Benzoic acid, 2,3,4,5-tetrachloro-6-cyano-, methyl ester, reaction products
Benzonitrile,3,3'-(2,3,5,6-tetrahydro-3,6-dioxopyrrolo[3,4-c]pyrrole-1,4-diyl)bis-
C.I. Pigment Blue 15
C.I. Pigment Green 7
C.I. Pigment Orange 13
C.I. Pigment Orange 34
C.I. Pigment Orange 64
C.I. Pigment Red 101
C.I. Pigment Red 122
C.I. Pigment Red 146
C.I. Pigment Red 176
C.I. Pigment Red 177
C.I. Pigment Red 184
C.I. Pigment Red 185
C.I. Pigment Red 2
C.I. Pigment Red 266
C.I. Pigment Red 48:1
C.I. Pigment Red 48:2
C.I. Pigment Red 48:3
C.I. Pigment Red 48:4
C.I. Pigment Red 81:5
C.I. Pigment Violet 19
C.I. Pigment Violet 23
C.I. Pigment Violet 3
C.I. Pigment Violet 3:4
C.I. Pigment Yellow 110
C.I. Pigment Yellow 111
C.I. Pigment Yellow 13
C.I. Pigment Yellow 138
C.I. Pigment Yellow 14
C.I. Pigment Yellow 150
C.I. Pigment Yellow 151
C.I. Pigment Yellow 155
C.I. Pigment Yellow 181

C.I. Pigment Yellow 194
C.I. Pigment Yellow 73
C.I. Pigment Yellow 74
C.I. Pigment Yellow 83
Calcium 3-hydroxy-4-[(4-methyl-2-sulphonatophenyl)azo]-2-naphthoate
Carbon black
Carbon black powcarbon B
Carbon Black, amorphous
Cellulose hydrogen sulphate sodium salt
Cerium dioxide
Chromate(1-), bis(2,4-dihydro-4-(2-(2-(hydroxy-kappaO)-5-nitrophenyl)diazenyl-kappaN1)-5-methyl-2-phenyl-3H-pyrazol-3-onato(2-)-kappaO3)-, sodium (1:1)
Chromium iron oxide
Colloidal silica
Copolymere de Chlorure de Vinylidene
Dichloromethyl
Diiron trioxide
dimethyl 2-[[1-[[(2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)amino]carbonyl]-2-oxopropyl]azo]terephthalate
Dimethyl Siloxane reaction with Silica
Dimethyldichlorosilane reaction with Silica
DIOXYDE DE SILICIUM
Dioxyde de silicium, prepare par voie chimique
Ethanaminium, N,N,N-trimethyl-2-[(2-methyl-1-oxo-2-propenyl)oxy]-, chloride, homopolymer
Ethene, homopolymere oxydee
Fumed metal oxide - aluminum oxide
Fumed silica, amorphous
Heucodur Brown 869
Heucosin Special Blue Grey G 6528 N
Heucosin Special Grey G 6556 N (Concrete grey RAL 7023)
Heucosin Special Red G 10345
Hexamethyldisilazane reaction with Silica
Hydrated, Amorphous Silica
hydrogen [[[(2-ethylhexyl)amino]sulphonyl][[(3-methoxypropyl)amino]sulphonyl]-29H,31H-phthalocyaninesulphonato(3-)-N29,N30,N31,N32]cuprate(1-), compound with N,N'-di#o-tolyl#guanidine
hydrogen bis[2-[(4,5-dihydro-3-methyl-5-oxo-1-phenyl-1H-pyrazol-4-yl)azo]benzoato(2-)]chromate(1-), compound with 2-ethylhexylamine (1:1)
Hydrogen hydroxy[2-hydroxy-3-[(2-hydroxy-3-nitrobenzylidene) amino]-5-nitrobenzenesulphonato(3-)]chromate(1-), compound with 3-[(2-ethylhexyl)oxy]propylamine (1:1)
Hydrophobic fumed silica
Hydrophobized highly dispersed silica, synthetic, x-ray amorphous silicon dioxide
Hydroxyde d'aluminium
Iron hydroxide oxide yellow
Iron manganese trioxide
KieselsΣure
Magnetite
methyl 4-cyano-5-[[5-cyano-2,6-bis[(3-methoxypropyl)amino]-4-methyl-3-pyridyl]azo]-3-methyl-2-thenoate
Molybdeendisulfide

N-(2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)-2-[(4-nitrophenyl)azo]-3-oxobutyramide
N-(2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)-3-oxo-2-[[2-(trifluoromethyl)phenyl]azo]butyramide
N,N'-(2,5-Dichloro-1,4-phenylene)bis(4-((2,5-dichlorophenyl)azo)-3-hydroxynaphthalene-2-carboxamide)
N,N'-(2,5-dichloro-1,4-phenylene)bis[4-[[2-chloro-5-(trifluoromethyl)phenyl]azo]-3-hydroxynaphthalene-2-carboxamide]
N,N'-naphthalene-1,5-diylbis[4-[(2,3-dichlorophenyl)azo]-3-hydroxynaphthalene-2-carboxamide]
N,N'-Phenylene-1,4-bis[4-[(2,5-dichlorophenyl)azo]-3- hydroxynaphthalene-2-carboxamide]
N-[4-(aminocarbonyl)phenyl]-4-[[1-[[(2,3-dihydro-2-oxo-1H-benzimidazol-5-yl)amino]carbonyl]-2-oxopropyl]azo]benzamide
Pigment Blue 15:1
Pigment Brown 23
Pigment Brown 43
Pigment Red 101
Pigment Yellow 110
Pigment Yellow 128
Pigment Yellow 138
Pigment Yellow 42
Pigment Yellow 93
Poly(tetrafluoroethylene)
Polyethylene oxide
Polyvinylchloride
Precipitated calcium carbonate
Precipitated calcium carbonate coated with fatty acids
Precipitated silica
Precipited calcium carbonate
Printex, Lamp black, Colour Black, XPB, Special Black
Printex, Lamp Black, XPB, Special Black
Pyrrolo[3,4-c]pyrrole-1,4-dione, 3,6-bis([1,1'-biphenyl]-4-yl)-2,5-dihydro-
Quaternary ammonium compounds, bis(hydrogenated tallow alkyl)dimethyl, salts with bentonite
Reaction mass of nickel, 5,5'-azobis-2,4,6(1H,3H,5H)-pyrimidinetrione complexes and melamine
Reaction mass of stannic oxide, zirconium oxide, antimony pentoxide and amorphous silica
Silane, dichlorodimethyl, reaction product with silica
Silica amorphous
Silica gel, pptd., cryst.-free
Silica gel, precipitated, crystalline free
Silica, Amorphous
Silica, amorphous, fumed crystalline free
Silica, amorphous, fumed, cryst.-free
Silica, smorphous, fumed crystalline free
Silicate(2-), hexafluoro-, disodium, reaction products with lithium magnesium sodium silicate
Silice
Silicic acid, lithium magnesium sodium salt
Silicium dioxide
Silico aluminate de sodium
Silicon dioxide
Silicon dioxide (synthetic amorphous silica)
Silicon dioxide, chemically modified
Silicones and siloxanes, dimethyl-, reaction products with silica

SIO2
sodium bis[2-[(4,5-dihydro-3-methyl-5-oxo-1-phenyl-1H-pyrazol-4-yl)azo]benzoato(2-)]chromate(1-)
Sodium bis[3-[[1-(3-chlorophenyl)-4,5-dihydro-3-methyl-5-oxo-1H-pyrazol-4-yl]azo]-4-hydroxy-N-methylbenzene-1-sulphonamidato(2-)]chromate(1-)
Sodium bis[3-[[1-(3-chlorophenyl)-4,5-dihydro-3-methyl-5-oxo-1H-pyrazol-4-yl]azo]-4-hydroxy-N-methylbenzenesulphonamidato(2-)]cobaltate(1-)
Sodium bis[4-hydroxy-3-[(2-hydroxy-1-naphthyl)azo]-N-(3-methoxypropyl)benzene-1-sulphonamidato(2-)]chromate(1-)
Sodium bis[4-hydroxy-3-[(2-hydroxy-1-naphthyl)azo]-N-(3-methoxypropyl)benzenesulphonamidato(2-)]cobaltate(1-)sodium bis[4-hydroxy-3-[(2-hydroxy-1-naphthyl)azo]-N-(3-methoxypropyl)benzenesulphonamidato(2-)]cobaltate(1-)
Solvent violet 13
Strontium 4-[(E)-(3-chloro-4-methyl-5-sulfophenyl)diazenyl]-3-oxidonaphthalene-2-carboxylate
Synthetic amorphous silica
Synthetic amorphous silica, fumed,
Synthetic amorpous silica
Tetramethyl 2,2'-[1,4-phenylenebis[imino(1-acetyl-2-oxoethane-1,2-diyl)azo]]bisterephthalate
Titanium dioxide
Xanthylium, 9-(2-carboxyphenyl)-3,6-bis(diethylamino)-, 4-[(5-chloro-2-hydroxyphenyl)azo]-4,5-dihydro-3-methyl-1-phenyl-3H-pyrazol-3-one 4,5-dihydro-4-[(2-hydroxy-5-nitrophenyl)azo]-3-methyl-1-phenyl-3H-pyrazol-3-one 3-[[1-[[(2-ethylhexyl)amino]carbonyl]-2-oxopropyl]azo]-2-hydroxy-5-nitrobenzoate cobaltate complexes
Zinc oxide

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