Exemption Request Form

Date of submission: 21st January 2021

(Updated version of 24th November 2021 with final LCA)

1. Name and contact details

1) Name and contact details of applicant:

Company:	Instrumentation Laboratory	Tel.:	+1 (781)861-4505
Name:	Jim Richard	E-Mail:	jrichard@ilww.com
Function:	Director Quality Engineering	Address:	180 Hartwell Road, Bedford, MA 01730, USA

2) Name and contact details of responsible person for this application (if different from above):

Company:	Intertek Health, Environmental & Regulatory Services	Tel.:	+4520577975
Name:	Torben Norlem	E-Mail:	Torben.norlem@intertek.com
Function:	Chief Counsel	Address:	Vesterbrogade 74, 1620, Copenhagen, Denmark

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2. Reason for application:

Please indicate where relevant:

- ☒ Request for new exemption in: Annex IV
- ☐ Request for amendment of existing exemption in
- ☐ Request for extension of existing exemption in
- ☐ Request for deletion of existing exemption in:
- ☐ Provision of information referring to an existing specific exemption in:
  - ☐ Annex III ☐ Annex IV

No. of exemption in Annex III or IV where applicable:

Proposed or existing wording: *Bis (ethylhexyl)-phthalate (DEHP) as a plasticizer in polyvinyl chloride (PVC), serves as a base material for amperometric, potentiometric and conductometric electrochemical sensors, which are used in in-vitro diagnostic medical devices for the analysis of whole blood.*

Duration where applicable: 3 years

☐ Other: _____

3. Summary of the exemption request

Instrumentation Laboratory is a leading manufacturer of equipment which analyses critical care analytes in whole blood, used in hospitals and laboratories in all world markets. We operate under ISO 14001 and are committed to meeting European and country specific environmental requirements.

Instrumentation Laboratory manufactures the GEM Premier 4000 diagnostic medical analyzer for the entire EU Market. These instruments are used to measure the blood of patients and provide clinicians with accurate measurements of specific analytes vital to medical diagnosis and patient treatment. The reported analytes include, among others, pH, pCO2, pO2, Na+, K+, Ca++, Cl-, glucose, lactate and hematocrit.

The heart of the GEM Premier 4000 is the sensor card where the electrochemical measurements of the above analytes take place. Since release, all sensor card resins on all GEM Premier systems (GEM Premier 3000/3500, GEM Premier 4000, and GEM Premier 5000) have contained a lead-based thermal stabilizer (tribasic lead sulfate, TBLS) required for heat stability during injection molding. The TBLS is addressed in a separate exemption application. However, the GEM Premier 4000, has an additional additive, Di(2-ethylhexyl)phthalate (DEHP), which is part of the resin formulation that aids in creating the mechanical properties required for the GEM Premier 4000. Due to slight differences in cartridge, electromechanical, and system designs, together with unique interactions with the sensor cards resins, removal of DEHP impacts analytical performance characteristics and thereby impedes the intended function of the GEM Premier 4000 analyzer.

As noted above the GEM Premier 4000 sensor card has proven to be more complex to convert to the reformulated RoHS resin in this platform, requiring a complete redesign of the resin formulation. In addition to analytical impacts for the GEM Premier 4000, significant optimization was required in manufacturing processes, which had to be tested, adjusted, and verified to meet the GEM Premier 4000 specifications.

In addition, the preliminary results of the LCA shows that there is no significant difference between the environmental performance of the current GEM Premier 4000 Sensor Card and the potential alternative Sensor Card.

Continued use of DEHP in the sensor card of the GEM Premier 4000 analyzer is required while the evaluation of the candidate resins continue with alternative plasticizers. The alternative plasticizers must not interfere with measurement of any analyte on the system over the intended specifications such as claimed product shelf life (up to 6 months at room temperature) and use life (up to 30 days in the analyzer).

We respectfully request that this application for an exemption be approved, as the sensor card is the most important part of our instrument, where all the electrochemical readings take place. Without this submission being approved, the supply of vital

analytical instruments that support hospitals and laboratories across the entire EU will be jeopardized with a clear negative impact on the EU Health Care Sector. The supply of the GEM Premier 4000 is currently of particular importance due to its critical role in the management of hospitalized patients with COVID-19. Meanwhile, we have an active project plan and are diligently evaluating new plasticizers compliant to RoHS.

Instrumentation Laboratory kindly invites the European Commission and the EU Member States to review this application for an exemption under RoHS and the supporting documentation accompanying the application. We hope for a constructive and positive review process, and we will proactively support all request and inquiries that Competent Authorities and relevant Stakeholders may have in this respect.

4. Technical description of the exemption request / revocation request

(A) Description of the concerned application:

1. To which EEE is the exemption request/information relevant?

   Name of applications or products: The Sensor Card Used in Cartridges for the GEM® Premier 4000 with iQM.

   a. List of relevant categories: (mark more than one where applicable)

   ☐ 1
   ☐ 2
   ☐ 3
   ☐ 4
   ☐ 5
   ☐ 6
   ☐ 7
   X 8
   ☐ 9
   ☐ 10
   ☐ 11

   b. Please specify if application is in use in other categories to which the exemption request does not refer: N/A

   c. Please specify for equipment of category 8 and 9:

   The requested exemption will be applied in

   ☐ monitoring and control instruments in industry

   X in-vitro diagnostics

   ☐ other medical devices or other monitoring and control instruments than those in industry

2. Which of the six substances is in use in the application/product?

   (Indicate more than one where applicable)

   ☐ Pb ☐ Cd ☐ Hg ☐ Cr-VI ☐ PBB ☐ PBDE

   X DEHP

3. Function of the substance: DEHP as a plasticizer in polyvinyl chloride (PVC) serves as a base material for amperometric, potentiometric and conductometric electrochemical sensors.

4. Content of substance in homogeneous material (%weight): 1.14% (GEM Premier 4000 Cartridge)

5. Amount of substance entering the EU market annually through application for which the exemption is requested: 1-10 kg.

Please supply information and calculations to support stated figure.

See details below:

6. Name of material/component: Electrochemical sensor cards composed of Polyvinyl chloride (PVC). Please refer to specific information provided below in point b).

Environmental Assessment:

Intertek has been retained by Instrumentation Laboratory to carry out an environmental Life Cycle Assessment (LCA) of four additives used or potentially used in sensor cards: DEHP (Di-2-Ethyl Hexyl Phthalate), Mineral Oil, Ester Lubricant and Acrylic Processing Aid. The three additives Mineral Oil, Ester Lubricant and Acrylic Processing Aid are potential alternatives to DEHP. DEHP is used as an additive on its own, in contrast to the other three additives, which must be used in a combination of all three to match the functional performance of DEHP. The LCA is included as Appendix F.

Results are per one kilogram of DEHP, and appropriate amounts of the other three additives to achieve equivalent functional performance, as detailed in the report. Full results are detailed in the report and summarised here (in all cases, a numerically lower result is a preferable result in environmental terms):

- The LCA for DEHP showed a global warming potential or 'carbon footprint' of 3.48 kgCO2eq, Mineral Oil of 2.69 kgCO2eq, Ester Lubricant of 4.05 kgCO2eq and Acrylic Processing Aid of 3.79 kgCO2eq.
- The alternatives to DEHP are required in combination, so the true comparison is DEHP with a carbon footprint of 3.48 kgCO2eq versus the combined alternative additives with a carbon footprint of 10.54 kgCO2eq.
- The USEtox LCA results in the 'Human Toxicity, Cancer' category were 76 nanoCases for DEHP versus 441 nanoCases for the combination of the other three additives.
- The USEtox results in the 'Human Toxicity, Non-Cancer' category were 256 nanoCases for DEHP versus 2130 nanoCases for the combination of the other additives.
- The results for Cumulative Energy Demand (CED) were lower in all cases for DEHP than for the combination of the other additives; for example, in the 'Non-Renewable,

Fossil' category, the result for DEHP was 97 Megajoules, while the result for the combination of the other additives was 251 Megajoules.

- The Ecopoint method results showed that DEHP achieved a score of 1.4 mPt versus 5.1 mPt for the combination of the other additives.

The overall conclusion is that the LCA provides evidence that DEHP is likely to be the preferred solution in terms of environmental impact and human health. The environmental impacts of the alternative additives when considered individually are within the same order of magnitude, but they must be used in combination in the sensor card to achieve equivalent functional performance, which makes their combined environmental impacts significantly higher (less desirable) than those of DEHP. However, the results should be kept in perspective: all these additives are only used in low concentrations in the sensor card, and their environmental impact is small compared to the environmental impact of the whole blood monitor.

GENERAL INFORMATION

Intertek was retained by Instrumentation Laboratory to carry out a Life Cycle Assessment (LCA) for four additives; DEHP, Mineral Oil, Ester Lubricant and Acrylic Processing Aid, which are added to Sensor Cards. The LCA was performed with guidance ISO 14040: Environmental Management – Life Cycle Assessment – Principles and Framework and ISO 14044: Environmental Management – Life Cycle Assessment – Requirements and Guidelines.

Instrumentation Laboratory manufactures the GEM Premier diagnostic medical analyzers for the EU Market. These instruments are used to measure the blood of patients and provide clinicians with accurate measurements of specific analytes, vital to medical diagnosis and patient treatment. This study was conducted to provide Instrumentation Laboratory with the environmental impacts associated with four additives:

- DEHP
- Mineral oil
- Ester Lubricant
- Acrylic Processing Aid

The primary goal of the study is to provide an analysis of the environmental impacts associated DEHP and with the combination of Mineral Oil, Ester Lubricant and Acrylic Processing Aid. Instrumentation Laboratory provided data on the functionally comparable material inputs for the additives: 1.000 kg DEHP versus the combination of 1.228 kg Mineral Oil, 1.404 kg Ester Lubricant and 1.404 kg Acrylic Processing Aid. The additives are added to aid the molding of the polymer in the sensor cards. DEHP – di-2-ethylhexyl phthalate, $C_6H_4(CO_2C_8H_{17})_2$ – is commonly added to plastics to make them malleable. Mineral oil, Ester Lubricant and Acrylic Processing Aid can act in a similar capacity when used in combination.

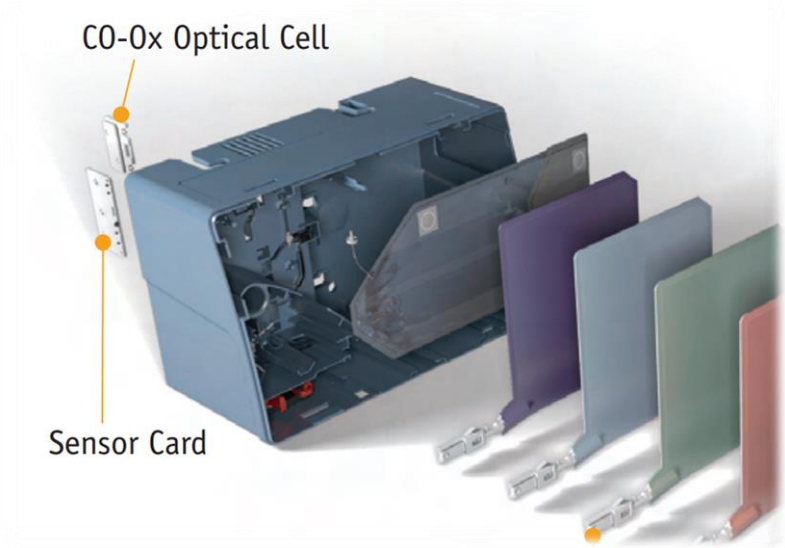

Figure 1. A small quantity of DEHP additive is used in the polymer of the Sensor Card

LCA METHODOLOGY

For the purposes of this study, the functional unit is defined as one kilogram of DEHP additive. Each additive requires different amounts in order to achieve similar functional results. The sensor card polymer would typically contain:

- DEHP: %

or

- Mineral Oil: %
- Ester Lubricant: %
- Acrylic Processing Aid: %

Therefore, normalization factors were used. The comparative reference flows are:

Additive	Unit	Factor
DEHP	kg	1.00
Mineral Oil	kg	1.228
Ester Lubricant	kg	1.404
Acrylic Processing Aid	kg	1.404
Combination of above three additives	kg	4.036

The LCA system boundary for the additives includes cradle-to-grave life cycle stages. This boundary considers raw material extraction, pre-production processes, production, transport and final disposal of the product (the additive). Aspects assigned to the card and its operation, such as electricity use during blood analysis, are not included. Further details of the LCA in conformity with the ISO Standards are provided in the full report.

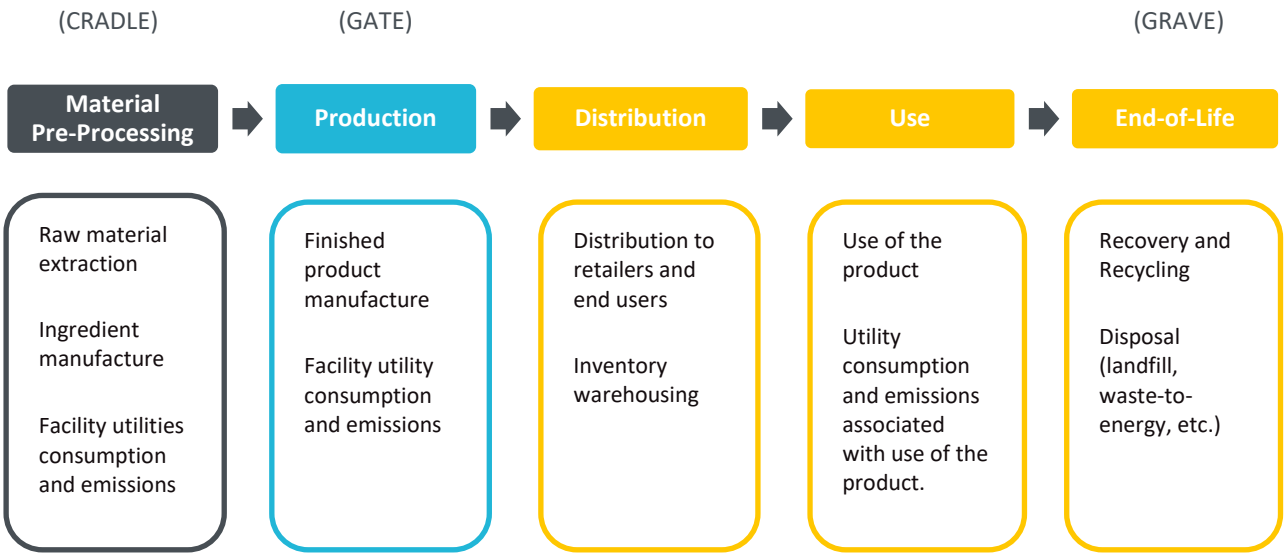

Figure 2. System boundary for the additives

Results

The tables below show the LCA results per functional unit using four environmental impact assessment methods: ReCiPe, USEtox, CED and Ecopoints. ReCiPe is the most commonly used LCA impact assessment method. ReCiPe reports global warming (carbon footprint) and a variety of other environmental impact metrics. USEtox reports human health impact. CED, Cumulative Energy Demand, reports life cycle energy requirements. Ecopoints, produced by the IMPACT 2002+ method, are a single number result that combines various environmental metrics.

Table 1. Cradle-to-grave ReCiPe LCA results for additives per functional unit

Impact category	Unit	DEHP 1kg	Mineral Oil 1.228kg	Ester Lubricant 1.404kg	Acrylic Processing Aid 1.404kg	Combined Additives 4.036kg
Global warming	kg CO2 eq	3.48	2.69	4.05	3.79	10.54
Stratospheric ozone depletion	kg CFC11 eq	0.000000552	0.000000134	0.000007520	0.000001368	0.00000902
Ionizing radiation	kBq Co-60 eq	0.111	0.000	0.163	0.460	0.623
Ozone formation, Human health	kg NOx eq	0.00499	0.00960	0.00809	0.00894	0.0266
Fine particulate matter formation	kg PM2.5 eq	0.00317	0.00586	0.00551	0.01219	0.0236
Ozone formation, Terrestrial ecosystems	kg NOx eq	0.00540	0.01005	0.00849	0.00922	0.0278
Terrestrial acidification	kg SO2 eq	0.00799	0.01880	0.01222	0.03707	0.0681
Freshwater eutrophication	kg P eq	0.000431	0.000000	0.001076	0.001834	0.00291
Marine eutrophication	kg N eq	0.0000419	0.0000152	0.0001207	0.0002291	0.000365
Terrestrial ecotoxicity	kg 1,4-DCB	3.01	0.67	10.05	12.78	23.496
Freshwater ecotoxicity	kg 1,4-DCB	0.0286	0.0099	0.0811	0.1850	0.276
Marine ecotoxicity	kg 1,4-DCB	0.0410	0.0136	0.1143	0.2586	0.387
Human carcinogenic toxicity	kg 1,4-DCB	0.0553	0.0033	0.1279	0.1818	0.313
Human non-carcinogenic toxicity	kg 1,4-DCB	0.968	0.466	2.423	5.262	8.151
Land use	m2a crop eq	0.0273	0.0000	2.9880	0.1536	3.142
Mineral resource scarcity	kg Cu eq	0.00410	0.00000	0.00786	0.15318	0.161
Fossil resource scarcity	kg oil eq	1.99	2.30	1.82	1.37	5.489
Water consumption	m3	0.0307	0.0000	0.0496	0.1008	0.150

Table 2. Cradle-to-grave USEtox LCA results for additives per functional unit

Usetox Impact Category	Unit	DEHP 1kg	Mineral Oil 1.228kg	Ester Lubricant 1.404kg	Acrylic Processing Aid 1.404kg	Combined Additives 4.036kg
Human toxicity, cancer	cases	0.0000000761	0.0000000023	0.0000001752	0.0000002637	0.000000441
Human toxicity, non-cancer	cases	0.000000256	0.000000370	0.000000636	0.000001120	0.00000213
Freshwater ecotoxicity	PAF.m3.day	6641	913	22047	33319	56279

Table 3. Cradle-to-grave CED LCA results for additives per functional unit

CED Impact Category	Unit	DEHP 1kg	Mineral Oil 1.228kg	Ester Lubricant 1.404kg	Acrylic Processing Aid 1.404kg	Combined Additives 4.036kg
Non renewable, fossil	MJ	97.3	105.4	83.1	62.7	251.2
Non-renewable, nuclear	MJ	3.48	0.00	4.11	8.96	13.07
Non-renewable, biomass	MJ	0.0000801	0.0000000	0.0004003	0.0006745	0.00107
Renewable, biomass	MJ	0.263	0.000	17.537	2.642	20.179
Renewable, wind, solar, geothermal	MJ	0.884	0.000	0.270	0.693	0.963
Renewable, water	MJ	0.545	0.000	1.203	2.045	3.248

Table 4. Cradle-to-grave Ecopoint LCA results for additives per functional unit

Ecopoints Damage Category	Unit	DEHP 1kg	Mineral Oil 1.228kg	Ester Lubricant 1.404kg	Acrylic Processing Aid 1.404kg	Combined Additives 4.036kg
Total	mPt	1.388	1.413	2.121	1.532	5.066
Human health	mPt	0.421	0.472	0.876	0.602	1.951
Ecosystem quality	mPt	0.025	0.009	0.309	0.098	0.416
Climate change	mPt	0.311	0.241	0.361	0.359	0.961
Resources	mPt	0.631	0.691	0.574	0.473	1.739

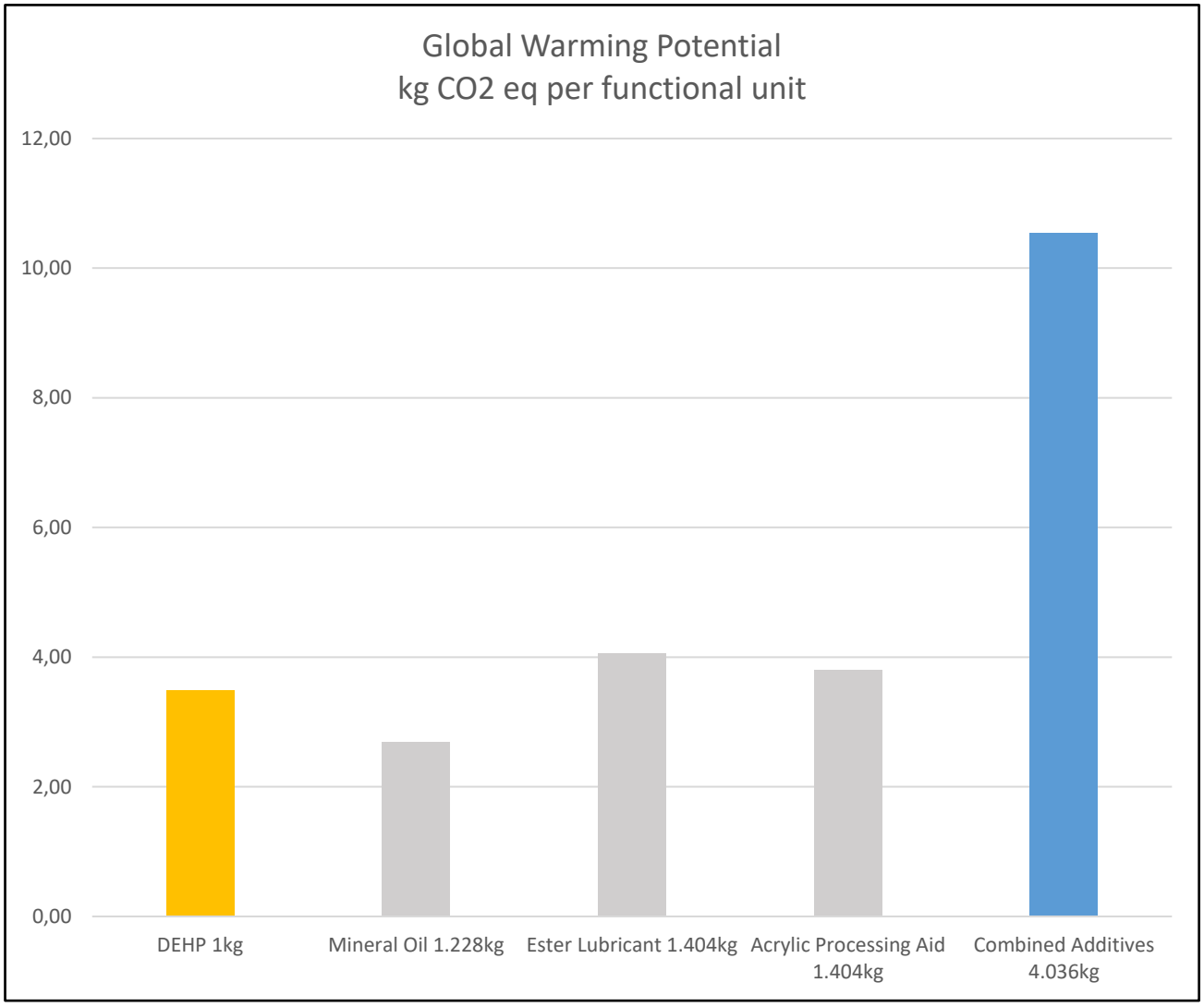

Figure 3. Carbon footprint results for additives DEHP, Mineral Oil, Ester Lubricant and Acrylic Processing Aid, and the combination of the three alternative additives

CONCLUSION

The overall conclusion is that the LCA provides evidence that DEHP is likely to be the preferred solution in terms of environmental impact and human health. The alternative additives, when used in combination in the sensor card to achieve equivalent functional performance, have a higher combined environmental and health impact than that of DEHP:

- The LCA for DEHP showed a global warming potential or 'carbon footprint' of 3.48 kgCO2eq, Mineral Oil of 2.69 kgCO2eq, Ester Lubricant of 4.05 kgCO2eq and Acrylic Processing Aid of 3.79 kgCO2eq.
- The alternatives to DEHP are required in combination, so the true functional comparison is DEHP with a carbon footprint of 3.48 kgCO2eq versus the combined alternative additives with a carbon footprint of 10.54 kgCO2eq.

- The USEtox LCA results in the ‘Human Toxicity, Cancer’ category were 76 nanoCases for DEHP versus 441 nanoCases for the combination of the other three additives.
- The USEtox results in the ‘Human Toxicity, Non-Cancer’ category were 256 nanoCases for DEHP versus 2130 nanoCases for the combination of the other additives.
- The results for Cumulative Energy Demand (CED) were lower in all cases for DEHP than for the combination of the other additives; for example, in the ‘Non-Renewable, Fossil’ category, the result for DEHP was 97 Megajoules, while the result for the combination of the other additives was 251 Megajoules.
- The Ecopoint method results showed that DEHP achieved a score of 1.4 mPt versus 5.1 mPt for the combination of the other additives.

LCA: X Yes
☐ No

(B) In which material and/or component is the RoHS-regulated substance used, for which you request the exemption or its revocation? What is the function of this material or component?

The RoHS-regulated substance, DEHP, is a constituent material in the sensor card of the disposable cartridge used with the GEM Premier 4000 analyzer.

The GEM Premier 4000 analyzer is used for blood analysis and serves as a critical analytical instrument in hospital labs, operating rooms, emergency rooms and point of care at bedsides across the Global and EU Health Care Sector. Blood analysis is a core element to virtually all diagnostic and therapeutic procedures carried out in the Health Care Sector today. Data from the GEM Premier 4000 critical care analyzer is used daily in hospitals around the world to make life-saving decisions regarding patient health. It is imperative that the data has the highest possible reliability and accuracy.

The sensor card is a vital component in the cartridges of the GEM Premier 4000 because it contains the electrochemical sensors used for measuring and reporting concentrations of critical care analytes in blood (pO2, pCO2, pH, Na+, K+, Ca++, Cl-, glucose, lactate and haematocrit). DEHP is part of the sensor card resin formulation that aids in creating the electrochemical and mechanical properties required for the GEM Premier 4000. Any change in the sensor card resin can directly impact analytical performance characteristics and thereby impede the intended function of the GEM Premier 4000 analyzer. To date, all improvements to the GEM Premier 4000 platform have been designed and optimized around the current sensor card resin.

For the GEM Premier 4000 analyzer to continue to provide patient blood data with uncompromised reliability and accuracy, continued use of DEHP in the sensor card of the GEM Premier 4000 analyzer is required while the search continues for alternative substances. The alternative substances must not interfere with measurement of any analyte, and must meet established product claims for the GEM Premier 4000 analyzer

over the claimed cartridge shelf life (up to 6 months at room temperature) and use life (up to 30 days in the analyzer).

(C) What are the particular characteristics and functions of the RoHS-regulated substance that require its use in this material or component?

The sensor card in the disposable cartridge is made of polyvinyl chloride (PVC). Use of PVC as the sensor card material dates back to the 1980s when the GEM- Stat and GEM 6 analyzers were first launched. The same molded sensor card has been carried forward to the currently manufactured GEM Premier platform analyzers (GEM Premier 3000, GEM Premier 3500, GEM Premier 4000 and GEM Premier 5000).

PVC has specific advantages as a sensor card material for the electrochemical sensors used in the GEM Premier products. Sensor membranes used for certain sensors (Na+, K+, Ca++, pH, pCO2) are based on PVC membranes and are solvent cast directly on the sensor card from a solution of tetrahydrofuran (THF). Because THF is a strong solvent for PVC, there is strong adhesion between the cast membranes and the PVC card. This membrane adhesion to the PVC is a critical requirement for sensor function and promotes long use life and shelf life.

The PVC sensor card is produced by injection molding. DEHP has been traditionally used as a plasticizer. The presence of DEHP in the PVC sensor card increases flexibility and reduces brittleness to improve durability and reliability under cyclical mechanical loading that the sensor card experiences during manufacturing and use in the GEM Premier 4000 analyzer. Importantly, DEHP performs this function without interfering in analyte measurements on the GEM Premier 4000 analyzer.

As mentioned above, any change in the sensor card resin can directly impact analytical performance characteristics of this system. This is critical because the quality management system, which ensures high quality and accurate blood measurements in the GEM Premier 4000 system, has been designed around the analytical performance of sensor cards containing DEHP, based on cartridge sensor data collected over a 20-year time period. The following advantages of the GEM Premier 4000 as compared to other existing technologies on the market today (examples of competing equipment are Siemens RapidPoint 500 and Roche Cobas 123) are directly related to resin formulation and require extensive validation for an alternative substance:

1. The GEM Premier 4000 analyzer utilizes the renowned Intelligent Quality Management (iQM™) System which automatically detects, corrects, and documents all 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 8 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 that reduce the need for user interpretation of results or repeat testing.

c. iQM results in a longer usable lifetime of the disposable cartridge, compared to other analyzers based on AQC technology. The iQM system conducts quality control as an integrated part of the testing process, whereas AQC counts quality control samples as separate tests thus reducing available number of patient blood samples during cartridge life.

2. The GEM Premier 4000 analyzer offers a single, disposable measurement cartridge which can be stored up to 6 months at room temperature. Other competing technologies utilize multiple cartridges to perform the same functions, some of which require refrigerated storage. This place 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. Every sensor card produced for the GEM Premier 4000 analyzer is 100% tested at the factory to ensure highest levels of quality to the customer. Other competing technologies use the concept of Acceptable Quality Limit (AQL) testing, where a sample of manufactured parts are tested to find whether the entire production lot meets the product specifications.

The combination of the iQM System, single measurement cartridge design, and rigorous testing procedure for each sensor card ensures that the GEM Premier 4000 analyzer provides the best possible results in all relevant use scenarios. This combination curtails the need for users to perform correctional analytical actions, enabling Healthcare staff to better focus on critical patient care tasks. These advantages are directly linked to the performance of the sensor card resin as a critical component of the measurement system.

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5. Information on Possible preparation for reuse or recycling of waste from EEE and on provisions for appropriate treatment of waste

1) Please indicate if a closed loop system exist for EEE waste of application exists and provide information of its characteristics (method of collection to ensure closed loop, method of treatment, etc.)

The GEM Premier 4000 cartridge is treated as medical waste, and its disposal is handled in each country per their local, state, and federal laws. In most cases, medical

waste is incinerated in specific designated facilities according to national requirements and supervision of the respective EU Member States.

2) Please indicate where relevant:

☐ Article is collected and sent without dismantling for recycling

☐ Article is collected and completely refurbished for reuse

☐ Article is collected and dismantled:

- ☐ The following parts are refurbished for use as spare parts: _____
- ☐ The following parts are subsequently recycled: _____

X Article cannot be recycled and is therefore:

- X Sent for energy return
- ☐ Landfilled

3) Please provide information concerning the amount (weight) of RoHS substance present in EEE waste accumulates per annum:

☐ In articles which are refurbished _____

☐ In articles which are recycled _____

X In articles which are sent for energy return 1-10 kg.

☐ In articles which are landfilled _____

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6. Analysis of possible alternative substances

(A) Please provide information if possible alternative applications or alternatives for use of RoHS substances in application exist. Please elaborate analysis on a life-cycle basis, including where available information about independent research, peer-review studies development activities undertaken

Instrumentation Laboratory has carried out an extensive RoHS compliance program to ensure compliance for equipment falling under the scope of RoHS and supplied to the EU by Instrumentation Laboratory. Please also refer to Point 4(A)(6) and Appendix F regarding the environmental assessment.

The compliance program identified the sensor card of the GEM Premier 4000 analyzer as a component with a content of DEHP exceeding the maximum concentration value of 0.1% as defined in Annex II of RoHS. DEHP is present in the PVC resin of the sensor card to act as a plastizicer to aid in creating the electrochemical and mechanical properties required for the GEM Premier 4000 analyzer.

Instrumentation Laboratory has been actively working to replace DEHP as a plastizicer in the PVC sensor card, working in close cooperation with commercial suppliers of PVC materials, academic institutions specializing in polymer chemistry and private consultants to identify alternatives for DEHP. Our progress toward this goal is

summarized in Point 7(A) of this application and detailed in Appendix B. This work is not yet complete, for reasons detailed in the following Points.

Instrumentation Laboratory is submitting this application for an exemption to allow additional time to complete this work while at the same time assuring uninterrupted supply to the EU healthcare sector of equipment critical to providing optimum care of critically ill patients.

The GEM Premier 4000 Blood Gas system plays a crucial role in the management of hospitalized patients with COVID-19. Arterial blood gas analysis is critical in evaluating and monitoring respiratory function in patients with pneumonia, acute respiratory failure, and acute respiratory distress syndrome. Patients with COVID-19 can suffer from these disorders and need routine blood gas testing as part of their care, especially if they require mechanical ventilation (Fang 2020[2]). Epidemiological studies have shown up to one-third of hospitalized COVID-19 patients require mechanical ventilation (Wunsch 2020[1]), making blood gas systems and reagents a high-demand product during the global pandemic. During the pandemic, our primary focus as a company has been to meet the increased demand for blood gas testing.

A key finding of the work completed until now was that replacement of DEHP as a plastizicer in the PVC resin of the sensor card resulted in deterioration in analytical performance of several parameters measured by the GEM Premier analyser. All resins tested prior to the current candidate (the CMR1345 resin), have shown issues of low amperometric oxygen sensor response and imprecise amperometric glucose sensor response. We therefore conclude that presence of DEHP in the PVC sensor card is aiding sensor performance, and published product claims were based on this optimum performance.

Appendix B shows the levels of performance we are trying to achieve after replacement of DEHP with an alternative RoHS-compliant resin.

At present, the evaluation continues for an alternative, RoHS compliant resin which will restore sensor functions to their original level of performance, consistent with product claims. EN ISO 13485:2012 (EN ISO 13485:2016 Medical Devices – Quality Management Systems – Requirements for Regulatory Purposes), EU Directive 98/79/EC (Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices) and European In Vitro Diagnostic Regulation (IVDR 2017/746), on in vitro diagnostic medical devices which is currently in progress. In vitro diagnostic medical devices requires that a manufacturer must demonstrate its ability to provide medical devices and related services that consistently meet customer and applicable regulatory requirements.

The legal obligation for the manufacturer to meet applicable requirements of the current EU Directive and the coming IVDR includes performance in terms of analytical sensitivity, analytical specificity, accuracy, repeatability, reproducibility, and limits of detection stated by the manufacturer. The Manufacturer needs to document

compliance with the above requirements of the EU Directive and the coming IVDR by updating the Technical File as appropriate.

Due to the aforementioned sensor response issues, the investigated alternative resins are not technically practical or viable alternatives at this time, as they affect the accuracy and reproducibility of test results carried out with the alternative sensor cards, thereby preventing the analyzer from performing its intended function within established product claims. Although the search for practical and viable alternatives is on-going, Instrumentation Laboratory must continue to manufacture the current sensor card using DEHP as a plasticizer until a new, non-DEHP resin is successfully identified, with performance equivalent to currently manufactured product.

Based on our evaluations we conclude that this application for an exemption falls within all three categories as established in Article 5(1)(a) with respect to the possibility to substitute the use of DEHP as a plasticizer in the PVC material of the sensor card:

1. Their elimination or substitution via design changes or materials and components which do not require any of the materials or substances listed in Annex II is scientifically or technically impracticable,
2. The reliability of the substances investigated for substitution is not ensured.
3. The total negative environmental, health and consumer safety impacts caused by substitution are likely to outweigh the total environmental, health and consumer safety benefits thereof.

As noted above the GEM Premier 4000 platform has proven to be more complex to convert to a RoHS resin than the other GEM Premier platforms, requiring a complete redesign of the resin formulation. Due to slight differences in cartridge, electromechanical, and system designs, together with unique interactions with the sensor cards resins, removal of DEHP was shown to impact analytical performance characteristics. These platform level differences requires additional molding process optimization and validation effort for GEM Premier 4000, to ensure the consistency of manufacturing, accuracy of results, and patient safety and effectiveness.

As noted above under Point 4(A)(6) the preliminary results of the LCA shows that there is no significant difference between the environmental performance of the current GEM Premier 4000 Sensor Card and the potential alternative Sensor Card.

(B) Please provide information and data to establish reliability of possible substitutes of application and of RoHS materials in application

Continued use of DEHP in the sensor card of the GEM Premier cartridge is required while the search evaluation of substances continues for an alternative resin with performance characteristics equivalent to the currently manufactured product. The alternative must not interfere with measurement of any analyte on the system over the

claimed product shelf-life (up to 6 months at room temperature) and use-life (up to 30 days in the analyzer).

Instrumentation Laboratory (IL), as referenced in previous studies in Section (A), is continuing to search evaluate for an alternative substance. IL recognizes that in addition to the environmental factors outlined in the Directive 2011/65/EU, the availability of the currently used PVC material in industry is also diminishing and is diligently investigating other materials and sources that could be a reliable substitute.

Upon identification of the RoHS compliant resin, additional time will be needed for development and update of the EU compliance documentation required for Medical Devices for a new sensor card according to applicable EU legislation and other applicable worldwide regulatory requirements for medical devices.

We are confident that the successful replacement of DEHP as a plasticizer in the PVC material of the sensor card across the entire GEM Premier product line will be concluded within the coming 3 years.

Specific to EU legislation, testing of the selected replacement resin and molded sensor cards for each GEM platform would be conducted by an independent outside laboratory to assure RoHS compliance. The report issued by the independent laboratory would then become part of our in-house Technical File for Compliance to European RoHS Directive 2011/65/EU. Also added to the Technical File will be documentation to prove compliance to European Directive 98/79/EC on in-vitro diagnostic medical devices as well as the coming IVDR, specifically in-house analytical verification testing reports for GEM Premier 4000 sensor cards, carried out to prove the RoHS compliant sensor cards meet product analytical performance claims throughout the claimed GEM cartridge shelf life and use life.

Currently Instrumentation Laboratory has gained information about specific failure modes resulting from replacement of DEHP as a plasticizer in the sensor card with alternative materials. Working with this baseline information and data from physical and chemical measurements with experimental card resins, we have narrowed the search to a few resin candidates with high probability of success in meeting product claims. We are confident as to the ultimate success of this project, within the Table 1 timeline.

In conclusion, the substitution of DEHP in the sensor card cannot be completed before the date of applicability of the restriction on use of DEHP according to the RoHS Directive. This application is therefore being submitted for an exemption allowing Instrumentation Laboratory additional time to complete this work. For further details, we refer to the included documentation regarding Project Plan and Schedule (Appendices C and D, cf. also below point 7(B)).

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7. Proposed actions to develop possible substitutes

(A) Please provide information if actions have been taken to develop further possible alternatives for the application or alternatives for RoHS substances in the application.

Actions to develop alternative substances are currently in progress. Table 1 shows milestones listed in the project schedule submitted as part of Appendix D. Also, included in the table is the progress (% Complete column) made towards each milestone.

Table 1: Project Plan

Task Name	Notes	% Complete
Feasibility	2010	**100%**
Feasibility Testing with off the shelf tin-stabilized rigid PVC (Alpha Gary, Georgia Gulf, Roscom, ViChem, Viking Polymer, Emmanual/UMASS custom resins)	2010-2012	100%
New compounder Teknor Apex created various resin formulations at external supplier	2012 - 2016	100%
Resin Formulation development transitioned to in-house	2016	100%
Tested variations of stearates	Apr-May 2016	100%
Tested different organic based stabilizer formulations	Apr-Jul 2016	100%
Pellet blending 1	Jul 2016	100%
Pellet blending 2	Sep 2016	100%
Molding of cards	Jul-Sep 2016	100%
Raw material blend	Oct 2016	100%
Testing	Q4 2016	100%
Molding of cards	Oct 2016	100%
Testing	Q4 2016	100%
Optimize formulation	Jan 2017	100%
CMR: 5 formulations tested (new thermal stabilizers)	Oct 2016-May 2017	100%
Literature research for chemical compound to optimize formulations	Aug 2016	100%

Test 1: Included CMR 1328, 1331, 1334	Oct 2016	100%
Test 2: Included CMR 1331, 1332, 1333	Nov 2016	100%
Identified gap in glucose sample precision	Jan 2017	100%
CMR: 6 formulations tested (additional additives)	Mar 2017	100%
Raw material blends of six new formulations	May 2017	100%
Test 1: Included CMR 1344, 1347, 1348	Aug 2017	100%
Test 2: Included CMR 1345, 1346, 1349	Sep 2017	100%
Shelf Life Assessment	Dec 2017	100%
Design and Process Optimization		**100%**
Down select top 3 formulations from CMR additional additives	Dec 2017	100%
Performance testing, shelf life stability	Jan 2018	100%
Testing on all GEM platforms for top 3 candidates from CMR additional additives	Feb 2018	100%
GEM 4000 testing (all 3 resins)	Apr-May 2018	100%
Repeat testing on all GEM platforms for top 3 candidates	Aug-Sep 2018	100%
Design Review	Oct 2018	100%
Material properties testing	Aug 2018	100%
Down select top 2 resins	Oct 2018	100%
Process Validation - Sensor Card Molding		**90%**
Molding Validations on all platforms	Q1-Q4 2019	100%
GEM 4000 molding validation IQ/OQ	Aug-Oct 2019	100%
PQ Validation	Nov 2019	100%
Retaining ring samples Round 1	Q3 2019	15%
Molding parameters	Q3 2019	100%
Molding of sample parts	Q4 2019	100%
Review parts in house	Q4 2019	100%
Identified poor adhesion of retaining ring to RoHS Resin	Q4 2019	100%
Complete validation of dried retaining rings	TBD	15%
Retaining ring samples Round 2	Q4 2019	100%

Molding parameters	Dec 2019	100%
Molding of sample parts	Jan-Feb 2020	100%
Review parts in house	Feb 2020	100%
Pull force testing at supplier with Round 1 and Round 2 retaining rings	Feb 2020	100%
Retaining ring Validation	Jan 2020	100%
IQ/OQ	Feb 2020	100%
PQ	Feb 2020	100%
Review parts - determine need to dry resin	Feb 2020	100%
Risk Assessment for drying resin	Feb 2020	100%
Complete validation of dried retaining rings	Mar 2020	100%
Re-validation 4k cards with dried resin	Apr 2020	100%
Process Validation - Sensor Card Pinning		**100%**
Pin dried cards	May 2020	100%
Verification and Validation*		**15%**
Build Material for Verification & Validation	June 2020	100%
Analytical Verification	Jul – Nov 2020	50%
Method Comparison	Jul 2020	60%
Aqueous Precision	Aug 2020	60%
Use Life	Aug 2020	30%
Systems Verification	Oct - Nov 2020	0%
Shelf Life Verification	Jul 2020 - Mar 2021	20%
ELM Testing	Jul 2020	100%
Process Validation (Manufacturing)	Jul - Nov 2020	50%
Dried Resin Process Validation	Oct-Nov 2020	25%
ELM Testing	Dec 2020	0%
Dried Resin Analytical Testing	Dec 2020	0%
Release Documentation	Apr-May 2021	0%

Controlled Distribution of RoHS Resin	Jun-Dec 2022	0%

*Delay due to increased demand to support COVID-19

Appendix B: **Testing Summary for GEM Premier Systems with Sensor Card Resins Compliant with Directive 2011/65/EU,** details the efforts completed to date to develop alternate substances.

Extensive investigative testing was performed on each platform for every RoHS resin evaluated to assess the ability to meet system and analytical performance requirements of each GEM platform. All resins were tested first on the GEM Premier 3000/3500 device, as it was the predicate for the GEM Premier 4000, to down-select resins to test on the rest of the GEM Premier family. Due to slight differences in cartridge, electromechanical, and system designs, analytical performance characteristics can vary due to unique interactions with the sensor cards resins. Therefore, testing across all platforms was used to evaluate the best resin to maintain the safety and effectiveness of all GEM Premier analyzers.

All resins tested prior to the current RoHS candidate (CMR1345) had analytical performance issues in various areas. In particular, all resins tested prior to the current candidate have shown issues of low amperometric oxygen sensor response (slope) and imprecise amperometric glucose sensor response.

Resin (CMR) 1345 has been successfully verified and validated on the GEM Premier 3000/3500 and GEM Premier 5000 platforms. Therefore, CMR1345 is the primary path of future testing on the GEM Premier 4000 platform. The GEM Premier 4000 sensor card requires unique mechanical characteristics from the other GEM platforms due to differences in system design. These differences require additional molding process optimization and validation efforts, to ensure the consistency of molding, accurate results, safety, and effectiveness.

(B) Please elaborate what stages are necessary for establishment of possible substitute and respective timeframe needed for completion of such stages.

Please see Appendix C and Appendix D: GEM 4000 Sensor Card RoHS Compliance Project Plan and GEM Premier 4000 Sensor Card RoHS Compliance Project Schedule, respectively.

Table 1 above shows milestones for executing project plan. Please note that we plan to complete the project between June and December 2022.

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8. Justification according to Article 5(1)(a):

(A) Links to REACH: (substance + substitute)

1) Do any of the following provisions apply to the application described under (A) and (C)?

☐ Authorisation

- ☐ SVHC
- ☐ Candidate list
- ☐ Proposal inclusion Annex XIV
- ☐ Annex XIV

☐ Restriction

- ☐ Annex XVII
- ☐ Registry of intentions

☐ Registration

2) Provide REACH-relevant information received through the supply chain.
Name of document: No information specific for REACH received

(B) Elimination/substitution:

1. Can the substance named under 4.(A)1 be eliminated?

☐ Yes. Consequences? _____

X No. Justification: Alternatives are currently not available

2. Can the substance named under 4.(A)1 be substituted?

☐ Yes.

- ☐ Design changes:
- ☐ Other materials:
- ☐ Other substance:

X No.

Justification: Alternatives are currently not available

3. Give details on the reliability of substitutes (technical data + information): Alternatives are currently not available
4. Describe environmental assessment of substance from 4.(A)1 and possible substitutes with regard to
   1) Environmental impacts: Please refer to point 4(A)(6) and Appendix F.
   2) Health impacts: Please refer to point 4(A)(6) and Appendix F
   3) Consumer safety impacts: EEE is only sold to professionals

⇨ Do impacts of substitution outweigh benefits thereof?

Please provide third-party verified assessment on this: Please refer to point 4(A)(6) and Appendix F.

(C) Availability of substitutes:

a) Describe supply sources for substitutes: Alternatives are currently not available

b) Have you encountered problems with the availability? Describe: Alternatives are currently not available

c) Do you consider the price of the substitute to be a problem for the availability?

☐ Yes X No

d) What conditions need to be fulfilled to ensure the availability? Alternative must not impede the reliability of test results carried out with the sensor card as the alternative must ensure that the analyzer performs its intended function within established product claims

(D) Socio-economic impact of substitution:

⇨ What kind of economic effects do you consider related to substitution?

☐ Increase in direct production costs

☐ Increase in fixed costs

☐ Increase in overhead

☐ Possible social impacts within the EU

☐ Possible social impacts external to the EU

X Other: Alternatives are currently not available

⇨ Provide sufficient evidence (third-party verified) to support your statement: Not relevant as alternatives are currently not available.

9. Other relevant information

Please provide additional relevant information to further establish the necessity of your request:

[1]Wunsch H. Mechanical Ventilation in COVID-19: Interpreting the Current Epidemiology. Am J Respir Crit Care Med. 2020;202(1):1-4.

[2]Fang B, Meng QH. The laboratory's role in combating COVID-19. Crit Rev Clin Lab Sci. 2020;57(6):400-414.

10. Information that should be regarded as proprietary

Please state clearly whether any of the above information should be regarded to as proprietary information. If so, please provide verifiable justification:
