Exemption Request Form

Non-confidential

Date of submission: 20th January 2022 – update 15th September 2023

1. Name and contact details

1) Name and contact details of applicant:

Company:	Werfen	Tel.:	+1 (781)861-4505
Name:	David Landis	E-Mail:	dlandis@werfen.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:

☐ Request for amendment of existing exemption in

X Request for extension of existing exemption in: Annex III, no. 7(c)-I

☐ 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: *Electrical and electronic components containing lead in a glass or ceramic other than dielectric ceramic in capacitors, e.g., piezoelectronic devices, or in a glass or ceramic matrix compound, which are used in in-vitro diagnostic medical devices for the analysis of whole blood.*

Duration where applicable: 5 years

☐ Other: _____

3. Summary of the exemption request

Werfen 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.

Werfen manufactures the suite of 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.

Based on the GEM Premier 5000 Werfen is currently in the process of developing an instrument incorporating a piezoceramic material. The Piezoceramic material is a vital component in the cartridges of the GEM Premier 5000 MARS used for measuring and reporting concentrations of critical care analytes in blood (pO2, pCO2, pH, Na+, K+, Ca++, Cl-, glucose, lactate and haematocrit). Lead is part of the Piezoceramic material of the piezoelectric transducer used to create acoustic power in a microfluidic detection flow chamber to separate plasma from whole blood patient samples by acoustofluidic separation. The purity and viability of the separated blood constituents is critical for diagnostic accuracy and for the therapeutic efficacy as well.

Any change in the Piezoceramic material can directly impact analytical performance characteristics and thereby impede the intended function of the GEM Premier 5000 MARS analyzer.

For the GEM Premier 5000 MARS analyzer to provide patient blood data with uncompromised reliability and accuracy, continued use of Lead in the Piezoceramic material of the GEM Premier 5000 MARS analyzer is required while the search continues for alternative substances.

The core obligation for our product in terms of meeting current EU requirements for diagnostic medical analyzers is limiting the use of alternative lead-free PZT material. Currently there is no lead-free material on the market meeting our product requirements with equivalent performance. Despite the achieved improvement in piezoelectric

properties, there are problems in the synthesis, processing and poling of the sintered ceramics.

For the reasons outlined above the substitution of Lead in the Piezoceramic material cannot be completed before the date of applicability of the restriction on use of Lead according to the RoHS Directive.

As noted above under Point 4(A)(6) the results of the LCA shows that Lead in certain aspects have a better environmental performance when compared to the environmental performance of the potential alternative materials.

We respectfully request that this application for an extension of the current exemption be approved, as the piezoceramic material is an important part of our instrument. 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 evaluating new piezoceramic materials compliant to RoHS.

Werfen 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 Piezoceramic material used in Cartridges for the GEM® Premier 5000 (MARS) with iQM.

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: 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)

X Pb ☐ Cd ☐ Hg ☐ Cr-VI ☐ PBB ☐ PBDE

☐ DEHP

3. Function of the substance: Lead as a constituent of piezoceramic material in piezoelectric transducer used to create acoustic power in a microfluidic detection flow chamber to separate plasma from whole blood patient samples by acoustofluidic separation.

4. Content of substance in homogeneous material (%weight):
5. Amount of substance entering the EU market annually through application for which the exemption is requested: 0,1 - 5 kg.

Please supply information and calculations to support stated figure.

6. Name of material/component: piezoceramic material with Lead zirconate titanate (PZT) used as piezoelectric transducer. Please refer to specific information provided below in point b).

Environmental Assessment:

Intertek has carried out an environmental Life Cycle Assessment (LCA) of Lead and alternatives for Lead used or potentially used in electronic piezo components.

Currently Lead is used in an electronic piezo component of blood analysis equipment. The alternatives considered to replace Lead in the component are … or .... All substances are expected to have the same weight to perform the same function.

The LCA was performed with guidance from *ISO 14040: Environmental Management – Life Cycle Assessment – Principles* and *Framework and ISO 14044: Environmental Management – Life Cycle Assessment – Requirements and Guidelines* [1]. A separate full LCA report provides a complete set of LCA methodological details as required by the ISO standards, summarised here.
The LCA study evaluates the environmental impacts at various stages of the life cycle of the three additives. Material and energy inputs and outputs are identified through the life cycle of the substances, summed up, and converted to measures of environmental impact. This permits quantified data analysis of environmental advantages and identification of opportunities to reduce environmental impacts.

The primary goal of the LCA study is to provide an analysis of the environmental impacts of the substances. The functional comparison is Lead additive versus the … and .... Each substance is considered to require the same amount in order to achieve similar results of replacing lead:

- **Lead 1 gram**

or

- **… 1 gram**

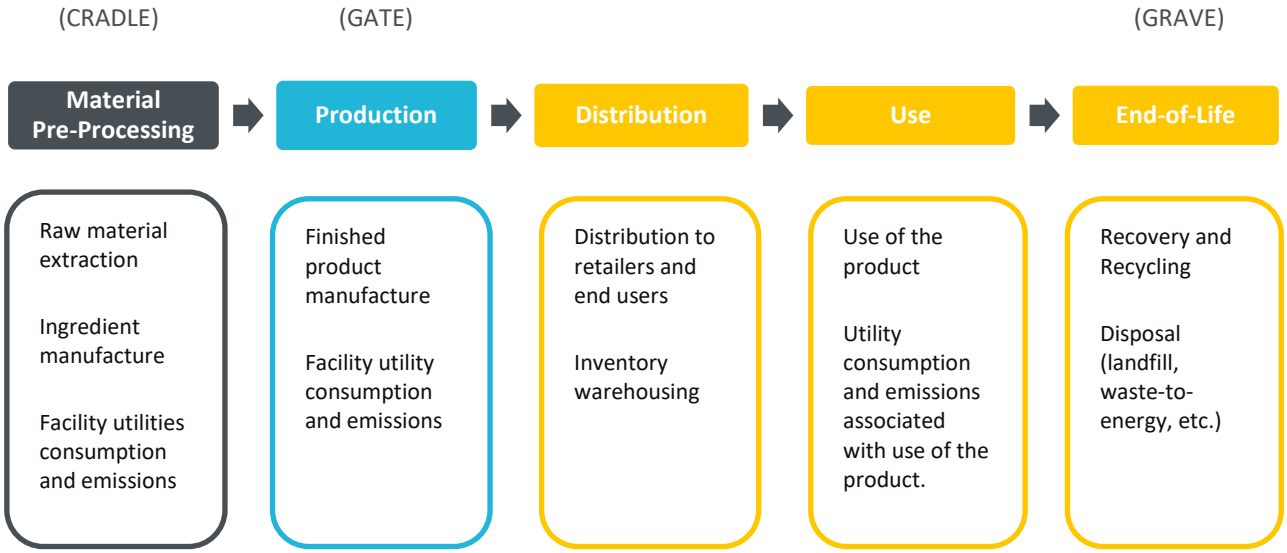
or

- **… 1 gram**

The relevant substances have been modelled in the weights as per above. In LCA terms, the functional unit is one gram of each substance.

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 additives. The rest of the electronic piezo component is not included. Operation of the equipment, such as electricity use during blood analysis, is not included.



Intertek utilised SimaPro 9.11 LCA software [2] to carry out the LCA, with data primarily from the Ecoinvent 3.6 database [3]. The data in these built-in resources were applied for commonly used materials, products and processes when internationally accepted generic information or secondary data is required for the study. The Ecoinvent 3.6 database is one of the most comprehensive and reliable resources for LCA data available globally.

While raw material and sub-component data sets within the Ecoinvent 3.6 database [3] typically include raw material extraction, transport, infrastructure, emissions, waste and energy use, they do not include any packaging and/or palletizing that is applied to sub-components in their transport to the finished product manufacturer. All input information is assumed to be as accurate as possible at the time of the study. For materials not being present in the Ecoinvent 3.6 database [3] the following assumptions have been made:

…

As the end electronic piezo component is to be used in Europe, a European waste scenario has been assumed for end-of-life processing. The Netherlands has been chosen as a reference country because Ecoinvent has data for the Netherlands.

The study limitations are considered to be as follows:

- Due to the inherent limitations of LCA methodology, this study should not be used as the sole source of environmental information on the materials and processes modelled. There may be other environmental issues outside the remit of LCA. This LCA has been performed according to best practices in modelling and allocation.
- Due to the limitation of some substances that were not available within the Ecoinvent database, these were created based on chemical composition information and desktop research.

- Intertek has not independently tested or verified that the stated quantities of alternative substances are in reality an accurate functional equivalent to the stated amount of Lead.

Results

Results are as follows:

ReCiPe impact assessment LCA results for the additives per gram
(ReCiPe is often considered to be the leading LCA method and reports a general range of environmental impacts):

Impact category	Unit	Lead
Global warming	kg CO2 eq	0.0020189551
Stratospheric ozone depletion	kg CFC11 eq	0.0000000014
Ionizing radiation	kBq Co-60 eq	0.0000102086
Ozone formation, Human health	kg NOx eq	0.0000054345
Fine particulate matter formation	kg PM2.5 eq	0.0000088323
Ozone formation, Terrestrial ecosystems	kg NOx eq	0.0000055084
Terrestrial acidification	kg SO2 eq	0.0000257259
Freshwater eutrophication	kg P eq	0.0000001400
Marine eutrophication	kg N eq	0.0000000907
Terrestrial ecotoxicity	kg 1,4-DCB	0.0758363440
Freshwater ecotoxicity	kg 1,4-DCB	0.0000660135
Marine ecotoxicity	kg 1,4-DCB	0.0001197735
Human carcinogenic toxicity	kg 1,4-DCB	0.0004877225
Human non-carcinogenic toxicity	kg 1,4-DCB	0.0298154890
Land use	m2a crop eq	0.0000980120
Mineral resource scarcity	kg Cu eq	0.0026434691
Fossil resource scarcity	kg oil eq	0.0003639480
Water consumption	m3	0.0000324070

USEtox impact assessment LCA results for additives per gram
(USEtox focuses on human health):

Impact category	Unit	Lead
Human toxicity, cancer	nanocases	0.00076232974000
Human toxicity, non-cancer	nanocases	0.00011830268000
Freshwater ecotoxicity	PAF.m3.day	0.00000181159590

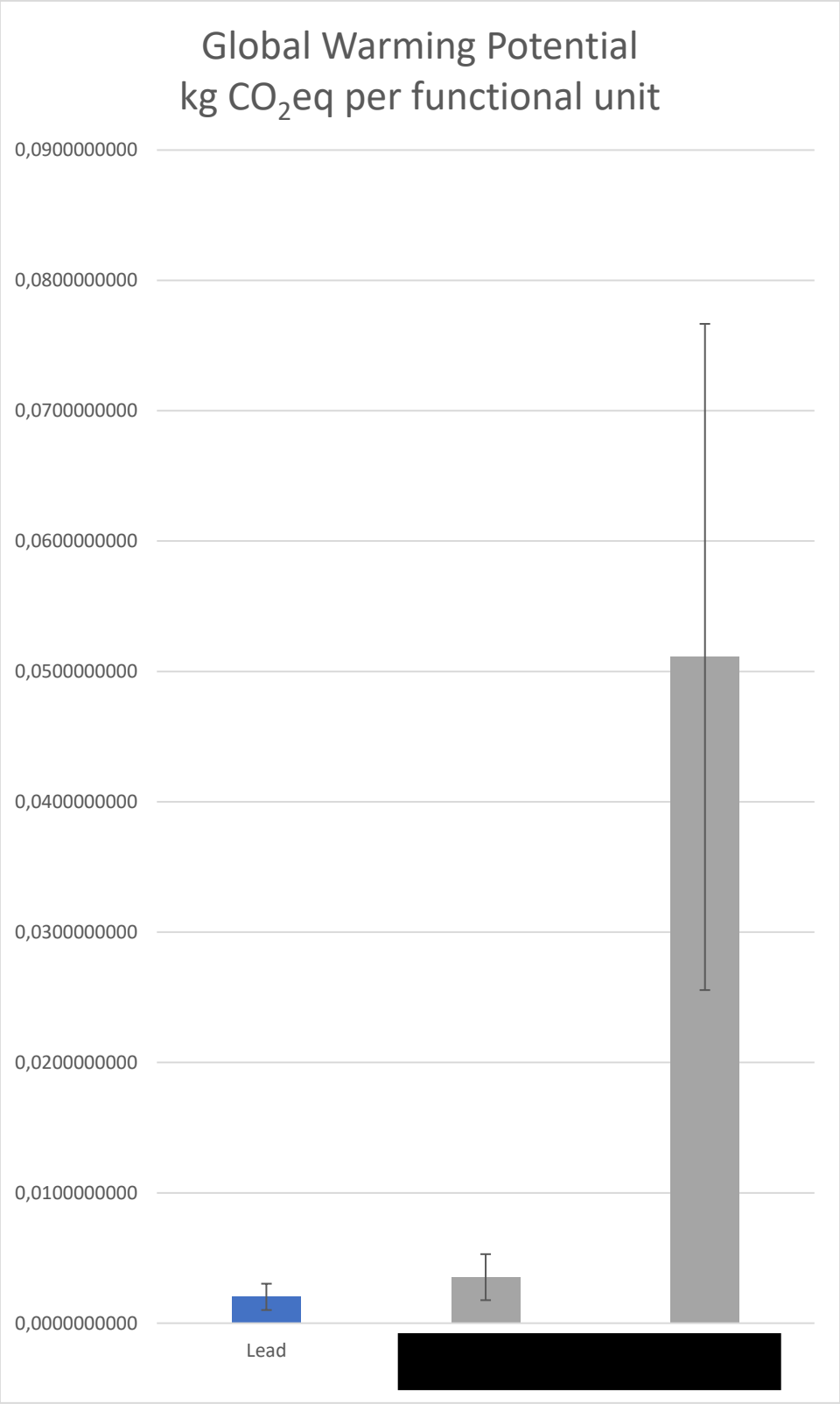
CED impact assessment LCA results for additives per gram
(CED, Cumulative Energy Demand, focuses on energy):

Impact category	Unit	Lead
Non renewable, fossil	kJ	16.67550
Non-renewable, nuclear	kJ	1.80514
Non-renewable, biomass	kJ	0.00028
Renewable, biomass	kJ	0.55916
Renewable, wind, solar, geothe	kJ	0.24489
Renewable, water	kJ	0.99629

Ecopoint impact assessment LCA results for additives per gram
(the Impact 2002+ method provides Ecopoints, a single-number result representing total environmental impact):

Damage category	Unit	Lead
Total	µPt	1.8061648
Human health	µPt	1.3128299
Ecosystem quality	µPt	0.16889245
Climate change	µPt	0.1891539
Resources	µPt	0.1352886

The following graph shows a summary of the global warming potential or carbon footprint for the additives modelled in the LCA study (per gram):



Carbon footprint results for the substances Lead, … (1 gram per substance)

Interpretation

- The LCA for Lead showed a global warming potential or 'carbon footprint' of 0.00202 $kgCO_2eq$, … of 0.0511 $kgCO_2eq$ and … of 0.00353 $kgCO_2eq$ (per kilogram of electronic piezo component polymer).
- The USEtox LCA results in the 'Human Toxicity, Cancer' category were 0.00076 nanoCases for Lead versus 0.00021 nanoCases for … and 0.019 nanoCases for ...
- The USEtox results in the 'Human Toxicity, Non-Cancer' category were 0.000118 nanoCases for Lead versus 0.000145 nanoCases for … and 0.00295 nanoCases for ....
- The results for Cumulative Energy Demand (CED) were lower in all cases for Lead than for the two other additives; for example, in the 'Non-Renewable, Fossil' category, the result for Lead was 16.67 Kilojoules, while the result for … was 32.93 Kilojoules and the result for … was 421.77 Kilojoules.
- The Ecopoint method results showed that Lead achieved a score of 1.80 µPt versus 1.13 µPt for … and 45.23 µPt for ....
- These results are per gram. The results are linear, so in future, if it is determined that different amounts of substances are required to fulfill the function of lead, the results can be multiplied by the weights to achieve new results. For example, if it turned out that twice as much … was required to perform equivalently to Lead, the … results could be doubled.

Conclusion

The overall conclusion is that the LCA provides evidence that Lead has lower environmental impact (in terms of the measures produced by LCA) in certain categories than the two alternatives. However, allowing for the uncertainties, it could be said that the environmental impact of Lead and … could be considered approximately equal, within the same order of magnitude. In contrast, … has higher environmental impacts than the other two substances. The alternative substances are different in their environmental impacts. … turns out to have higher environmental impacts than …, which can compete with Lead and is in some categories better than Lead. The alternative substances have, in some categories, a potential environmental and health impact significantly higher than that of Lead, in terms of the measures produced by LCA, especially ....

REFERENCES

[1] ISO, "ISO 14044:2006/AMD 1:2017 , Environmental Management - LCA - Requirements and guidelines - Amendment 1," ISO, 1 December 2017. [Online]. Available: https://www.iso.org/standard/72357.html.

[2] P. Sustainability, "Simapro," Pre Sustainability, [Online]. Available: https://simapro.com/.

[3] B. e. a. Weidema, "Overview and Methodology: Data Quality Guidelines for the Ecoinvent Database version 3," Ecoinvent Centre, St. Gallen, 2013.

[4] …

[5] R. e. a. Golroudbary, "Environmental Sustainability of Niobium Recycling: The Case of the Automotive Industry," *Recycling,* 2019.

[6] "Niobium (Columbium)," U.S. Geological Survey, Mineral Commodity Summaries, 01 2021. [Online]. Available: https://pubs.usgs.gov/periodicals/mcs2021/mcs2021-niobium.pdf. [Accessed 20 10 2021].

[7] U. S. o. A. Environmental Protection Agency, "Solders in Electronics: A Life-Cycle Assessment Summary," 2005.

[8] European Commission - Joint Research Centre - Institute for Environment and Sustainability, "International Reference Life Cycle Data System (ILCD) Handbook - General Guide for Life Cycle Assessment," Publiciations Office of the European Union, Luxembourg, 2010.

[9] International Standards Organization (ISO), *ISO 14040 Environmental management - Life Cycle Assessment - Principles and Framework,* Geneva: International Standards Organization (ISO), 2006.

[10] International Standards Organization (ISO), *Environmental management - Life Cycle Assessment - Requirements and guidelines,* Geneva: International Standards Organization (ISO), 2006.

[11] RIVM, Radbound Nijmegan, Leiden University and Pre Sustainability, "ReCiPe Midpoint Method," 2017. [Online]. Available: (http://www.rivm.nl/en/Topics/L/Life_Cycle_Assessment_LCA/Downloads/Documents_ReCiPe2017/Report_ReCiPe_Update_2017). [Accessed February 2020].

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, Lead, is a constituent material in the Piezoceramic material of the disposable cartridge to be used with the GEM Premier 5000 MARS analyzer.

The GEM Premier 5000 MARS analyzer is currently under development and will be 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 5000 MARS critical care analyzer is to be 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 Piezoceramic material is a vital component in the cartridges of the GEM Premier 5000 MARS used for measuring and reporting concentrations of critical care analytes in blood (pO2, pCO2, pH, Na+, K+, Ca++, Cl-, glucose, lactate and haematocrit). Lead is part of the Piezoceramic material of the piezoelectric transducer used to create acoustic power in a microfluidic detection flow chamber to separate plasma from whole blood patient samples by acoustofluidic separation. The purity and viability of the separated blood constituents is critical for diagnostic accuracy and for the therapeutic efficacy as well

Any change in the Piezoceramic material can directly impact analytical performance characteristics and thereby impede the intended function of the GEM Premier 5000 MARS analyzer.

For the GEM Premier 5000 MARS analyzer to provide patient blood data with uncompromised reliability and accuracy, continued use of Lead in the Piezoceramic material of the GEM Premier 5000 MARS analyzer is required while the search continues for alternative substances. The alternative substances must not interfere with measurement of any analyte and must meet product claims for the GEM Premier 5000 MARS analyzer over the claimed cartridge shelf life (up to 6 months at room temperature) and use life (up to 31 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?

Lead is a constituent of the Piezoceramic material used in the disposable cartridge in the form of Lead zirconate titanate (PZT) used as piezoelectric transducer due to superior performance referring to high Q-value and more. As noted the piezoelectric

transducer used to create acoustic power in a microfluidic detection flow chamber to separate plasma from whole blood patient samples by acoustofluidic separation.

Acoustofluidic separation is based on the interaction of acoustic waves with fluids and inclusions within the fluids. One convenient way to generate acoustic waves is to use transducers made of piezoelectric materials. Piezoelectric materials can generate electrical polarization under an applied mechanical stress or, vice versa, mechanical deformation arise from electrical polarization.

There are various types of piezoelectric transducers based on their material properties, configurations, and actuation modes. Some materials like quartz show natural piezoelectric properties due to its crystal structure yielding a net electrical dipole, while others like lead zirconate titanate can be made piezoelectric by applying an external electric polarization. Depending on the material and orientation, the vibration mode can be different. The most common vibration modes used in piezoelectric transducers are thickness expansion mode. When an alternating current (AC) signal is applied to the planer electrodes of a transducer, piezoelectric materials vibrate at the frequency of the AC signal. In both the thickness expansion and thickness shear modes, the whole body of the piezoelectric material vibrates, producing waves that are usually referred as “bulk acoustic waves” (BAW).

Based on the combined action of ultrasound waves and the flow of carrier fluids, acoustofluidics has emerged as a useful tool for manipulation of biofluids and biological suspensions in microfluidic devices. These devices exploit standing acoustic pressure waves that through the purely mechanical parameters, such as compressibility, density and size, induce fluid- and particle-specific forces leading to acoustophoresis this phenomenon is the basis of the development of gentle and robust methods for concentrating, trapping, washing, aligning and separating cells [2]. To be used for manipulation purposes, the acoustic pressure wave inside the microchannel must exhibit well defined pressure nodes and intense pressure fields, that effectively attract or repel particles.

For these reasons, acoustofluidic devices operate at acoustic resonance frequencies. Because the speed of sound in water is around 1500 m/s, and the typical characteristic dimensions of acoustofluidic microchannels range in 200 − 500 μm, it is seen that ultrasound frequencies of about 1.5 − 2.5 MHz are ideally suited for creating effect.

The effectiveness of the device in focusing microparticles is quantified by two mechanical indicators: the average direction of the pressure gradient and the amount of acoustic energy localized in the microchannel. Further, we derive the relations between the Lagrangian, the Hamiltonian and three electrical indicators: the resonance Q-value, the impedance and the electric power (Bruus et al.). The acoustic standing

wave formed by the channel walls continuously translated blood cells from their original medium to clean plasma solution with virtually no mixing of the fluids.

As mentioned above, any change in the Piezoceramic material 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 5000 MARS system, is designed around the analytical performance of the Piezoceramic material containing Lead.

The following advantages of the GEM Premier 5000 MARS as compared to other existing technologies on the market today are directly related to the material and require extensive validation for an alternative substance:

1. The GEM Premier 5000 MARS 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 5000 MARS 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. Transducers produced for the GEM Premier 5000 MARS analyzer are tested at the factory to ensure highest levels of quality to the customer.

The combination of the iQM System, single measurement cartridge design, and rigorous testing procedure for the transducer ensures that the GEM Premier 5000 MARS 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 transduceras a critical component of the measurement system.

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 5000 MARS 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 0,1 - 5 kg.

☐ In articles which are landfilled _____

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

Werfen 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 Werfen. Please also refer to Point 4(A)(6) and Appendix C regarding the environmental assessment.

The compliance program identified the Piezoceramic material of the GEM Premier 5000 MARS analyzer as a component with a content of Lead exceeding the maximum concentration value of 0.1% as defined in Annex II of RoHS.

Werfen has been actively working to replace Lead in the Piezoceramic material, working in close cooperation with commercial suppliers of Piezoceramic materials, academic institutions and private consultants to identify alternatives for Lead. 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.

Werfen 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.

A key finding of the work completed until now was that replacement of Lead in the Piezoceramic material resulted in deterioration in analytical performance of the GEM Premier analyser. We therefore conclude that presence of Lead in the Piezoceramic material is aiding performance, and published product claims were based on this optimum performance.

At present, the evaluation continues for an alternative, RoHS compliant material which will restore 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 requirements mandates 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 requirements 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 by updating the Technical File as appropriate.

Due to the aforementioned issues, the investigated alternatives are not technically practical or viable alternatives at this time, as they affect the accuracy and reproducibility of test results carried out with the alternatives, thereby preventing the analyzer from performing its intended function within established product claims. Although the search for practical and viable alternatives is on-going, Werfen must continue to manufacture the current cartridge using Lead until a new, non-Lead material 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 Lead in the Piezoceramic material:

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 5000 MARS platform has proven to be more complex to convert to a RoHS compliant Piezoceramic material, requiring a redesign of the material.

As noted above under Point 4(A)(6) the results of the LCA shows that Lead in certain aspects have a better environmental performance when compared to the environmental performance of the potential alternative materials.

(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 Piezoceramic material of the GEM Premier cartridge is required while the search evaluation of substances continues for an alternative material 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 31 days in the analyzer).

Werfen is continuing to search and evaluate for an alternative substance. Werfen recognizes that in addition to the environmental factors outlined in the Directive

2011/65/EU, the industry is diligently investigating other materials and sources that could be a reliable substitute.

As noted above the core requirement for our product is limiting the use of alternative lead-free PZT material. Currently there is no lead-free material on the market is meeting our product requirements with equivalent performance [1, 2]. There is no lead-free ferroelectric ceramics product on the market yet with high piezoelectric properties needed for our application. Despite the achieved improvement in piezoelectric properties, there are problems in the synthesis, processing and poling of the sintered ceramics.

Lead free piezo ceramics are available on the market today, (i.e., by one of the market leaders and key suppliers, PI Ceramics, based on …, see TABLE below), suffer from their low Q-value (a Q-value of >>1 is needed for the application used in the MARS product).

…

TABLE 1: Comparison PZT Materials

Lead-free material suffers either from low acoustic power, low Q-value, generation of heat, or the characteristics of the bulk material shows low mechanical strength; brittle material [3]

Current lead-free alternatives such as … are not good enough to reach energy level and Q-value we need for efficient separation [4]. Other alternative materials such as wismute oxide are not meeting performance requirements either, and are not industrialized.

Literature

[1] Bell and Deubzer (2018) Lead-free piezoelectrics - The environmental and regulatory issues. MRS Bulletin, 43 (8). pp. 581-587. ISSN 0883-7694, https://doi.org/10.1557/mrs.2018.154

[2] Lead-free piezoelectrics: Current status and perspectives. Coondoo et al. JOURNAL OF ADVANCED DIELECTRICS; Vol. 3, No. 2 (2013) 1330002 (22 pages) DOI: 10.1142/S2010135X13300028

[3] Microscale Acoustofluidics, Thomas Laurell, 2014, (ISBN 978-1-84973-671-8)

[4] Performance study of acoustophoretic microfluidic silicon-glass devices by characterization of material- and geometry-dependent frequency spectra, Fabio,1, ∗ Thomas Laurell,1, and Henrik Bruus.

Upon identification of the RoHS compliant material, additional time will be needed for development and update of the EU compliance documentation required for Medical Devices for a new transduceraccording 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 transduceracross the entire GEM Premier product line will be concluded within the coming 5 years.

Specific to EU legislation, testing of the selected replacement material for the 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 5000 MARS Piezoceramic material, carried out to prove the RoHS compliant material meet product analytical performance claims throughout the claimed GEM cartridge shelf life and use life.

Currently Werfen is investigating specific failure modes resulting from replacement of Lead in the Piezoceramic material with alternative materials. Working with this baseline

information and data from physical and chemical measurements with experimental materials, we are investigating different candidates with 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 Lead in the Piezoceramic material cannot be completed before the date of applicability of the restriction on use of Lead according to the RoHS Directive. This application is therefore being submitted for an extension of the current exemption allowing Werfen 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 B. Also, included in the table is the progress (% Complete column) made towards each milestone.

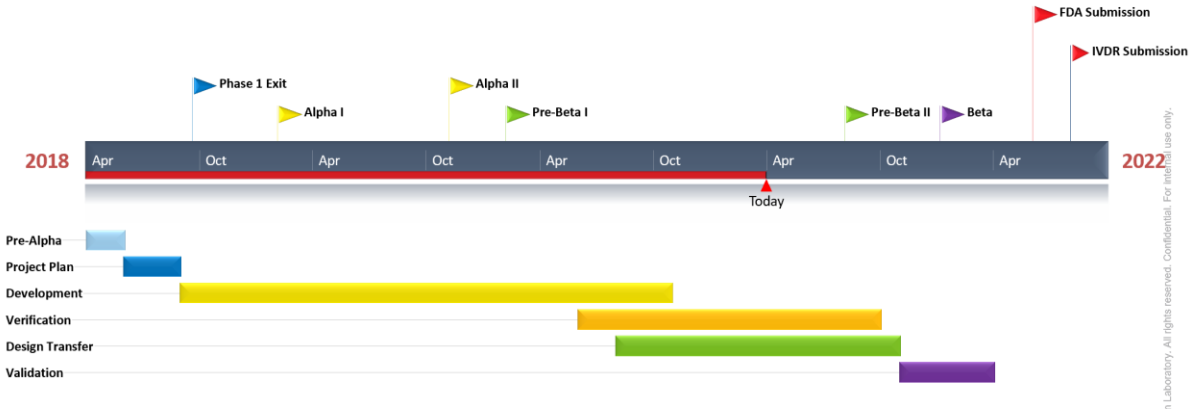
Table 1: Project Plan

These phases are defined in the Design Control Procedure (QMDD-20001-00) for Design Control projects.

- Project Proposal
- Design Input (Phase 1)
- Design Output (Phase 2)
- Design Verification (Phase 3)
- Design Transfer (Phase 4)
- Design Validation (Phase 5)
- Product Launch (Phase 6)

Currently, Project MARS is still a Design Control project within Phase III – Verification. See the project schedule below. The development cycle covers the Design Input and Design Output phases. Product Launch will be begin after FDA and IVDR submission when approval is attained.

Project Schedule in Phases



Below is a summary table of key external evaluation milestone tests.

Milestone Test	Configuration	Planned Date	High-level Test Objective
Alpha I	R&D Prototype	Q1 2019	• Integrated prototypes without bench equipment (with exception of laptop for H value) • Single LED configuration • Baseline performance established using clinical samples in full syringe mode and correlated to predicate device Cobas
Alpha II	R&D Prototype	Q4 2019	• Fully integrated prototypes • Production-grade camera that supports Analytical and Software • Hemolysis module drive settings established • Software integrated with “interim” CentOS • Software data acquisition, ROI, and processing implemented • Micromode testing in the clinical setting
Pre-Beta I	MFG Prototype	Q2 2021	• Mechanical parts all molded or proto-molded in the final design (only the touchscreen may be 3D printed) • Focus on assessing impact to existing sensors • iQM Checks and reporting (H flag)
Pre-Beta II	MFG Prototype	Q4 2021	• All software support coded • Optimized coefficients and algorithms • Final fluidic scripts

			• Hardware lock
Beta	Production Equivalent	Q2 2021	• Final locked configurations across all disciplines (hardware, analytical, software) • Configuration matches PAK users will receive • Summative Human Factors Report

Once on market, changes are managed as a Design Change project. Upon release of Project MARS, the product will be managed in accordance with Werfen Quality System processes and procedures including but not limited to items such as product feedback, complaint handling, investigations and trending, configuration management, design change management, and risk management. This plan will be updated a later time to accurately capture all of these activities.

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

Please see Appendix B: Project MARS RoHS Exemption Plan.

Section 7 above shows milestones for executing project plan.

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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 C.
   2) Health impacts: Please refer to point 4(A)(6) and Appendix C
   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 C.

(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 cartridge 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:

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:
