Exemption Request Form

Date of submission: 25th May 2017

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:	Omøgade 8, 2100 Copenhagen, Denmark

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2. Reason for application:

Please indicate where relevant:

☐ Request for new exemption in:

☐ Request for amendment of existing exemption in

X 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 X Annex IV

No. of exemption in Annex III or IV where applicable: Entry 41

Proposed or existing wording: *Lead as a thermal stabilizer in polyvinyl chloride (PVC) used as base material in amperometric, potentiometric and conductometric electrochemical sensors which are used in in-vitro diagnostic medical devices for the analysis of blood and other body fluids and body gases.*

Duration where applicable: 31st December 2018

☐ Other: _____

3. Summary of the exemption request

Instrumentation Laboratory is a leading manufacturer of equipment used for analysis of critical care analytes in 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 diagnostic medical analyzers 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 family is the sensor card where the electrochemical measurements of the above analytes take place. Due to the complex electrochemical processes in the sensor card, it has not been possible to find a stabilizer other than lead that works, without affecting analytical performance of analyte measurements using our GEM Premier 3000/3500/4000/5000 instruments, thereby impeding the intended function of the GEM Premier analyzers.

In addition, the results of the Life Cycle Assessment show that the Current GEM Sensor Card performs better in environmental terms than the potential alternatives.

Continued use of lead in the sensor card of the GEM Premier analyzers is required while the search continues for an alternative stabilizer. The alternative stabilizer must not interfere with measurement of any analyte on the system over the claimed product shelf life (up to 9 months at room temperature) and use life (up to 4 weeks in the analyzer).

We respectfully request that this application for renewal of 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. Meanwhile, we have an active project plan and are diligently researching new stabilizers compliant to RoHS.

Instrumentation Laboratory kindly invites the European Commission and the EU Member States to review this application for renewal of 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 Family of Critical Care Analyzers.

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

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

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

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)

X Pb ☐ Cd ☐ Hg ☐ Cr-VI ☐ PBB ☐ PBDE

3. Function of the substance: Lead as a thermal stabilizer in polyvinyl chloride (PVC) used as base material in amperometric, potentiometric and conductometric electrochemical sensors

4. Content of substance in homogeneous material (%weight): 2,7% (GEM Premier 4000 Cartridge) and 6,6% (GEM Premier 3000, 3500 and 5000 Cartridge)

5. Amount of substance entering the EU market annually through application for which the exemption is requested: 48.14 kg.

Please supply information and calculations to support stated figure.

Based on the 2017 forecast for GEM Premier cartridge shipments to the EU, the estimated total amount of lead contributed to the EU by the sensor card will be 48.14 kg.

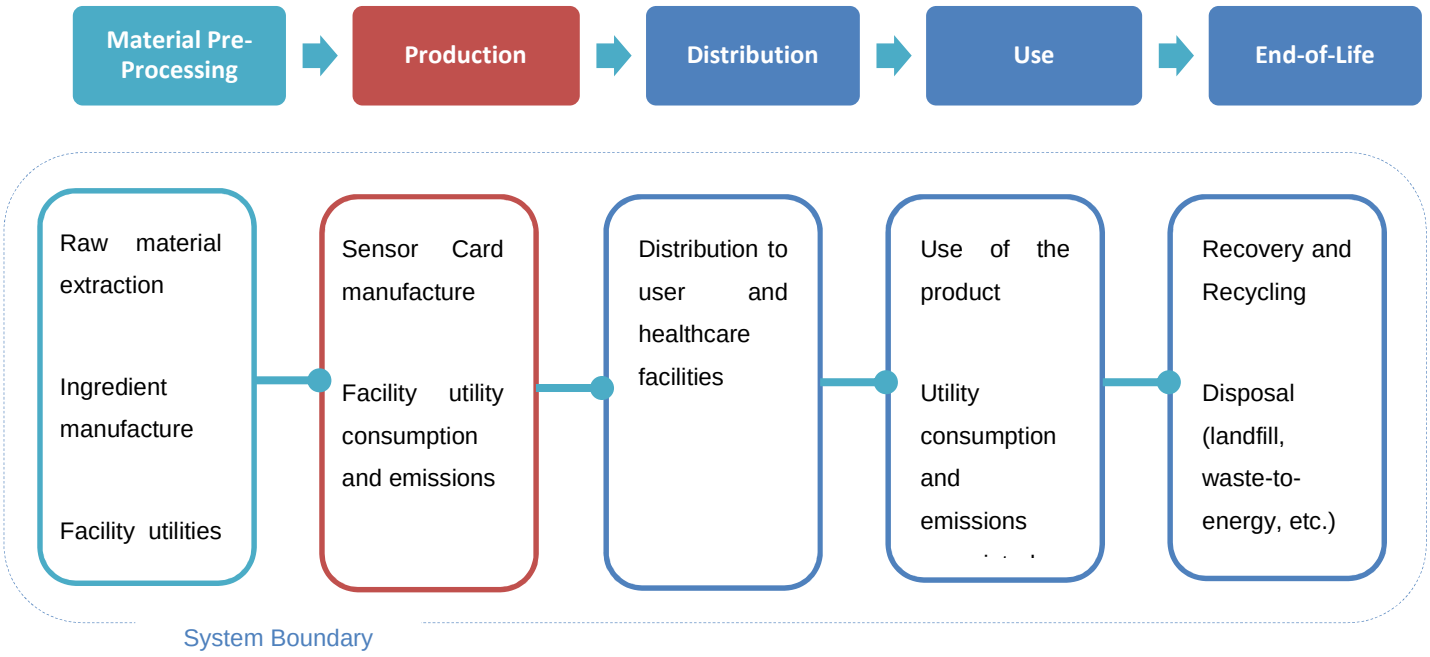
6. Name of material/component: Polyvinyl chloride (PVC) used as base material in amperometric, potentiometric and conductometric electrochemical sensors. Please refer to specific information provided in point b) of the Application document dated 15th May submitted by Instrumentation Laboratory.

Environmental Assessment: A report providing an analysis of the current GEM Card and identified alternatives from a Life Cycle Assessment perspective is included as Appendix F.

The analysis provided in the Life Cycle Assessment (LCA) report is based on a scientific method quantifying the environmental impacts of the Card and the alternatives. The LCA investigates the whole life cycle, from extraction of raw materials, processing and transport, through product manufacture, use and disposal/recycling. At each of these stages, inputs (energy and materials used), and outputs (the products made and emissions released) are measured. These are then summed up to show the total energy and materials used, and emissions released. These energetic and physical material results are then converted into environmental impact measures, such as global warming potential (carbon footprint). In this way, the environmental performance of a product can be analyzed in a quantified way, and, if required, compared with other products in an unbiased, scientific way.

The LCA report produced as part of this exemption application is contained in the Appendix F and is summarized here. The LCA was prepared in accordance with the ISO standard ISO 14044: 2006 Environmental Management – Life Cycle Assessment – Requirements and Guidelines. The LCA analyzed the current card, compared with two potential alternative cards. The results are shown for 1 GEM Premier 3000/3500 Sensor Card (the product).

The whole life cycle of the product was analyzed:



The LCA made the following assumptions:

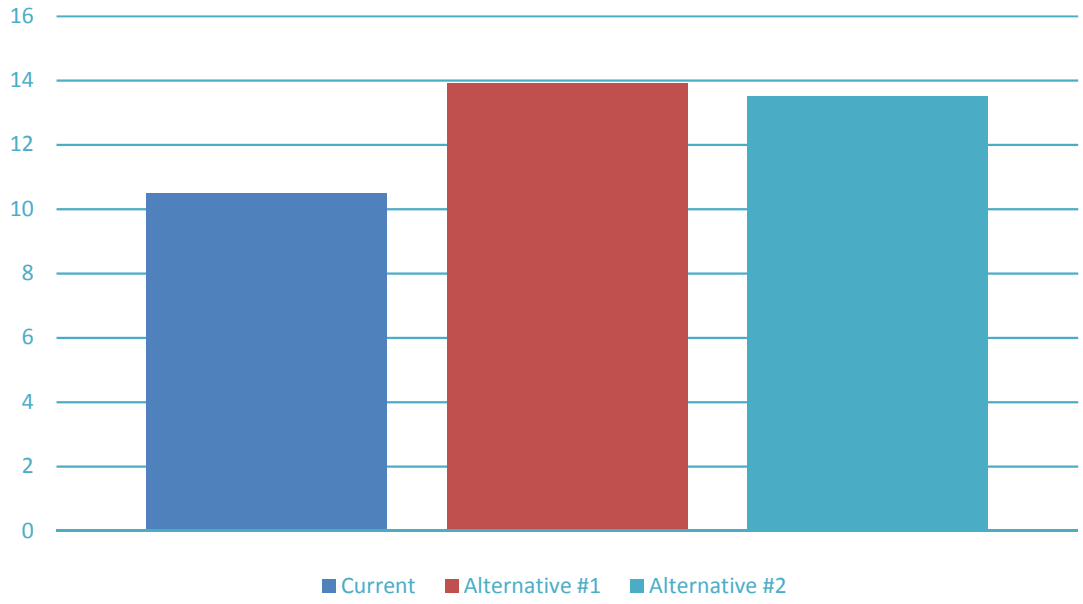
- The card is manufactured in the US, and used in Europe
- The current card and the two alternatives are all assumed to provide the same functionality and lifespan
- Both potential alternative cards contain an Organic Based Stabilizer (OBS) to replace the lead in the current card

The results of the LCA are as follows:

Carbon Footprint, a common term for Global Warming Potential (GWP), is a recognized measure of Greenhouse Gas (GHG) impact. The life cycle carbon footprint of 1 card is summarized below for the three options:

- Current card: 10.5 gCO2 eq.
- Alternative card 1: 13.9 gCO2 eq.
- Alternative card 2: 13.5 gCO2 eq.

The chart below illustrates the carbon footprint comparison between the current card material configuration and the two alternatives.



Carbon Footprint, Three GEM Premier Sensor Card versions

The carbon footprint results show that the current card has a carbon footprint of 10.5 gCO2eq, compared with 13.9 and 13.5 for the two alternatives (lower carbon footprint is better). The carbon footprint of the current card is 22% lower than the next lowest card.

The LCA also analyzed other environmental measures as shown in the Appendix F. Considering 23 environmental impact measures, the current card was found to have the lowest environmental impacts in 20 categories, and the highest in the remaining 3 categories. The current card was found to consume less energy in its production, distribution, use and disposal than both alternative cards.

LCA methodology focuses on environmental (ecological) impacts rather than human toxicology. However, the European LCA methodology used in this LCA does provide one approximate general human health parameter termed Human Toxicity. All three card configurations showed Human Toxicity results within the same order of magnitude. To further investigate human health issues, another LCA methodology was also applied, the US Environmental Protection Agency (EPA) methodology. This showed that the combined Human Toxicity values were not significantly different for the three cards, supporting the European methodology results.

In conclusion, the overall results of the LCA show that the Current GEM Premier Sensor Card has lower environmental impacts in most environmental impact

categories. The carbon footprint of the current card is lower than that of both alternative cards.

Based on the results of the LCA, the current GEM Premier Sensor Card performs better in environmental terms than the potential alternatives.

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 sensor card is a vital component in the cartridges of the GEM Premier family of Critical Care Analyzers. The GEM analyzer is used for blood testing and serves as a critical analytical instrument in hospital labs, operating rooms, emergency rooms and point of care at bedside across the Global and EU Health Care Sector. Blood testing is a core element to virtually all diagnostic and therapeutic procedures carried out in the Health Care Sector today.

The disposable cartridge functions as the heart of the GEM Premier analyzer where the actual testing process takes place. The sensor card is the primary unit of the cartridge and is the location of all electrochemical sensors which the GEM Premier systems use for measuring and reporting concentrations of critical care analytes in blood.

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, and the same molded card has been carried forward to the currently manufactured analyzers (GEM Premier 3000, GEM Premier 3500, GEM Premier 4000 and GEM Premier 5000). The sensor card is located in the disposable cartridge which is used in these instruments. Electrochemical sensors for the following critical care analytes are located on the sensor card: partial pressure of oxygen and carbon dioxide (pO2 and pCO2), pH, Na+, K+, Ca++, Cl-, glucose, lactate and hematocrit.

PVC has specific advantages as a sensor card material for the electrochemical sensors used in the GEM Premier products. Sensing 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, which is a critical requirement for sensors to have long use life and shelf life.

The PVC sensor card is produced by injection molding. Lead compounds have been traditionally used as a thermal stabilizer to prevent breakdown of the polymer at the high temperatures required for the injection molding process. We have determined that

the presence of lead in the PVC sensor card does not interfere with measurement of any analytes on the GEM Premier family of analyzers. In fact, recent testing has shown that presence of lead in the plastic sensor card appears to enhance performance and is required for proper functioning of certain sensors deposited on the PVC sensor card; specifically, pO2, glucose, lactate and hematocrit. However, alternative thermal stabilizers, such as those including tin, have been tested and shown to produce interference, especially with measurement of electrolytes.

Data from the GEM Premier family of critical care analyzers are used daily in hospitals around the world to make life-saving decisions regarding patient health. It is imperative that these data have the highest possible reliability and accuracy. This consideration was acknowledged by the EU Commission when the current exemption was adopted.

The sensor card in the cartridge of the GEM Premier analyzers is the heart of the analyzer, where sensors for measuring concentrations of critical care parameters in blood are located. For the GEM Premier analyzers to continue to provide patient blood data with uncompromised reliability and accuracy, continued use of lead in the sensor card of the GEM Premier analyzers is required while the search continues for an alternative thermal stabilizer.

The alternative stabilizer must not interfere with measurement of any analyte, and must meet established product claims for the GEM Premier systems over the claimed cartridge shelf life (up to 9 months at room temperature) and use life (up to 4 weeks 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?

Compared to other existing technologies on the market today (Examples of competing equipment are Siemens RapidPoint 500 and Roche Cobas 123) the GEM Premier analyzers offer several advantages:

1. The GEM analyzers utilize 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, improve significantly patient safety by

producing rapid and correct results thereby reducing the need for user interpretation of results and the need for 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 analyzers are the only systems of their kind to offer a single, disposable measurement cartridge which can be stored up to 9 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 family of analyzers is 100% tested at the factory to assure 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.

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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 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 48.14 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 family of analyzers as a component with a content of Lead exceeding the maximum concentration value of 0.1% as defined in Annex II of RoHS. Lead is present in the PVC resin of the sensor card to act as a thermal stabilizer and prevent breakdown of the PVC resin during the high temperature injection molding process required to produce the sensor card.

During the existing exemption period, Instrumentation Laboratory has been actively working to replace lead as a thermal stabilizer in the PVC sensor card as this was the basis of the initial exemption. 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 renewal of the exemption to allow additional time to complete this work at the same time assuring uninterrupted supply to the EU healthcare sector of equipment critical to providing optimum care of critically ill patients.

An unexpected finding of the work completed until now was that replacement of lead as a thermal stabilizer in the PVC resin of the sensor card resulted in deterioration in performance of several parameters measured by the GEM Premier analyzer. We

therefore conclude that presence of lead in the PVC sensor card is enhancing 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 lead with an alternative RoHS-compliant thermal stabilizer, especially with respect to precision of the glucose sensor and pO2 sensor sensitivity (slope).

At present, the search continues for an alternative, RoHS compliant thermal stabilizer 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 proposed In Vitro Diagnostics Device Regulation (Interinstitutional File: 2012/0267 (COD) - Adoption of a REGULATION OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL on in vitro diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU - IVDR) on 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 performances in terms of analytical sensitivity, diagnostic sensitivity, analytical specificity, diagnostic specificity, accuracy, repeatability, reproducibility, including control of known relevant interference, 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.

Based on our evaluations we conclude that this application for renewal of an exemption falls within all three categories as established in Article 5(1)(a) with respect to the possibility to substitute the use of lead as a stabilizer 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.

With respect to the above criteria, Instrumentation Laboratory is working in close cooperation with commercial suppliers of PVC materials, academic institutions specializing in polymer chemistry and private consultants to identify alternative thermal

stabilizers for PVC. These efforts have produced some promising candidates including several organic-based stabilizers and stabilizers based on zinc or calcium-zinc.

Several initial candidates, considered as thermal stabilizers to replace lead in the sensor card, have been investigated and shown to produce: deterioration in accuracy of the sodium sensor, decreased sensitivity of the oxygen sensor, and increased imprecision for measurement of glucose, lactate and hematocrit in blood on the GEM Premier family of instruments.

The EU Directive 98/79/EC on in vitro diagnostic medical devices specifically mandates that a manufacturer must meet its product claims for analytical sensitivity, diagnostic sensitivity, analytical specificity, diagnostic specificity, accuracy, repeatability, reproducibility, including control of known relevant interference, and limits of detection.

Therefore the investigated alternative stabilizers are not technically practical or viable alternatives at this time as they impede the reliability of test results carried out with the sensor card, thereby preventing the analyzer from performing its intended function within established product claims.

However, some of these alternative PVC thermal stabilizers, when used in addition to minimal quantities of Lead in concentrations below 0.1% in the sensor card (i.e. Lead in a concentration below the limit specified by the EU RoHS directive), have shown results moving in a positive direction to address the performance problems seen with the alternative thermal stabilizers alone. The focus of continued investigations includes optimizing the selection of an alternative thermal stabilizer in addition to presence of 0.098% lead in the PVC resin of the GEM Premier sensor card. See Section g for detailed technical information concerning failure modes seen for the alternative thermal stabilizers with and without addition 0.098% lead and plans for future direction.

As stated previously, the, GEM Premier 3000, GEM Premier 3500, GEM Premier 4000 and GEM Premier 5000 instruments are critical care instruments used in

hospital laboratories, operating rooms, emergency rooms and point of care at bedside. The cartridges that these instruments use (which contain lead in the sensor card) are integral to the diagnosis and treatment administered to critically ill patients, based on results from these analyzers.

Although the search for practical and viable alternatives is on-going, Instrumentation Laboratory must continue to manufacture the current sensor card using lead as a stabilizer until a new, non-lead stabilizer is successfully identified, with performance equivalent to currently manufactured product.

As noted above under Point 4(A)(6) the overall results of the Life Cycle Analysis show that the Current GEM Premier Sensor Card has lower environmental impacts in most

environmental impact categories. The carbon footprint of the current card is lower than that of both alternative cards.

Based on the results of the LCA, the current GEM Premier Sensor Card performs better in environmental terms than the potential alternatives.

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

Continued use of lead in the sensor card of the GEM Premier cartridge is required while the search continues for an alternative stabilizer with performance characteristics equivalent to currently manufactured product. The alternative stabilizer must not interfere with measurement of any analyte on the system over the claimed product shelf-life (up to 9 months at room temperature) and use-life (up to 4 weeks in the analyzer).

Instrumentation Laboratory, as referenced in previous studies in Section (A), is continuing to search 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 looking at 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 lead as a stabilizer in the PVC material of the sensor card across the entire GEM Premier product line will be concluded within the coming 7 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: 1) In-house proof of performance testing reports for sensor cards in each GEM product platform, carried out to prove the RoHS compliant sensor cards meet product analytical performance claims throughout the claimed GEM cartridge shelf life and use life, and 2) Clinical testing conducted at customer sites to assure each GEM platform continues to meet product claims and customer expectations in the hands of intended users.

During the time since the original exemption was granted, Instrumentation Laboratory has gained information about specific failure modes resulting from replacement of lead

as a thermal stabilizer 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. The final resin will likely contain 0.098% lead in the form of tribasic lead sulfate, in addition to a RoHS compliant thermal stabilizer which we will select based on the optimized analytical performance. We are confident as to the ultimate success of this project, within the Table 3 timeline.

In conclusion, the substitution of lead in the sensor card cannot be completed before the expiration date of the current exemption. This application is therefore being submitted to extend the 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.

Table 2 shows milestones listed in the project plan submitted in our original exemption application. Also, included in the table is the progress (% Complete column) made towards each milestone.

Table 2: Original Project Plan

Name	Start	Finish	% Complete
Design Controls	November 14, 2011	November 30, 2011	100%
Formulation and Molding Color master resin	September 16, 2011	January 31, 2012	100%
Performance Verification	December 6, 2011	May 28, 2012	100%
Formulation and Molding Teknor Apex resin	May 29, 2012	August 19, 2013	100%
Review of Performance Teknor Apex Stabalizers	January 11, 2013	January 24, 2013	100%
Stablizer Down Selection	January 25, 2013	January 29, 2013	100%

Mold Optimization on selected resin	January 30, 2013	March 6, 2013	100%
Validation Planning	January 30, 2013	February 12, 2013	100%
POP & Beta	January 31, 2013	February 20, 2013	0%
Card Manufacture (drilled)	February 13, 2013	March 4, 2013	100%
ELM Testing (3 rounds)	March 5, 2013	December 4, 2013	0%
Alpha Beta Testing	November 18, 2013	September 8, 2014	37%

The critical milestone for the completion of original project plan was dependent on successful testing (Alpha Beta Testing milestone in Table 2) using sensor cards molded with RoHS compliant resins supplied by the Teknor-Apex Corp. However, in our internal and external clinical testing we found that the precision and bias of Glucose and Lactate sensors along with pO2 sensor slopes (sensitivity) did not meet our requirements. Because of these technical issues, we continued exploring new resin materials. For detailed information of test results see attached Appendix B.

A new project plan is shown in Table 3 (***See below Point 7(B)***). Instrumentation Laboratory has been working with the companies and consultants shown in Table 4, screening many potential RoHS-compatible resin candidates for: (1) physical and mechanical properties required to produce the sensor card by injection molding, and (2) chemical compatibility of the resins with sensor formulations on sensor cards across all our GEM Premier Instrument platforms. Only the most promising resin candidates

were considered for the formal evaluations based on the revised project plan shown in Table 3.

See attached Appendices B - E for detailed information.

Appendix B: **Testing Summary for GEM Premier Systems with Sensor Card Resins Compliant with Directive 2011/65/EU,** includes the following information:

- A list of PVC card resins containing alternative thermal stabilizers tested since 2012, the stabilizers they contain and performance of these materials during testing on GEM Premier systems
- Card resins currently under test and new candidate materials to be tested
- Results of literature searches conducted
- Since testing of PVC resins containing alternative thermal stabilizers was started in 2012, the following is a summary of the findings from experimental work conducted at Instrumentation Laboratory:
    - All RoHS compliant resins had decreased sensitivity (slope) of the pO2 sensor.
    - All resins containing organo-tin compounds resulted in deterioration in accuracy of the GEM Premier sodium sensor outside of product specifications. In addition, thioorgano-tin compounds resulted in increased glucose and lactate sensor imprecision outside of GEM Premier product specifications.
    - CaZn stearate and Zn stearate stabilizers resulted in increased glucose and lactate sensor imprecision outside of product claims. These stabilizers also resulted in decreased pCO2 sensor slope (sensitivity).
    - The majority of PVC resins containing organic based stabilizers (OBS) resulted in increased glucose and lactate sensor imprecision outside of product claims. However, two resins containing OBS stabilizers (Teknor Apex 8009B-1 and 8009B-2), considered proprietary formulations by the Teknor Apex Corp., passed specifications for glucose and lactate imprecision, but were significantly worse than that of production resin containing lead thermal stabilizer. Results were close to the limit and are considered at risk for not meeting product specifications with normal variation in product performance.
    - Color Master 1304 resin, containing various thermal stabilizers *plus* 0.098% lead (in the form of tribasic lead sulfate, TBLS) met product specifications, however even these formulations were significantly worse than that of production resin containing lead thermal stabilizer.

Results were close to the limit and are considered at risk for not meeting product specifications with normal variation in product performance.

- Conclusions from testing conducted on GEM Premier systems:
    - No RoHS-compliant resin has yet demonstrated acceptable performance for all sensors, although resins containing 0.098% lead have shown improved performance.
    - The consistency of negative impact on glucose and lactate precision and loss of pO2 sensor slope (sensitivity) across tests of different RoHS-compliant resins containing various thermal stabilizers, leads us to conclude that the problem is likely from the reduction of lead rather than from addition of some unknown interfering substance.
- Future evaluation will include multiple paths explored in parallel, as explained in further detail in Table 3 and Appendix C and D:
    - Design and Process optimizations are in progress for the best RoHS-compliant resin identified to date (Color Master 1304 + 0.098% lead).
    - In parallel, exploration will continue to optimize the RoHS compliant resin formulation to better align performance with that of the current production sensor card. While the above resin may be able to achieve minimum requirements, attempts will continue to minimize performance losses as compared to the current production resin.
        - Root cause analysis will continue to understand the contribution of lead, even in small quantities, to the physical and chemical properties of the sensor card.
        - Other RoHS-compliant compounds that can generate similar properties to lead will be explored as co-stabilizers.
        - If feasibility testing identifies a new compound with performance that can equal current production, then work will proceed with the new resin.
    - Once optimizations are complete, the required process and design verification and validation activities will commence. These activities include:
        - Evaluation of Risk to all design and process requirements impacted by the change
        - Process Validations of all impacted processes at suppliers and internally
        - Complete system design verifications and validations, including real time shelf life of all impacted products as well as clinical trials within critical care units with patient samples
        - Submission and approval of changes to regulatory bodies of every region impacted by this change
    - The extensive verification and validation required by our Design Control procedures will ensure performance does not adversely affect the safety

or effectiveness the device, and is necessary to maintain compliance with Directive 98/79/EC, cf. Article 3 and Annex 1. This is the focus of the Project Plan and Schedule contained in Appendix C and D, with distribution planned for 2022.

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

Appendix C and Appendix D: RoHS Compliance of GEM Sensor Card Resin Project Plan and RoHS Compliance of GEM Sensor Card Resin Project Schedule, respectively.

Table 3 shows milestones and timeline for executing revised project plan. Please note that we plan to complete updating the CE technical file in January 2022. For executing this project plan we have allocated 2 full time employees and committed in excess of $2.5mm (USD) from 2017 until the end of 2021 and we are committed to provide more resources as and when needed for the success of this project in timely fashion.

Table 3: Revised Project Plan. Duration column represents number of working days for each activity and start/finish dates columns include non-working days except Shelf Life testing.

Task Name	Duration (number of working days)	Start	Finish	% Complete
RoHS Compliance of GEM Sensor Card Resin	**1975 days**	**September 8, 2014**	**April 1, 2022**	**21%**
Procure vendors and resin materials	**180 days**	**September 8, 2014**	**May 15, 2015**	**100%**
Procure vendors and raw materials	90 days	September 8, 2014	January 9, 2015	100%
Mold and prepare sensor cards	90 days	January 12, 2015	May 15, 2015	100%
Screen new resin candidates	**330 days**	**May 18, 2015**	**August 19, 2016**	**100%**
Evaluate new resin candidates	180 days	May 18, 2015	January 22, 2016	100%
Optimize internal processes	90 days	January 25, 2016	May 27, 2016	100%
Data analysis and review	60 days	May 30, 2016	August 19, 2016	100%
Feasibility	**220 days**	**August 22, 2016**	**July 07, 2017**	**90%**
Select Top 2 resin candidates using GEM 3000	90 days	August 22, 2016	December 23, 2016	100%
Cartridge use life study GEM 3000	30 days	December 26, 2016	February 3, 2017	100%
Cartridge use life study GEM 4000	30 days	March 20, 2017	April 28, 2017	100%
Cartridge use life study GEM 5000	30 days	May 23, 2017	June 23, 2017	50%
Select top resin candidate (Data analysis and review)	10 days	June 26, 2017	July 07, 2017	0%
Design and Process Optimization	**270 days**	**June 26, 2017**	**July 6, 2018**	**0%**

Compounding and evaluation of new co-stabilizers with top resin using GEM 3000 candidate	90 days	June 26, 2017	October 27, 2017	0%
Cartridge use life study GEM 4000 - Optimized resins	30 days	October 30, 2017	December 8, 2017	0%
Cartridge use life study GEM 5000 - Optimized resins	30 days	December 11, 2017	January 19, 2018	0%
Data analysis and review to select top candidate	30 days	January 22, 2018	March 2, 2018	0%
Improve internal processes to get optimal performance of top resin candidate	90 days	March 5, 2018	July 6, 2018	0%
Pre-POP GEM 3000 and 4000	30 days	March 5, 2018	April 13, 2018	0%
Pre-POP GEM 5000 and ChemSTAT	30 days	April 16, 2018	May 25, 2018	0%
Data analysis	10 days	May 28, 2018	June 8, 2018	0%
Formal Design Review	5 days	June 25, 2018	June 29, 2018	0%
Process Validation - Resin Compounding	90 days	March 5, 2018	July 6, 2018	0%
Process Validation - Sensor Card Molding	**240 days**	**April 16, 2018**	**March 15, 2019**	**0%**
Mold Validation GEM 3000 sensor card	60 days	April 16, 2018	July 6, 2018	0%
Mold Validation GEM 4000 sensor card	60 days	July 9, 2018	September 28, 2018	0%
Mold Validation GEM 5000 sensor card	60 days	October 1, 2018	December 21, 2018	0%
Mold Validation GEM ChemSTAT sensor card	60 days	December 24, 2018	March 15, 2019	0%
Shelf Life	**240 days**	**June 30, 2018**	**February 24, 2019**	**0%**
Shelf life GEM 3000 sensor card	8 mons	June 30, 2018	February 24, 2019	0%
RoHS Compliance of GEM Sensor Card Resin	**1975 days**	**September 8, 2014**	**April 1, 2022**	**21%**
Procure vendors and resin materials	**180 days**	**September 8, 2014**	**May 15, 2015**	**100%**
Procure vendors and raw materials	90 days	September 8, 2014	January 9, 2015	100%
Mold and prepare sensor cards	90 days	January 12, 2015	May 15, 2015	100%
Screen new resin candidates	**330 days**	**May 18, 2015**	**August 19, 2016**	**100%**
Evaluate new resin candidates	180 days	May 18, 2015	January 22, 2016	100%
Optimize internal processes	90 days	January 25, 2016	May 27, 2016	100%
Data analysis and review	60 days	May 30, 2016	August 19, 2016	100%
Feasibility	**220 days**	**August 22, 2016**	**June 23, 2017**	**75%**
Select Top 2 resin candidates using GEM 3000	90 days	August 22, 2016	December 23, 2016	100%
Cartridge use life study GEM 3000	30 days	December 26, 2016	February 3, 2017	100%
Cartridge use life study GEM 4000	30 days	March 20, 2017	April 28, 2017	75%
Cartridge use life study GEM 5000	30 days	May 1, 2017	June 9, 2017	0%
Select top resin candidate (Data analysis and review)	10 days	June 12, 2017	June 23, 2017	0%
Design and Process Optimization	**270 days**	**June 26, 2017**	**July 6, 2018**	**0%**
Compounding and evaluation of new co-stabilizers with top resin using GEM 3000 candidate	90 days	June 26, 2017	October 27, 2017	0%
Cartridge use life study GEM 4000 - Optimized resins	30 days	October 30, 2017	December 8, 2017	0%
Cartridge use life study GEM 5000 - Optimized resins	30 days	December 11, 2017	January 19, 2018	0%

Data analysis and review to select top candidate	30 days	January 22, 2018	March 2, 2018	0%
Improve internal processes to get optimal performance of top resin candidate	90 days	March 5, 2018	July 6, 2018	0%

Appendix E: Comparison of Material Properties of Apex RM 8009 B NT1 Grey 3141 with CMX 2151 Grey 10 & JLD 91221 for GEM Family Sensor Card Material Replacement by Xiujun Wang

• Appendix E, Section 9 provides test results for mechanical properties important for proper resin formulation and molding of the current production sensor cards using PVC resins from Color Master Inc. and Zhejiang Jinlida Plastics Co. The RoHS compliant replacement resin which is ultimately selected should show similar mechanical properties as the production resins. Appendix E shows such data for only one possible resin candidate (Apex RM 8009B) and is not intended to be a comprehensive review of mechanical properties of all the RoHS compliant resins under consideration.

In addition to the information listed in Appendix B, since the original 2012 application for exemption for the GEM Premier sensor card, Instrumentation Laboratory has

engaged the services of the following companies and consultants in an effort to replace lead as a thermal stabilizer in the PVC sensor card.

Table 4: Companies and Consultants Engaged by Instrumentation Laboratory to Replace Lead as a Thermal Stabilizer in the GEM Premier Sensor Card

Company or Consultant	Contribution to Sensor Card Project
Teknor-Apex Co., Pawtucket, RI	Compounded RoHS-compliant resins for evaluation
Color Master Inc., Butler, IN	Compounded RoHS-compliant resins for evaluation
Zhejiang Jinlida Plastics Co. Lanxi, Zhejiang, China	Compounded RoHS-compliant resins for evaluation
SMC Corp., Devens, MA	Molding house which produced sensor cards using RoHS-compliant PVC resins
Premier Polymers & Processing Consultants Inc., Algonquin, IL	Provided consultation in formulating RoHS-compliant PVC resins
Polymer Diagnostics Inc. Avon Lake, OH	Tested thermal stability of RoHS-compliant PVC resins
Jordi Labs, Mansfield, MA	Provided testing services, particularly molecular weight determinations and chemical compatibility studies of RoHS-compliant PVC resins
Intertek Plastics Technology Laboratory Pittsfield, MA	Tested mechanical properties of RoHS-compliant PVC resins such as tensile strength, impact resistance, density and rheology
Akron Rubber Development Laboratory Akron, OH	Tested oxygen permeability of RoHS-compliant PVC resins
Nano Composix, San Diego, CA	Tested zeta potential (surface charge) of RoHS-compliant PVC resins
SEM Tech Solutions, N. Billerica, MA	Examined sensor cards made with RoHS-compliant PVC resins for physical features (sensor pin heights and gaps around pins) and measurements of leaching of contaminants from resins into glucose and lactate sensing membranes
Inspection Plus, Three Rivers, MI	Provided first article inspection of sensor cards molded with RoHS-compliant PVC resins vs. dimensional specifications

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 stabilizers must not impede the reliability of test results carried out with the sensor card as the alternative stabilizers 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:

…

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:

…