PUBLIC VERSION OF THE SOCIO-ECONOMIC ANALYSIS

Legal name of applicant:	Instrumentation Laboratory SpA
Submitted by:	EPPA S.A. on behalf of the applicant
Date:	21 June 2019
Substance:	4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated (4-tert-octylphenol ethoxylates) (4-tert-OPnEO) (OPnEO) (EC 618-541-1, CAS 9036-19-5)
Use title:	Use as a lysing agent for red blood cells in blood analysis diagnostic device
Use number:	1

CONTENTS

LIST OF ABBREVIATIONS

AoA = Analysis of Alternatives

CSR = Chemical Safety Report

EBIT = Earnings Before Interest and Taxes

ECHA = European Chemicals Agency

ED = Endocrine Disruptor

EEA = European Economic Area

EU = European Union

IL = Instrumentation Laboratory

IVD = In Vitro Diagnostics

kg = Kilogram

L = Litre

MA= Massachusetts

NPV = Net Present Value

NY = New York

RAC = Committee for Risk Assessment

R&D = Research and Development

REACH = Registration, Evaluation, Authorisation and Restriction of Chemicals

SEA= Socio-Economic Analysis

SEAC = Committee for Socio-Economic Analysis

US/USA = United States of America

DECLARATION

The Applicant is aware of the fact that evidence might be requested by ECHA to support information provided in this document.

Also, we request that the information blanked out in the "public version" of the Socio-economic analysis is not disclosed. We hereby declare that, to the best of our knowledge as of today (21 June 2019) the information is not publicly available, and in accordance with the due measures of protection that we have implemented, a member of the public should not be able to obtain access to this information without our consent or that of the third party whose commercial interests are at stake.

Signature  21 June 2019, Bedford, MA (USA)

Jim Richard

Director of Quality Engineering, Instrumentation Laboratory Company

1. SUMMARY OF SOCIO-ECONOMIC ANALYSIS

OPnEO [4-(1,1,3,3-Tetramethylbutyl)phenol, ethoxylated] was added to Annex XIV of the European Union's (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Regulation (EC) No 1907/2006 due to its classification as an endocrine disruptor (ED), because of the suspected endocrine disrupting properties of its biodegradation product octylphenol. OPnEO was prioritized for inclusion in Annex XIV by a recommendation of the European Chemicals Agency (ECHA) and was formally added to Annex XIV under entry 42 on 13 June 2017, with a sunset date on 4 January 2021. After this date the substance cannot be placed on the EEA market or used in the EEA unless an authorisation has been granted.

Based on the scientific knowledge available to date, no eco-toxicological threshold can be derived. Therefore, an authorization can be granted if there are not suitable alternatives and the socio-economic benefits of using OPnEO outweigh the risks (and costs) to the environment. However, as it will be shown, concerning the use highlighted in this authorization for application, all risks are adequately controlled during the substance's lifecycle.

Werfen is a global healthcare leader in vitro diagnostic (IVD) products, headquartered in Barcelona, Spain. Instrumentation Laboratory (IL) is an integral part of Werfen since 1991. IL is headquartered in Bedford (MA, USA). Additional R&D and Operations sites of IL are located in Orangeburg (NY, USA), San Diego (CA, USA), and Munich (Germany). Some of IL's product development takes place in Barcelona, Spain at Werfen.

Instrumentation Laboratory (IL) employs more than 1,800 people worldwide and its 2017 revenue accounts for USD 970 million. IL products are distributed in over 130 countries around the world. Today, more than 1.1 million patient samples are tested on IL systems every day.

IL develops, manufactures and distributes instruments, related reagents and data management solutions, for hospitals around the world, at the point-of-care, and in the laboratory. IL solutions include Hemostasis and Acute Care Diagnostic products and services, all designed with a common goal: to help healthcare providers enhance patient care and efficiency.

This SEA focuses on IL business related to the production of lysing bags contained indisposable cartridges, which are used in two Blood Gas Systems (Acute Care Diagnostics): GEM® Premier™ 4000 and GEM® Premier™ 5000. These two types of instruments are used in different clinical settings (laboratories, intensive care units, operating rooms, and emergency departments) to measure and to report concentrations of critical analytes in blood (e.g., pressure of oxygen and carbon dioxide as well as haemoglobin and haemoglobin fractions through CO-Oximetry).

The applicant of this application for authorization (Instrumentation Laboratory S.p.A.) is an Italian company (based in Milan) that imports into the EEA the in-scope products, disposable cartridges manufactured in Bedford (MA, USA) containing lysing bags that are manufactured in Orangeburg (NY, USA). The applicant is the sole importer into the EEA of the in-scope products for this application for authorization.

The commercial production of the lysing bags contained in the GEM® Premier™ 4000 and GEM® Premier™ 5000 cartridges started in 2006 and 2017, respectively. The

applicant is planning to import 6 ton/year of OPnEO, which is contained in the lysing bag as a lysing agent for red blood cells in blood analysis diagnostic device, in concentrations of [redacted]% and [redacted]% for GEM® Premier™ 5000 and GEM® Premier™ 4000, respectively.

The applicant is applying for an authorization to import into the EEA the cartridges containing OPnEO because, to date, there are not technically and economically suitable substitutes that could immediately replace OPnEO function in the GEM® Premier™ 5000 and GEM® Premier™ 4000 instruments for acceptable diagnostic performance, as shown in the Analysis of the Alternatives (AoA). As a consequence, in the event of refused authorisation ("non-use" scenario), many hospitals and commercial laboratories in the EEA are likely to face a shortage in their equipment and the consequent negative impact of EEA national health-care systems and patient care.

In terms of socio-economic benefits to the EEA society of the continued importation of OPnEO, the monetized residual risk for the environment is *zero*, because there will be no (zero) OPnEO emissions from the hospitals and commercial laboratories that use the in-scope cartridges, as reported in the CSR. This finding will not change during the whole period of the requested authorization. This means that there are no benefits for the EEA society to be considered from refusing this application for authorization, but only costs.[1] Conversely, the total costs for the EEA society from refusing the authorization would be *more than* 70 million EURO/year over 12 years after the sunset date. We have also assessed the "non-use" scenario with conservative assumptions to show the robustness of this finding.

Specifically, the main costs for the EEA society due to the refusal of the authorization are:

- The loss of the expected business (calculated by using EBIT) for the applicant and for Werfen affiliate organizations across the EEA;
- The net additional financial impact that the EEA customers of the applicant would face;
- [redacted] FTE employees currently working in the EEA for the applicant and for Werfen affiliate organizations would become redundant;
- The lost benefits of using the two Blood Gas Systems (GEM® Premier™ 5000 and GEM® Premier™ 4000) at EEA hospitals and commercial laboratories.

In line with the main findings of this SEA – which shows that the benefits of the "applied for use" scenario outweigh its costs to the EEA society (which are zero) – the applicant is applying for an authorisation to import OPnEO for 12 years after the sunset date (2021). Based on the results of this SEA and the potential benefits of GEM® Premier™ 5000 and GEM® Premier™ 4000 to the EEA society, the applicant should be granted the authorisation to import the cartridges (GEM® Premier™ 5000 PAK and GEM® Premier™ 4000 PAK) containing OPnEO, in accordance with the article 60(4) of REACH.

[1] Throughout this SEA a "." separates units from decimals, whereas a "," indicates thousands and millions.

2. AIMS AND SCOPE OF SEA

2.1. Aims and scope of SEA

OPnEO [4-(1,1,3,3-Tetramethylbutyl)phenol, ethoxylated] was added to Annex XIV of the European Union's (EU) Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) Regulation (EC) No 1907/2006 due to its classification as endocrine disruptor (ED), because of the suspected endocrine disrupting properties of its biodegradation product octylphenol. OPnEO was prioritized for inclusion in Annex XIV by a recommendation of the European Chemicals Agency (ECHA) and was formally added to Annex XIV under entry 42 on 13 June 2017, with a sunset date on 4 January 2021. After this date the substance cannot be placed on the EEA market or used in the EEA unless an authorisation has been granted.

Based on the scientific knowledge available to date, no eco-toxicological threshold can be derived for OPnEO. Therefore, the application for authorisation has to be submitted under the Socio Economic Analysis (SEA) route foreseen under REACH, as the substance is considered to be without a safe threshold (being an ED).

When the application is submitted under the SEA route, an authorisation can only be granted if there are not suitable alternatives to OPnEO for the concerned use and the costs for the environment are outweighed by the benefits of the continued use. However, all risks of using OPnEO are adequately controlled during the substance's lifecycle as shown in the CSR, because the only customers of the in-scope products for this application for authorization are hospitals and commercial laboratories located in the EEA.

The aim of this SEA is to assess the lost benefits (*whereas the costs are equal to zero*) for the EEA society in the event of authorization not being granted to the applicant. In line with the Costs and Benefits Analysis (CBA) methodology, this SEA has covered all the relevant impacts (environmental, economic, social, and wider economic impacts).

The substance use has been defined as:

"Use as a lysing agent for red blood cells in blood analysis diagnostic device"

On the basis of the projected demand for the disposable cartridges for the 12 years starting from 2021, the applicant is applying for the authorisation to import 6 ton/year of OPnEO contained in the produced cartridges to be used in GEM® Premier™ 5000 and GEM® Premier™ 4000, because there is no technically and economically suitable substitute to OPnEO to date, as shown in the AoA.

From a geographical point of view, the focus of this SEA is on the EEA. However, when assessing all possible impacts in the "non-use" scenario, the analysis has been qualitatively extended, when needed, to other EEA companies as well as to non-EEA countries.

In line with the ECHA guidance on the preparation of the Socio-Economic Analysis (2011),[2] this SEA aims to assess and quantify (if feasible) all main impacts expected in the "non-use" scenario (i.e., refused authorization). All future monetized impacts will be discounted at 4% discount rate. All monetized values have been adjusted to a base year, which is 2021 (the sunset date for OPnEO). The identification of the most likely non-use scenario and the assessment of the related impacts are based on information provided by the applicant and no third parties have been interviewed.

2.2. Market and business trends including the use of the substance

Werfen is a global healthcare leader in vitro diagnostic (IVD) products headquartered in Barcelona, Spain. IL is an integral part of Werfen since 1991. IL is headquartered in Bedford (MA, USA). Additional R&D and Operations sites of IL are located in Orangeburg (NY, USA), San Diego (CA, USA), and Munich (Germany). Some IL's product development is done in Barcelona, Spain at Werfen.

IL employs more than 1,800 people worldwide and its 2017 revenue accounts for USD 970 million. IL products are distributed in over 130 countries around the world. Today, more than 1.1 million patient samples are tested on IL systems every day.

IL develops, manufactures, and distributes instruments, related reagents and data management solutions, for hospitals around the world, at the point-of-care and in the laboratory. IL solutions include Hemostasis and Acute Care Diagnostic products and services, all designed with a common goal: to help healthcare providers enhance patient care and efficiency.

IL has revolutionized the world of clinical diagnostics. From the first direct-reading pH/blood gas analyzer (IL105) for routine testing in 1959; to the Flame Photometer (IL143) for chemistry electrolyte testing in 1964; to the invention of CO-Oximetry measurement (IL182) for haemoglobin and haemoglobin fractions in 1968; to the introduction of continuous on-board calibration (IL813) for blood gas quality assurance; from the first fully automated mid-sized Hemostasis analyzer (ACL810) in 1985 to the most advanced platform for automated Hemostasis testing (ACL TOP) in 2004. In 2016 the first fully automated on-demand assay for Heparin-Induced Thrombocytopenia (HIT) testing was introduced, as well as the Lab Automation workcell for Hemostasis testing (Hemocell).

Integrated on GEM® Premier™ 4000, proprietary Intelligent Quality Management (iQM™) provides quality checks before and after every sample. Error detection time is reduced from hours to minutes and errors are automatically corrected and documented, ensuring quality results, eliminating maintenance, delivering cost-efficient outcomes, and improving patient care. New iQM2 with IntraSpect™ technology is integrated on GEM® Premier™ 5000; it provides intelligent analysis and automated quality assurance with every sample, continuously and in real-time, unlike traditional (auto or manual) QC offerings.

[2] ECHA (2011): Guidance on the preparation of socio-economic analysis as part of an application for authorisation, Reference: ECHA-11-G-02-EN, available at: https://echa.europa.eu/documents/10162/23036412/sea_authorisation_en.pdf/aadf96ec-fbfa-4bc7-9740-a3f6ceb68e6e

Error detection time is reduced from hours to minutes and errors are automatically corrected and documented for a complete picture of quality.

This SEA focuses on IL business related to the use of lysing bags contained in disposable cartridges, which are used in two Blood Gas Systems (Acute Care Diagnostics): GEM® Premier™ 4000 and GEM® Premier™ 5000. These two types of instruments are used in different clinical settings (laboratories, intensive care units, operating rooms, and emergency departments) to measure and to report concentrations of critical analytes in blood (e.g., pressure of oxygen and carbon dioxide as well as CO-Oximetry).

The applicant of this application for authorization (Instrumentation Laboratory S.p.A.) is an Italian company (based in Milan) that imports into the EEA the in-scope products, disposable cartridges manufactured in Bedford (MA, USA) containing lysing bags that are manufactured in Orangeburg (NY, USA). The applicant is the sole importer into the EEA of the in-scope products for this application for authorization.

One should also bear in mind that a significant supplier base for the GEM products is in the EEA, [redacted]

Figure 1 presents an overview of the market shares of IL and those of its main competitors in the EU.

Figure 1. Market shares of IL and those of its main competitors in the EU

[redacted]

2.2.1 GEM background

The GEM Premier analyzer is a portable critical care system for use by health care professionals to analyse rapidly whole blood samples. It serves as a critical analytical instrument in hospital labs, operating rooms, emergency rooms and other point-of-care at locations around the world. Blood testing using critical care analysers such as GEM® Premier™ 4000 and GEM® Premier™ 5000 is a core element of diagnostic and treatment procedures carried out in the health-care sector today.

The GEM Premier analysers are comprised of an instrument housing and a disposable cartridge (PAK) that can measure many parameters of blood such as: pH, pCO_2, pO_2, sodium, potassium, ionized calcium, chloride, glucose, lactate, hematocrit, total bilirubin (tBili), total hemoglobin (tHb), oxygen saturation (sO_2), and hemoglobin fractions including oxyhemoglobin (O_2Hb), deoxyhemogobin (HHb), carboxyhemoglobin (COHb) and methemogobin (MetHb). These analytes, along with derived parameters, aid in the diagnosis of a patient's acid/base status, electrolyte and metabolite balance and oxygen delivery capacity.

The disposable cartridge contains all the components required to perform whole blood testing. This includes a sensor card, an oximetry module, and individually packaged process control and lysing solutions. The sensor card provides a low volume, gas tight chamber in which whole blood samples are presented to the sensors. The process control solutions are utilized in performing calibrations, quality control and other assay specific functions. The lysing solution is used to lyse the whole blood cells prior to optical measurements.

The sensor values of the GEM Premier cartridge are measured and monitored with Process Control Solutions (PCS). These solutions are pre-tonometered (adjusted gas saturation) to specific levels of pO_2 and pCO_2, and contain known quantities of analytes and dyes tested using (NIST traceable, CLSI, or internal) standards to establish target values for ensuring accuracy of results at medical-decision levels, where clinical actions are necessary. All process control solutions are used to monitor and correct performance of the system during use, as part of the Intelligent Quality Management (iQM™) system.

Figure 2. Components of a GEM Premier 4000 disposable PAK/cartridge

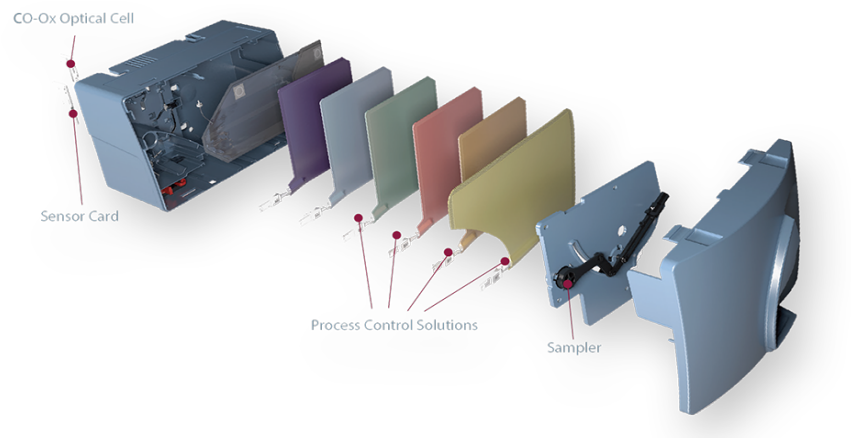


Figure 2 shows the components that are assembled into a GEM Premier 4000 disposable PAK/cartridge (lysing bag shown in purple). The minimum number of samples that can be tested with each cartridge depending on the cartridge type is 75 and the most commonly used sample capacity is 450. OPnEO is formulated in the lysing solution in concentration of [redacted]% and [redacted]% for GEM® Premier™ 5000 and GEM® Premier™ 4000 cartridges, respectively.

OPnEO is the surfactant used as a lysing agent to rupture the cell membranes of the red blood cells in whole blood sample in blood analysis diagnostic device. The blood measurement algorithms of the GEM Premier analysers require complete and fast lysis for accurate measurements and reporting results in 45 seconds to diagnose and treat critically ill patients.

Data from the GEM Premier family of critical care analysers are used daily in hospitals and commercial laboratories around the world to make life-saving decisions regarding patient health. It is imperative that these data have the highest possible reliability and accuracy. The use of OPnEO in the GEM Premier analysers is critical to the performance of the CO-Oximetry system, providing results for total hemoglobin, oxyhemoglobin, carboxyhemoglobin, methemoglobin, deoxy-hemoglobin, oxygen saturation, and total bilirubin.

2.2.2 Competing Equipment

Compared to other existing technologies (not requiring OPnEO) on the market for blood gas analysers,[3] the GEM Premier analysers offer a number of unique advantages:

1. The GEM analysers utilize the renowned Intelligent Quality Management (iQM™) System that automatically detects, corrects, and documents different forms of errors, and confirms resolution ensuring patient safety and the highest quality of test results.

   a. iQM™ continuously monitors on-board Process Control Solutions (PCS), reducing the time to error detection to minutes instead of the hours required by traditional manual or Automated Quality Control (AQC) that normally are run every eight hours, as regulated by CLIA in the United States and by applicable national legislation in EU Member States.

   b. iQM™ eliminates manual intervention to correct sensor errors, such as removal of blood clots from the system, thereby significantly reducing time needed for the testing process and enhancing ease of use. The reduced testing time will, in critical situations, significantly improve patient safety, by producing rapid and correct results thereby reducing the need for user interpretation of results and the need for repeating tests.

2. The GEM Premier analysers are the only systems of their kind to offer a single, disposable measurement cartridge that can be stored up to six months at room temperature.

[3] For example, Siemens RapidPoint 500 and Radiometer ABL 800 and ABL 90.

Other competing technologies utilize multiple cartridges to perform the same functions, some of which require refrigerated storage. This places an additional burden on the customer of stocking multiple consumable cartridges and providing refrigerated storage at point-of-care testing locations, where space is often limited.

3. Other competing technologies approach CO-Oximetry measurements in various ways, including ultrasonic lysis and measurement of whole blood without hemolysis. One distinct advantage of the current chemical lysis method employed by GEM Premier analysers is that the Triton X-100 is contained in a solution that buffers the pH of the sample, eliminating the potentially extreme effect of pH on measured Methemoglobin. Thus, the GEM Premier family of analyzers are better able to provide an accurate result in the presence of varying pH.

4. Some of the competing technologies (e.g. ultrasonic lysing) require exposing the blood samples to analyser components for measurement of CO-Oximetry parameters. On the GEM Premier systems blood is exposed only to the disposable cartridge components, allowing for simplicity in biohazard waste disposal and easy analyser decontamination.

2.3. Definition of "applied for use" scenario

The commercial production of the lysing bags contained in the GEM® Premier™ 4000 and GEM® Premier™ 5000 started in 2006 and in 2017, respectively.

The "applied for use" scenario is that in which the applicant can continue to import the disposable cartridge containing OPnEO to be used in GEM analysers, and the related business linked to the import of GEM® Premier™ 4000 and GEM® Premier™ 5000. This is so because the GEM analysers can be used only with the GEM PAK disposable cartridge (from a microeconomic viewpoint, they are complementary goods).

2.3.1 Supply chain

Supplying of OPnEO

OPnEO is sourced as a 100% solution that is formulated at a later stage in the plant in Orangeburg (NY, USA). IL expects that, to cover the peak market demand for in-scope products (GEM PAK cartridges), 6 ton/year of OPnEO are needed. Therefore the applicant applies for importing 6 ton/year of OPnEO (contained into the catridges) into the EEA.

Filling bags to be contained into the disposable cartridges

In Orangeburg (NY, USA), the small lysing bags (volume: [redacted] and [redacted]) are filled in with different compounds. In one of these lysing bags is contained, among others, a quantity of OPnEO (concentration: [redacted]% or [redacted]%, respectively).

From Orangeburg (NY, USA) to Bedford (MA, USA)

The filled lysing bags are then shipped to the IL plant in Bedford to be assembled into the GEM PAKs (cartridges) as well as for packaging and shipment.

The GEM® Premier™ 4000 and GEM® Premier™ 5000 cartridges are shipped to the EU as individual PAKs or as a bulk shipment. The individual PAKs are enclosed in a sealed foil bag and then placed into Styrofoam, which is then placed into a cardboard box for shipment. This is the same for both individual cartridge shipments and bulk shipment to the EEA with only difference being the size of the cardboard box.

Importing into the EEA, distributing, use, and hazardous waste

The applicant, which currently employs [redacted] people, imports into the EEA the GEM cartridges. The applicant is the sole importer into the EEA of the in-scope products for this application for authorization.

There is no further processing in the EU other than labelling the GEM PAKs with the specific saleable part number based on customer sales order, as well as the reprogramming the electrically erasable programmable read-only memory (EEPROM).

All products containing OPnEO are imported as finished products (pre-loaded cartridges) and no further processing (mixing or chemical reactions) takes place in the EEA before the product is supplied to customers (i.e., hospitals and commercial laboratories). The cartridges do not allow, during the normal use, for any possibility that the operators at hospitals and commercial laboratories open them. All OPnEO therein remains inside the cartridges.

Any liquid waste (including empty lysing bags containing OPnEO remainders) is assumed to be disposed (as indicated in the SDS provided by IL to its customers) via special containers (for hazardous medical waste). All operators who use GEMs are all qualified personnel using personal protection equipment.

2.4. Definition of “non-use” scenario

The AoA concludes that a suitable alternative to OPnEO in the manufacturing process of the cartridges to be used in GEMs, that would be able to replace the functions of OPnEO without adversely affecting the final product, has not been found yet. Furthermore, no alternative will be validated by the sunset date.

This means that, without being allowed to import the cartridges containing OPnEO many hospitals and commercial laboratories in the EEA will face a shortage in blood gas systems and the critical patient results they deliver.

As outlined in the AoA, the whole substitution process to an alternative requires 12 years beyond the sunset date. On the basis of the considerations mentioned above, the most likely “non-use” scenario in the event of no authorization being granted is a shortage in blood gas systems for many hospitals and commercial laboratories in the EEA.

2.5. Information for the length of the review period

In order for the GEM Premier analysers to continue to provide patient blood data with uncompromised reliability and accuracy, the continued use of OPnEO in the GEM Premier cartridges is required during the search for an alternative lysing agent. The alternative lysing agent must be capable of quickly (in about two seconds) and fully lysing red blood cell (a capability not exhibited by all surfactants), must not interfere with the intended optical measurements, must not interact with blood haemoglobin chemistry or chemistry of other analyte measurements, must exhibit a low degree of foaming, and must meet established product claims for the GEM Premier systems over the claimed cartridge shelf life (up to six months at room temperature) and use life (up to four weeks in the analyser).

The iQM™ processes for CO-Oximetry are designed around the use of OPnEO and its fluidic and optical interactions with patient blood and aqueous process control solutions. The use of an alternative lysing agent will require a redesign and reimplementation of iQM™ processes for CO-Oximetry.

The substitution of OPnEO with another substance will require an estimated time period of 12 years starting from the sunset date (2021), as detailed in the AoA. This is due to many specific constraints the applicant has to face, as the substitution plan shows.

In line with the conclusions reported in the AoA, the applicant requests an authorisation for importing OPnEO contained in the manufactured cartridges to be used in GEM analysers for 12 years, starting from the sunset date (2021). This request is based on the following considerations:

- For the time being no viable alternative to OPnEO has been identified with equal performance;
- Even if a both technically and economically viable alternative to OPnEO were to become available, it would take at least 12 years to develop and to validate a new manufacturing process to meet equal quality standards.
- The adoption of an alternative will require specific administrative measures. In particular, the revalidation of the production process and re-approval of market authorizations by regional and national authorities. A major change in the cartridges, and therefore in its quality, may force national authorities to request the applicant to redo clinical trials.
- There will be no risk of introducing OPnEO to the environment, as shown in the CSR, and the socio-economic benefits are high (and costs are zero). This costs-benefits balance will not change during the requested review period.

Therefore, the applicant believes that any review period shorter than 12 years would not be sufficiently long for identifying a viable alternative, developing and testing the impacted process steps, and completing the transition to an OPnEO free process.

A review (substitution) period shorter than 12 years would create a shortage of blood gas systems in the EEA hospitals and commercial laboratories. In addition, a shorter review period would require a re-application for authorization, which will take resources to the applicant that would be used for R&D. A 12-year review period will prevent a disruption in

the supply chain and help to protect the health of the EEA population. Thus, the applicant is strongly convinced that a review period of 12 years is appropriate and justifiable, as all criteria that are laid out by ECHA (2013) are fulfilled.[4]

3. IMPACTS OF GRANTING THE AUTHORIZATION

3.1. Human health and/or environmental impacts

3.1.1 Number of people exposed

This section is not relevant for this application for authorization because OPnEO has been added to Annex XIV due to its classification as *environmental* endocrine disruptors (EDs), because of the suspected endocrine disrupting properties of its biodegradation products octylphenol.

The assessment of the impacts of the use of OPnEO on workers' and general population's human health is not relevant for this application, as the reason to apply for an authorization is the concern for the environmental compartment.

Operators at hospitals and commercial laboratories use the substance under controlled conditions. No contact with the substance will occur during normal operations.

The health impacts on potential people who could benefit from the data generated by GEM Premier analysers are deferred to Section 3.4 (Social impacts).

3.1.2 Impact on the environment

The production process of the lysing bags exclusively happens in the USA, therefore is out of scope for this application for authorization. As shown in Sections 9 and 10 of the CSR, there will be no (zero) emission of OPnEO from the use of GEM® Premier™ 4000 and GEM® Premier™ 5000 cartridges at hospitals and commercial laboratories in the EEA, because the operators work under controlled conditions and all waste containing OPnEO will be collected and treated as hazardous waste (as indicated in the SDS provided by IL). Therefore, there is no risk for the environment (no negative impact to be assessed) from granting the authorization.

3.2. Economic impacts

3.2.1 Suppliers of the applicant

Table 1 reports the financial impact on the IL suppliers in the EU that fabricate material used in the GEM instrument and PAK.

[4] ECHA (2013), Setting the Review Period when RAC and SEAC Give Opinions on an Application for Authorisation (SEAC/20/2013/03), available at: https://echa.europa.eu/documents/10162/13580/seac_rac_review_period_authorisation_en.pdf

Table 1. Financial impact for the suppliers

The total annual revenue that the EEA suppliers of GEM PAK materials will lose in the non-use scenario (stop shipping to the EEA) is equal to [redacted] EURO (rounded; exchange rate of 11 May 2019: 1 EURO = 1.12 USD).

We conservatively assume that, on average, suppliers' EBIT is equal to 25% sales, therefore the annual impact is equal to 25% times [redacted] EURO = [redacted] EURO (rounded). This implies that **over 12-year review period the negative impact from the non-use scenario (or the benefit of avoiding it) for suppliers is equal to [redacted] EURO (NVP, 4%; rounded)**,[5] **which is equivalent to an annualized value of [redacted] EURO (rounded)**.[6]

3.2.2 Customers of the applicant

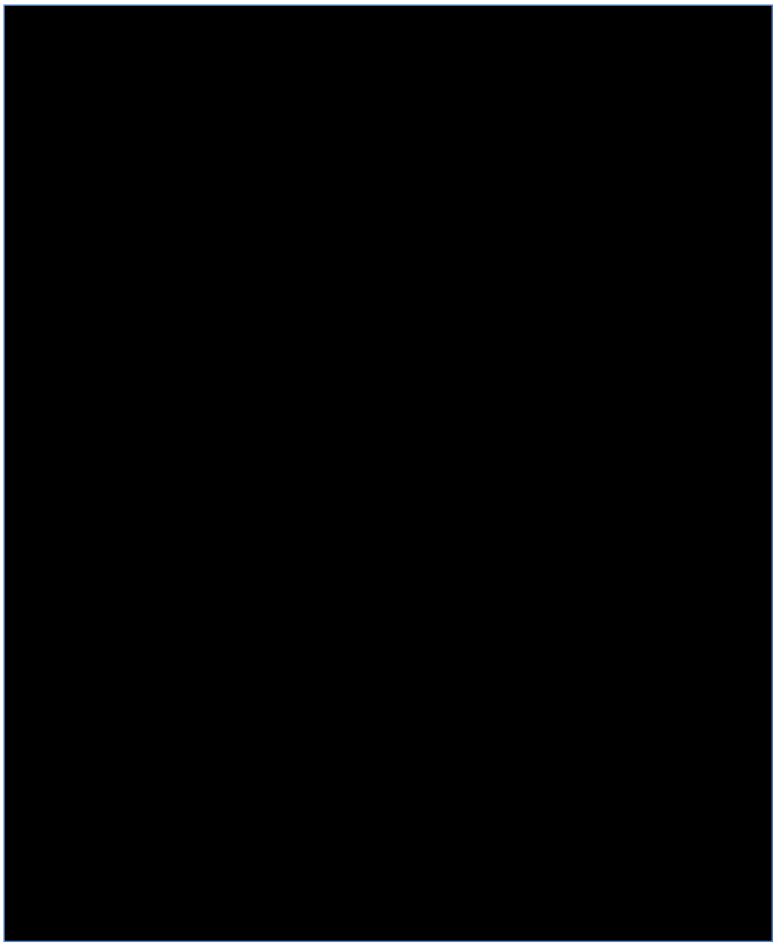
The installed base of GEM Premier 4000 and GEM Premier 5000 instruments in the EEA is estimated to be [redacted]. The instrument installations are split between the lease (instrument rental) [redacted]% and sale [redacted]%. In both cases the customers would need to replace their instruments if the applicant was no longer able to supply GEM PAKs in the non-use scenario. However, we can reasonably assume that those customers using a lease contract would continue to use similar contract with competitors (to simplify we assume at the same conditions), without facing capital costs. Therefore only [redacted]% of the sales would represent the capital costs, which should be taken into account. Therefore, we can plausibly assume that approximately [redacted] instruments ([redacted]% times [redacted] instruments) will be replaced by sales (not lease contracts) from competitors. For the remaining [redacted]% we conservatively assume that competitors will provide instruments without requiring customers to pay a rental price in exchange of purchasing their cartridges.

The main costs of replacing an instrument would include: capital cost of a competitive instrument (this should be multiplied by [redacted]); the costs to train medical technical staff (this should be multiplied by [redacted], being independent by the type of sale/lease contract); the costs of correlation studies for validation of the replacement instrument (this should be multiplied by [redacted], being independent by the type of sale/lease contract).

[5] Using the Excel function =PV(4%,12,-[redacted],0,0).
[6] Using the Excel function =PMT(4%,12,-[redacted],0,0).

The applicant has asked one of its customers (from Benelux) to provide data on the costs for replacing (i.e., repurchasing) the GEM instruments and PAKs. Table 2 shows the capital cost and other expenses for repurchasing 6 GEM instruments.

Table 2. Costs (data from a customer) to replace 6 GEM instruments[7]



This is a representative example of what costs the applicant's customers across the EEA would face in the non-use scenario.

For [redacted]% of instruments (repurchases) we can make reference to the whole Table 2. The labour costs (man hour) are assumed to be internal resources of customers. Therefore those costs, though not requiring paying additional money, can be considered as losses in productivity due to the diversion of workforce away from productive activities.

This means that one has a one-off cost the first year equal to [redacted] EURO and the subsequent years (11 years, assuming the instruments are able to continue working to during the whole requested 12-year review period) equal to [redacted] EURO/year. Applying these values to the estimated number of impacted instruments across the EEA ([redacted]) yields to:

[7] Labor costs are expressed in EURO-equivalent man hours.

- One-off costs (first year): [redacted] EURO times [redacted]/6 = [redacted] EURO;
- Annual costs (subsequent 11 years): [redacted] EURO (NPV, 4%, rounded)[8] times [redacted]/6 = [redacted] EURO.

For the remaining [redacted]% of instruments (lease) we do not consider the following two impacts in the second row of Table 2: [redacted] EURO (capital costs) and [redacted] EURO (ongoing impact). This means that one has a one-off cost the first year equal to [redacted] EURO and the subsequent years (11 years, similarly to what we have assumed above) equal to [redacted] EURO/year. Applying these values to the estimated number of impacted instruments across the EEA ([redacted]) yields to:

- One-off costs (first year): [redacted] EURO times [redacted]/6 = [redacted] EURO (rounded);
- Annual costs (subsequent 11 years): [redacted] EURO (NPV, 4%, rounded)[9] times [redacted]/6 = [redacted] EURO (rounded).

Therefore, over 12-year review period the negative impact from the non-use scenario (or the benefit of avoiding it) for the EEA customers of the applicant is equal to [redacted] EURO. [redacted] This means that the monetized costs derived above are underestimated.

Being aware that tenders organized by customers differ across the EEA countries, to be conservative in the estimation, we take into account only 75% of the total estimate above, that is [redacted] EURO (rounded), which is equivalent to an annualized value of [redacted] EURO (rounded).[10]

Moreover, customers in the EEA that have recently bought GEM® Premier™ 4000 and GEM® Premier™ 5000, and therefore the **equipment is not totally amortized**, will face a negative impact. [redacted] **These additional impacts have been quantified** below, assuming a 10% of margin and 50% of remaining value at 2021: [redacted] **EURO**, **which is equivalent to an annualized value of [redacted] EURO (rounded).**[11]

[8] Using the Excel function =PV(4%,11,-[redacted],0,0)/(1+4%).
[9] Using the Excel function =PV(4%,11,-[redacted],0,0)/(1+4%).
[10] Using the Excel function =PMT(4%,12,-[redacted],0,0).
[11] Using the Excel function =PMT(4%,12,-[redacted],0,0).

Hence, the grand total of the impacts on the customers of the applicant is equal to [redacted] EURO, which is equivalent to an annualized value of [redacted] EURO (rounded).[12]

3.2.3 Suppliers of the applicant's customers (benefits from the non-use scenario)

The fact that the customers of the applicant (considered above) will need to face additional costs mean they indirectly create benefits for the suppliers/competitors of some services listed in Table 2. We have previously assumed that internal resources of the applicant's customers will cover labour costs; therefore we do not consider them here (second column of Table 2). To be conservative in the estimation, we assume that in this case EBIT is equal to 50% of sales of suppliers/competitors of the applicant's customers.

This means that for the [redacted]% of instruments (sales), the positive economic impact from the non-use scenario is:

- First year: [redacted] EURO times 50% times [redacted]/6 = [redacted] EURO (rounded);
- Subsequent 11 years: [redacted] EURO (NPV, 4%, rounded)[13] times [redacted]/6 = [redacted] EURO.

For the remaining [redacted]% of instruments (lease) we do not consider the following two impacts (besides labour costs) in the second row of Table 2: [redacted] EURO (capital costs) and [redacted] EURO (ongoing impact). This means that one has the benefit from one-off financial entrance the first year equal to [redacted] EURO and the subsequent years (11 years, similarly to what we have assumed above) equal to [redacted] EURO/year. Applying these values to the estimated number of impacted instruments across the EEA ([redacted]) yields to:

- First year: [redacted] EURO times 50% times [redacted]/6 = [redacted] EURO (rounded);

[12] Using the Excel function =PMT(4%,12,-[redacted],0,0).
[13] Using the Excel function =PV(4%,11,-[redacted]*50%,0,0)/(1+4%).

- Subsequent 11 years: [redacted] EURO (NPV, 4%, rounded)[14] times [redacted]/6 = [redacted] EURO (rounded).

Therefore, over 12-year review period the positive impact from the non-use scenario for the suppliers of the applicant's customers is equal to [redacted] EURO, which is equivalent to an annualized value of [redacted] EURO (rounded).[15]

3.2.4 The applicant

The applicant is the legal entity representing Werfen for imports from Werfen affiliate companies into the EEA. Therefore, the values reported in Table 3 are for the applicant though other Werfen affiliate companies sell its products.

As a refused authorisation to this application will be equivalent to halt its imports and therefore its business, the relevant economic measure to quantify the impact is given by EBIT. The direct cost of a refused authorisation (or the benefit of granting it) is represented by the loss of the contribution to the EEA economy of the EBIT generated by the applicant with the sales of GEM® Premier™ 4000 and GEM® Premier™ 5000, [redacted]

Table 3. The applicant's sales and EBIT in million EURO

Year	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032
Value of production	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
EBIT	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

The lost EBIT is equal to [redacted] EURO over the period 2021-2032, which is equivalent to an annualized value of [redacted] EURO (rounded).[16]

3.3. Social impacts

This section summarizes the main expected social impacts of the "non-use" scenario. The most important ones are:

- The EEA populations affected by the absence of GEM® Premier™ 4000 and GEM® Premier™ 5000;
- The unemployment associated with the layoff of workers across the EEA.

[14] Using the Excel function =PV(4%,11,-[redacted]*50%,0,0)/(1+4%).
[15] Using the Excel function =PMT(4%,12,-[redacted],0,0).
[16] Using the Excel function =PMT(4%,12,-[redacted],0,0).

With a refused authorization, the employment of the applicant's suppliers is also likely to be negatively affected, but the applicant is not in a position to quantify this additional impact.

The applicant does not expect negative social impacts from changes in working conditions, job satisfaction, training and skill development, and social security within the whole organization.

3.3.1 Reduction of medical equipment

Table 4. Number of hospitals in EU

TOTAL - EU	
Bed size category	# of Hospitals
<100	1,845
100-299	2,774
300-499	1,594
>500	1,406
Other, non-hospital site	3,276
Total	10,895

Table 3 reports an estimation of the entire market (IL and competitors) for some EU countries (not all because some countries did not report this information to IL/the applicant). To estimate what share of these hospitals belong to IL business, one can reasonably estimate this share by using IL total market share in the EU (i.e., about xx%). This means that more than xxxxx hospitals in the EEA are expected to have in their equipment portfolio GEM® Premier™ 4000 and/or GEM® Premier™ 5000. Therefore, those same hospitals have to use GEM® Premier™ 4000 GEM PAK and/or GEM® Premier™ 5000 GEM PAK cartridges.

The applicant expects to import into the EEA in the period 2021-2032 on average xxxxx GEM® Premier™ 4000 cartridges and xxxxx GEM® Premier™ 5000 cartridges. Considering that the standard number of samples that can be tested with each cartridge is 450 (min. 75, max. 600), **in the use scenario the average annual testing capacity that the EEA hospitals and commercial laboratories would be able to provide to the EEA society is equal to more than [redacted] of tested samples of blood** (that is, 450 x [redacted]).

3.4.2 Unemployment

In the non-use scenario the applicant expects a negative impact on employment across the whole EEA (viz., across [redacted] countries). This is due to the fact that the distribution of the in-scope products is done by Werfen affiliate organizations that operate across the EEA. The expected headcount reduction is based on the proportional expected reduction in sales of in-scope products as well as the reduction in other products in that business.

In total [redacted] FTE workers will be redundant in 2021, according to the estimations of the applicant regarding the dynamics of its EEA businesses in the non-use scenario. The total annual gross salaries (including the employer's social security contributions) that will be paid

by the applicant as well as by the other Werfen affiliate organizations to these workers is equal to [redacted] EURO.

We proceed according to the ECHA document on the evaluation of the unemployment (SEAC/32/2016/04)[17] and the paper of Dubourg (2016)[18] endorsed by ECHA. Therefore:

- Using Table A7 (column G, considering that we take into consideration the gross wage including the employer's social security contributions) in Dubourg's paper, the total social costs of unemployment in the EU-28 is equal to 2.16 times the annual gross salary reported above.[19]
- Table 5 presents the statistics from Eurostat (data for 2018Q4) on the average duration of the unemployment for both men and women with the age of 15-64 years in the EU-28.[20]
- We consider only 50% of the average duration of the employment to take into account the fact that some workers are high skilled and would need less time to find a job.

Table 5. Duration of unemployment in EU-28

Duration Grouping	Thousand units	Proportion (A)	Assumed duration (B)	Weighted average (A*B)
Less than 1 month	1495.1	0.093215954	0.5	0.046607977
From 1 to 2 months	2997.7	0.186899514	1.5	0.280349271
From 3 to 5 months	2515.9	0.156860422	4.5	0.705871901
From 6 to 11 months	2176.1	0.135674695	8.5	1.153234907
From 12 to 17 months	1878.3	0.117107568	14.5	1.698059742
From 18 to 23 months	761.3	0.047465257	20.5	0.973037764
From 24 to 47 months	2030.5	0.126596879	35.5	4.4941892
48 months or over	2184.2	0.136179711	48	6.53662612
Total	16039.1	1		**15.88797688**

The social costs of employment in the non-use scenario (or the benefits of avoiding it) are:

[17] ECHA (2016). The Social Cost of Unemployment. Available at: https://echa.europa.eu/documents/10162/13555/seac_unemployment_evaluation_en.pdf/af3a487e-65e5-49bb-84a3-2c1bcbc35d25

[18] Richard Dubourg, 2016. Valuing the Social Costs of Job Losses in Applications for Authorization. The Economics Interface Limited.

[19] This value is greater than 1 because it takes into account the following components: lost wage, costs of job searching, recruitment costs, scarring costs (i.e. the impact of unemployment status on future wages and employment possibilities), and leisure time (which is a benefit and therefore subtracted from the previous components).

[20] Data extracted from http://appsso.eurostat.ec.europa.eu/nui/show.do?wai=true&dataset=lfsq_ugad

[redacted] EURO x 2.16 x 15.88797688/12 months times 50% = [redacted] **EURO (rounded), which is equivalent to an annualized value of [redacted] (rounded).**[21]

3.4. Wider economic impacts

With the refusal of the authorization there could be some benefits for the EEA economy because European competitors producing in the EEA could gain market shares from IL/Werfen. This will imply a small benefit from the non-use scenario (a small cost from granting the authorization), that is the consequent decrease of imports from outside the EEA, improving the EEA trade balance. However, it is very likely that EEA competitors would need years to produce enough to replace of GEM instruments, and the customers would have no instrument during that period, creating a serious healthcare issue from this shortage, as highlighted in Section 3.3.1

Table 6: Socio-economic benefits of continued use

Description of major impacts	**Quantification of impacts [annualised to € per year]**
1. Benefits to the applicant(s) and/or their supply chain	
1.1 Avoided profit loss due to investment and/or production costs related to the adoption of an alternative	[redacted]
1.2 Avoided profit loss due to ceasing the use applied for	[redacted]
1.3 Avoided relocation or closure cost	N/A
1.4 Avoided residual value of capital	[redacted]
1.5 Avoided additional cost for transportation, quality testing, etc.	N/A
Sum of benefits to the applicant(s) and / or their supply chain	[redacted]
2. Quantified impacts of the continuation of the SVHC use applied for on other actors	
1.1 Avoided net job loss in the affected industry	[redacted]
1.2 Foregone spill-over impact on surplus of alternative producers	-[redacted]
1.3 Avoided consumer surplus loss (e.g. because of inferior quality, higher price, reduced quantity, etc.)	++
1.4 Avoided other societal impacts (e.g. avoided CO_2 emissions or securing the production of drugs)	N/A
Sum of impacts of continuation of the use applied for	> -[redacted]
3. Aggregated socio-economic benefits (1+2)	> [redacted]

[21] Using the Excel function =PMT(4%,12,-[redacted],0,0).

4. COMBINED ASSESSMENT OF IMPACTS

4.1. Comparison of impacts

When analysing all the impacts in the "non-use" scenario (or the benefits of avoiding it), the monetization of the environmental risks (associated with the use of OPnEO) represents a benefit to the society (or a cost of granting the authorization), but this is zero, because of zero emissions, whereas the economic and social impacts are the expected costs of a refused authorization (or benefits of granting it). The wider economic impacts are also benefits for the EEA society in the "non-use" scenario because of the potential reduction of the EEA trade balance. The following table aims to summarize all the monetized impacts derived in the previous sections.

Table 7: Comparison of socio-economic benefits and risks of continued use

Socio-economic benefits of continued use		**Monetised excess risks associated with continued use**	
Benefits to the applicant(s) and/or their supply chain [annualised to € per year]	[redacted]	Monetised excess risks to workers directly exposed in the use applied for [annualised to € per year]	N/A (0)
Quantified impacts of the continuation of the SVHC use applied for on other actors [annualised to € per year]	> -[redacted]	Monetised excess risks to the general population and indirectly exposed workers [annualised to € per year]	N/A (0)
Additional qualitatively assessed impacts	Avoided shortage in the annual testing capacity that the EEA hospitals and commercial laboratories would be able to provide to the EEA society	Additional qualitatively assessed risks	N/A (0)
Aggregated socio-economic benefits [annualised to € per year]	> [redacted]	Aggregated monetised excess risk [annualised to € per year]	N/A (0)

Table 8: Benefit/ risk summary

Net benefits (€)	> [redacted] per year
Benefit/monetised risk ratio	N/A (monetized risk is zero)

Table 9: Cost of non-use per kg and year (for PBT/vPvB substances and endocrine disruptors)

	Per year
Total cost (€)[annualised to € per year]	[redacted]
Total emissions (kg)	Zero
Ratio (€/kg)	N/A

4.2. Distributional impacts

Table 10: Distributional impacts

Affected group[1]	**Economic impact [annualised to € per year]**	**Health and environmental impact**
Economic operator		
Applicant	[redacted]	N/A (0)
Suppliers of alternatives in the EU	-	N/A
Suppliers of alternatives outside the EU	-	N/A
Competitors in the EU and other suppliers to the applicant's customers	-[redacted]	N/A
Competitors outside the EU	-	N/A
Customers of the applicant	[redacted]	N/A
Supplier of the applicant	[redacted]	N/A
Public at large in the EU (the whole EEA population)	Testing capacity that the EEA hospitals and commercial laboratories would be able to provide to the EEA society (++)	N/A (0)
Geographical scope		
The whole EEA (with business/employment impacts in [redacted] countries)	+++	N/A (0)
Within the applicant's business		
Employers/Owners	[redacted]	N/A (0)
Exposed workers	N/A (0)	N/A (0)
Non-exposed employees	[redacted]	N/A (0)

4.3. Uncertainty analysis

As there is no cost for the EEA society from granting the authorization (because of zero emission from EEA downstream users), any more restrictive assumptions that could be alternatively adopted (e.g., on the social costs of unemployment, loss of value added, impact on patients) will not change in any way the main result of this SEA: the benefits of granting (or the costs of not granting) the authorization (estimated by with the conservative approach) to the applicant are and remain over time larger than costs (or the benefits of not granting the authorization), which are actually zero.

5. CONCLUSIONS

The applicant is applying for an authorisation to import into the EEA cartridges containing OPnEO to be used in Blood Gas Systems. These cartridges are produced by IL in the US and then shipped to Italy (i.e., imported by the applicant) for the distribution to EEA hospitals (the applicant's sole customers). To date there are not technically suitable substitutes that could immediately replace OPnEO used in the manufacturing of these cartridges.

This SEA has analysed all main impacts expected in the "non-use" scenario. There will be no (zero) benefit for the EEA society over 12 years after the sunset date in case of a refused authorisation. Conversely, the total costs for the EEA society would be *more than* 70 million EURO/year over 12 years after the sunset date.

Given the above considerations, the applicant believes that it should be granted the authorisation in accordance with the article 60(4) of REACH. In line with the conclusions reported in the AoA, the applicant requests an authorisation for 12 years, starting from the sunset date because, as this application for authorisation has shown, all criteria laid out by ECHA (2013)[22] are fulfilled.

[22] ECHA (2013), Setting the Review Period when RAC and SEAC Give Opinions on an Application for Authorisation. Available at: https://echa.europa.eu/documents/10162/13580/seac_rac_review_period_authorisation_en.pdf

ANNEX I – JUSTIFICATIONS FOR CONFIDENTIALITY CLAIMS

Blanked out item	Page number	Justification for confidentiality
Details of lysing bag	*6, 11, 12*	*The information is a business secret whose publication could harm the interests of the applicant. The information is claimed confidential in line with Article 119 of the REACH Regulation.*
Data on workers	*6, 13, 21, 22, 23, 24, 25*	*The information is a business secret whose publication could harm the interests of the applicant. The information is claimed confidential in line with Article 119 of the REACH Regulation.*
Details of production and organization	*9, 18, 20*	*The information is a business secret whose publication could harm the interests of the applicant. The information is claimed confidential in line with Article 119 of the REACH Regulation.*
Market share	*9*	*The information is a business secret whose publication could harm the interests of the applicant. The information is claimed confidential in line with Article 119 of the REACH Regulation.*
Financial data	*16, 17, 18, 19, 20, 21, 23, 24, 25*	*The information is a business secret whose publication could harm the interests of the applicant. The information is claimed confidential in line with Article 119 of the REACH Regulation.*
Data on customers and contracts	*16, 17, 18, 19, 20 21, 23, 24, 25*	*The information is a business secret whose publication could harm the interests of the applicant. The information is claimed confidential in line with Article 119 of the REACH Regulation.*