# Exemption Request Form

Date of submission: 20th December 2019

## 1. Name and contact details

### 1) Name and contact details of applicant:


| | | | |
|---|---|---|---|
| Company: | COCIR | Tel.: | 00327068966 |
| Name: | Riccardo Corridori | E-Mail: | corridori@cocir.org |
| Function: | EHA Policy Senior Manager | Address: | Blvd A. Reyers 80, 1030 Bruxelles |


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

| | | | |
|---|---|---|---|
| Company: | _____ | Tel.: | _____ |
| Name: | _____ | E-Mail: | _____ |
| Function: | _____ | Address: | _____ |

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## 2. Reason for application:

Please indicate where relevant:

☐ Request for new exemption in:

☐ Request for amendment of existing exemption in

☒ Request for extension of existing exemption in Annex IV

☐ 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: 29

Existing wording: Lead in alloys, as a superconductor or thermal conductor, used in cryo-cooler cold heads and/or in cryo-cooled cold probes and/or in cryo-cooled equipotential bonding systems, in medical devices (category 8) and/or in industrial monitoring and control instruments.

Proposed wording: Lead in alloys as a thermal conductor in cryo-cooled cold probes in medical devices (category 8)

Duration where applicable: Maximum Validity period

☐ Other: _____

## 3. Summary of the exemption request / revocation request

Cryo-cooled cold probes are used in cryoablation therapy to generate local low temperatures in medical therapy to destroy abnormal or diseased tissue. The interface between the components of the cryo-cooled cold probe are joined together using lead-tin-silver solder. The solder wicks in between the components, joining them mechanically and thermally. The cryo-cooled cold probe functionality depends directly on its ability to cool (freeze) and heat (thaw) rapidly during a cryoablation procedure and so a high thermal conductivity of the solder is essential. In turn this is dependent upon the ability of the internal components including the cryostat (machined heat exchanger) to reach the desired temperatures rapidly and uniformly.

The lead alloy solder joints are required to be able to withstand a large amount of stress (mechanical, chock and temperature) while having suitable ductility. Due to the substrates the solder has to join (stainless steel, copper, and brass) and wick between the manufacturability of the joint is technically challenging.

Lead free solders of tin-silver and tin-copper have been trialled and deemed unsuitable, with current testing on tin-copper-silver solder being undertaken. Alternative technologies have been considered, including the use of brazing/welding, adhesives, mechanical bonds and additive manufacturing; all of which are unable to demonstrate the required technical performance required for cryo-cooled cold probes.

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## 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: Cryo-cooled cold probes used in cryoablation therapy

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

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

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

c. Please specify for equipment of category 8 and 9:
The requested exemption will be applied in
☐ monitoring and control instruments in industry
☐ in-vitro diagnostics
☒ other medical devices or other monitoring and control instruments than those in industry

2. Which of the six substances is in use in the application/product?
(Indicate more than one where applicable)
☒ Pb ☐ Cd ☐ Hg ☐ Cr-VI ☐ PBB ☐ PBDE

3. Function of the substance: Lead in solder as a thermal conductor, used in cryo-cooled cold probes

4. Content of substance in homogeneous material (%weight): 50-60% (54% nominal)

5. Amount of substance entering the EU market annually through application for which the exemption is requested: 2.8kg of lead
Please supply information and calculations to support stated figure.
This is provided separately as the calculation includes confidential market information.

6. Name of material/component: Lead Solder alloy

7. Environmental Assessment: Not applicable as there are no technically suitable substitute materials or designs that are known to be sufficiently reliable.
LCA: ☐ 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?**

Cryo-cooled cold probes are used in cryoablation therapy to generate local low temperatures in medical therapy to destroy abnormal or diseased tissue. The cryotherapy delivered by the system is based on the Joule Thomson effect where high-pressure argon gas (generally at 3,100 psi) is circulated through cryo-cooled cold probes to induce tissue freezing at the distal end (far end) of the probe, creating an ice ball. A cryostat is used to maintain a low temperature within the shaft and allow for rapid cooling and heating during the procedure. Once the freezing is complete, active tissue thawing is then achieved by circulating helium gas under pressure (generally 1,700 psi) through the cryo-cooled cold probes creating a warming effect to melt the ice ball. The freezing and thawing is repeated until the ablation (tissue destruction) of targeted tissue is complete and is typically repeated at least two times, as shown in Figure 1.

Figure 1 Cryo-cooled cold probe example, showing with the integrated ice length slider adjustment feature allowing the user the ability to vary the size and shape of the ice ball, depending on clinical requirements

The Cryocare CS Surgical System is an example of a system which can control up to eight, single-use, disposable cryo-cooled cold probes which are provided sterile to the user.

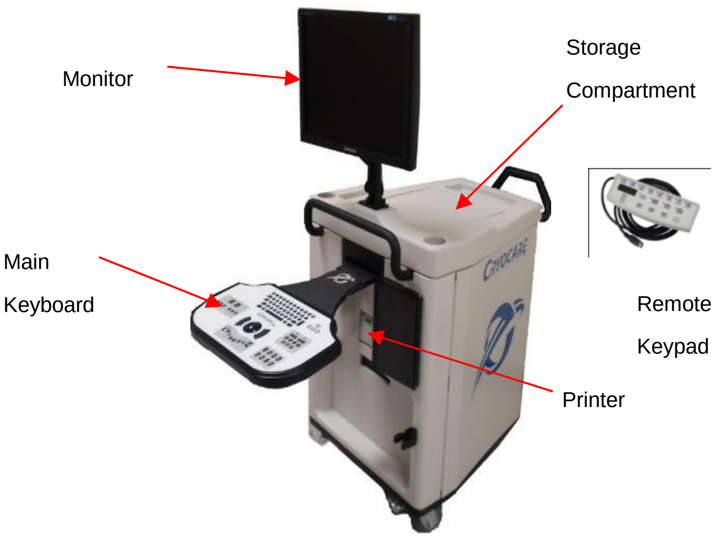


Figure 2 Cryocare CS™ Surgical System (Front)

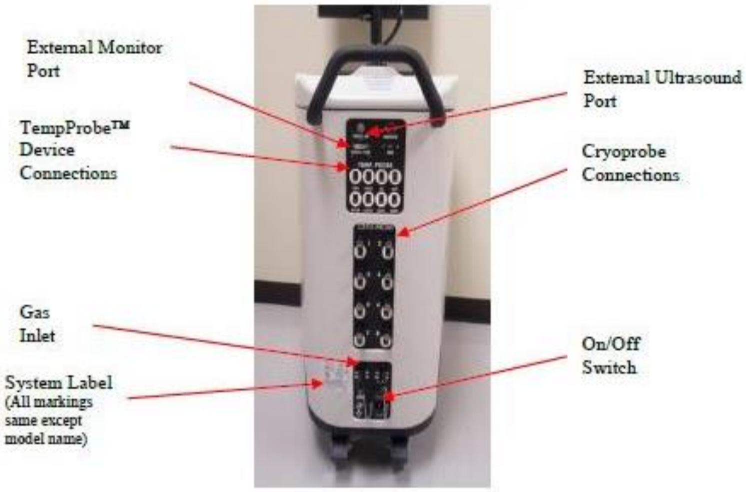


Figure 3 Cryocare CS$^{TM}$ Surgical System (Back)

Each cryo-cooled cold probe is assembled using several components consisting of items formed from stainless steel, copper, and brass, connected to the sharp tipped probe shaft that is inserted into the body. At the distal end of the shaft is the expansion chamber where argon gas under pressure (at greater than 3,000 psi) expands and causes the tip, and a controlled length of the shaft, to reach -180°C to allow the rapid freezing of the surrounding tissue. As the cold argon gas travels away from the active freezing area it passes into a vacuum sleeve that protects the rest of the shaft from the freezing temperatures. After reaching the handle area of the cryo-cooled cold probe the released cold argon gas travels through a cryostat which serves as a heat exchanger to allow the incoming argon gas to be pre-cooled. A thermocouple is used to verify functionality of the freezing and thawing cycles by measuring the temperature of the return gas, with the thermocouple and lead solder experiencing temperatures of at least as low as -80°C during freezing application.

The interface between the components of the cryo-cooled cold probe are joined together using lead-tin-silver (54% Pb, 45% Sn, 1% Ag w/w) solder, with each probe having between 8 – 10 connections. The solder wicks in between the components, joining them mechanically and thermally. The cryo-cooled cold probe functionality depends directly on its ability to cool (freeze) and heat (thaw) rapidly during a cryoablation procedure and so a high thermal conductivity of the solder is essential. In turn this is dependent upon the ability of the internal components including the cryostat (machined heat exchanger) to reach the desired temperatures rapidly and uniformly. The lead alloy solder joints allow this to occur during a procedure.

The reliability of the solder joint is crucial for patient safety, as if it were to fail, the shaft which normally would be at non-freezing temperature may become extremely cold causing damage to non-targeted tissues including arteries, veins, or nerves and the skin at the insertion site. Lead based solder joints in cryo-cooled cold probes have had a very long and successful history of use for cryogenic medical procedures for over 20 years and have proven to be very safe and reliable.

Cryo-cooled cold probes are crucial for medical treatment and offers advantages over other methods of cancer treatment:

- They are less invasive than surgery, reducing pain, bleeding and other complications;
- Shorter recovery time of patients, therefore reducing the need for prolonged or any hospital stay, reducing procedure costs to the healthcare systems;
- Reduction of damage on nearby healthy tissue due to the focused nature of the treatment;
- Can be used in combination with standard treatments such as surgery, chemotherapy, hormone therapy and radiation; and
- May offer an alternative to treating cancers that are considered inoperable, due to other medical factors or are not responding to standard treatments.

The following are some examples of applications in which the cryo-cooled cold probes are used:

- Prostate cryosurgery[1,2];
- Renal cryosurgery[3] offering lower rates of local tumour progression versus Radiofrequency ablation[4];
- Pulmonary (lungs and thoracic (chest) tumours;
- Liver metastases (secondary malignant cancer growths)[5];
- Gynaecological tumours[6];

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[1] Wenske, S., Quarrier, S., Katz, A. et al. Salvage Cryosurgery of the Prostate for Failure After Primary Radiotherapy or Cryosurgery: Long-term Clinical, Functional, and Oncologic Outcomes in a Large Cohort at a Tertiary Referral Centre; European Urology, V.64, 1-7 (2013)

[2] Sze, C., Tsivian, E., Tay, K.J. et al. Anterior gland focal cryoablation: proof-of-concept primary prostate cancer treatment in select men with localized anterior cancers detected by multi-parametric magnetic resonance imaging. BMC Urol 19, 127 (2019)

[3] Rodriguez, R., Chan, D., Bishoff, J. et al. Renal ablative cryosurgery in selected patients with peripheral renal masses. Urology, V.55, 25-30 (2000)

[4] Kunkle DA and Uzzo RG: Cryoablation or Radiofrequency Ablation of the Small Renal Mass: A Meta-analysis. Cancer 113: 2671-2680 (2008)

[5] Kawamura, M., Izumi, Y. et al Percutaneous cryoablation of small pulmonary malignant tumours under computed tomographic guidance with local anaesthesia for nonsurgical candidates, The Journal of Thoracic and Cardiovascular Surgery, V.131, Issue 5, 1007-1013 (2006)

[6] Butros, S., DelCarmen, M. Et al. Image-Guided Percutaneous Thermal Ablation of Metastatic Pelvic Tumor From Gynecologic Malignancies, Obstertics & Gynecology, V123, Issue 3, 500-505 (2014)

- Dermatolgical (skin) tumours[7];
- Otorhinolaryngology (ear, nose and throat surgery);
- Proctology (rectum, anus, and colon); and
- Tissue in pain management[8].

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

The internal components of the cryo-cooled cold probe are assembled together using a tin-lead solder alloy with approximately eight to ten soldered joints per probe. The lead solder has to have the following functionality:

- The ability to withstand large amounts of stress from the following factors and maintain a reliable bond:
  - Cryo-cooled cold probe use involves manual manipulation of the probe during use and thus mechanical stresses are induced which could lead to brittle joint failure;
  - Ability to withstand mechanical shock which the probe may experience during transportation and in service use due to being dropped;
  - The use of high pressure gas (argon - typically at 3,100 psi) is introduced into the cryo-cooled cold probe (for at least two ten minute cycles) during routine one-time use (treatment procedure) which places stress on the solder joints;
  - Very large temperature changes including to very low temperatures;
- The lead solder must have high thermal conductivity and thermal capacity at cryogenic temperatures. The thermal properties of materials at ambient temperatures are very different to those at cryogenic temperatures and so the commonly used metals used in domestic refrigerators are not suitable at such low temperatures. Research has shown that lead is a particularly good material in this application and has 20 years of data supporting its use due to its high thermal conductivity and thermal capacity;
- Lead / tin solder is relatively ductile at low temperatures and able to withstand the thermal shock that occurs when cryo-cooling begins (freeze cycle) and ends (thaw cycle);
- Lead provides a strong flexible bond between components of different materials (stainless steel, brass, and copper) that have differing coefficients

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[7] Goncalves, JCA., Fractional Cryosurgery for Skin Cancer, Dermatologic surgery, V.35, Issue 11, 1788-1796 (2009)

[8] Moore M, et al: CT Guided Percutaneous Cryoneurolysis for Post Thoracotomy Pain Syndrome. Acad Radiol 17:603-606 (2010)

of thermal expansion (the material distorts to accommodate movement between adjacent materials due to differential thermal expansion and contraction when temperatures change);

- Resistance to oxidation and corrosion in conditions of use; and
- Ability to form very small and well defined, continuois circumferential solder joints, requiring good flow and wetting properties of the bond on difficult-to-solder metals.

Wetting refers to the capacity of molten solder to interact with a substrate, at the interface of solder and substrate, to form a certain amount of intermetallic compound that acts as an adhesion layer to join the solder and the substrate. The reaction between the solder and substrate is important as it may affect the micro-structure and eventually the mechanical strength of the solder joint.

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

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

A closed loop system does not exist as the cryo-cooled cold probes are disposed of as infected medical waste after each procedure.

**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: _____

☐ Article cannot be recycled and is therefore:

- ☒ 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 _____

☒ In articles which are sent for energy return 2.8kg of lead (as used probes are contaminated medical waste, they must be incinerated, however, the probes are mostly metal so very little, if any, energy is returned

☐ In articles which are landfilled _____

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## 6. Analysis of possible alternative substances

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

Lead based solders have had a very long and successful history of cryogenic medical procedure use at cryogenic temperatures, for over 20 years and have proven to be very reliable. The cryo-cooled cold probe undergoes a large amount of stress during it lifetime, as described in Section 4A, which includes thermal cycling.

Lead free solders have been trialled by a manufacturer with both a tin-silver alloy (96% Sn, 4% Ag w/w) and a tin-copper alloy (97% Sn, 3% Cu w/w) trialled on 10 and 4 (including two different designs) cryo-cooled cold probes respectively. The trial of alternatives showed manufacturability issues where the very small and continuous circumferential solder joints in the cryo-cooled cold probe were unable to be formed to the required standard as is achieved using lead solder due to inferior flow and wetting properties of the lead-free alternatives.

It is well known that wetting of lead-free solder alloys, such as tin-silver-copper, on copper and other metal surfaces is inferior to tin-lead solder[9]. This is due to many variables which include the composition of the metal being soldered, the type of flux, the solder composition and the temperature. These variables affect the "wetting force" which allows solder to spread across a metal surface. This is important in cryo-cooled cold probes as the solder has to spread such that it flows across metal surfaces and between two adjacent metal parts to form a strong bond. In the cryo-cooled cold probes, soldering is to copper, brass and stainless steel. Solder wetting of brass is more difficult than to copper because the zinc content of brass is readily oxidised and so more aggressive fluxes are required to achieve wetting. Soldering to stainless steel is very difficult as its air-formed oxide is very inert requiring very aggressive fluxes. Solder wetting by solder on stainless steel can be very poor and the solder spread will be minimal if all oxide is not removed. The known difference in solder spread of tin/lead solders compared with lead-free solders can be exacerbated on metals such as brass and stainless steel that have air-formed oxides that are difficult to remove[10].

A feasibility study including the review of currently available data is under way on a tin-copper-silver alloy (97% Sn, 0.25% Ag w/w, 2.75% Cu).

[9] For example, http://www.techni-tool.com/ARTICLES/Kester-Lead-free-SMT-Soldering-Defects-How-to-Prevent-Them

[10] For example https://www.digikey.co.uk/en/maker/blogs/rohs-vs-non-rohs-soldering

Due to the complex geometric arrangement of the components in the cryo-cooled cold probe the solder is required to wick between components, requiring good wettability. Effective wetting is determined depending on the alloy composition, flux (and its ability to remove surface oxides), substrate and their interactions with one another. Stainless steel due to its inherent oxide film is difficult to solder in comparison with other metallic substrates as it limits solder adhesion to the surface. Although with careful pre-treatment and selection of alloy composition and a suitable flux, soldering is possible, there will always be differences in the wetting properties of lead-free solders compared with lead-solders due to differences in surface tension forces.

A contributing factor to the ability to substitute for lead free solders is the concern about reliability at low temperatures. It is known that all solders become harder and much more brittle as temperature decreases and most lead-free solders are harder than SnPb. Lead-free solders are less ductile than tin lead at room temperature, examples of hardness values for un-annealed alloys are (with a lower hardness value indicating a softer more ductile material):

- Eutectic tin 37% lead Vickers hardness = 12.9
- Tin 4.7% silver 0.7% copper Vickers hardness = 21.9

Harder solders are likely to induce higher stress levels that would be more likely to cause damage to the solder (e.g. cracks or de-bonding). Relatively soft and ductile materials can deform to relieve any stresses that will occur as a result of differential thermal expansion that will occur when temperature changes, whereas brittle materials will not deform so high stress forces will be induced, potentially leading to bond failure.

Solder is not routinely tested down to the temperatures experienced in the cryo-cooled cold probe and therefore there is limited data available. Lead-free solders have been shown to have very sharp transition from ductile to brittle behaviour at cold temperatures whereas lead alloy solders do not, with sources demonstrating the transition temperature for many lead-free solders to be in the range of -50°C to -150°C which correlates with the expected cryo-cooled probe solder joint temperatures[11,12]. The lack of substitutes with proven reliability is a concern to users of these devices as they require high reliability.

**Potential alternative technologies:**

A review of common alternative bonding methods is outlined below with their potential applicability for use in cryo-probes analysed:

- **Brazing or welding:** The advantage of this would be its ability to form strong, thermally conductive joining of the components. However high temperatures are required (500°C for brazing and >1000°C for welding) which would damage other components in the cryo-cooled cold probe. Also, braze alloys do not flow into gaps like solder and so will not form good gas-tight seals.
  Automated micro-welding equipment may overcome the damage to surrounding material however; the weld bead produced by this method is less desirable for leak prevention under high pressure than the smooth and uniform soldered joint and so will not form good gas-tight seals.
- **Thermally conductive adhesives** are commercially available however when they are cooled to very low temperatures, the adhesive has the propensity to become extremely brittle and therefore is likely to cause bond failure due the stresses imposed. Commercial thermal conducting adhesives are not specified for use at very low temperatures. Also, they have inferior thermal conductivity when compared with metals such as solder.
- **Mechanical connections:** Mechanical connections are used to make electrical connections such as with connectors but these cannot be gas-tight and so are unsuitable in cryo-cooled probes.
- **Additive manufacturing process (3D printing):** Although state of the art of additive manufacturing has been raised to a high level within the last few years, it is not possible to accurately deposit structures that form gas-tight bonds in the internal small diameter structures that are required inside the cryo-cooled probes. Due to the design of the cryo-cooled cold probe utilising multiple materials it is unlikely that additively produced structures would meet all of the technical requirement. Furthermore, additive manufacturing may introduce micro-porosity which

[11] Ratchev, P., Loccufier, T., Vandevelde, B. Et al. A Study of Brittle to Ductile Fracture Transition Temperatures in Bulk Pb-Free Solders, EMPC, 12-15 (2005)

[12] Lupinacci, A., Shapiro, AA. Et al. A study of solder alloy ductility for cryogenic applications, IEEE Interational Symposium on Advanced Packaging Materials (2013)

could jeopardize the integrity of the vacuum sleeve, thereby endangering the user and patient during use.

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

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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.**

Refer to Section 6 for recent research into substitution of lead. Manufacturers have in the past tested SnAg but found it to be unsuitable as described above. SnAgCu is being assessed but as these alloys are very similar to SnAg, these alloys are unlikely to give good reliability without extensive and lengthy research.

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

Work with SnAgCu (the most commonly used lead-free solder) will continue but if unsuitable, alternative alloys that are uncommon in electrical equipment could be assessed. At present, no alternative alloy with wetting and flow properties that are similar or better than SnPb on the metals used in the probes has been found.

When a new lead free connection design has been developed, extensive testing, often followed by clinical trials are needed before approval requests can be submitted. Typical timescales are as follows:

**Table 1 Predicted timescales for the development of lead free connections**

| **Phase** | **Elapsed time** |
|---|---|
| Research to identify potential alternatives | 1-2 years |
| Testing of alternative materials in cryo-probes | 1-2 years (if successful) |
| Design control documentation of design change | 3 months |
| Process Development for new material | 3-6 months |
| Fabrication and sterilization of test articles | 3 months |
| Reliability assessment, aging trials, sterilization testing | 1-2 years |
| Accelerated Aging (3-year shelf life | 4 months |
| Real-Time Aging (3-Year shelf life) | 3 years |
| Functional testing after aging | 2 months |
| Submission for global approvals | 1-2 years |
| **Total Cumulative Time** | Over 8 years to 12.5 years |

The timescales as outlined in Table 1 are based on the assumption that a potential alternative with the required performance as outline in Section 4(C) is found.

## 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: Lead metal registration – see https://ila-reach.org/our-substances/lead-metal/ and https://echa.europa.eu/registration-dossier/-/registered-dossier/16063

### (B) Elimination/substitution:

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

☐ Yes. Consequences? _____

☒ No. Justification: There are no current alternatives that provide a technical solution

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

☐ Yes.

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

☒ No.

Justification: _____

3. Give details on the reliability of substitutes (technical data + information):_____
4. Describe environmental assessment of substance from 4.(A)1 and possible substitutes with regard to
   1) Environmental impacts: _____
   2) Health impacts: _____
   3) Consumer safety impacts: _____

⇨ Do impacts of substitution outweigh benefits thereof? Not Applicable
Please provide third-party verified assessment on this: _____

**(C) Availability of substitutes:**

a) Describe supply sources for substitutes: _____

b) Have you encountered problems with the availability? Describe: _____

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

☐ Yes ☐ No

d) What conditions need to be fulfilled to ensure the availability? _____

**(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- Without this exemption cryo-cooled cold probes would not be able to be sold in the EU. If this system were no longer available in the EU, patients would be required to seek alternative therapy likely more expensive and possibly more invasive surgery.

In 2008 2.45 million EU citizens were diagnosed with cancer and 1.23 million died because of cancer. Cancer cost the EU €126 billion in 2009 with healthcare accounting for €51 billion. Cryo-cooled cold probes offer unique functionality and cost effective treatment in cancer treatment in areas such as lung cancer which costs the EU €18.8 billion and prostate cancer which costs the EU €8.43 billion[13].

☐ Possible social impacts external to the EU

☐ Other: _____

⇨ Provide sufficient evidence (third-party verified) to support your statement: _____

## 9. Other relevant information

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

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## 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:**

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[13] Luengo-Fernandes, R., Leal, J. et al Economic burden of cancer across the European Union: a population-based cost analysis, Lancet Oncology, V.14, Issue 12, 1165-1174 (2013)

Confidential market data is used by COCIR to calculate the quantity of lead entering the EU market annually used in cryo-cooled cold probes. Additionally the possible social impacts within the EU relating to the number of affected patients in the EU which benefit from the use of cryo-cooled cold probes. Both of these have been submitted separately.