Study to assess three (3) exemption requests relating to Annex IV to Directive 2011/65/EU: request for amendment of existing exemption 31a; request for a new exemption for bis-(ethylhexyl) phthalate (DEHP) in ion selective electrodes for point of care analysis of ionic substances in human body fluids; and request for a new exemption for DEHP in plastic strain relief devices used to prevent damage to cable connections to MRI imaging coils (Pack 17) – Final Report

Under the Framework Contract: Assistance to the Commission on technical, socio-economic and cost-benefit assessments related to the implementation and further development of EU waste legislation

May 2020

Prepared by Oeko-Institut e.V., Institute for Applied Ecology, and Fraunhofer-Institut for Reliability and Microintegration (IZM)

Carl-Otto Gensch, Oeko-Institut

Yifaat Baron, Oeko-Institut

Katja Moch, Oeko-Institut

Viviana López, Oeko-Institut

Otmar Deubzer, Fraunhofer IZM

05 May 2020

Oeko-Institut e.V.

Freiburg Head Office, P.O. Box 1771

79017 Freiburg, Germany

Tel.:+49 (0) 761 – 4 52 95-0

Fax +49 (0) 761 – 4 52 95-288

Web: www.oeko.de

Fraunhofer IZM

Gustav-Meyer-Allee 25

13355 Berlin, Germany

Tel.: +49 (0)30 / 46403-157

Fax: +49 (0)30 / 46403-131

Web: www.fraunhofer.de

Acknowledgements

We would like to express our gratitude towards stakeholders who have taken an active role in the contribution of information concerning the requests for exemption handled in the course of this project.

Disclaimer

Oeko-Institut and Fraunhofer IZM have taken due care in the preparation of this report to ensure that all facts and analysis presented are as accurate as possible within the scope of the project. However, no guarantee is provided in respect of the information presented, and Oeko-Institut and Fraunhofer IZM are not responsible for decisions or actions taken on the basis of the content of this report.

EUROPEAN COMMISSION

Directorate-General for Environment

Directorate B - Circular Economy & Green Growth

Unit B3 - Waste Management & Secondary Materials

Contact: Karolina Zázvorková

E-mail: Karolina.ZAZVORKOVA@ec.europa.eu

European Commission

B-1049 Brussels

6. Request 2019-1: DEHP ion selective electrodes for point of care analysis

"Bis-(ethylhexyl) phthalate (DEHP) in ion selective electrodes for point of care analysis of ionic substances in human body fluids"

Declaration

In the sections that precede the "Critical review" the phrasings and wordings of stakeholders' explanations and arguments have been adopted from the documents provided by the stakeholders as far as required and reasonable in the context of the evaluation at hand. Formulations were only altered or completed in cases where it was necessary to maintain the readability and comprehensibility of the text. These sections are based exclusively on information provided by applicants and stakeholders, unless otherwise stated.

Acronyms and definitions

XXwt %	Following a number, this formulation refers to the percent weight of a substances from a component or from the homogenous material within which it is contained, depending on used formulation.
COCIR	European Coordination Committee of the Radiological, Electromedical and Healthcare IT Industry
BGA	Blood gas analysis
DEHP	Bis (ethylhexyl)-phthalate
EEE	Electrical and electronic equipment
EoL	End of life
ISE	Ion selective electrodes
IVD	In-vitro diagnostics
PoC	Point of care
RoHS	Directive 2011/65/EU on the restriction of hazardous substances in electrical and electronic equipment

6.1. Background

COCIR (2018b) has requested a new exemption for

„Bis (ethylhexyl) phthalate (DEHP) in ion selective electrodes for point of care analysis of ionic substances in human body fluids"

The exemption is requested to be added to RoHS Annex IV and to be valid for the maximum validity period of 7 years for EEE in Category 8.

COCIR explains that medical personnel in emergency departments, intensive care units, neonatal units and in operating theatres often need to rapidly analyse various fluids of their patients, including pleural fluid[13], blood and dialysate[14]. These situations are referred to as "point of care" and analysis is usually needed within a few minutes. Point of care testing requires a much shorter time to obtain results compared to traditional laboratory testing. As explained by COCIR "*Point of Care (PoC) analysers are medical devices used in these situations where results of body fluid analysis are required in the shortest time possible in order to enable quick therapeutic intervention" (COCIR 2018b).*

These type of devices operate with disposable cartridges containing ion selective electrodes (ISE) and other chemicals used for analysis and measurements of ions in blood or other body fluids, as well as washing and waste disposal, aqueous quality controls and electronics.

Some ISE contain Bis (ethylhexyl) phthalate (DEHP)",

DEHP has been added to the list of restricted substances specified in Annex II of the RoHS Directive and shall be prohibited in medical devices covered by the Directive as of 22 July 2021[15]. An exemption is thus requested to allow further placing of cartridges on the market for use in PoC blood analysis devices, where these apply ion selective electrodes containing DEHP.

6.1.1. Amount of Bis-(ethylhexyl) phthalate (DEHP) in ion selective electrodes used under the exemption

COCIR estimates a total of 2.2 kilograms of DEHP entering the EU market annually through the application described for this exemption request. This amount of RoHS-restricted substance would therefore be avoided should the exemption not be granted.

Supporting this estimation the applicant details the general composition of the membranes as 29 wt % Polyvinyl Chloride (PVC), 70wt % DEHP and an ionophore that imparts specificity for the particular ion of interest (COCIR 2018b).

As part of the answers to the first Clarification Questionnaire, the applicant provides more information regarding average size and weight of one cartridge that contributes to understanding the dimensions of the products under the scope of this exemption. According to COCIR, the size of one cartridge is 29 cm x 26 cm x 20 cm and "*For one manufacturer the weight of a cartridge is 1.34 kg. Therefore each unit cartridge contains 0.00021 weight % of DEHP*" (COCIR 2019b).

COCIR also provided data referring to a scenario in which an exemption would not be granted, for details see section 6.3.2.

[13] Pleural fluid is defined as the fluid that is found between the layers of the pleura, the membranes of which line the cavity and surround the lungs.

[14] In the process of dialysis, dialysate is the fluid passing through the dialyser, used for drawing toxins out of the patient's blood stream.

[15] Directive (EU) 2015/863 of 31 March 2015 amending Annex II to Directive 2011/65/EU

6.2. Technical description of the requested exemption

COCIR indicates that "*DEHP is used as a membrane solvent for the ion selective electrode (ISE) constituents"* (COCIR 2018b) that are used in PoC analysers to measure the concentrations of analytes such as partial pressure of carbon dioxide (pCO2), pH, concentration of sodium and potassium ions.

An important requirement of the functionality of ISE in this type of PoC analysers is the fact that they can analyse very small samples of whole blood. As highlighted by COCIR (2018b), this translates into reducing the need for blood transfusions and saving valuable time in emergency situations in comparison to central lab systems.

Regarding the component in which DEHP is used, COCIR describes that these ISE sensors "*are supplied to hospitals as components of disposable cartridges which contain the chemicals used for the analysis and carry out measurement, washing and waste disposal, aqueous quality controls and electronics*" (COCIR 2018b). In reference to the cartridges, COCIR describes that *„The measurement cartridge is a device that contains all the sensors used to make the measurements, liquid reagents to calibrate the sensors over its use-lifetime […]. The sensors are housed in a sensor module. The reagents are contained in foil laminated bags"*. (COCIR 2018b)

However, COCIR refers to the fact that ISE cartridges that contain DEHP are designed specifically for each type/model of instrument. Considering that *"many EU hospital already own or will buy before 21 July 2021 analysers that utilise ISE cartridges"*, new disposable cartridges must be compatible with PoC analysers already in the market.

Based on the above, the consultants understand that these cartridges containing DEHP are consumables of the PoC analysers, which are nevertheless to be considered as electrical and electronic equipment (EEE)[16]. They are disposed of after the chemicals used for the analysis have been consumed. In addition, these must be compatible with the type of analyser model that are already being used by hospitals in the EU. In this sense, the consultants understand that the exemption is at least in part concerned with the provision of such cartridges on the EU market, so as to ensure that devices already on the market can continue to be operated.

In its original application for exemption, the applicant lists the functions that the ‚DEHP cartridge is required to fulfil in the ISE cartridges of PoC blood analysers. These include:

> *„must be able to analyse whole blood directly,*
>
> *must not affect stability of membrane or electrodes during use or in storage,*
>
> *Cartridges must be compatible with analysers already on the market and in use within EU hospitals,*
>
> *Give analysis results within as short time as possible, ideally within one minute,*

[16] ISE cartridges are consumables with an equipment constituent meeting the specific definition of EEE in Article 3(1) and 3(2) of RoHS 2, comparable e.g. to printer cartridges, see FAQ 7.2. https://ec.europa.eu/environment/waste/rohs_eee/pdf/faq.pdf, last accessed 10.09.2019.

Change-over time to replace the used cartridges should be as short as possible, ideally less than 30 minutes."

As plasticiser, the substance must have the following properties:

"be liquid over a wide range of temperatures,

be compatible with, and solvate the other membrane components,

not induce phase separation,

not exhibit crystallization,

be lipophilic so it does not leach from the membrane during the use" (COCIR 2018b).

According to the applicant, this exemption request is requested for EEE in category 8, medical devices for in-vitro diagnostics (IVD) and relevant for devices used for *"chemical analysis of blood gases, electrolytes, metabolites, total hemoglobin, and hemoglobin derivatives in arterial and venous whole blood samples, dialysate and other body fluids such as pleural fluids"* (COCIR 2018b).

6.3. Applicant's justification for the requested exemption

Based on premises of technical unreliability of substitution alternatives, COCIR justifies the exemption with the argument that substitution is not technically practical. In the original application, COCIR declares that this exemption is needed because alternatives to DEHP have been found to give less accurate and incorrect test results and alternative methods to ion selective electrodes (ISE) take more time and may also provide inaccurate results.

6.3.1. Substitution or elimination of Bis-(ethylhexyl) phthalate (DEHP) in ion selective electrodes

Arguments for the justification of the need for this exemption in terms of substitution or elimination provided by the applicant address two levels: First, the level of substance substitution, regarding substances that could be applied as alternative plasticisers. Second, the technological level referring to elimination through the use of other methods or analysis devices or to elimination by developing an alternative design for the analysing cartridge.

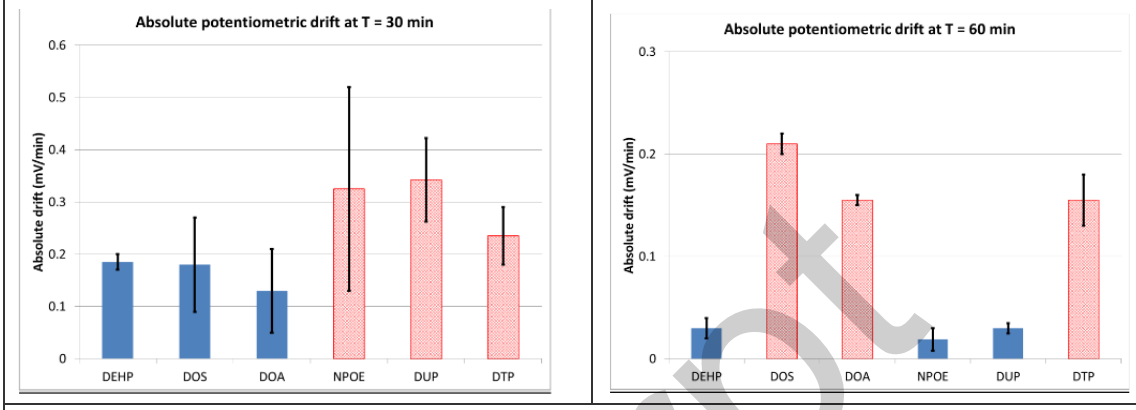
Substance substitution (Alternative plasticisers)

COCIR argues that attempts to replace DEHP with possible alternative plasticisers with similar properties have resulted in incorrect analysis translating into technical unreliability.

Regarding this, the applicant claims that several manufacturers of IVD ISE have attempted to replace DEHP with alternative substances with similar properties. The original application for exemption includes details about tests conducted with a range of plasticiser classes (ether, diester, phthalates). These tests were aimed at identifying a class which would yield sensors with the best balance and later life stability in terms

of potential (mV) drift[17] per unit timer. Sensors using nitrophenyloctylether (NPOE), dioctyl sebacate (DOS), dioctyl adipate (DOA), diundecyl phthalate (DUP), ditridecyl phthalate (DTP) resulted in unacceptable drift that cannot be used to give reproducible and accurate results.

Figure 6-1: Measured change in millivolts (mV) over the tested time period in minutes (mV/min) with measurements from several sensors



The above plots show the initial drift (mV/min) at T = 30 minutes and drift at T = 60 minutes after exposure to aqueous solutions for each of the tested plasticizers. DEHP exhibits the best balance of initial drift after one hour and reproducibility and is therefore the preferred plasticiser

Source: COCIR (2018b)

Based on the tests shown in Figure 6-1 of the original application for exemption, COCIR claims that *"research by manufacturers has shown that current models of analysers have to use the current design of ion selective electrode cartridges that contains DEHP"* (COCIR 2018). COCIR argues that alternatives to DEHP (substitution on the substance level) give less accurate test results than current ISE PoC analysers with DEHP.

Elimination on the Device Level (Alternative Analysis Methods and Devices)

Referring to alternative analysis methods, COCIR describes the range of currently available techniques and methods that could be used to measure the same analytes as done by PoC analysers.

The listed alternative methods are ion chromatography, flame photometry, atomic adsorption spectroscopy and glass pH electrodes for pH. Required time, materials, measurement procedure and calibration are clarified for each one of these methods. In addition, critical limitations pointing at reasons why they fail to perform the same

[17] Sensors Drift [mV/min]: Drift is a natural phenomenon for sensors. It affects all sensors regardless of the vendor. It is caused by physical changes in the sensor. Sensor precision often remains high. Drifting will affect the sensor's accuracy, causing it to be off target.
https://serverscheck.com/lab/sensor-drifting.asp

function as ISE PoC analysers, which perform up to the required time and sample sizes, are highlighted.

Ion chromatography for example, is a laboratory based technique that requires a skilled operator and the analysis time is much longer than with ISE. Similarly, flame photometry and atomic adsorption spectroscopy are also laboratory-based methods for which the samples should be prepared and separated before the analysis. On the other side, devices such as the glass pH electrode for pH, require more fluid to immerse the electrode, which may sometimes be more than is available from a patient. This represents a critical difference in contrast to the small samples required for ISE analysers. Further details can be viewed in the application (COCIR 2018b).

Further details as to alternative technologies are compiled in Table 6-1 below.

Table 6-1: Comparison of operation characteristics and parameters for alternative analysis technologies

Method	Ions that can be analysed	Analysis time per sample	Limitations	Total elapsed time from taking sample to results	Analyse whole blood	Measure ion activity	No maintenance needed	Automatic calibration	Automatic quality control	Can analyse all analytes (Na+, K+, Ca2+, H+, pCO2, Cl-, Glu, Lac, pO2, total haemoglobin, hematocrit) simultaneous-ly	Positive ID of patient	Connection to hospital IT system
ISE PoC analyser	Na+, K+, Ca2+, H+, pCO2 (bicarbonate), Cl-, Glu, Lac, pO2, total haemoglobin, hematocrit	1 minute for all analytes simultaneously. It is important to note that measuring blood gases (pO2) and metabolites (glu, lac) together is critical for a full and rapid diagnosis of the patient.	All ions can be analysed simultaneously and rapidly from a very small quantity of fluid.	1 minute	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Ion chromatography	Na+, K+, Ca2+, total CO2 (bicarbonate), Cl-	Whole blood cannot be analysed as it will block the small capillary and so additional time (at least 15 minutes) is needed to separate blood to extract the clear plasma that contains the ions (e.g. by centrifuge). Analysis requires calibration with at least at two standards (these contain for example all cations Na+, K+, Ca2+,) each standard taking typically 30 minutes.	Cannot measure ion activity. Anions and cations must be analysed separately, either by using two instruments or changing columns which will add at least one additional hour to the analysis time as the column has to equilibrate before it can be used. Ion chromatograph must be used by trained analysts and so are not suitable for	15 + (2 x 30) + 30 + 30 = ca. 2 hours for one sample, then >30 minutes for subsequent samples plus queuing time.	No	No	No	No	No	No	No	No

Method	Ions that can be analysed	Analysis time per sample	Limitations	Total elapsed time from taking sample to results	Analyse whole blood	Measure ion activity	No maintenance needed	Automatic calibration	Automatic quality control	Can analyse all analytes (Na+, K+, Ca2+, H+, pCO2, Cl-, Glu, Lac, pO2, total haemoglobin, hematocrit) simultaneous-ly	Positive ID of patient	Connection to hospital IT system
		Recalibration is advisable every 2 – 3 hours. Analysis time per sample is up to 30 minutes and in addition is data processing time of up to another 30 minutes. Note that Ca2+ ions take the longest time for analysis[18].	PoC locations. Samples therefore need to be taken from PoC facilities to these labs, where the samples join a queue, which can typically add 1 hour.									
Atomic adsorption	Na+, K+, Ca2+,	If a sufficient volume of blood is available, it can be centrifuged to obtain the clear aqueous phase, which will take about 15 minutes to separate the phases. Alternatively, acid digestion is an option but will take at least one hour (it also determines total calcium which is not the	Cannot measure ion activity This method is slow because whole blood cannot be analysed directly and only one ion is analysed at a time. These instruments are fairly large and require gas cylinders of acetylene and oxygen. These are very hazardous and	At least 2 hours including waiting time - 15 to 30 + 18 + (3x3) = 42 to 57 minutes	No	No	No	No	No	No	No	No

[18] See figure 4 in https://webcache.googleusercontent.com/search?q=cache:wI4xJ6tlCb8J:https://www.mdpi.com/2297-8739/5/1/16/pdf+&cd=1&hl=en&ct=clnk&gl=uk&client=firefox-b-d and figure 11 of https://www.unil.ch/idyst/files/live/sites/idyst/files/shared/Labos/Jackson_2000.pdf

Method	Ions that can be analysed	Analysis time per sample	Limitations	Total elapsed time from taking sample to results	Analyse whole blood	Measure ion activity	No maintenance needed	Automatic calibration	Automatic quality control	Can analyse all analytes (Na+, K+, Ca2+, H+, pCO2, Cl-, Glu, Lac, pO2, total haemoglobin, hematocrit) simultaneous-ly	Positive ID of patient	Connection to hospital IT system
		same as the concentration of the ISE method). Calibration of the spectrometer requires analysis of the ion at least at two concentrations so will take at least 6 minutes[19] per ion and sample analysis about 3 minutes per ion[20]. Total elapsed time for four ions is 15 to 30 + 18 + (3x3) = 42 to 57 minutes. In addition, time is required to set up the spectrometer and allow it to equilibrate (ca. 1 hour) before any analysis can be carried out.	are unsuitable in an emergency hospital environment. They can therefore only be used at a different location away from patients and untrained staff. Samples therefore need to be taken from PoC facilities to these labs, where the samples join a queue, which can typically add 1 hour.									

19 It is good practice to flush out the instrument after each sample for about 10 minutes to avoid cross-contamination, so this time would be in addition per sample.

20 https://www.sciencedirect.com/topics/materials-science/atomic-absorption-spectrometry

Method	Ions that can be analysed	Analysis time per sample	Limitations	Total elapsed time from taking sample to results	Analyse whole blood	Measure ion activity	No maintenance needed	Automatic calibration	Automatic quality control	Can analyse all analytes (Na+, K+, Ca2+, H+, pCO2, Cl-, Glu, Lac, pO2, total haemoglobin, hematocrit) simultaneous-ly	Positive ID of patient	Connection to hospital IT system
Flame photometry	Na+, K+, Ca2+,	Very similar to atomic adsorption spectroscopy, but can be quicker as Na+, K+ and Ca2+ can be analysed simultaneously, but has to be calibrated for each ion has to be separate taking about 18 minutes for three ions. Total elapsed include blood separation time is 15 + 18 + 3 = 36 minutes plus 1 hour equilibration time.	Cannot measure ion activity Flame photometry is a type of atomic adsorption spectroscopy and so analysis time is similar and the limitations described above are the same	1 - 2 hours = 15 + 18 + 3 = 36 minutes plus 1 hour equilibration time.	No	No	No	No	No	No	No	No
pH electrode	H+ only	Requires at least 10cm^3. This quantity will not always be available, for example very little blood can be taken from premature babies.	Measuring blood analytes, particularly pH, needs to be done at 37C (body temperature) and the system/sample controlled to +/- 0.1C for acceptable clinical performance. The electrode would need to be cleaned between each sample	Ca. 1 plus time for temperature equilibration and recalibration, probably 30 minutes per sample, although not likely to be sufficiently accurate	Yes	Yes	Yes	No	No	No	No	No

Method	Ions that can be analysed	Analysis time per sample	Limitations	Total elapsed time from taking sample to results	Analyse whole blood	Measure ion activity	No maintenance needed	Automatic calibration	Automatic quality control	Can analyse all analytes (Na+, K+, Ca2+, H+, pCO2, Cl-, Glu, Lac, pO2, total haemoglobin, hematocrit) simultaneous-ly	Positive ID of patient	Connection to hospital IT system
			to remove adsorbed proteins. The adsorption of proteins can cause the sensor to drift, requiring calibration. In addition, exposure of the sample to air will change the pH. Taking these together, a bench top pH electrode would not be capable of achieving the minimum +/-0.04 pH unit total analytical error expectation									

Source: COCIR 2019d, Personal communication by email submitted 2.10.2019

In reference to alternative methods, COCIR adds that "[…] *central lab systems use an indirect method of measuring these ions whereas blood gas systems measure them directly."* (COCIR 2018b).

COCIR argues that alternative methods to ion selective electrodes used in blood gas analysis devices (elimination on the technological level) have either been found to give less accurate and incorrect test results or require more time and are less reliable than ISE PoC analysers.

As for the possibility of elimination by developing an alternative analysis technique, in its original application for exemption COCIR poses that the "lab-on-a-chip" is the main focus of IVD equipment manufacturers (COCIR 2018b). Considering that this entails the development of a very different design, from mid-2018, the stages leading to the development of this alternative technology are expected to take between 8 and 10 years (see Table 6-2).

Table 6-2: Expected timescale for the development of alternative designs of analyser

Development phase	Elapsed time
Design of new miniaturised analysers and construction of prototypes	2 years from mid 2018
Testing to determine accuracy, adjustments to calibration. Establish manufacturing capabiltiy, site location and validation.	3 years
Clinical trials	1 year
Notified Body approval	6 months in EU, up to 2 years globally
Total elapsed time	**8 years (so by 2026)**
Support installed base of IVD analysers in EU hospitals	Current design of cartriges will be needed until **2030**

Source: *COCIR (2018b)*

As part of the answers to the first clarification questionnaire, COCIR provided further information about the work on this alternative which began before 2015. There they clarified that "*the "lab-on-chip" development is in feasibility phase and will take 8 to 10 years before complete replacement will be possible"* (COCIR 2019b).

Elimination on the Component Level (Alternative design or technology to the cartridge for ISE analyser)

Regarding the option of replacing DEHP in the current design, COCIR explains that different design for analyser cartridges that could substitute ISE cartridges containing DEHP is only expected to be available after 21 July 2021.

In their original application, COCIR explicitly claims that *"These analysers are planned to be sold in the EU until alternative technology is developed which is expected to be after 21 July 2021. Therefore this exemption will be needed for new analysers sold after 21 July 2021 as well as for consumable ion selective electrode modules that are supplied to hospitals in the EU to use with these analysers"* (COCIR 2018b).

This claim is based on the likely duration of the stages that would need to be carried out for this option. Timescales estimations for these stages are provided in the original application for exemption and include 7-8 years of technical development work as well as 2 years of subsequent regulatory path. Based on this, the total period could be up to 10 years.

Even so, COCIR highlights that "*modified ISE modules will however not be compatible with existing analysers that were designed with DEHP ISE modules and so an exemption would still be needed for these"* (COCIR 2018b). The consultants understand this to refer to reverse compatibility with devices already operating on the EU market. In this respect, in a later communication, COCIR (2019d) provided N estimation as to the lifetime of the analysers in which the ISE is applied: "*The average life-time of ISE PoC Analyzer is 9.7 years, with >50% of the install base older than 10 years*"

Considering that hospitals and clinics in the EU already using devices that require DEHP-membranes on its ISEs would need to obtain consumables until the analysers reach end of life, the applicant estimates that: *"cartridge consumables will be needed in the EU at least until 2030 and so this exemption will be needed for these until this date."* (COCIR 2018b)

6.3.2. Environmental arguments

Information provided in reference to the environmental aspects of this request for exemption address two main points: The end-of-life (EoL) treatment of the ISE cartridges, and the amount of WEEE generated in a forced substitution scenario, where current analysers are subject to premature obsolescence in the event that DEHP-based ISE cartridges would no longer be available for these to operate.

Regarding possible preparation for reuse, recycling or provisions for appropriate treatment of waste, in the original application, COCIR indicates that ISE cartridges cannot be recycled and are therefore sent for energy return. On this, it is added that after its use, ISE and membranes become bio-hazards so they are excluded from the WEEE Directive (COCIR 2018b).

In terms of environmental impacts, COCIR claims that *"without this exemption, hospitals would be forced to dispose of IVD analysers prematurely resulting in electrical equipment being disposed of before its normally expected end of life giving an increase in electrical waste" (COCIR 2018b)*. According to the applicant, the manufacture of substitute equipment to replace these, will also have environmental and health impacts.

In the answers to the clarification questionnaire, COCIR provided estimations about the possible amounts of waste generated through a forced substitution. This was

declared to be roughly > 1,000 t per year including all associated consumables and relates to the substitution of blood analysis devices already operating on the market. These estimations are based on (COCIR 2019b):

- an average weight of 16.6 kg per device of approximately 30,000 instruments currently placed on the EU market, which would generate around 500 tonnes of WEEE; and
- additional foreseeable generated waste which is based on a weight of 1.34 kg/cartridge of approximately 12 cartridges used per year per analyser.

The applicant also highlights the fact that even though these are theoretical calculations, these amounts of waste would be the result of avoiding a small amount of DEHP.

> *"There would be a large disposable cost for the >1000 t of waste as compared to preventing approximately 2.2 kg of DEHP from being placed on the market."* (COCIR 2019b)

In relation to the PoC analysis devices to be scrapped prematurely, COCIR furthermore estimates that "*Replacing these 500t by new devices would also lead to additional RoHS substances entering the EU market (e.g. lead in steel up to 0.35%, lead in aluminium with up to 1.5%, lead in copper with up to 4%). Assuming that 20% steel, 10% aluminium and 5% copper are being used, with a lead content of 0.35% in steel, 1.5% in aluminium and 4% in copper, the total weight of additional lead put on the market would be 2,100 kg (compared to a saving of 2.2 kg DEHP)*" (COCIR 2019b). This is data is compiled in Table 6-3 below.

Table 6-3: Estimation of the total weight of lead (Pb) entering the market through the replacement of PoC analysers currently in stock

Total Weight of EEE which need to be replaced [kg]	**500.000**
% Steel	20,00%
% Aluminum	10,00%
% Copper	5,00%
% Lead content in Steel	0,35%
% Lead content in Aluminum	1,50%
% Lead content in Copper	4,00%
Total Weight of Lead entering the market by products replacing the installed base [kg]	**2.100**

Source: *(COCIR 2019b)*

6.3.3. Socioeconomic impacts

Regarding the foreseeable socioeconomic impacts of the substitution, COCIR indicates an increase in fixed costs and possible social impacts within the EU. In the original application for exemption, COCIR further describes human health and economic impacts (See section 6.3.2 for environmental impacts).

The implications of a scenario where EU hospitals PoC units already using this type of cartridge analysers will not be able to obtain ISE module consumables include human health impacts:

> *"There will be serious implications if delays in obtaining analysis results occur or if they are not accurate. Any delay in treatment could, as a worst case, result in unnecessary deaths (although it is impossible to estimate a quantitative impact)" (COCIR 2018b)*

The economic impacts refer to the economic expenditures which hospitals and clinics in the EU will incur either by buying alternative analysers or by replacing them with new equipment. Besides, the applicant points at possible job losses if cartridges cannot be sold in the EU.

As part of the answers to the first clarification questionnaire and based on theoretical calculations, COCIR provided more specific estimations about these aspects (COCIR 2019b):

- "Approximately 30,000 instruments are [used; the consultants] in the EU and each uses 12 measurement cartridges/year and each cartridge can measure 500 samples [this; the consultants] yields approximately 180 [million; the consultants] measurements or 90 million patients (2 samples/patient) negatively impacted." (COCIR 2019b)
- "One manufacture estimates that approximately 158 million measurements are made per year and 432K [i.e. 432,000; the consultants] samples are measured each day world-wide. Assuming 50 % is in the EU and typically more than one sample is taken from each patient therefore roughly 40 million patients would be impacted for one manufacture. For 3 manufactures approximately 120 million patients would be negatively impacted per year" (COCIR 2019b).

To summarise, based on an estimate of approximately 30,000 instruments currently placed on the EU, it is estimated that between 90 and 120 million patients could be negatively impacted. These numbers consider the amount of measurement cartridges and samples per year reported and calculated from different manufacturers.

As for impacts on employment inside and outside the EU, COCIR refers to negative impacts along a range of industries e.g. manufacturing, supply chain, service, R&D, marketing, quality, regulatory, information technology, associated distributors, medical services and hospitals.

Clarifications from COCIR, regarding additional costs, estimate that hospitals would incur in unanticipated costs of more than 250 million in order to replace all systems currently placed on the EU market.

On this, COCIR points out that the overall impact to hospital infrastructure is similar to that described in Exemption 41, Section 7.4.5 of Gensch et al. (2019). These refer to hospitals across the EU conducting time- and money-consuming decision processes towards purchasing new blood analysers. Additionally, these impacts consider unanticipated investment costs of over 300,000 euros for one single hospital as well as further expenses from connecting the new instruments to existing information systems which are estimated at 20,000 euros. Finally, the need for training the staff on the new instruments would represent costs that could be measured in terms of number of employees and the hours invested per person. According to data from one German hospital, training their staff for just one hour could translate into 1,200 hours of unproductive work time (Gensch et al. 2019).

Despite providing detailed information about these aspects, COCIR clarifies that:

"This exemption is justified on the basis that substitution is not technically practical and does not rely on socio-economic issues to justify the maximum validity period" (COCIR 2018b).

Considering this, even though there is information about the socioeconomic impacts, the main focus of the justification for this exemption is on arguments of technical practicability of substitution.

6.4. Stakeholder contributions

During the public consultation, one contribution was submitted by **Radiometer Medical ApS,** who manufacture "acute care solutions in labs and at the point of care"[21]**.** Radiometer addressed the following arguments:

Radiometer agrees with the scope of the exemption and the wording proposed by COCIR. As evidence supporting this exemption request, Radiometer declares to have an ongoing project aimed to substitute the DEHP in ISE. This project has, however, not succeeded in the substitution so far.

As for alternatives that may cover part or all of the applicability range of DEHP, Radiometer claims that they cannot point today at a suitable substitute. No quantitative data about application specifications to support their view was provided in the contribution. In addition, this stakeholder declares that DEHP is used in all the relevant electrodes in the cartridges of their device so that it is not possible for them to make a partial substitution. On that matter it is indicated that their plan is to substitute DEHP before July 21, 2021.

About research initiatives currently looking into the development of possible alternatives this contribution states that:

> *"To Radiometer's knowledge the "lab-on-chip" technology will not be available in the foreseeable future"* (Radiometer Medical Aps 2019).

[21] See Radiometer Website: https://www.radiometer.co.uk/

In relation to their own PoC devices, Radiometer declares that the total amount of DEHP placed on the EU market as part of disposable sensor cassettes is about 35 g per year. Therefore, Radiometer considers the total of 2.2 kg DEHP provided in the estimation of COCIR in the original application as a reasonable estimation. (Radiometer Medical Aps 2019)

In quantitative terms, Radiometer estimates that as of January 1, 2019 a total of 7,800 of their analysers have already been placed on the EU market. This number is understood by the consultants to be mentioned as it clarifies the number of Radiometer devices that would need to be scrapped should cartridges no longer be available. Regarding possible additional waste to be generated in the event of a forced substitution the contribution includes the following statement:

> *"If accessories should not be available after 2021, the analysers cannot be used and must be scrapped. The amount of scrap from Radiometer equipment in this case is estimated to 73 ton"* (Radiometer Medical Aps 2019).

Finally, this stakeholder poses that in the event of a forced substitution, the main costs will be the replacement of all the impacted PoC equipment. In addition, Radiometer has estimated that total replacement costs, which include among others costs for equipment replacement and for training the staff on new equipment, to add up to € 130 million. It is highlighted that most of these costs will be allocated to the public sector apart from private hospitals and clinics.

6.5. Critical review

6.5.1. REACH compliance – Relation to the REACH Regulation

Art. 5(1)(a) of the RoHS Directive specifies that exemptions from the substance restrictions, for specific materials and components in specific applications, may only be included in Annex III or Annex IV "*provided that such inclusion does not weaken the environmental and health protection afforded by*" the REACH Regulation. The article details further criteria which need to be fulfilled to justify an exemption, however the reference to the REACH Regulation is interpreted by the consultants as a threshold criterion: an exemption could not be granted should it weaken the protection afforded by REACH. The REACH regulation has been consulted in this respect: the first stage of the evaluation thus includes a review of possible incoherence of the requested exemption with the REACH Regulation.

With regards to **Annex XIV of the REACH Regulation**: DEHP has been included in the SVHC REACH candidate list for the reason of being toxic for reproduction in 2008 and has been added to Annex XIV in 2012. In July 2017, DEHP has been additionally recognized for endocrine disrupting properties. Thus, DEHP as substance cannot be placed on the market or used after the 21 February 2015 (Sunset date), unless an authorisation is granted.

In the original application for exemption COCIR indicated that *"ion selective electrode membranes containing DEHP are manufactured outside of the EU and so only articles are imported into the EU and DEHP is not used as a chemical substance in the EU"*

(COCIR 2018b). Thus they are imported as articles in the EU and REACH Annex XIV is not applicable.

Additionally, DEHP is referred to in **REACH Annex XVII**:[22]

- **Entry 51** in Annex XVII of the REACH Regulation[23] stipulates that DEHP shall not be used in concentrations greater than 0.1 % by weight of the plasticised material, in toys and childcare articles. Toys and childcare articles containing DEHP in a concentration greater than 0.1 % by weight of the plasticized material shall not be placed on the market.
  Whereas basically, this restriction concerning toys and childcare articles could apply to certain articles within the scope of Directive 2011/65/EU (RoHS 2), it is not in the scope of this requested exemption concerning medical devices; the use of DEHP in ISE cartridges for PoC analysers is not related to applications in toys or childcare articles.
  Furthermore entry 51, paragraph 3, contains the recent amendment of December 2018 that stipulates that the four phthalates that are restricted under RoHS (DEHP, DBP, BBP, DiBP individually or in any combination), shall not be placed on the market after 7 July 2020 in articles in a concentration equal to or greater than 0,1 % by weight of the plasticised material in the article. However, it is further stipulated that this paragraph shall not apply to medical devices within the scope of Directives 90/385/EEC, 93/42/EEC or 98/79/EC, or parts thereof and shall not apply to electrical and electronic equipment within the scope of Directive 2011/65/EU. Thus, the restriction of entry 51 does not apply to the exemption here at hand.
- **Entry 30** of Annex XVII is also relevant (entry 30 refers to substances in Appendix 5 or Appendix 6 and DEHP is listed in Appendix 6). According to entry 30, DEHP shall not be placed on the market, or used, as substances, constituents of other substances, or in mixtures for supply to the general public.
  In the consultants' understanding, the restrictions for substances under entry 30 of Annex XVII do not apply to this requested exemption.

COCIR also mentions a proposed restriction on DEHP for *"materials which have prolonged skin contact. However, hospital staff and patients can not touch the membranes as they are inaccessible inside the cartridge."* This proposal to which COCIR is referring to has been decided and forms part of the amendment of entry 51 of Annex XVII. The prolonged skin contact is meant for plasticised material for use exclusively in the open air, which comes into contact with human mucous membranes or into prolonged contact with human skin. Thus, this does not apply to the request here at hand.

[22] See also the Appendix of this report at page 108.

[23] Please note that this entry has been amended quite recently:
COMMISSION REGULATION (EU) 2018/2005 of 17 December 2018 amending Annex XVII to Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, valuation, Authorisation and Restriction of Chemicals (REACH) as regards bis(2-ethylhexyl) phthalate (DEHP), dibutyl phthalate (DBP), benzyl butyl phthalate (BBP) and diisobutyl phthalate (DIBP);
https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32018R2005&from=EN

No other entries, relevant for the use of DEHP in the requested exemption could be identified in Annex XIV and Annex XVII (status September 2019). Based on the current status of Annexes XIV and XVII of the REACH Regulation, the requested exemption would not weaken the environmental and health protection afforded by the REACH Regulation. An exemption could therefore be granted if other criteria of Art. 5(1)(a) apply.

No other entries, relevant for the use of DEHP in the requested exemption could be identified in Annex XIV and Annex XVII (status August 2019). Based on the current status of Annexes XIV and XVII of the REACH Regulation, the requested exemption would not weaken the environmental and health protection afforded by the REACH Regulation. An exemption could therefore be granted if other criteria of Art. 5(1)(a) apply.

6.5.2. Scientific and technical practicability of substitution

As justification of the exemption, COCIR offers arguments first and foremost based on the lack of reliability of the substitutes. COCIR's Members have attempted to comply with the substance restriction through efforts to replace DEHP with possible alternative plasticisers with similar properties. These efforts have concluded in incorrect analysis results which evidences technical unreliability for the intended application.

- COCIR (2018b) summarises the results from manufacturer's tests with alternative plasticisers detailing that NPOE, DUP and DTP exhibit unacceptable drift[24] and cannot be used to give reproducible and accurate results (See also section 6.3.1).
- Information from COCIR (2018b) intends to show that in contrast, DEHP exhibits the best balance between initial drift after one hour and reproducibility, and is therefore the preferred plasticiser out of all of the alternatives tested. This characteristic is seen as key for the technology to meet the needs of PoC environment as well as the short period of time needed to obtain analysis results.

The consultants understand that even though a broad range of RoHS compliant plasticisers exist and have been tested, the compatibility with the intended use of the sensors in PoC situations, makes time and precision of results a critical feature that needs to be ensured for the ISE application described by the applicant.

Looking into the initiatives of other producers of PoC blood gas analysis devices to substitute DEHP in the ISE of such devices, shows that at least a few manufacturers have difficulties to find alternatives.

- (COCIR 2019b) states that "*for 3 manufactures approximately 120 million patients would be negatively impacted per year*" in relation to the estimation of socio-economic impacts and the consultants thus conclude that three of the at least four manufacturers[25] of blood analysis devices have not achieved substitution and

[24] Sensors Drift [mV/min]: Drift is a natural phenomenon for sensors. It affects all sensors regardless of the vendor. It is caused by physical changes in the sensor. Sensor precision often remains high. Drifting will affect the sensor's accuracy, causing it to be off target.
https://serverscheck.com/lab/sensor-drifting.asp

[25] The consultants are aware from the review of exemption 41 of Annex IV for lead in blood gas analysis cartridges, that there are at least four manufacturers placing equipment in the EU market (Roche,

would need the exemption. This would suggest that one manufacturer may be compliant and would not need an exemption for DEHP[26].

- Radiometer Medical Aps contributed to the stakeholder consultation in full support of the request given that it uses DEHP in disposable sensor cassettes and that DEHP covers all the relevant electrodes at the sensor device. When asked about the status of ongoing research for substitution, Radiometer expressed that *"Our plan is to substitute before July 21, 2021"* (Radiometer Medical Aps 2019).

Technical information regarding the use of DEHP as plasticiser in ISEs was provided by Professor Mark Meyerhoff from the University of Michigan in the form of technical comments, following an inquiry by the consultants.

In his comments, Professor Meyerhoff explains in detail the scientific principles of the functionality of plasticisers in polymeric membrane-based ion-selective electrodes. In this document, he acknowledges that the nature of the plasticizer employed can play a significant role in the ion-selectivity exhibited by polymer membrane ISEs. In order to explain the criteria governing this selectivity, he elaborates on the two following processes (Meyerhoff 2019a):

(1) the single ion partition coefficients from aqueous phase of sample solution into organic phase of the membrane (primarily the plasticized PVC) (k_i and k_j; where $k_i = [i]^{org} / [i]^{sam}$ [27] and for j ions: $k_j = [j]^{org} / [j]^{sam}$. ; where "i" is the primary target ion and "j" is some potential interferent ion; and

(2) the formation constants of the ions to form a complex with the selective ionophore (L) in the plasticized membrane phase (i.e., K_f for rxn: $i_{org} + L_{org} <-> iL_{org}$ and $j_{org} + L_{org} <-> jL_{org}$).

Meyerhoff (2019a) explains that these two processes dictate the selectivity coefficient (K^{pot} observed with any given ionophore used to prepare polymer membrane ISEs), in accordance with the following equation[28]:

$$K_{i,j}^{pot} = \frac{k_j}{k_i} \frac{K_f^j}{K_f^i}$$

Based on these criteria, Professor Meyerhoff elaborates on how changing the plasticiser would affect selectivity:

Siemens, Instrumentation Laboratories and Radiometer). Abbot also manufactures PoC devices, but using single use cartridges in a hand held device and thus their equipment is irrelevant in respect of this comparison.

[26] From publicly available data, only two of the named companies are specified as COCIR Members and it can thus not be concluded if COCIR has full information on the compliance of all relevant actors or not. For detail see: https://www.cocir.org/about-cocir/members.html

[27] The consultants understand "sam" to be an abbreviation for sample and "org" to be an abbreviation for organic phase, whereas the equation is related to the analysed ion in the aqueous phase of the sample solution and in the organic phase of the membrane. "I" represent the target ion, whereas j represents other, potentially interfering ions.

[28] K^{pot} represents the selectivity coefficient. K_f is the binding constant of the ionophore, whereas K_i and K_j are the binding constants of the target ion and the interfering ion respectively.

> *"In most cases, the ratio of the formation constants of the ion with the ionophore dominate the selectivity term. Hence, changing plasticizer from one to another will not usually have dramatic effect, unless the dielectric constant of the plasticizer changes significantly. Such large changes in dielectric constant can cause exudation of the plasticizer or ionophore from the membrane phase, and also alter the solvation energy of the free ion within the plasticizer phase (k_i). If it makes the k_i value lower, but does not change the k_j value equally in the same direction, then the selectivity constant will increase, making the electrode less selective. (Meyerhoff 2019a)"*

Moreover, this expert's comments also consider possible exceptions in which changing the plasticisers would indeed affect selectivity:

> *"So, in most cases, I would expect that changing from DEHP to some other plasticizer that has a similar lipophilicity/dielectric constant is not going to dramatically change the selectivity and analytical performance of any ionophore-based ISE. The only exception could be in the case of polymeric membrane electrodes that utilize ionophores that are not especially selective in their binding constants (K_f values, above) with the target analyte ion over potential interferent ions. In such cases, if the plasticizer helps extract the target ion to a greater extent than interferent ions into the membrane phase, then the overall selectivity could be enhanced or vice versa."* (Meyerhoff 2019a)

On this, the document provides an example of DEHP use as plasticisers in certain Ca^{++} selective membrane electrodes that employ dialkyl-phosphate carrier type ionophores to obtain enhanced calcium ion selectivity. For these membranes it is considered that the electrode selectivity could be negatively impacted by altering the plasticiser. Even in this case, the substitution might represent higher costs but it is still not considered technically unfeasible.

As Professor Meyerhoff puts it: *"Given the rather small sizes and quantities of the membrane materials employed to create the ISE sensors employed in modern blood analyzers, this is not a particularly compelling argument not to change to an ionophore system (e.g., to ETH 1001) that does not require the use of DEHP"* (Meyerhoff 2019a).

Building on this, his comments conclude with the following statement on the practicability of DEHP substitution:

> *"For sure, all other ISE ionophore systems[29] (for Na^+, K^+, H^+, etc.) do not require the use of DEHP as the plasticizer to achieve the desired selectivity for measurement of the target ions in undiluted blood samples."* (Meyerhoff 2019a)

The consultants understand this to mean that even in the cases where ion selectivity could be affected by a change in the plasticiser (e.g. Ca^{++}), the constraints for DEHP substitution are rather economical than technical. Moreover, it is understood that for

[29] Besides Calcium ions

the following analytes, the application of DEHP as a plasticiser does not play a role in the ion selectivity of the polymer membrane ISE: Na^+, K^+, H^+.

From the content of these technical comments, the consultants conclude that substituting the plasticiser in an ISE in modern blood analysers would require technical re-design and calibration, but is in principle a feasible process. The status of substitution of the various manufacturers appears to depend on whether DEHP is used in ISE of a specific device to begin with and how far the efforts to substitute are (testing of plasticisers, redesign, recertification of device, etc.). In a later follow up communication with Professor Meyerhoff it was enquired about whether his technical comments are limited to the feasibility of substitution for blood analysers (Meyerhoff 2019b). The consultants wanted to clarify whether ISEs measuring a broader range of fluids represent larger technical difficulties of substitution. This, considering that the subject of this specific request for exemption, are ISE used in Point of Care devices which, besides whole blood samples, serum and plasma, also provide analysis for other body fluids (e.g. urine, cerebral spinal fluid, pleural fluid and dialysate).

To this, Professor Meyerhoff expressed that whole blood is surely the most complex matrix, but for sure other plasticisers can function effectively for all the relevant ISEs for reliable measurements in whole blood samples. Besides, he expressed scepticism about the impossibility of DEHP substitution under those conditions.

> *"I truly doubt that these other types of samples really would have some components that would make it impossible to use another plasticizer, other than DEHP, to make the polymeric membrane ISEs function with good accuracy/adequate selectivity"* (Meyerhoff 2019b)

With this, as a technical consultant on the electrochemical sensor technology with more than 30 years of experience, Professor Meyerhoff confirms his initial position about this exemption, by which he states that it is possible that all ISE sensors within other whole blood analysers can indeed be prepared without the need to employ DEHP in the sensing membranes.

COCIR were asked to comment on the input of Prof. Meyerhoff and provided the following input: the "*technical input on the ISE selectivity impact from changing plasticizers in sensor membrane formulations is correct. However this is only one requirement for a clinically useful blood analysis system.*

There are complex interactions between the sensor membrane formulations, internal electrolyte formulations, system calibration reagent surfactants, calibration reagent preservatives and compatibility with internal system materials used to house the sensors. The membrane formulations are specifically optimized to function within the system and all components that contact the sensors. All these aspects need to be addressed to yield a stable, reproducible and useful system.

In our exemption request we also noted that the system utilizes mathematical formulas (algorithms) that are specifically designed for each sensor (membrane formulation). Therefore it is the total integrated system (instrument, reagents, sensor formulation, algorithms) that is the complete system device which yields clinically acceptable performance and results.

Overall system stability and availability is very important to enable quick treatment of patients. In our exemption request we showed data that alternative plasticizers do not enable a stable system and will result in delayed treatment of patients. This delay can negatively impact patient outcomes. We also showed data that alternative plasticizers yield sensors with more variability. This can cause low quality clinical results leading to improper treatment of patients.

The conclusion of our data was the following; DEHP exhibits the best balance of initial drift after one hour and reproducibility and is therefore the preferred plasticizer. This has allowed the technology to meet the needs of the critical care environment in particular a short period of time to obtain results and a short time before first measurement with a new cartridge." (COCIR 2019d)

Though the consultants understand that various parameters may affect the time needed to develop a substitute for DEHP in this application, it can also be understood that at least one manufacturer expects complete substitution by July 2021. This leads to the conclusion that substitution is possible in the time frame available before the DEHP restriction is to come into force for medical devices, though it can also be followed that finding a compatible substitute may be more time-consuming for some manufacturers as it is a trial and error process.

As to the comparability of PoC devices with alternative blood analysis technologies, COCIR provide a comparison of the operation characteristics and parameters of alternative analysis technologies in Table 6-1. The comparison shows that the alternative technologies mentioned either do not provide the same functions (e.g. ion chromatography, atomic adsorption spectroscopy, flame photometry) or only cover part of the functions provided by the ISE PoC analysers (pH electrode). Furthermore, all technologies addressed in the table require a substantially longer time to provide results in comparison with the ISE PoC analyser (between 30 minutes to over two hours in comparison with the relatively short time period of 1 minute in which results are obtained with the ISE PoC analyser).

Referring to the use of alternative technologies for blood analysis, this review emphasizes that "point-of-care" equipment is used by medical practitioners to measure various blood parameters in proximity to where the patient is being taken care of (emergency rooms, intensive care units, and operation rooms). Thus the short time in which such devices provide results is of importance to allow rapid diagnosis and decisions as to further care. *"The alternative of sending blood samples to the central laboratory requires more time and also does not provide results for parameters unique to blood gas analysis devices (pH, pO2, pCO2, HCO3)"* (Gensch et al. 2019, p. 60).

6.5.3. Environmental arguments and socioeconomic impacts

Environmental arguments for this exemption request were provided by COCIR referring to the amounts of waste generated in possible scenarios in which an exemption shall not be granted.

The first aspect to be considered is the End of Life (EoL) treatment of the ISE cartridges after they have been used and discarded. In the original application, COCIR

details that since these cartridges are considered a bio-hazard, they cannot be recycled and are sent for energy return (see section 6.3.2).

In this regard, the consultants understand that a decision about granting the exemption would not modify the EoL treatment of such medical waste. Therefore, in terms of additional material flows containing DEHP that could lead to emissions and health risks in EEE waste management facilities, whether an exemption is granted or not shall not affect possible impacts in such facilities. In other words, not granting an exemption is not expected to lead to environmental benefits in the form of reducing such emissions.

The second aspect to be considered refers to the amount of WEEE that would be generated as result of premature obsolescence of the PoC analysers, which currently use ISE cartridges containing DEHP. The applicant provided information about the amount of waste that would possibly be generated highlighting the difference between > 1000 t of waste (from scrapped equipment and consumables, containing an estimated 2,100 Kg of Pb) compared to 2.2 kg of DEHP prevented from being placed on the EU market annually (see section 6.3.2).

In light of these estimations, the consultants enquired about the possibility of selling the stock of consumables outside the EU in the event that the exemption is not granted. Addressing this enquiry, COCIR provided additional information regarding the EU stock of cartridges for PoC blood analysis devices that would go to waste (COCIR 2019b):

> *"… each instrument uses a range of cartridges (1 -3), quality control materials and accessory consumables (e.g. syringes) all of which would be in stock. The cartridges would not be sold outside of the EU as there are other distribution centres which support the rest of the world. Manufacturing production and distribution centres are pre stocked based on forecast demand so all material is accounted for. In addition there is a limited shelf life so all stock would go to waste. Even if the manufacturer could sell outside of the EU the stock at the other centres would go to waste. Therefore millions of consumables would not be used and would become waste"* (COCIR 2019b)

In this case it could be argued that in a substitution scenario, it is possible for hospitals to stock up on cartridges to keep operating the PoC equipment to avoid premature obsolescence. According to information included in the review of Ex. 41, Annex IV for this type of sensors the expected shelf life is up to 9 months (Gensch et al. 2019, p. 58). Though the shelf-life may vary between manufacturers, COCIR also refer to a limited shelf-life. This means that the limited shelf life of consumables of this type would critically constrain this possibility and PoC devices will cease to be operational shortly after ISE cartridges containing DEHP are no longer available. Though this means on the one side that such devices may be scrapped prematurely, it is also assumed that as long as consumables are available (stocked) with a suitable shelf-life, that they would be used and not "go to waste" as suggested by (COCIR 2019b). As manufacturers are aware of the legislation, it is also assumed that restocking of manufacturer distribution points would be avoided after mid-2021 if the exemption is not approved, avoiding such stock going to waste.

Information provided by COCIR regarding the various socio-economic impacts that could result should the exemption not be granted is summarised in Table 6-4.

Table 6-4: Possible socioeconomic impacts in a scenario in which the exemption is not granted

Impact area	Detail	Estimations from COCIR (referring to three manufacturers)*	Consultants comments on information
DEHP avoided on the market and in the waste stream	DEHP not to be placed on the market through ISEs used in compatible PoC analysers.	2.2 kg of DEHP to be avoided on the market annually.	It is noted that the amount of 2.2 Kg DEHP to be placed on the market is an annual estimation, meaning that every year for which the exemption is needed shall result in an additional 2.2 Kg of DEHP being placed on the market. It is also noted that consumables are treated as medical waste and not as EEE waste. Therefore, the exemption will not affect the amount of restricted substances in EEE waste streams.
Generation of additional waste	Equipment subject to premature obsolescence and waste from consumables should ISE cartridges containing DEHP no longer be available.	>1000 tons of waste would be generated if ISEs containing DEHP are no longer available on the EU market. Around 500 tons of WEEE from scrapped obsolete PoC equipment (containing ca. 2,100 Kg of Pb) and the rest from millions of unused associated consumables at the end of shelf life.	It is not clear why COCIR considers that consumables would be scrapped ahead of their EoL. The PoC devices already on the market are expected to be RoHS compliant and could be used as long as consumables are available. As long as the consumables are compliant at the time placed on the market, they can be used afterwards. The shelf life of the cartridges is understood to be limited (assumed up to 9 months) and would suggest that the PoC device obsolescence would follow shortly after cartridges could no longer be placed on the market. However, this would suggest only the obsolescence of these devices - ca. 500 tonnes containing ca. 2,100 Kg of Pb.

Impact area	Detail	Estimations from COCIR (referring to three manufacturers)*	Consultants comments on information
Health impacts	EU hospital PoC units that use DEHP-ISE analysers will not be able to obtain DEHP-ISE module consumables and so will not be able to analyse patients' body fluids.	The impact will be felt directly by the end users in hospitals and clinics where these critical care devices could no longer be used. This will negatively impact patient care as proper treatment would not be given and put lives at risk. Based on estimations from analysers from 3 manufactures approximately between 90 and 120 million patients would be negatively impacted per year.	In the consultants opinion it needs to be assumed that manufacturers would communicate to facilities that the consumables shall no longer be available and thus that hospitals would prepare for this process and acquire new equipment. It is not clear if devices are available on the market at present that do not use DEHP, but at least Radiometer plans to be compliant by July 2021, when the restriction of DEHP for medical devices comes into force. As a minimum, health facilities would be expected to seek compliant equipment and acquire it as fast as possible. This unplanned investment may affect the general ability to provide patients with other services in light of limited budget, but it cannot be followed that medical facilities would not replace equipment as quickly as possible.
Economic impacts	Hospitals and clinics in the EU would need to buy alternative analysers if cartridges are no longer available in the EU.	There would be a large disposable cost for the >1000 t of waste as compared to preventing approximately 2.2 kg of DEHP from being placed on the market annually. > $250 million would be incurred by hospitals to replace all systems (decision process for new equipment, unanticipated invest-ment, new stocks of consumables, staff training, connection to internal system, etc.).	Where the cartridges use DEHP, the emissions and economic impacts on waste EEE treatment facilities should only be considered for 500 tonnes of obsolete devices. Where the cartridges cannot be placed on the market, there will be a decrease in respective treatment services – either the range of such services provided is to decrease or where new equipment will be bought, there will be decreases in other services that would be invested in were the exemption available. In this sense, the estimation of $250 million represents an estimation of the maximum decrease of services provided to patients. The impact on patients described above which is

Impact area	Detail	Estimations from COCIR (referring to three manufacturers)*	Consultants comments on information
			the result of this decrease is unknown in range. (See also comments on generation of additional waste and health impacts).
Impacts on manufac-turers	Manufacture of substitute equipment (if and when suitable designs are available) to replace non-compliant ones will have environmental and health impacts.		It can be followed that new manufacture to replaced devices reaching EoL early shall result in additional use of resources, i.e. in resources used not reaching their full potential. It is assumed that other environmental or health impacts of manufacture are controlled, as required by legislation of emissions of facilities, for example by the Industrial Emissions Directive where EU manufacture is concerned.
Employ-ment	Impacts on employment in total, in the EU and outside the EU	All functions and a range of industries would be negatively impacted e.g. manufacturing, supply chain, service, R&D, marketing, quality, regulatory, Information technology, associated Distributors, medical services and hospitals.	Assuming that at least one manufacturer shall be compliant by July 2021 (e.g., Radiometer), alternatives are likely to be available before the restriction comes into force and it is thus assumed that some negative effects on employment might be offset by the industry sector which has reached compliance.

Source: *Summary from data presented in COCIR (2018) and COCIR (2019)*

Note: *COCIR Refer in their information to impacts related to three manufacturers, though it is not clear which manufacturers are meant. In relation to impacts on end-users, the previous review of Ex. 41, Annex IV also offered examples from typical German hospitals regarding the possibility of using other devices should the non-RoHS compliant cartridges no longer be sold within the EU. To support the critical review, it is noted that blood analysers used in German hospitals are usually from one vendor and one single model. This is done to facilitate standardization and harmonization in training and use procedures within the hospital staff (Gensch et al. 2019).

According to the information above, it is understood that even though stocking-up with consumables for the current compatible PoC analysers is an eventual possibility for hospitals, the limited shelf time would result in premature obsolescence of these

equipment (expected once the maximum shelf life of stocked cartridges is reached). Subsequently, it would be necessary to replace the PoC analysers with alternative RoHS-compliant PoC equipment, which would lead to unexpected financial and operational challenges for the end-users (both for hospitals and staff). These challenges translate into negative health impacts and delays in health services for patients.

The consultants' understanding of considerations in terms of the environmental and socioeconomic arguments provided for this exemption are summarised as follows:

- The EoL waste treatment of cartridges for PoC blood analysis equipment is not understood to be affected by the compliance of the ISE sensors with the substance restriction. Discarded cartridges are managed as medical waste and treated by energy recovery regardless of whether the ISEs contain DEHP or not. In this sense, whether an exemption will be granted or not shall not affect possible emissions related to the treatment of waste in WEEE facilities - the restriction of the DEHP cartridges on the market shall not have a benefit in terms of possible DEHP emissions at EEE waste management facilities.
- Considering the limited shelf life of consumables for PoC analysers and the design compatibility between cartridges with specific devices, an eventual premature obsolescence of the equipment currently on the market (ca. 30,000 instruments) is unavoidable, should the exemption not be granted. In this respect, it is not that additional waste shall be generated, but rather that the waste of such devices shall be generated prematurely. Considering COCIR's estimation that the "*life-time of ISE PoC Analyzer is 9.7 years, with >50% of the install base older than 10 years*" and considering the limited shelf-life of cartridges, suggests that early obsolescence of equipment is to affect a large part of the equipment in stock.
- Though the amount of 2.2 kg DEHP to be avoided annually should the exemption not be granted is to be viewed as a benefit for the environment/health, this scenario shall also result in ca. 500 t of waste being generated of devices scrapped early in light of the unavailability of ISE consumables on the EU market, i.e. in a cost in terms of resource use. It is not straightforward to determine if the benefits of avoiding DEHP justify the costs of the early scrapping of materials such as aluminium, steel and copper contained in the PoC devices.
- In order to replace the scrapped PoC obsolete equipment, around 2,100 kg of lead would enter the EU market through new devices replacing the installed base. It is noted that such impacts are expected anyway when new devices will be placed on the market and in this sense, this is viewed as an acceleration of an impact expected in the further future.
- Costs for hospitals and other health providers represent the main negative economic impacts.

6.5.4. Scope of the Exemption

Following the initial review of the exemption request application, and in light of the information made available, an effort was made to detail the range of body fluids falling under the scope of the requested exemption. In its original application, COCIR specifies that the exemption is "for point of care analysis of ionic substances in human body fluids" (COCIR 2018b). However, based on the information presented in the

exemption application, analyses are currently only performed on the following fluids: blood samples, pleural fluids and dialysate.

In this respect, in the first round of clarification questions, COCIR was asked to provide a complete list of body fluids of relevance to this type of ISE measures, to which they listed the following: (COCIR 2019b):

- Whole Blood
- Serum
- Plasma
- Urine
- Cerebral Spinal Fluid
- Pleural fluid

Additionally, it was clarified that although dialysate is not a body fluid, the instrument and sensors are also used to measure this in cases of patients undergoing lifesaving dialysis. Therefore, according to the applicant, other body fluids and dialysate also need to be included within the scope of the exemption.

In this case, the consultants consider that the initially proposed scope of this exemption to be too narrow to cover all application areas and would propose to add dialysate fluids to the formulation. The following formulation, which was agreed with the applicants, should be used should an exemption be granted:

„Bis (ethylhexyl) phthalate (DEHP) in ion selective electrodes applied in point of care analysis of ionic substances present in human body fluids and/or in dialysate fluids."

6.5.5. Conclusions

Article 5(1)(a) provides that an exemption can be justified if at least one of the following criteria is fulfilled:

- 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**;
- the **reliability** of substitutes is not ensured;
- 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.

In the review of this request for exemption, in relation to scientific and technical progress, it can be understood that alternative plasticisers are available on the market. Professor Meyerhoff claims that other plasticisers can function effectively for all the relevant ISEs for reliable measurements in whole blood samples.

Nonetheless, COCIR puts forward that some producers, have conducted tests with alternative plasticisers, but have not yet found and implemented a substitute suitable for the reliability and time requirements of results provided by PoC analysers. COCIR has provided sufficient information to show that efforts with alternative plasticisers have resulted in unreliable results, which do not meet the time standards and

replicability required for the intended use in PoC situations. Nevertheless, Radiometer declares that a substitution would be achieved in their PoC analysis devices before 21 July of 2021, when the DEHP restriction shall apply to medical devices under the scope of RoHS. The consultants thus question the need for an exemption with the maximal duration as requested by COCIR. Seeing as Radiometer expects to achieve substitution by 2021 confirms that substitution is possible, and also considered reliable, though it can be followed that the time needed to achieve compliance may vary from manufacturer to manufacturer to some degree.

In terms of environmental impacts, where substitution is achieved, there is no information as to the identity of the substitute used, and thus the comparison of the negative impacts of the alternative substances with that of the use of DEHP is not feasible at the substance level on the base of the publicly available information. It is noted that Radiometer intend to apply the substitute before 21 July 2021. This is understood to mean that in the recertification of the cartridges it has not been found that the use of the substitute would "*compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons*", as placing such devices on the market would not be allowed according to Directive 3/42/EEC concerning medical devices (Annex I, Essential Requirements, 1.1, stipulating the conditions to be fulfilled for a medical devices to be placed on the Union market).

Nonetheless, additional environmental and socio-economic aspects are of relevance. These relate to a substitution scenario in which DEHP can no longer be used and include socio-economic impacts (Article 5(1)(a) sentence four). They do not refer directly to the environmental comparison of the DEHP-based cartridges and their substitutes (compliant cartridges or alternative technologies).

Environmental impacts include:

- It is expected that the annual placing on the market of 2.2 kg DEHP could be avoided as a consequence of not granting this exemption request. Seeing that as of July 2021, at least one manufacturer is expected to be compliant, this annual amount would decrease. This decrease will further continue as additional manufacturers become compliant. This impact is understood to be of absolute nature - expected in an exemption scenario and prevented where the exemption is not granted, however it is not expected to have an actual benefit. Despite the fact that DEHP is to be placed on the market, it is understood not to lead to impacts that are not acceptable in the use phase (as this would not be allowed through the Medical Devices Directive) nor to impacts in the waste management of EEE, seeing as all analysis cartridges (with DEHP or without) are to be disposed of as medical waste. In other words, as the exemption scenario is not expected to result in actual negative impacts, vice versa it cannot be assumed that a substitution scenario will result in benefits (prevention of impacts).
- In contrast, not granting an exemption shall lead to negative impacts from resulting premature waste flows and new materials needed for manufacturing and placing new devices on the market. This is related to the approx. 500 tonnes of WEEE from scrapping PoC equipment subject to premature obsolescence, but also a similar amount of materials required to manufacture new equipment prematurely

in replacement of the ones that can no longer be operated, also containing other restricted substances such as lead (2,100 kg of lead foreseen). In this case, the impacts are not absolute but considered only as an acceleration of impacts expected anyway. Though premature scrapping of equipment is to be understood as an impact, however, under an exemption scenario, the equipment would be expected to be scrapped at the end of its service life (approx. 10 years) and it can be expected that some of the analysers in the EU stock shall be newer and some older.

It is not straightforward to weigh the prevention of 2.2 kg of DEHP being placed on the market against the acceleration of impacts related to premature obsolescence of the existing stock (500 tonnes) and premature manufacture and placing on the market of new equipment produced from various resources and containing about 2.1 tonnes of lead.

A further indication for a weighting of the amount of 2.2 kg of DEHP being placed on the market by this exemption request, is to consider the tonnages of DEHP brought on the market by all applications:

- DEHP is registered under REACH for manufacture and use in the EU in a tonnage band of 10,000 – 100,000 tonnes per annum.[30] This does not include the import of DEHP in articles.
- The European PRODCOM statistics on the production of manufactured goods contains an entry for the group 'dibutyl and dioctyl orthophthalates'[31] to which but not exclusively DEHP belongs; thus, the total volume for the EU28 of 281,379 tons in 2018 that even exceeds the tonnage band for DEHP indicated by the registration dossier cannot only be ascribed to DEHP.

Though the RoHS Directive does not foresee a threshold for total amounts per year of restricted substances to be considered in exemption requests, a comparison of amounts of DEHP applied in total might support the socio-economic impacts. Against the amounts of DEHP for all applications ranging from 10 000 to 100 000 tons per year of DEHP manufactured and/or imported in the European market per year,[32] the amount 2.2 kg of DEHP can be considered a minor amount that has to be weighed against the following impacts on health:

In terms of **impacts on health**, it can be followed that not granting the exemption would also result in a significant impact on healthcare facilities currently using ISE PoC analysers that contain DEHP. In such cases, devices currently on the market are expected to become non-operational shortly after ISE cartridges containing DEHP are no longer available. Such devices would need to be replaced relatively quickly after cartridges can no longer be placed on the market and could no longer be operated. This would mean that health facilities would not be able to operate the equipment over intended lifetime (loss of benefits related to past investments) and would also need to liquidate sufficient funds to allow purchasing compliant equipment relatively quickly

[30] ECHA Registered Substance Database: Entry for Bis(2-ethylhexyl) phthalate; https://echa.europa.eu/de/registration-dossier/-/registered-dossier/15358

[31] PRODCOM Code 20143410.

[32] As a substance; this does not cover the import of DEHP in articles.

and to train staff on how to use it. Such investments would not have been planned and could affect the range of other services to be provided by such facilities. COCIR estimates that the overall impact to hospital infrastructure is similar to that described in Exemption 41, Section 7.4.5 of Gensch et al. (2019). In this report, an estimation was made for a single hospital of medium size and referred to unanticipated investment costs of over 300,000 euros for new equipment; another 20,000 euros for connecting the new instruments to existing information systems and costs related to the training of staff on the new equipment estimated at 1,200 hours of non-productive work (Gensch et al. 2019).

The first two Article 5(1)(a) criteria are not considered to be fulfilled, seeing as substitutes shall exist by the time the DEHP restriction comes into force for medical devices (22 July 2021) and are considered reliable.

In terms of Article 5(1)(a) third criteria, in past evaluations, fulfilment has been based on a comparison of health and environmental impacts of the RoHS substance in a specific application and impacts of its direct substitute (substance or technology to substitute the initial application). In the current case, the comparison cannot be based on a direct substitute but perceives the general scenario of substitution (i.e., impacts referred to are not tied to the available substitute but to a scenario in which DEHP can no longer be used. Assuming the European Commission can follow this interpretation, this criteria could be observed as fulfilled, i.e., meaning that "*the total negative environmental, health and consumer safety impacts caused by*" the substitution scenario in which DEHP cannot be used "*are likely to outweigh the total environmental, health and consumer safety benefits thereof*."

Article 5(1)(a) also specifies that "*decisions on the inclusion of materials and components of EEE in the lists in Annexes III and IV and on the duration of any exemptions shall take into account [...] the socioeconomic impact of substitution*".

In this regard, the non-availability of cartridges, subsequently leading to early EoL of devices already on the market, is expected to lead to various socio-economic impacts including environmental impacts (early obsolescence, premature manufacture of new EEE) and particularly to high costs for replacement of the devices by medical facilities which shall subsequently lead to health impacts, i.e. impacts on the range of services provided. Though not granting an exemption shall reduce the amount of DEHP to come on the market, this scenario should be weighed against:

- the premature obsolescence of ISE PoC analysers in stock;
- the accelerated use of resources for manufacturing new equipment (including ca. 2.1 tonne Pb); and
- the burden of compliance for health facilities that is expected to affect the quality and range of health services and thus to affect the health of patients.

To summarise, in the current case, it is observed that DEHP technologies shall be available in July 2021, when the DEHP restriction comes into force for medical devices. These substitutes are, however, not compatible with analysis devices of all manufacturers. Not providing an exemption, however, will lead to certain environmental and health impacts: Though the placing of DEHP on the market would be avoided, it would result in ca. 500 t of analysis devices being scrapped prior to

their end-of-life and in a use of around 2,100 kg of lead in the manufacture of devices to replace those scrapped early. It will also result in a decrease in health services to patients, either directly where analysis devices are not available to provide the services currently available at facilities or through funding being allocated from other services towards purchase of new analysis devices. Though it cannot be quantified, this is expected to have an impact on patient health that shall differ from case to case. It is also noted that avoiding the placing on the market of DEHP is not expected to have an actual environmental benefit, seeing as ISE are considered medical waste and sent to incineration, regardless of whether they contain DEHP or not.

It is observed that at least one manufacturer shall be compliant with the DEHP restriction as of July 2021, meaning that developing alternatives is feasible, even if other manufacturers may require additional time to complete this task. Should the exemption be granted, it is recommended to provide a validity of 7 years from the date of approval. Should a request for renewal of the exemption be made, the status of compliance of other manufacturers should be asserted to conclude whether the range of expected impacts would still warrant a renewal.

6.6. Recommendation

Seeing as Radiometer expects to achieve compliance by 22 July 2021 for ISE PoC analysis devices, it is concluded that after this date or in close proximity to it, the first two main Article 5(1)(a) criteria shall no longer be fulfilled for the requested exemption: substitutes shall be available and reliable. Assuming that the third Article 5(1)(a) criteria applies to the scope of a substitution scenario and not just the impacts of the actual substitute, this criterion can be considered fulfilled. Socio-economic aspects also support the exemption, seeing as not granting an exemption is expected to result in the early obsolescence of analysers of other manufacturers already on the market. Translating into socio-economic costs of a no-exemption scenario, particularly those expected for health facilities, and the impact related to the early scrapping of devices currently operating in the EU stock, are seen as significant.

It is further recommended to grant the exemption requested by COCIR for a duration of 7 years from the date of approval.

In this case, the exemption should be granted with the following formulation:

Exemption formulation	Duration
Bis (ethylhexyl) phthalate (DEHP) in ion selective electrodes applied in point of care analysis of ionic substances present in human body fluids and/or in dialysate fluids	7 years