LIGHTINGEUROPE
THE VOICE OF THE LIGHTING INDUSTRY

Request to renew Exemption 18b, 18(b)-I and Annex IV 34

under the RoHS Directive 2011/65/EU

Lead as activator in the fluorescent powder (1 % lead by weight or less) of discharge lamps when used as sun tanning lamps containing phosphors such as BSP (BaSi2O5 :Pb) & Lead as activator in the fluorescent powder (1 % lead by weight or less) of discharge lamps containing phosphors such as BSP (BaSi2O5:Pb) when used in medical phototherapy equipment

and

Annex IV exemption 34 for "Lead as an activator in the fluorescent powder of discharge lamps when used for extracorporeal photopheresis lamps containing BSP (BaSi2O:Pb) phosphors

Date: 20 January 2020

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Contents

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2 Reason for application

LightingEurope submits this application to:	*request for the renewal of existing **Annex III exemption no. 18(b) and 18(b)-I and Annex IV exemption no. 34***
LightingEurope proposes to continue using the existing wording which is:	*18(b) Lead as activator in the fluorescent powder (1 % lead by weight or less) of discharge lamps when used as sun tanning lamps containing phosphors such as BSP (BaSi2O5 :Pb)* *And* *18(b)-I Lead as activator in the fluorescent powder (1 % lead by weight or less) of discharge lamps containing phosphors such as BSP (BaSi2O5:Pb) when used in medical phototherapy equipment* *And* *Annex IV exemption 34 for "Lead as an activator in the fluorescent powder of discharge lamps when used for extracorporeal photopheresis (ECP) lamps containing BSP (BaSi2O:Pb) phosphors*
LightingEurope requests a duration of	*Maximum validity period required.*

3 Summary of the exemption request

This request concerns the extension of the current Annex III exemption:

- **18(b)** regarding Lead as activator in the fluorescent powder (1 % lead by weight or less) of discharge lamps when used as sun tanning lamps containing phosphors such as BSP (BaSi2O5 :Pb).

And

- **18(b)-I** Lead as activator in the fluorescent powder (1 % lead by weight or less) of discharge lamps containing phosphors such as BSP (BaSi2O5:Pb) when used in medical phototherapy equipment

And

- **Annex IV exemption 34** for "Lead as an activator in the fluorescent powder of discharge lamps when used for extracorporeal photopheresis lamps containing BSP (BaSi2O:Pb) phosphors"

As recommended in the report of Oeko-Institut e..V. Assistance to the Commission on Technological Socio-Economic and Cost-Benefit Assessment related to Exemptions from the Substance Restrictions in Electrical and Electronic Equipment: Study to Assess 3 RoHS Exemption Requests (Pack 8) dated 16 February 2016.

LightingEurope further asserts that Directive 2011/65/EU Annex IV is for products which are specific to medical devices and monitoring and control instruments. Annex III currently requests products be listed in accordance with their applications including those categories listed in Annex 1 Categories 8 and 9. In order to avoid ambiguity or repetition in the application for exemptions renewals and in further consideration of the extremely small volume of lamps entering the EU and their total lead content in Annex IV products, LightingEurope requests and recommends the incorporation of Annex III Exemption 18(b)1 and Annex IV Exemption 34 for these three applications of "Lead as activator in the fluorescent powder (1 % lead by weight or less) of discharge lamps containing phosphors such as BSP (BaSi2O5:Pb)"

It is further declared as evidence to support the recommendation that the total lead content of all lamps in Annex IV ex. 34 currently in use in the EU and projected for use during the recommended maximum duration of 5 years is less than 1 kg.

This exemption covers indoor sun tanning discharge lamps containing lead as an activator in the fluorescent powder. These lamps are produced in T12, T8 and T5 diameters and CFL (compact fluorescent lamp) configurations. The phosphors contained in these lamps are manufactured from the same components but can vary in spectral discharge across the UVA and UVB spectrum by the specified proportional phosphor mix. The lamps, and equipment

they are installed in, are governed by EU regulations concerning the allowable output of ultraviolet radiation permitted within a determined exposure time. The EU regulates and tanning equipment and the installed lamps which are marked on the lamps by a specific “X, Y” code system for the erythemally-weighed UV radiation in accordance with EN standard 61228 Ed.2 (2008-01). The lamps are installed in various commercial and residential indoor tanning equipment. This can be in the form of a sun tanning bed or booth or a tabletop appliance for facial tanning. The abovementioned EN standard forms the basis of lamp marking and is required. It clearly limits room for substitution by lead-free phosphors. The regulatory demands come from the LVD ADCO group, see below reference.

At the 18th meeting of the LVD Administrative Co-operation working group (ADCO) in Brussels on the 14th November 2006 the following was unanimously agreed by the Member States present:

- The Scientific Committee on Consumer Products (SCCP) Opinion on: Biological effects of ultraviolet radiation relevant to health with particular reference to sun beds for cosmetic purposes represents the basis for good engineering practice in Europe in relation to the safety matters for such products.

- The recommendations shall be applied with effect six months from the publication of this Declaration.

- The maximum erythemal-weighted irradiance should not exceed 11 SED/h (0.3 W/m2). *Published on 22 January 2007*

Other UV lamp types are produced for dermatological and phototherapeutic use under medical supervision in Annex 3 exemption 18(b)1 or as above indicated in Annex IV exemption 34. These lamps are not used to produce visible light so general lighting efficacy standards are not relevant and therefore do not apply.

4 Technical description of the exemption request

4.1 Description of the lamps and their applications

4.1.1 Lamps covered by this exemption 18b

This exemption covers indoor sun tanning discharge lamps containing lead as activator in the fluorescent powder. The lamps produce UVA and UVB in predetermined dosages and ratios for the purpose of producing artificial sunlight. The lamps are installed in tanning equipment

which are calibrated for the use of specific lamp types and they are marked in accordance with EU regulations for tanning lamps and equipment. Brochures and data about these lamps can be seen in several websites, e.g.:

- Lighttech http://www.light-sources.com/tanning/tanning-lamp-products
- Cosmedico http://www.cosmedico.de/en/tubes.html
- Sylvania: https://www.sylvania-lighting.com/product/en-int/category/special-lighting/bodycare-and-tanning/families/

4.1.2 Lamps covered by this exemption 18(b)1

This exemption covers UV discharge lamps containing lead as activator in the fluorescent powder. These lamps are used for (medical) skin treatment such as PUVA phototherapy purposes (see brochures [1], [2]). PUVA phototherapy is a very specific application enabling effective skin treatments used in Medical applications and is explained in the brochures, for instance, a photochemical treatment where a combination of a drug e.g. Psoralen in

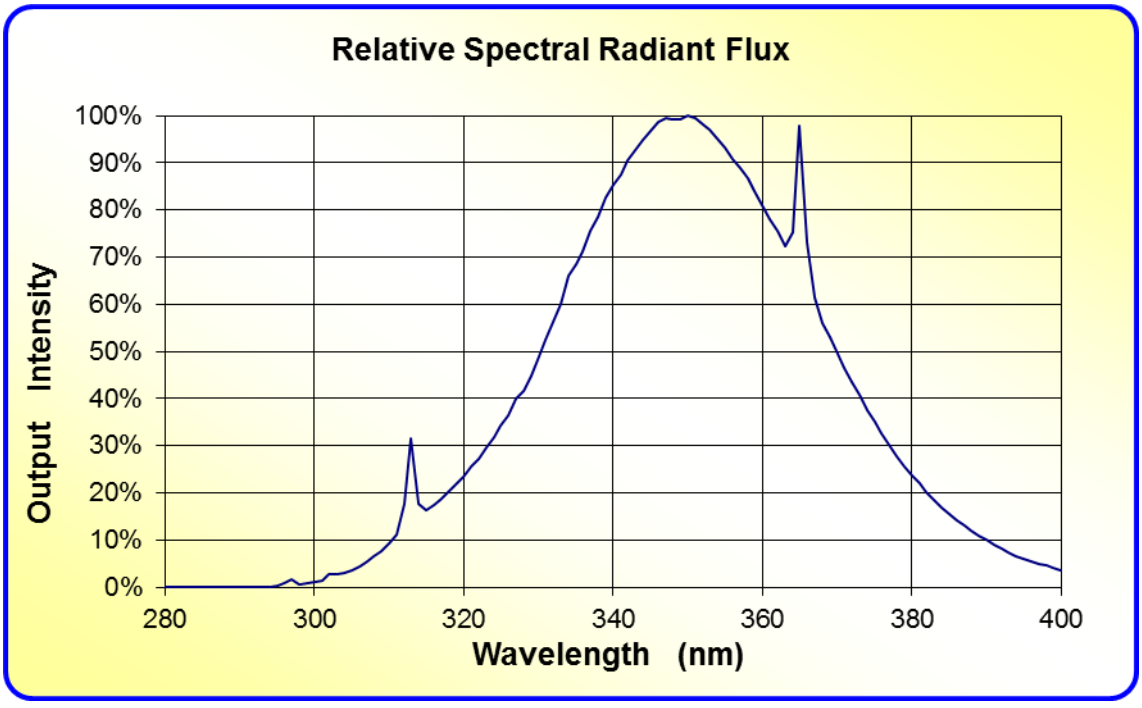
[1] Brochure Philips: http://www.lighting.philips.com/pwc_li/main/subsites/special_lighting/assets/pdf/Medical-treatment-with-phototherapy-2013.pdf

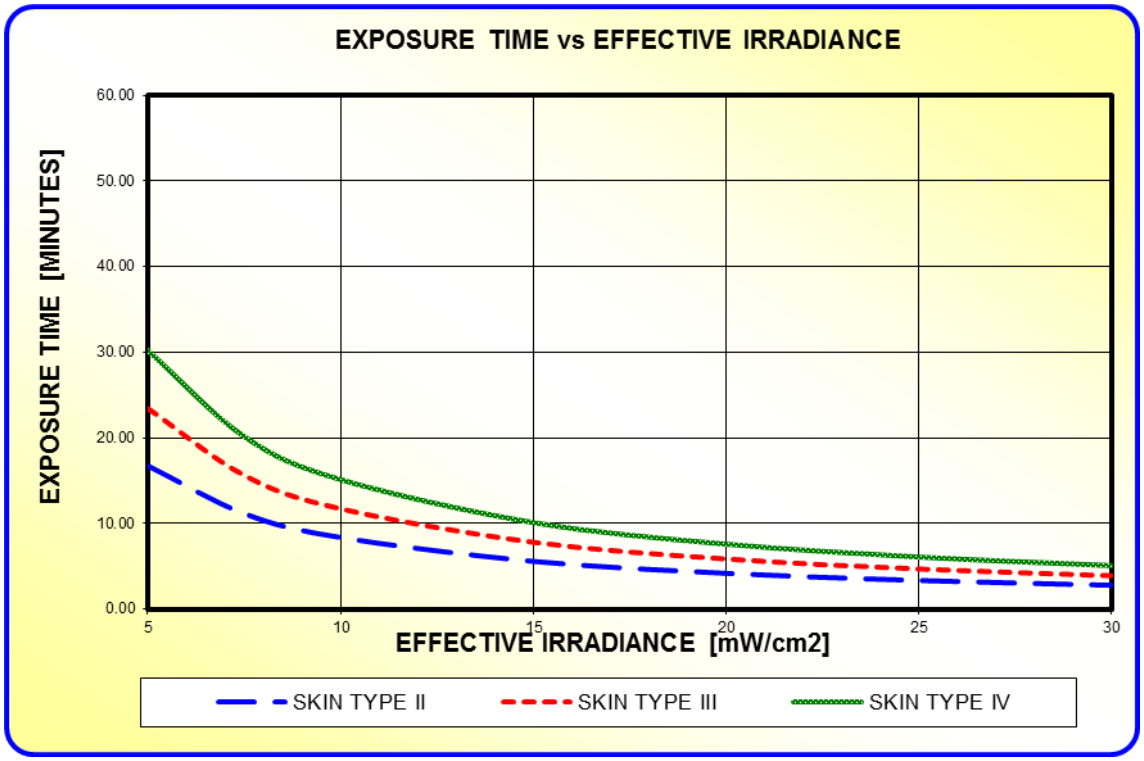
[2] Brochure LightSources: http://www.light-sources.com/specialty/applications/medical-phototherapy-photonic-activated-dermatological-treatments-and-light-t)

combination with UVA radiation is used to treat skin diseases as psoriasis, vitiligo, atopic dermatitis etc.

These lamps are produced in T12, T8 and T5 diameters and single capped configurations – see illustrations below.

The phosphors contained in these lamps are manufactured from the same components but can vary in spectral discharge across the UVA and UVB spectrum which provide a variety of erythemal outputs and exposure limits.





Graph 1: Example of a typical UVA/UVB spectrum of an indoor tanning lamp

The lamps and equipment are governed by EU regulations concerning the allowable output of ultraviolet radiation permitted within a determined exposure time. The EU regulates tanning equipment and the installed lamps which are marked on the lamps by a specific “X, Y” code system. For example, see, IEC 606335-2-27 and EN standard 61228 Ed.2 (2008-01). The lamps are installed in various commercial and residential indoor tanning equipment which can be in the form of a tanning bed or booth or a tabletop appliance for facial tanning.

The typical lifetime of these lamps ranges from 600 to 1000 hours with a session or usage time that ranges approximately from 5-30 minutes.

These lamps are not used for the production of visible light so general lighting efficacy standards do not apply. UV output efficacy (UVA radiation out vs electrical power in) is typically between 15% and 25%, but the real measure is with what power the desired effect is reached.

This is governed by the equipment, lamp type, lamp power, UV output measured by standardized means, user skin type and other such factors.

The market demand for tanning lamps remains stable for the coming years.

Regarding Annex III Exemption 18(b)1

- PUVA phototherapy lamps and equipment have always used BSP phosphors (> 25 years). Extensive literature is available on the effectiveness of PUVA phototherapy with BSP containing lamps. No studies with effective results have been done with either fluorescent lamps with other phosphors, or other technologies (LED) giving UVA/UVB spectra. PUVA equipment release and approval has always been based on extensive patient tests with lamps containing BSP

- The lamps are used for dermatological and phototherapeutic use under medical supervision and installed in dedicated phototherapy equipment.

- Although PUVA phototherapy lamps are very similar to tanning lamps in construction and incorporate lead-activated phosphors, they may have small differences in spectral distribution and exposure schedules depending on the application and the patient needs.

- The typical lifetime of these lamps ranges from 600 to 1000 hours with a session time that ranges approximately from 5-30 minutes.

- These lamps are not used for the production of visible light so general lighting efficacy standards do not apply. UV output efficacy (UVA radiation out vs electrical power in) is typically between 15% and 25%, but the real measure is with what power the desired effect is reached (e.g. clearance rate for PUVA phototherapy lamps).

- The market demand PUVA phototherapy-lamps remain stable for the coming years.

Regarding Annex IV Exemption 34

Annex IV exemption 34 was previously requested by Therakos, Inc. for the use of lead activated phosphors in the lamps used in their Extracorporeal Photopheresis (ECP) equipment. LightingEurope members have worked directly with Therakos to assist in the preparation and submission of this exemption renewal request which is attached hereto in its entirety. We are submitting this request to harmonize the exemptions for medical products contained in Annex 3 and Annex IV and as written in this request for renewal. We will make reference to the ECP

products throughout this document but consider the separate application to be a more efficient method for your review and consideration.

We refer to the comments regarding the BSP phosphors used in 18b1 PUVA medical lamps. The same phosphor is a major component used in the design and manufacture of the ECP lamps. The separate renewal request document will elaborate on the critical need for this phosphor in these lamps and the extended development, clinical testing and approval processes that were required to approve this product for medical use.

LightingEurope is unaware of any current development efforts in the manufacture or availability of alternate lead-free phosphors for this application. Given the changes in the lighting industry and movement to alternate light sources such as LED, LightingEurope is unaware of and does not expect that new phosphors will be developed for this application. LED technology has been investigated by the equipment manufacturer for their medical device products but at the time of this writing there are no LED solutions available.

As stated in the Therakos renewal request "This exemption is required to allow the use of lead in a UVA lamp phosphor used for extracorporeal photopheresis (ECP) treatment of cutaneous T-cell Lymphoma (and other T-cell related diseases). The treatment involves exposure of leukocytes that are temporarily removed from patient's blood to light from lamps with lead doped barium silicate phosphor. The light activates a drug which has been introduced into the leukocyte fraction of the blood. This type of phosphor emits a unique spectrum that is optimum for this medical treatment. All other UVA phosphors contain less light of the effective wavelengths or have shorter wavelengths that cause further damage to cells. Therefore, there is currently no substitute lamp type for treatment of this disease by extracorporeal photopheresis as described in this application."

4.1.3 Applications covered by this exemption 18b

Indoor tanning lamps are light sources that produce ultraviolet light in the regions of the UVA and UVB spectrums. Their intent is to produce artificial sunlight to replicate sunlight exposure for the human body (similar to that as produced by the sun) yet applied in calculated doses per European regulations. It is estimated that over 90% of indoor tanning lamps produced and used throughout Europe are manufactured with BSP ($BaSi_2O_5$:Pb) phosphors containing 1% or less lead as an activator. There is no feasible alternative for this phosphor that will yield the same or similar results and has undergone the extensive European and US regulatory testing associated with the application of the tanning lamps using these phosphors.

Almost 100% of the tanning lamps using these phosphors are produced in the EU. Below are three examples of typical indoor suntanning equipment.

Left and center photos are tanning beds and right photo is a tanning booth.

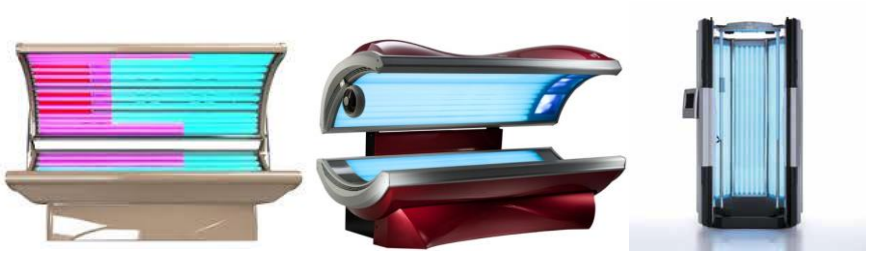


Figure 2: Examples of Indoor tanning equipment

4.1.4 Applications covered by exemption 18(b)1

PUVA phototherapy lamps are light sources that produce ultraviolet light in the regions of the UVA and UVB spectrums. Their intent is to produce artificial sunlight to replicate sunlight exposure for the human body (similar to that as produced by the sun) yet applied in calculated doses as regulated by European regulations. It is estimated that over 90% of indoor UVA phototherapy lamps produced and used throughout Europe are manufactured with BSP (BaSi2O5:Pb phosphors containing 1% or less lead as an activator). There is no feasible alternative for this phosphor that will yield the same or similar results and has undergone the extensive European and US regulatory testing associated with the application of UVA phototherapy lamps using these phosphors.

Over 80% of phototherapy lamps do not use BSP. These are so-called (Narrowband) UVB lamps. However, a substantial group of patients cannot be effectively treated by (NB –) UVB

– phototherapy. For this group, PUVA phototherapy is the only effective treatment therapy available, see footnotes [3] [4].

Almost 100% of the medical skin treatment lamps using these phosphors are produced in the EU.

Figure 3: Examples of PUVA Phototherapy units

4.1.5 Applications covered by Annex IV exemption 34

Therakos Photopheresis Immunotherapy

[3] see http://psoriasis-cure-now.org/uvb-puva/,

[4] Sami S. Yones; Roy A. Palmer; Trish T. Garibaldinos; John L. M. Hawk. "Randomized Double-blind Trial of the Treatment of Chronic Plaque Psoriasis: Efficacy of Psoralen-UV-A Therapy vs Narrowband UV-B Therapy." Arch Dermatol 2006 142: 836-842.)

4.1.6 Annex I category covered by this exemption

List of relevant Annex I categories for this exemption

☐ 1 ☐ 2 ☐ 3 ☐ 4 ☒ 5

☐ 6 ☐ 7 ☒ 8 ☒ 9 ☐ 10 ☐ 11

Application in other categories, which the exemption request does not refer to: N/A

4.1.7 Annex I category covered exemption 18(b)1 and Annex IV exemption 34

Equipment of category 8 and 9: N/A

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

LightingEurope is of the opinion that lamps in general are category 5 products, but having a character of a component, a consumable as well as a spare part.

There are numerous applications where lamps can also be regarded as component of a product belonging to any of the other categories 1 - 11 e.g. lamps/lighting in ovens, refrigerators [category 1], clocks [2], copy machines, projectors [3] TV sets [4], background lighting of tools [6], video games [7], UV lamps in medical equipment [8], control panels for industrial installations [9], UV in automatic dispensers [10] or lamps fixed installed in furniture [11].

LightingEurope believes that lamps covered by some exemptions might not belong to category 5 equipment only if it is specifically designed as part or component of only one specific other category and there is no intended possibility to use it in others. Examples for the latter case are specific lamps for medical equipment, which have a certain special function in such equipment only, e.g. lamps for vitreoretinal surgical systems.

LightingEurope is aware of the difficulty to unambiguously classify certain lamps in the categories set out by RoHS legislation. For lamp producers it is essential to have legal certainty regarding the possibility to put the products on the market irrespective of the planned application as we are not able to control the use of the lamps in products. Specific special

purpose lamps indeed can be considered also as a spare part (or consumable) in certain applications such as sun-tanning cabins and medical equipment.

4.2 Description of the substance

4.2.1 Substance covered by this exemption

Lighting Europe is asking for exempting

☒ Pb ☐ Cd ☐ Hg ☐ Cr-VI ☐ PBB ☐ PBDE

4.2.2 Function of lead

Lead is used in the phosphor for UV radiation in tanning and phototherapy and ECP lamps. The lead activator is required to allow the barium silicate phosphor to fluoresce. It transforms the 254 nm radiation to the designed UV (290nm-400nm) radiation. A fluorescent lamp uses phosphors which, when activated, will produce light in different wavelengths. The primary wavelengths of “light” produced by indoor tanning and phototherapy and ECP lamps are in the UVA and UVB regions or 290-400nm. Lead is the primary activator for the barium silicate phosphors to fluoresce and is used in over 95% of the indoor low-pressure mercury vapour fluorescent lamps used for tanning and certain medical applications which are not covered by this exemption.

4.2.3 Location of lead in lamps

The lead is evenly distributed throughout the phosphor coating of the lamps to radiate in the range of 290-400nm when excited by radiation at 254nm. The lead content of the phosphors is less than 1% of the total weight of the phosphor.

4.2.4 Amount of lead

The phosphor coating represents the homogenous material used in the fluorescent lamps with respect to this exemption. The lead content of the phosphor is less than 1% of the total phosphor weight.

There is no published data available for the quantity of tanning lamps entering the EU.

However, based on market estimations of LightingEurope the lead content of tanning lamps is limited to 190 kg of lead total per year entering the EU. This amount is approximately 10%

less in the phosphor and taking into account the decrease in available market, compared to the amount in the 2015 exemption renewal request.

Lead is also used in similar lamp types for medical and phototherapy applications in exemption 18(b)1 such as PUVA light therapy for skin conditions such as psoriasis.

The phototherapy application is a small niche market compared to the total lighting market.

With respect to this exemption, the phosphor coating represents the homogenous material used in the fluorescent lamps. The lead content of the phosphor is less than 1% of the total phosphor weight.

There is no published data available for the quantity of phototherapy lamps entering the EU. However, based on market estimations of LightingEurope the lead content of medical lamps in 18b1 and Annex IV 34 is limited to 2.5 kg of lead total per year entering the EU.

4.2.5 Environmental assessments, LCAs

Additional information is not available as no alternate phosphor types are available that will yield the same result nor have undergone the regulatory testing of the EU or US. There are no statistical data available specific to the Life Cycle Analysis of the tanning and medical lamps represented in this exemption request, however due to the relatively low market quantities for special lighting, the total environmental impact is expected to be limited.

Research conducted about fluorescent lamps for general lighting applications does not specifically equate to these specialty lamps as they are not designed to produce visible light. Efficacies, expressing the amount of visible light in Lumen per Watt, are normally related to e.g. fluorescent lamps for general lighting, do not apply to tanning lamps. Cradle to grave estimates for the production of the components and the finished lamps in this exemption request are similar to those of general lighting fluorescent lamps.

We refer to the fact however that the use of lead as an activator of the phosphor in these lamps allows the transmission of the specific wavelengths of light to be emitted in such a fashion to be the most effective form for its purpose, which is not achievable with other phosphor types or other technologies. Therefore, efficacies of any alternate product types would not be an adequate comparison.

The potential substitution or replacement to other wavelengths or ultraviolet dosages would require revalidation of all existing equipment in the EU market or could cause the elimination

of such equipment causing great hardship to the small business owners of tanning salons throughout the EU. These current lamp types have been tested, studied and regulated in the EU and changes to these products would require a duplication of the clinical testing which has been compiled over years of study and regulation. It is further noted that the overall lead content of such lamps, as in general lighting, has been reduced in the past five years with the less than 0.1% lead content to allow for recycled glass in the glass envelop of the lamp.

5 Waste management

5.1 Waste streams

☒ 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

Sun tanning lamps are in the scope of EU Directives 2002/96/EC - WEEE and 2012/19/EU– WEEE Recast. Take back systems are in place in all EU Member States: end users and most commercial customers can bring back the lamps free of charge. Sun tanning lamps are collected separately from general household waste and separately from other WEEE waste. Also, a dedicated recycling process exists for lamps.

European legislation on Waste Electrical and Electronic Equipment makes producers responsible for end of life products within this category as from August 13th 2005. Target setting as a consequence of the present legislation is 4kg per inhabitant per year for all categories.

European lamp manufacturing companies have founded Collection & Recycling Organizations in the EU Member-States, represented EucoLight, with the objective to organize the collection

and recycling of gas discharge lamps. The goal is to comply with present and probable future EU legislation and meet or exceed national targets.

In general, the following channels have been established in the respective member-states providing countrywide coverage:

- Direct collection from large end users and professional installers:

Containers have been made available, ad hoc or permanently, and will be collected upon notification by the end user that the container is full.

- Collection through distribution:

Wholesalers and Retailers place collection means at their premises respectively in their shops. Collection is done upon notification.

- Collection through municipalities:

Where the infrastructure allows collection, means are placed at municipality depots.

5.2 Amount of lead in WEEE

☐ In articles which are refurbished
☒ In articles which are recycled
☐ In articles which are sent for energy return
☐ In articles which are landfilled

Phosphor coating represents the homogenous material used in the fluorescent lamps with respect to this exemption. The lead content is less than 1% of the total phosphor weight.

There is no published data available for the quantity of tanning lamps entering the EU. However, based on market estimations of LightingEurope the lead content of tanning lamps is limited to 190 kg of lead total per year entering the EU. This amount is approximately 10%

less in the phosphor and taking into account the decrease in available market, compared to the amount in the 2015 exemption renewal request.

6 Substitution

Can the substance of this exemption be substituted?

☐ Yes, by
- ☐ Design changes:
- ☐ Other materials:
- ☐ Other substance:

☒ No
Justification: see in chapters below

6.1 Substituting lead in the fluorescent powder of discharge lamps when used as sun tanning lamps

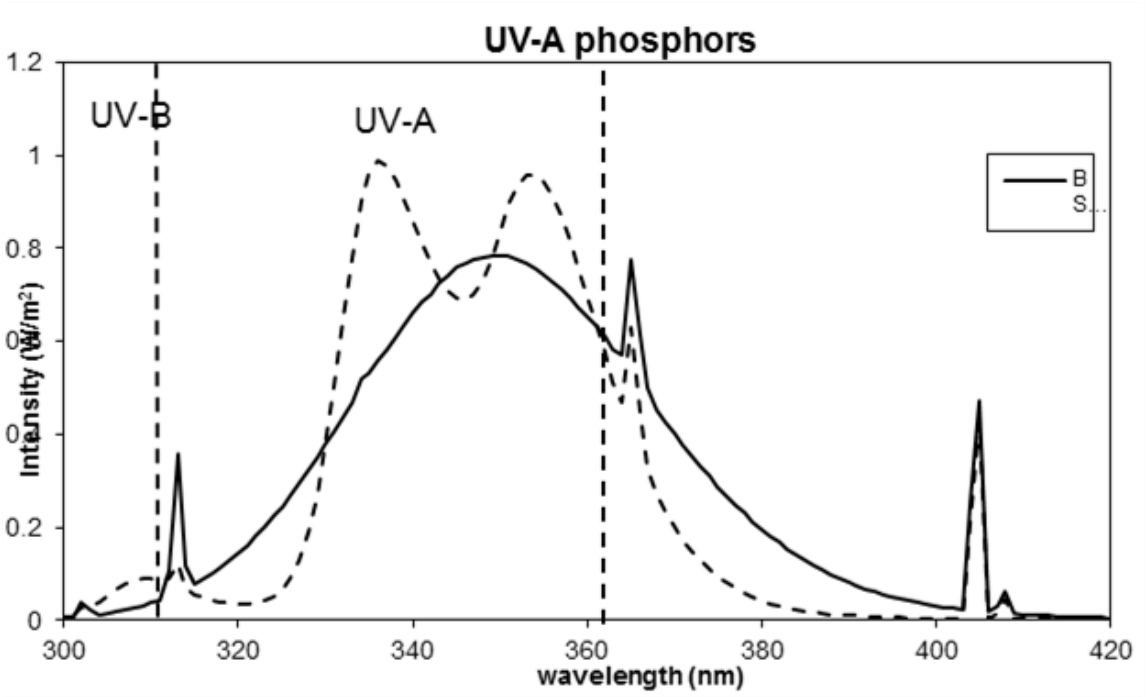
6.1.1 Spectrum incompatibility

The application for tanning equipment is strictly regulated in the EU. Any possible alternative to lead in BSP type of phosphor would need to fulfil the following criteria:

- Lamp specification must be the same with regard to
  - UVA and UVB output, and with that Erythema
  - Spectral power distribution
  - Compatibility (electrical/mechanical spec) must be OK
  - Reliability must be OK
  - Safety must be OK
  - Lamp operation must be the same in the different equipment in the market
  - Lamp start-up and time to peak intensity must be the same.
  - Lamp intensity must be the same.
  - Lamp maintenance/depreciation must be the same,
- Tanning result on patients must be equal
- Compliance with CE regulations (X/Y coding system for tanning lamps according to EN 60335-2-27)
- No (negative) side effects
- (Psoriasis) Clearance rate on phototherapy patients
- Economically feasible. Equipment in use today is calibrated and requires lamps to meet output limits using X/Y coding system. Different lamps would need revalidation.

Only one alternative material comes close: Ce doped YPO phosphor. Please see below spectrum of Ce doped YPO phosphor in comparison to BSP.

Phosphor coating represents the homogenous material used in the fluorescent lamps with respect to this exemption. The lead content is less than 1% of the total phosphor weight.



Graph 2: Emission spectrum of a Cerium-doped phosphor – UV lamp

Based on the above measurement results, it can be concluded that:

1. The spectral power distribution shows differences in the UVA and UVB range.
2. The ratio for UVA and UVB output is different which is an important factor for tanning applications and is governed by EU regulations.
3. Therefore, the Cerium based material has a lower expected treatment effectiveness, with regard to Erythema and NMSC (non-melanoma skin cancer).

Tanning lamp output is measured on a weighted distribution of UVA and UVB output measured by the output by nanometer. The lamps are coded using the X/Y system by lamp type which is then applied for use in each specific piece of equipment. Tests have been done using these phosphors for tanning lamps showing that the spread in UVA and UVB output is too high to be viable as a practically feasible alternative. It would not be able to comply with CE regulations for tanning lamps (due to spectral incompatibility).

For phototherapy lamps the spectral incompatibility has resulted in a lack of interest by the medical community. Therefore, no adequate tests and clinical studies have been set up on patients to prove the effectiveness from Ce doped YPO phosphor for PUVA phototherapy and no approvals for such equipment exist.

Therefore, this Ce-based material is not allowed for this application.

6.1.2 UV output variations of Cerium phosphors in UV lamps

A second problem for the Ce doped phosphors is the variations of the UV output over the lamp length due to coating thickness. When fluorescent lamps are coated with a phosphor the thickness of the coating varies over the length of the lamp. For current UV-fluorescent coatings used, like BSP, the thickness variations do not lead to a severe inhomogeneous output. However, for Cerium doped phosphor this thickness difference leads to unacceptable UV output variations which will affect the skin treatment effectiveness (see table below).

	thin coated side		thick coated side	
	UVB		UVB	
1 P	594		325	
2 P	567		313	
3 P	614		322	
4 P	614		322	
5 P	604		350	
6 P	600		325	
7 P	595		301	
8 P	615		265	
9 P	599		283	
10 P	622		409	
AVG	602,4		321,5	
STDV	14,87	2%	36,96	11%
MAX	622,00		409,00	
MIN	567,00		265,00	
Range	55,00	9%	144,00	45%

Table 1: Thickness variations of Ce-doped coatings and the impact on UV output

6.2 Substituting fluorescent technology by lead free technology

In principle other technologies can be evaluated for replacing fluorescent technology for tanning and phototherapy including ECP applications. One could think of e.g. LED, OLED, HID, and incandescent or halogen technology.

However, for any new technology one needs to address the replacement market (replacing lamps in existing fixtures) and the market for new equipment using the new technology.

The criteria to determine whether a new technology can replace existing fluorescent technology using BSP (and Hg) in existing equipment are:

- Lamp specification must be the same with regard to
    - UVA and UVB output
    - Spectral power distribution
- Safety must be OK
- Compatibility must be OK (Electrical and mechanical specification)
- Reliability must be OK
- Tanning result
- Compliance with CE regulations (X/Y coding system for tanning lamps according to EN 60335-2-27)
- No (negative) side effects
- Effective treatment results for phototherapy patients (e.g. clearance rates for psoriasis, effective chemotherapy, etc.)
- Economically feasible (cost of replacement technology)

For new equipment similar criteria hold as mentioned above.

6.2.1 Feasibility of the alternatives

In this paragraph we only discuss LED as an alternative radiation technology as Incandescent, halogen and OLED simply do not emit radiation in the UVA/UVB range.

LEDs in principle could be chosen as radiation technology for special purposes, provided the following criteria are fulfilled.

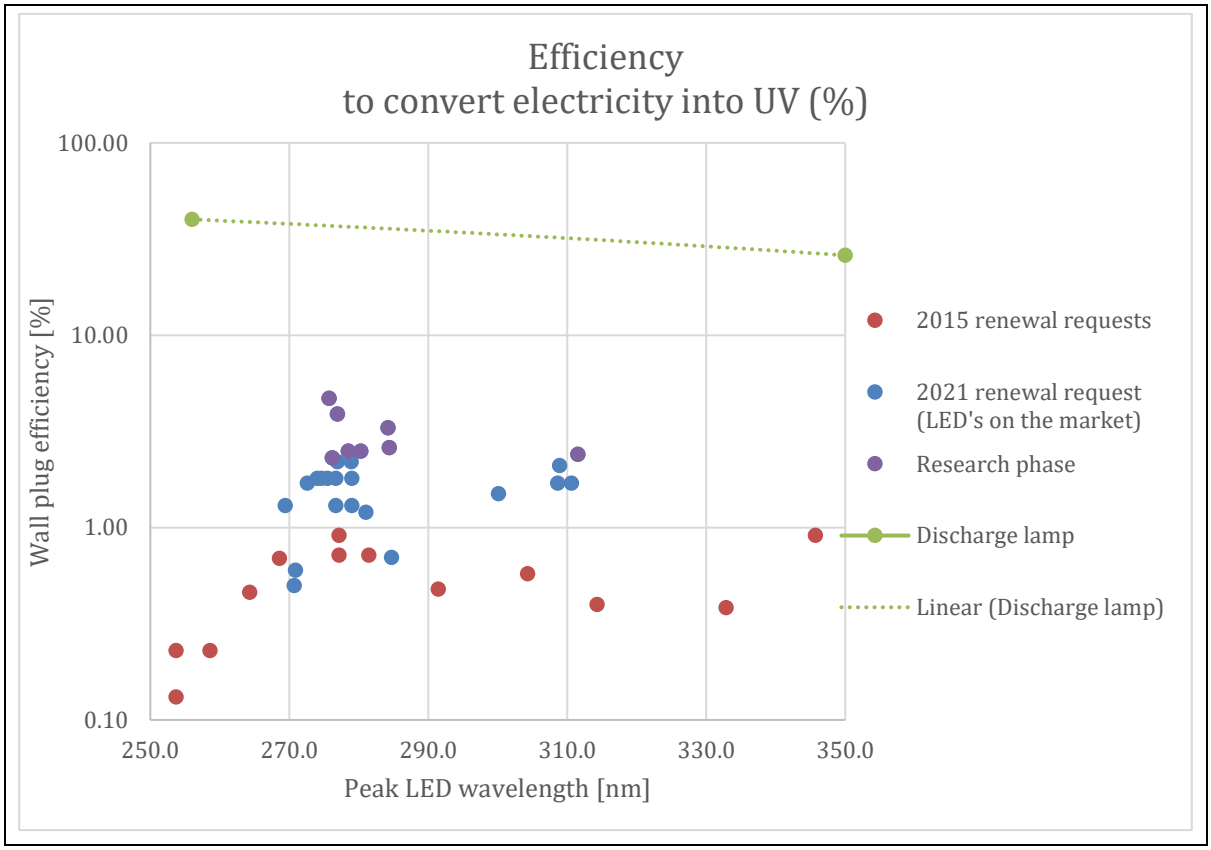
- Wall Plug Efficiency is comparable to fluorescent lamps
- Effectiveness is comparable to fluorescent lamps (i.e. same tanning or photo-therapeutic effect)
- Regulation/approval is passed

In the following paragraphs each of these 3 criteria is discussed.

6.2.1.1 Wall Plug Efficiency

a. In contrast to general lighting lamps, (compact) fluorescent lamps for special purposes emit radiation in UV or blue wavelength bands. LEDs for general lighting purposes are made of InGaN, a material that emits blue light which with the help of phosphors is converted into the desired visible wavelengths. Theory says you can only convert from shorter wavelengths to longer. It is therefore impossible to create UV light with LED material as used for visible light LEDs.
b. There are other materials available from which LEDs can be made that generate UV light (like AlGaN), however the efficiency (radiated power out / electrical power in) of LEDs with those materials is still very low. In the UVC (100-280nm) and UVB (280-315nm), the WPE (wall plug efficiency) of LEDs are now close to 1%, where the wall plug efficiency of fluorescent lamps are close to 20% or even higher. See below pictures in which public data from several manufacturers are put together into a single graph.
c. Most of the sources in the figure below are single wavelength devices. It is unsure how these should be combined in equipment that radiates over a wider wavelength range in order to obtain the desired photo therapeutic effect.

Graph: LEDs (UVB, UVA and Blue): WPE vs. wavelength (data of several manufacturers)



Graph 3: Efficiency to convert electricity into UV (%)

Conclusion:

There is no comparable WPE for LEDs below 380 nm. Therefore, LED lamps are not suitable soon as a practical alternative for tanning or phototherapy applications.

6.2.1.2 Effectiveness data

For tanning no tests results are available yet regarding effectiveness in reaching the desired effect in a comparison study between equipment using fluorescent lamps and equipment using LEDs. For most of these applications that is not done yet as no LEDs were available. Hence effectiveness data are not available.

For PUVA phototherapy applications no tests results are available yet regarding patient effectiveness to reach the desired effect in a comparison study between equipment using

fluorescent lamps and equipment using LEDs. For most of these applications that is not done yet as no promising LEDs were available. Therefore effectiveness data are not available.

In narrow band applications the LED replacements have to generate UVB at an exact wavelength and in a narrow wavelength band. Binning the LEDs at the right wavelength is already a major task, making the LED's with that exact wavelength then generate a narrow wavelength band is not possible yet. Below 308 nm there is a serious risk of skin burn, above 314nm the treatment is less effective. The spectra are shown in Figure 1.

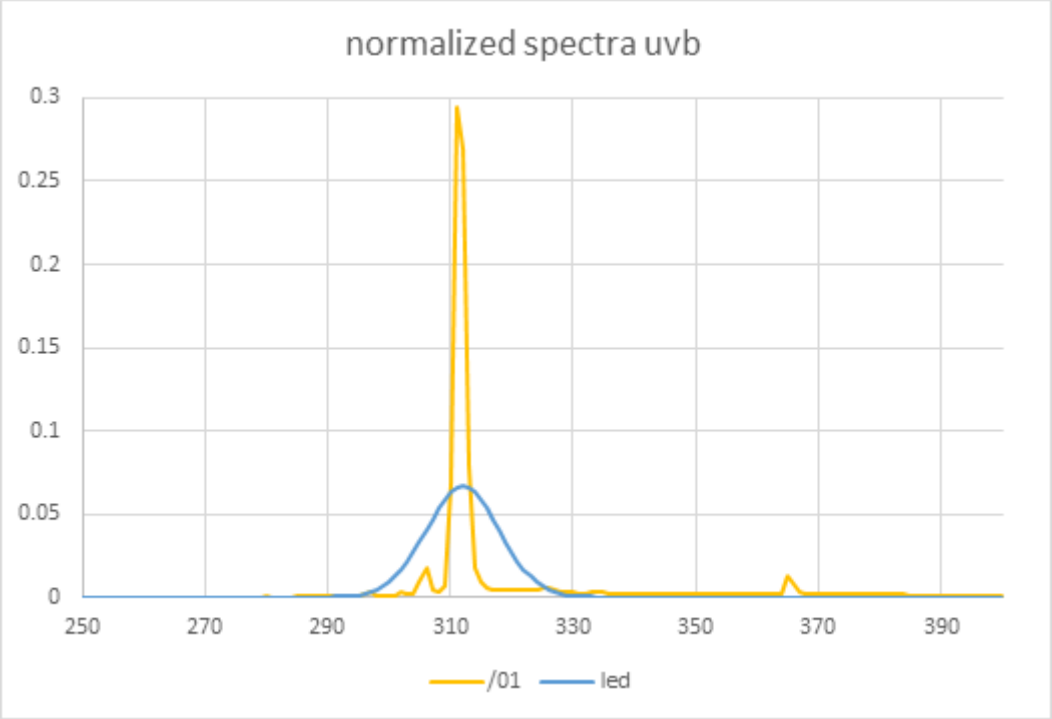


Figure 1 LED narrowband spectra compared to the colour /01 spectrum of conventional lamps of exemption 18(b) I

6.2.1.3 Regulation/approval

CE conformity and other European directives for special purpose applications (like for instance approval of medical devices for phototherapy and CE regulations on tanning lamps (CE 60335-2-27)) is based on fluorescent discharge lamps (with respect to safety and system

responsibility). No CE conformity is available for other lamp technologies.

6.2.2 Availability of substitutes

UVA LEDs are available from several suppliers. However, as is clear from the above their efficiency is very low. No public roadmaps exist that predict when UVA LEDs with acceptable output and efficiency will be available. Only after that can the design and development of LED based equipment start and then be followed by customer/patient tests.

6.2.3 Impacts of substitution

Apart from feasibility and availability also the potential impacts of substitution must be considered.

Amongst the impacts are:

- Environmental impact
- Health & Safety impact
- Socio-economic impacts
- Impact on innovation

6.2.3.1 Environmental impact of substitutes

Though LED technology is developing at a rapid pace for general lighting, there is today no viable LED alternative available for phototherapy applications. Therefore, this section is not applicable.

6.2.3.2 Health and safety impact of substitutes

The fluorescent tanning lamps in use today have undergone extensive testing and calibration in the equipment. The effect of Ce doped phosphor may have considerable impact on health and safety of customers as the manufacturing tolerance in output and spectrum cannot be

controlled to the extent required by EU regulations. For LED as an alternative technology the effects on health and safety will have to be investigated.

6.2.3.3 Socio-economic impact of substitution

Economic effects related to substitution:

☒ Increase in direct production costs
☒ Increase in fixed costs
☒ Increase in overhead
☒ Possible social impacts within the EU
☒ Possible social impacts external to the EU
☒ Other:

It is expected that even if UVA LEDs become available with feasible specifications, tanning equipment may become much more expensive. It will become therefore an economically unattractive solution and this can have a significant impact on the application.

The possibility for lead free technology for these lamps is not feasible for replacements lamps in existing equipment due to the scientific and clinical evaluations that would need to be done on every type of fixture or appliance that is in the field. The economic burden this would impose on the small business owners such as tanning salons and dermatologists would cause the closing of many businesses.

It could be imagined that new equipment could be changed to non-lead phosphors. However over 90% - and it is estimated that it may be as much as 99%- of the tanning phosphors are

lead activated. There are no alternative non-lead activated phosphors available today that provide the same or equivalent spectral radiation.

Social impacts

As there are no reliable substitutes if the renewal of the exemption is not allowed it would shut down the indoor tanning industry in Europe.

It is estimated that almost 100% of these lamps used in Europe are manufactured in Europe by fluorescent lamp companies.

It is estimated that almost 100% of the indoor tanning equipment sold in Europe is manufactured in Europe.

It is estimated that almost 100% of the tanning lamps sold as aftermarket lamps are sold by manufacturers or distributors located in Europe.

It is estimated that over 90% of the tanning lamps used in the US are manufactured in Europe.

It is estimated that over 75% of the tanning equipment sold in the United States is made in Europe.

As there are no reliable substitutes, if the renewal of the phototherapy exemption is not allowed it would leave the patients in Europe that need PUVA phototherapy without a suitable treatment.
It is estimated that almost 100% of these lamps used in Europe and even in the whole world are manufactured in Europe by fluorescent lamp companies. It is estimated that almost 80% of the phototherapy equipment sold in Europe is manufactured in Europe.

Other impact

Economic impact due to the loss of the entire tanning application in Europe.

6.2.3.4 Impact of substitution on innovation

If UVA LEDs will become available in the future, new equipment will have to be developed and approved for PUVA phototherapy.

6.2.4 Future trends of substitution

Given the market size and in combination with strict regulations, efforts to substitute BSP containing lamps are extremely limited (to non-existent).

No plans are made to replace Pb with Ce as earlier tests were unsuccessful and no new insights have been created.

As regards LEDs: other UVA applications are available in LEDs but tanning development has been limited. At this moment it is impossible to predict if and when UVA LED based equipment will become feasible.

With respect to the current LED developments, some other UVA applications are already switching to LEDs but on medical applications the developments are limited. It is at this moment impossible to predict if and when UVA LED based equipment will become feasible, however the patient tests and approval process would take a very long period. Therefore, we request a renewal for the maximum validity period.

6.3 Links to REACH, according to RoHS Directive Article 5(1)(a)

Do any of the following provisions apply to the application described?

no

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

☐ Restriction
- ☐ Annex XIV
- ☐ Annex XVII
- ☐ Registry of intentions

☐ Registration

Provide REACH-relevant information received through the supply chain.

Not Applicable

7 Removal of lead from lamps

Can lead be eliminated?

☐ Yes.
☒ No.

It is not practical to remove the lead from these lamp types. The lead is required as an activator for the phosphors that produce the specific wavelengths of light necessary to provide the

necessary spectrum and meet the clinical and regulated requirements imposed by the EU regulatory agencies.

8 Reduction of lead content of lamps

The less than 1% lead content of these lamps as a percentage of the weight of the homogenous phosphor material is needed to activate the phosphor.[5] A reduction in the lead content would cause either a loss of output or not be sufficient to activate the phosphor. As a result, the lamp would no longer satisfy EU regulations.

9 Other relevant information

The tanning industry is closely monitored and regulated by European authorities and is subject to standards such as EN 60335-2-27 and EN 61228.

EN 60335-2-27 : This International Standard deals with the safety of electrical equipment on exposing the skin to ultraviolet or infrared radiation, for household and similar use in tanning salons, beauty parlours and similar buildings.

Tanning and medical equipment in Europe is subject to unscheduled auditing and measurement of the lamps and equipment which has been certified for use with lamps that are equivalent or the same as the lamps originally installed by the original equipment manufacturer (OEM). This equipment has undergone extensive testing to assure compliance with ultraviolet exposure schedules and the use of any lamps other than those substantially equivalent are restricted.

It would be a significant financial burden if not impossible to the independent salon owners to try to retrofit their equipment and have each unit certified by the regulating bodies.

10 Information that should be regarded as proprietary

All information regarding total available market and the calculations to estimate substance weights such as lead content is confidential and provided by Lighting Europe as a total summation of estimates provided by the members.

[5] For more details on the lead content in glass, please refer to the LightingEurope exemption renewal request for Exemption 5(b), Annex III, of 16 January 2020, document: LE RoHS Exemption 5b - 20200116 – FINAL.

PART-2017-156760V2 (1).pdf

PART-2017-156760V2 RoHS 3 18b exemp

Extracorporeal Photopheresis.pdf

Additional Information provided by Mallinckrodt Pharmaceuticals c/o Therakos, Inc. in support of Exemption request: Lead as an activator in the fluorescent powder of discharge lamps when used as Photopheresis lamps containing phosphors such as BSP (BaSi2O5:Pb)

Summary

This exemption is required to allow the use of lead in a UVA lamp phosphor used for extracorporeal photopheresis (ECP) treatment of cutaneous T-cell Lymphoma (and other T-cell related diseases). The treatment involves exposure of leukocytes that are temporarily removed from patient's blood to light from lamps with lead doped barium silicate phosphor. The light activates a drug which has been introduced into the leukocyte fraction of the blood. This type of phosphor emits a unique spectrum that is optimum for this medical treatment. All other UVA phosphors contain less light of the effective wavelengths or have shorter wavelengths that cause further damage to cells. Therefore, there is currently no substitute lamp type for treatment of this disease by extracorporeal photopheresis as described in this application.

- **Description of materials and equipment required for exemption**

An ECP treatment is comprised of the *ex vivo* exposure of autologous leukocytes (a type of white blood cells transferred from the patient's own body) to a liquid formulation of 8-methoxypsoralen and ultraviolet A (UVA) light, followed by the subsequent reinfusion of the white blood cells to the patient. During an ECP treatment, whole blood is drawn from the patient into the Therakos Photopheresis system instrument and is subjected to centrifugation in order to separate the whole blood into its components. The red blood cells and plasma components are returned

back to the patient. The white blood cells are collected (the collected cells are known as buffy coat), concentrated and prepared for treatment with 8-methoxypsoralen and ultraviolet A light. The treated white blood cells are then returned back to the patient. The 8-methoxypsoralen is inert until exposed to UVA light and its activation is dependent on exposure to UVA light frequencies. The activation of the 8-Methoxypsoralen is critical to the entire process. This drug (brand name UVADEX™ 20 mcg/mL Solution) is exposed to a computer controlled specific dose of intense ultraviolet light from a BSP lamp of 1-2 joules per cell. The UV light causes a photochemical reaction to occur between the drug and DNA of the white blood cells which forms cross links between the drug molecules and the DNA. The exposure to psoralen and subsequent photoactivation of the white blood cells in the buffy coat induces apoptosis (normal programmed cell death) of the treated white cells. Administration of cells which have been induced to undergo apoptosis has the effect of creating a state of immunologic tolerance. The overall effect of this therapy can be thought of in terms of having an anti-inflammatory effect.

ECP is used to treat several medical conditions worldwide including:

- Cutaneous T-cell Lymphoma (CTCL), which is a type of Non-Hodgkin's lymphoma cancer that manifests itself primarily in the skin
- Graft versus Host disease which is a serious complication of bone marrow transplants
- Cardiac transplant rejection
- Lung transplant rejection

The above medical conditions are characterized by states of immunologically induced inflammation. Patients with these conditions are for the most part extremely acutely ill. ECP is frequently the last therapeutic option offered to patients and therefore frequently represents salvage treatment status. ECP is administered only in medical centers which have undergone specific training for the administration of this unique therapy. The above conditions are also considered as "orphan conditions"[1] since the numbers of patients who have these conditions is very small. In fact, the cumulative number of patients (< 20,000) with the above 4 conditions who would be candidates for this therapy still meets the criteria for orphan status (less than 200,000 cases in EU annually).

In the EU, the Therakos Photopheresis systems are indicated for the administration of a Photopheresis treatment.

Research has shown that the wavelength of the UV light used is critical to photo activate the drug and that the BSP lamps are ideally suited having a relatively narrow UVA emission spectrum. The wavelength peaks at 350nm, the spectral range and light dose (1-2 joules per cell) of this lamp is specified in the US FDA PMA and NDA approval and the EU Medical Device Directive (CE Mark) approvals for this equipment. Although the 350nm peak is important, the entire curve of the UVA spectrum generated by the custom BSP lamp has been proven to be safe and effective

[1] "Orphan" diseases are defined in the EU as ones which affect less than 5 per 10,000 of the population (<1 in 200,000 in the USA) http://www.nice.org.uk/niceMedia/pdf/smt/120705item4.pdf

in delivering the 1-2 joules of energy to each collected cell. 1-2 joules has been deemed (by cell viability testing post Photopheresis) to be the appropriate dose of UVA energy to elicit the photochemical reaction described above between the drug and the leukocytes' DNA. The shape of the emission spectrum is required to elicit the desired response and avoid the negative consequences as discussed below:

- Light of longer wavelengths have too low energy to promote the photochemical reaction
- Light of shorter wavelengths have higher energy which can cause damage to DNA and could promote undesirable side-reactions between the drug and DNA such as incomplete cross linking of the DNA and sister chromatid exchanges of the DNA
- Broader spectra have less energy at the critical 350nm wavelength so that longer treatment times are needed for the same effect which increases the risk of infection. The risk of infection will be proportional to the time that the patient is connected to the treatment system.

In this treatment the current passed to the BSP lamps is much greater than is normally used for other applications for BSP lamps. This is to produce as much UV light as possible from the lamp to achieve the shortest possible treatment time. This type of use greatly shortens the lamp's life to 150 hours. Once the lamps have been used for 150 hours the computer controlled Photopheresis instrument instruct the operator to change the lamps. As the lamps decay the photoactivation time set by the computer increases. To treat a patient, the UV exposure unit contains 18 special BSP lamps that are designed solely for this treatment.

As discussed above, the exact mechanism by which this treatment works is not understood, but it is clear that many complex processes are induced that alleviate the patients' devastating symptoms. These symptoms include extensive itching, fissuring, scaling and edema. The skin of many patients resembles burn victims. In these cases, and without Photopheresis treatment, 50% of these patients die from infection. Therefore, any changes to the UV light wavelength will alter the proportions of desired light spectrum to adequately photoactivate the drug combined with the DNA of the collected cells and disturb the desirable balance that is created to benefit the patient. In addition, shorter wavelengths could cause patient safety issues, undesirable damage to DNA, side-effects and certainly lack of efficacy.

- **Photochemistry**

To understand why these specific UV light wavelengths are important, the photochemical reactions that can occur between organic molecules and ultraviolet light are described here. When organic substances are exposed to UV light, bonding and paired electrons are excited from their ground states to excited σ^* and π^* states. UV radiation energy is inversely proportion to its wavelength so that long wavelengths (e.g. visible light) have less energy than short wavelengths (e.g. UV):

$$E = h\nu = hc/\lambda$$

Where E = energy, h = planks constant, ν = frequency, c= speed of light and λ = wavelength.
The energy required to excite an electron depends on the type of bond. For example, a C-C single bond has σ electrons which are excited only by short UV wavelengths of <140nm to σ* states whereas C=C double bonds require lower energy radiation of ~180nm to excite π electrons to excited π*. Single bonds have only σ electrons which require the most energy to excite whereas double bonds have π electrons which require lower energy from longer wavelengths than is needed for σ electrons. Double bonded oxygen and nitrogen atoms also have unbonded electrons that can be excited into excited π energy bands with lower energy that is needed to excite double bond π electrons. The structure of organic molecules governs the minimum energy required to excite electrons so that adjacent bonds affect the minimum excitation energy of a bond. For example, two double bonds separated by a single bond are referred to as being conjugated and the minimum energy required to excite a conjugated π electron is less than a non-conjugated π electron and is excited by longer wavelengths, typically ~220nm.
The electrons in each bond of a complex molecule are excited by different minimum energy levels and so, the UV light spectrum will affect which electrons are affected. As the UV wavelength decreases, its energy increases and can excite more of the bonds in a molecule potentially causing additional chemical interactions.
The drug used for this treatment is 9-methoxy-7H-furo[3,2-g][1]-benzopyran-7-one. This complex molecule has several conjugated C=C double bonds and these are also conjugated to a C=O ketone bond and so the peak adsorption wavelength is ~300nm. When an electron is excited by UV light, three things can occur.

- The electron falls back to its unexcited state with the emission of radiation
- The electron falls back to its unexcited state with the heat radiation
- A chemical reaction occurs

Of these, the first two are harmless although are in effect a waste of UV energy whereas the desired chemical reaction between the drug and DNA gives the beneficial treatment to the patient. It is important however to avoid undesirable photochemical reactions. With light of 350nm, the desired reaction between the drug and DNA occurs to give covalently bonded methoxsalen to single DNA strands or bridging pairs of DNA strands. If shorter wavelengths are used, additional photochemical reactions would occur as the higher energy level would excite different electrons in the methoxsalen molecule and also in the white blood cell molecules causes different chemical reactions to occur some of which will be harmful and could also destroy the desired reaction product.

- **UV lamps**

Ultraviolet light is generated by the interaction between the emission spectrum from excited mercury vapour with specially designed phosphors that adsorb the mercury emission wavelengths and emit their own characteristic spectrum. UV lamps therefore consist of a glass tube containing a partial vacuum with a small amount of mercury and there are electrodes at each end. When a voltage is passed between the two electrodes, a plasma is created in the low-pressure gas inside the tube that vaporizes the mercury that emits light of high energy and relatively short wavelengths with most between 200 – 360nm. The short wavelengths are very harmful so these must be

completely converted into longer wavelength light which is achieved by the coating of phosphor material on the inside of the glass tube. The chemical composition of the phosphor controls the emission spectrum. Phosphors are available for a very wide variety of spectral emissions. Phosphors used in fluorescent lamps that are used for ambient lighting convert all of the mercury emission into visible light with no dangerous UV. Several phosphors have been developed that emit UV light with wavelengths that are longer than the mercury emission. One composition, barium silicate doped with lead, gives the optimum narrow spectrum with a maximum emission at 350nm. This is the BSP lamp.
The light emission spectrum is governed by the crystal structure dimensions of the phosphor. Each crystalline chemical compound has different crystal lattice dimensions and so is capable of emitting different ranges of light output wavelength. To emit light, the crystal lattice needs to be distorted by a dopant atom and the size and valency of the dopant affect the amount of distortion and as a result the output wavelengths. Several compounds are used for UV phosphors apart from barium silicate including several borates, phosphates and silicates although these emit UV light only with the correct dopant atoms.
BSP lamp phosphors use lead as the dopant in barium silicate. Both lead and barium are divalent so lead can easily bond inside the barium silicate lattice but as lead is larger than barium, the lattice is distorted. There are no other large divalent ions that can be used in the barium silicate lattice. In the periodic table, the other large atoms are stable only in different valency states and so will not be able to bond in the same way to the barium silicate. The largest divalent ion apart from lead is Europium but this is significantly smaller and so gives a completely different spectrum. If even smaller ions such as manganese are used as the dopant, only visible light emission occurs.

- **Justification for this exemption**

This exemption request is based on there being no suitable alternative fluorescent lamp that has a lead-free phosphor that emits ultraviolet light with a spectrum that is identical to the spectrum from the BSP lamp. There would be a risk to human health from using alternative UV lamps that emit shorter, more energetic wavelengths as these could cause harmful side-effects. Alternative lamps would not be permitted as these are not approved by the medical devices directive and approval will require many years of clinical trials as described below. The spectra from alternative phosphors would also not provide effective treatment when these emit less desirable wavelengths. UVA lamps that emit longer wavelengths will have no medical effect and shorter wavelengths could be harmful to human health.

Alternately, a feasibility study using LED light technology in lieu of fluorescent for the current lamps in the Cellex Photopheresis System was completed. However this study indicated that current LED technology is unlikely to precisely match the spectral (wavelength) output of the current lamp system and would have a reduced wavelength range, or at best a modified distribution of irradiance for the full wavelength range. No alternative LED lamps have shown to have the desired medical effect comparable to the current fluorescent lamps.

- **Analysis of possible alternatives**

Fluorescent lamp alternatives:

In addition there are about 17 phosphors that emit in the ultraviolet spectrum. The characteristics of the UV phosphors are compared in the table below.

- **Table 1. UV lamp phosphors**

Reference	Chemical composition	Peak wavelength (nm)	Band width (nm)
2011	BaSi2O5:Pb	**350**	41
2030	YMgB5O10:Gd,Ce,Pr	312	2
2040	YPO4:Ce	335 & 357	35
2052	SrB4O7:Eu	371	18
2080	LaPO4:Ce	318 & 335	41
2090	(Sr,Mg)Al11O19:Ce	338	53
2091	(Ba,Mg)Al11O19:Ce	**347**	53
2093	(Ba,Mg)Al11O19:Ce	**347**	54
2094	CaAl11O19:Ce	333	39
2095	(Y,Mg)Al11O19:Ce	344	51
2096	(Sr,Mg)Al11O19:Ce	309	38
	(Ca,Na)P2O7:Ce	330	40
	(Mg,Sr)P2O7:Eu	395	40
	CaSO4:Eu	388	16
U738	(La,Gd)B3O6:Bi	312	2
NP-804	Ca3(PO4)2:Ti	326	57
NP-803	(Ca,Zn)3(PO4)2:Ti	306	39

The currently used BSP phosphor is 2011 which has a symmetrical spectrum with a peak wavelength of 350nm and a bandwidth of 41 nm. This has a symmetrical spectrum which is the basis for the entire safety and effectiveness profile of this lamp. The entire procedure is based on this requirement given the unique photoactivation properties of Methoxsalen. There is very little radiation emitted below 310nm and also very little above 390 nm. Of the phosphors in the above table, only types 2091 and 2093 have similar peak wavelengths but they have broader spectra and 2093 also has a secondary peak at ~380nm. So with both 2091 and 2093, there is less energy available at the important 350nm. 2095 will also be less suitable as its peak wavelength is at a higher energy of 344nm and has a broader spectrum than 2011.

Spectra of UV phosphors which are similar to the BSP phosphor (reference number 2011) are compared below with the spectrum of the BSP phosphor for comparison. Note that these spectra are of light from the phosphor only as mercury emission lines have been omitted.

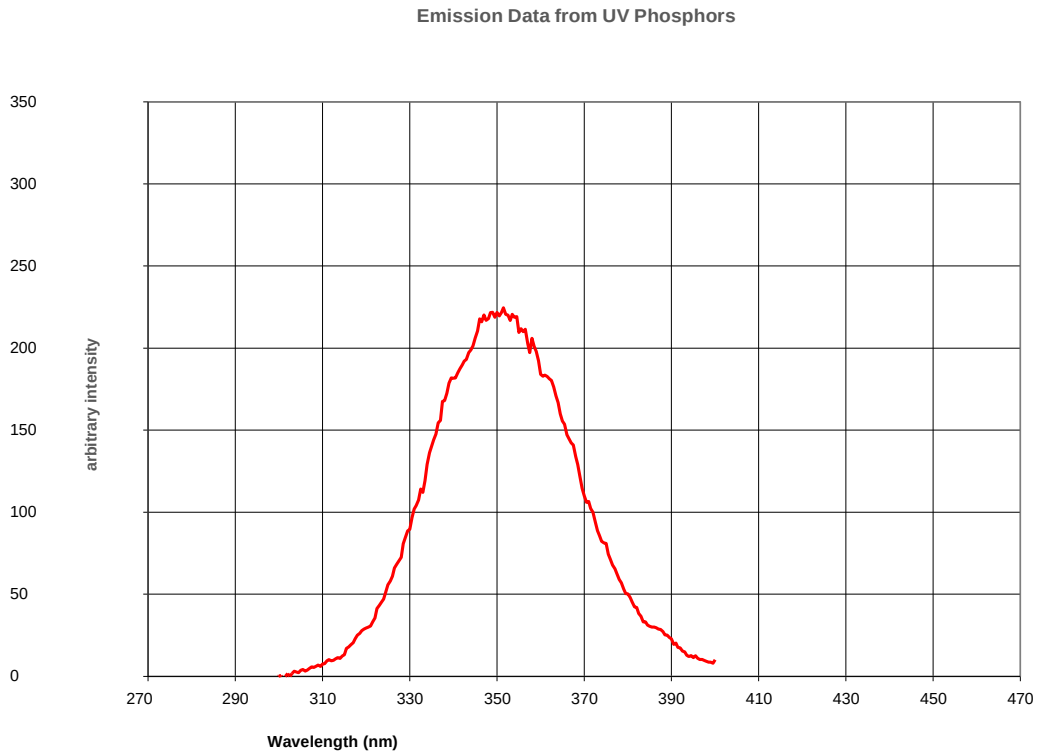


Figure 1. Spectrum of light emission from BSP lead-doped barium silicate phosphor (2011)

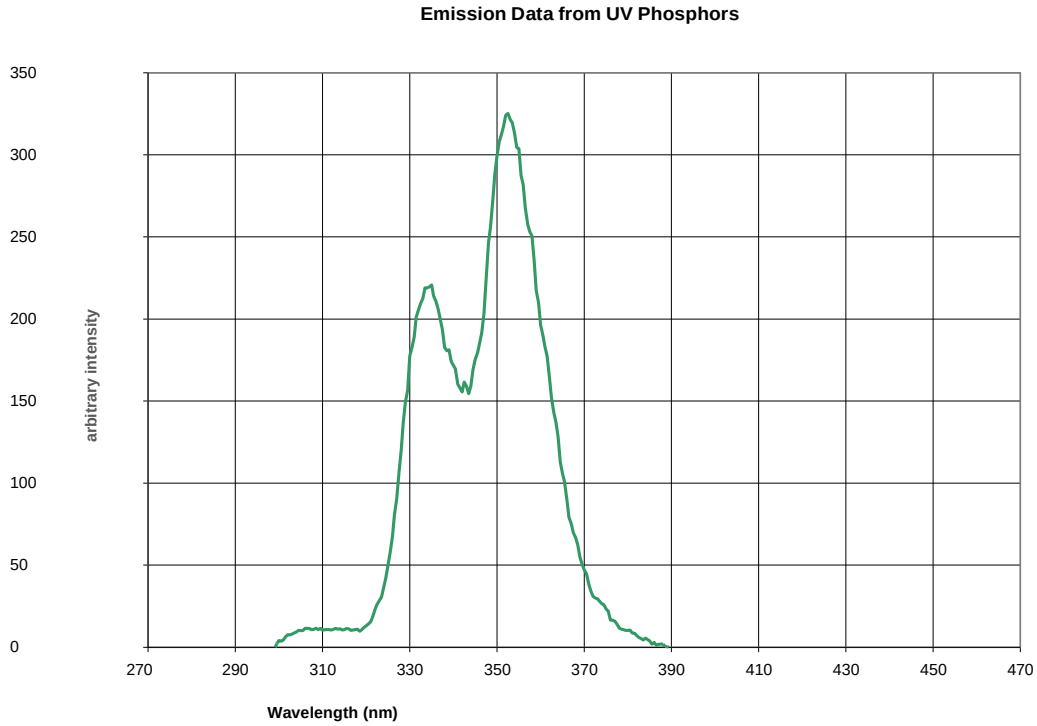


Figure 2. Spectrum of light emission from cerium-doped-yttrium phosphate phosphor (2040)

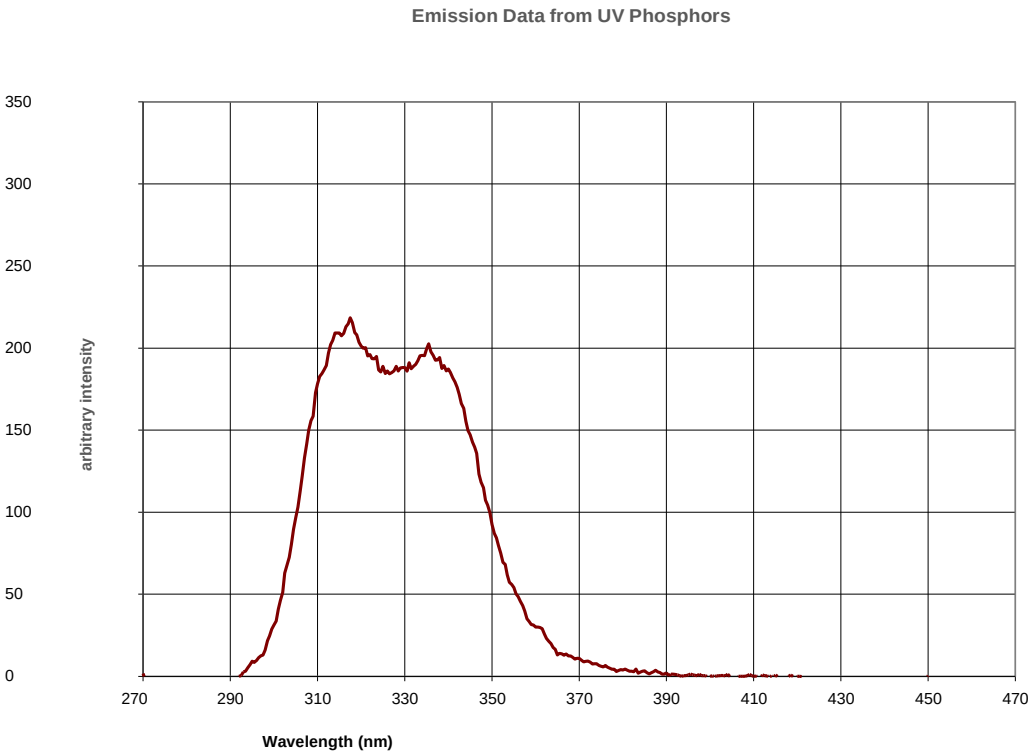


Figure 3. Spectrum of light emission from cerium doped lanthanum phosphate phosphor (2080)

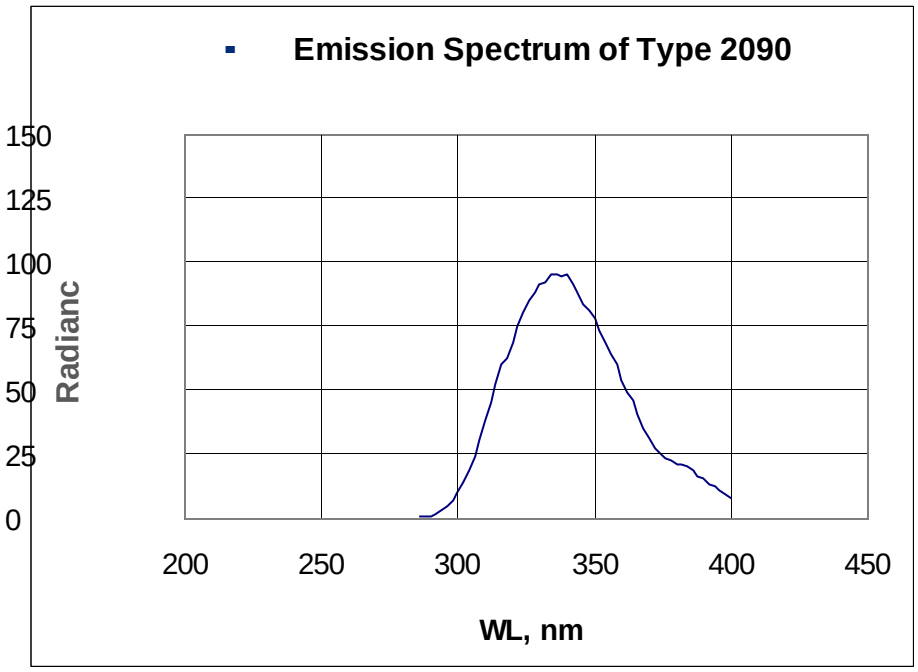


Figure 4. Spectrum of light emission from cerium doped strontium, magnesium aluminate phosphor (2090)

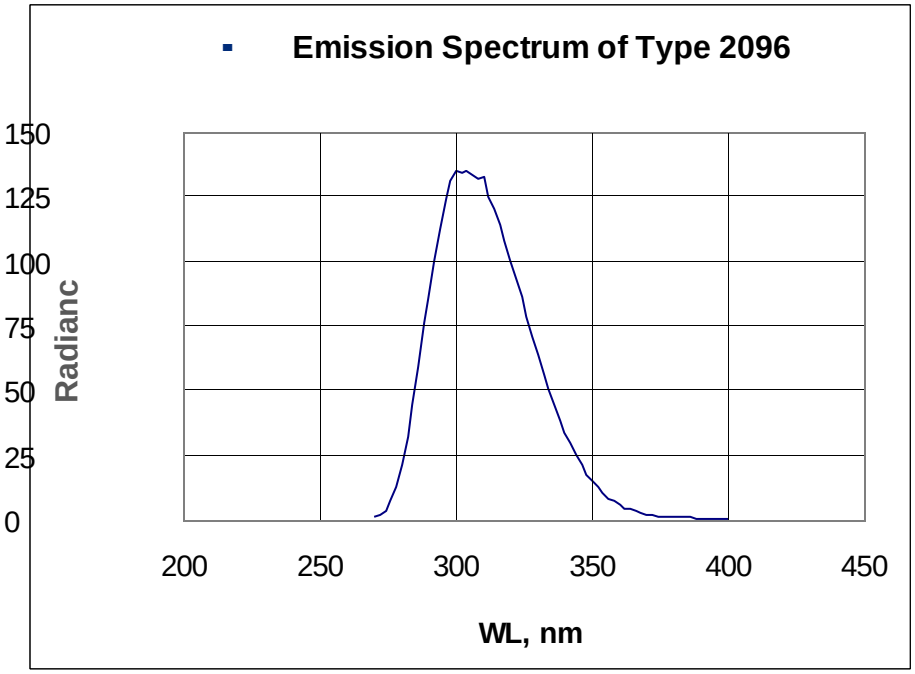


Figure 5. Spectrum of a different composition of cerium doped strontium, magnesium aluminate phosphor (2096)

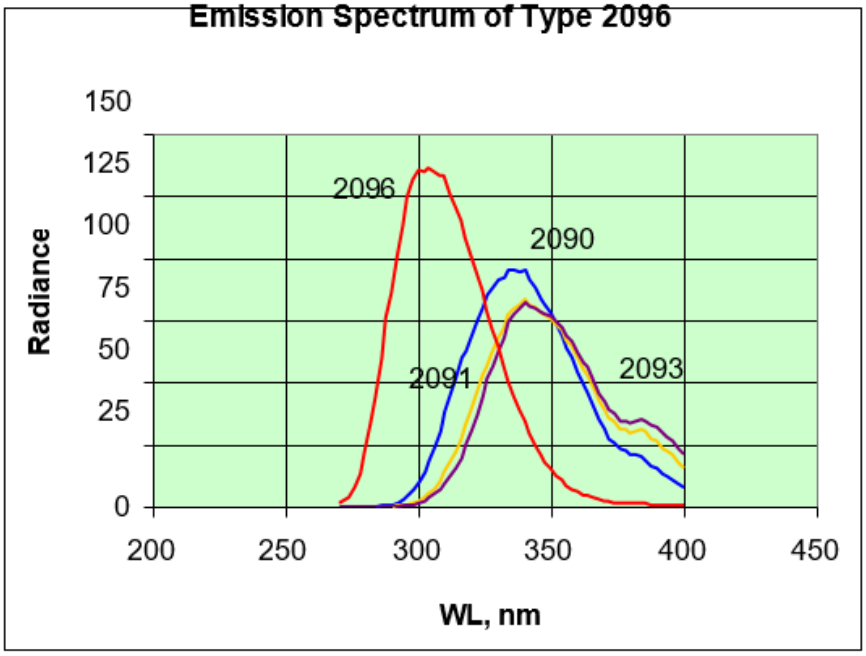


Figure 6. Comparison of doped Ba,Mg and Sr,Mg aluminosilicate phosphors

LED Lamp Technology:

Mallinckrodt has performed assessments of LED three Concepts as potential replacements to the current UV-A lamp solution on the THERAKOS Cellex using arrays of LEDs as follows:

1. Array of single wavelength LEDs designed to maximize efficiency.
2. Array of multiple wavelength LEDs designed to best replicate the gas-lamp emission spectrum.
3. Array of multiple wavelength LEDs designed to partially replicate the gas-lamp emission spectrum while limiting the total number of LED types, and their power consumption.

The following equivalence requirements were used for the Mallinckrodt LED analysis:

- LED irradiance over the entire window of interest shall be equivalent to or exceed the irradiance median of 46.5 mW/cm^2
- The maximum irradiance value shall not exceed 93 mW/cm^2. The specification derives from the relative maximum irradiance from a single lamp (24 mW/cm^2) to the average irradiance (12 mW/cm^2) listed in Table 2.
- The distribution width of average energy delivered to a cell using the LED system shall not exceed the width of the UV gas lamp distribution.
- The power dissipated as heat of the system shall not be greater than the current power dissipation of the UV lamps

The currently available off the shelf LEDs are summarized graphically in Figure 7 below. It is apparent that below 365 nm there are few LEDs and they have low wall-plug efficiencies. Within the wavelength band matching the currently used Phosphor coating, the majority of high efficiency, high power output LEDs are at 365 nm. As a consequence, concept 1 concentrates on using solely LEDs at 365nm for maximum efficiency.

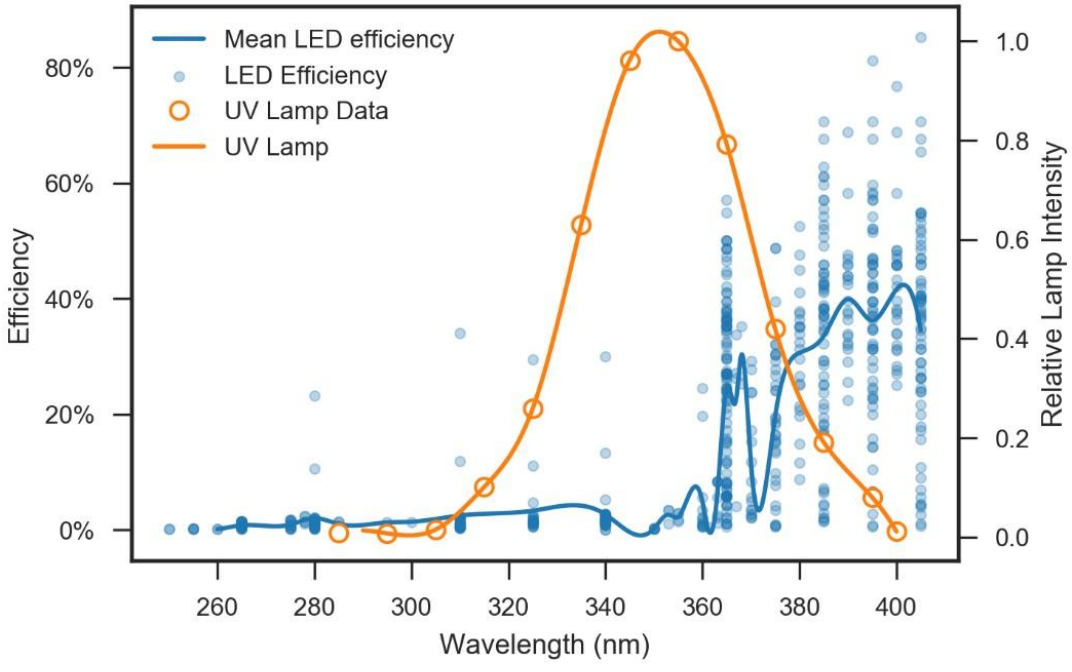


Figure 7. Results of LED component search with current Phosphor spectrum superimposed.

Concept 1 – Array of Single Wavelength LEDs at Maximum Efficiency

The output from the Zemax simulations was imported into Mathworks MATLAB data analysis software to create a composite image representing the LED irradiance over the entire serpentine channel. This was then analyzed in an identical fashion to the UV lamp for equivalence analysis.

The LEDs were modelled on a square array, centered on the serpentine. The pitch between the LEDs was increased from 20 mm – 40 mm. A selection of the irradiance distributions are illustrated in Figure 8 with associated probability distributions in Figure 9.

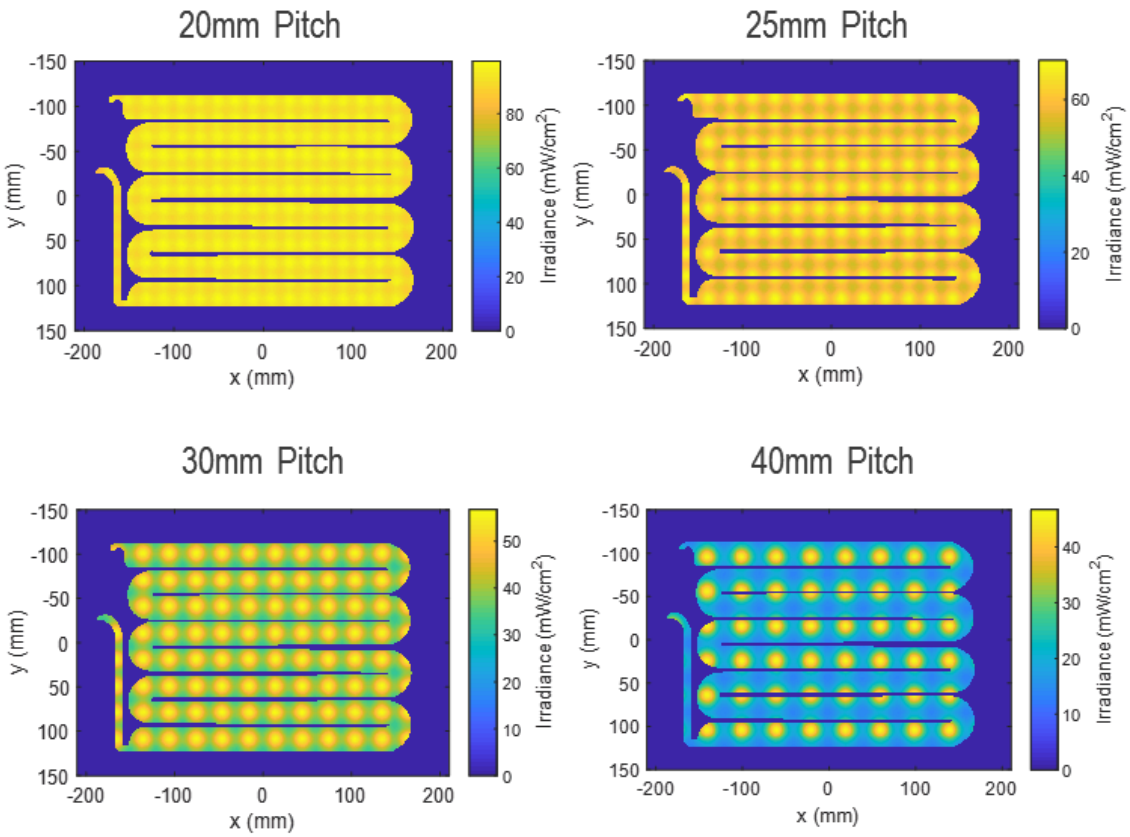


Figure 8: LED irradiance distribution incident on serpentine channel for increasing LED pitches. Each LED is operated at 450 mW.

It can be seen from Figure 9 that the probability distributions are not skewed for low pitches, ≤ 20 mm, and skewed negatively for higher pitches ≥ 26 mm (tail on the right). This suggests that there is likely to be hotspots for high pitch values. Note that the mean value of the irradiance can be adjusted by altering the LED drive current (i.e. the distribution can be translated along the x-axis).

One of the key specifications for the spatial distribution of the LED array is to ensure there are no hotspots that occur at ~2x the median irradiance. As a consequence, the simulations suggest that the pitch of the LEDs must be less than ~30 mm. This enforces a lower limit on the number of LEDs required (~ 8 x 11 array, for a total of 88 LEDs).

These probability distributions can be used to estimate the average energy incident of a

cell (assuming no absorption by the media) during the duration of treatment, in a similar fashion to the UV gas lamp energy distribution (Figure 10).

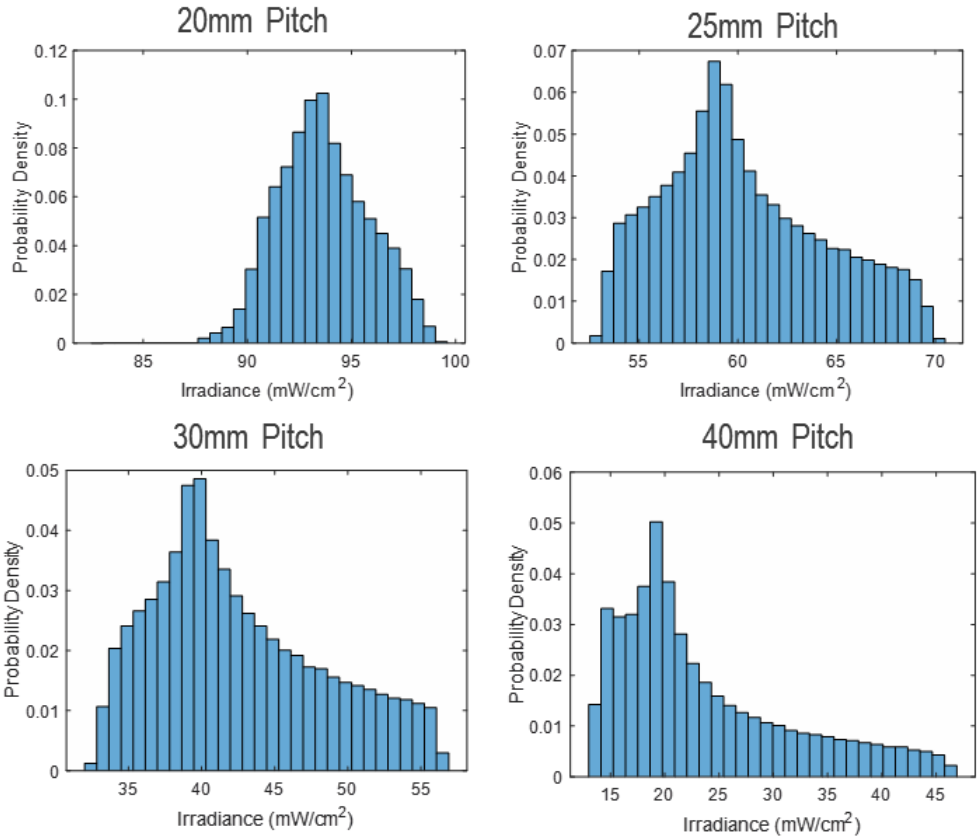
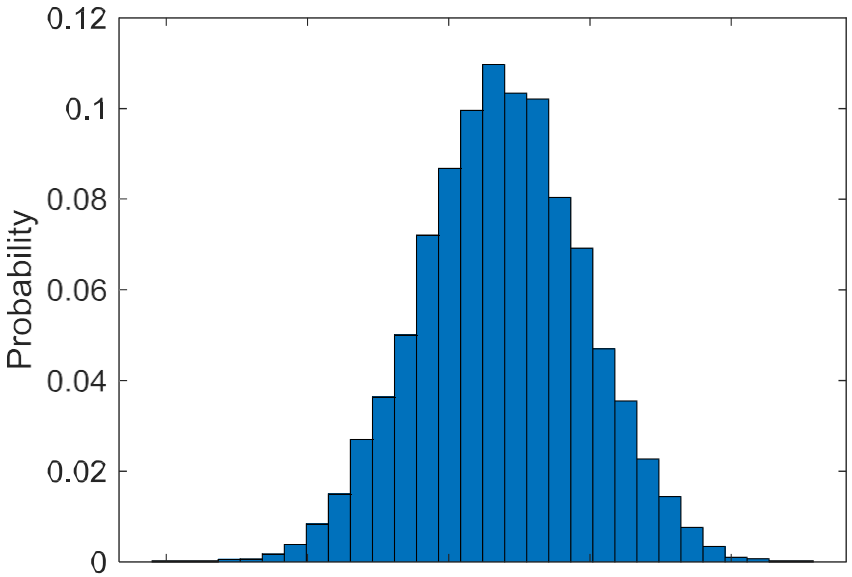


Figure 9: Associated irradiance probability distributions for simulations shown in Figure 8.

The average energy incident on the serpentine channel during the procedure is illustrated in Figure 10 (for 10,000 cells). This defines the specification for the LED light source, in terms of total energy delivered during a single procedure. This will affect the nominal LED optical power, and the spatial distribution of the LED array, which can thus be optimized in order to meet this dose requirement.



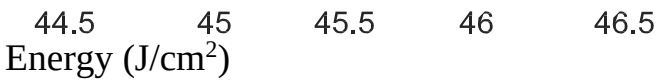


Figure 10: Probability of incident energy on flowing location within serpentine channel during the UV treatment with the current argon-mercury lamp. Based on average of ~45 mW/cm^2 irradiance over ~17 minutes

The LED median energy dose can be compared to the required dose from the gas lamp, to calculate the necessary optical power of each individual LED. The number of LEDs required can be calculated from the LED pitch and the serpentine dimensions. These results are illustrated in Figure 11.

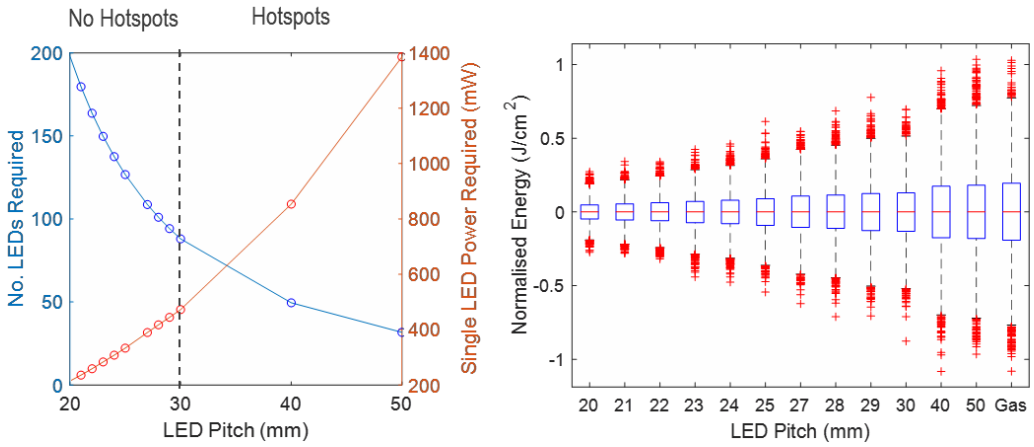


Figure 11: Left – number of LEDs and optical power of each single LED required to provide equivalent energy to UV gas source. Right – box and whisker plot of energy distribution for increasing LED pitches. Energy has been normalized about zero. Note that the variation in energy increases with increasing LED pitch. The distribution width of LED energy is less than or equal to the width of the UV gas lamp distribution for all LED pitches.

The number of LEDs required ranges from 90-200, and the optical power required from a single LED ranges from 200-475 mW. Note that the minimum number of LEDs required for no hotspots is ~90, operating each with an optical power of ~475 mW (the pitch between the LEDs can be decreased beyond 20 mm, but the number of LEDs scales with the power of the pitch leading to very large numbers of LEDs in a single array). As the simulation only represents a single-side illumination, the optical powers required can be halved if illuminating from both sides, but the number of LEDs will have to be doubled to avoid the generation of hot-spots.

The last specification for equivalence is that the width of the energy distribution does not exceed the UV gas lamp. This is satisfied for all LED pitches (up to the max simulated 50 mm), as shown by Figure 11(right).

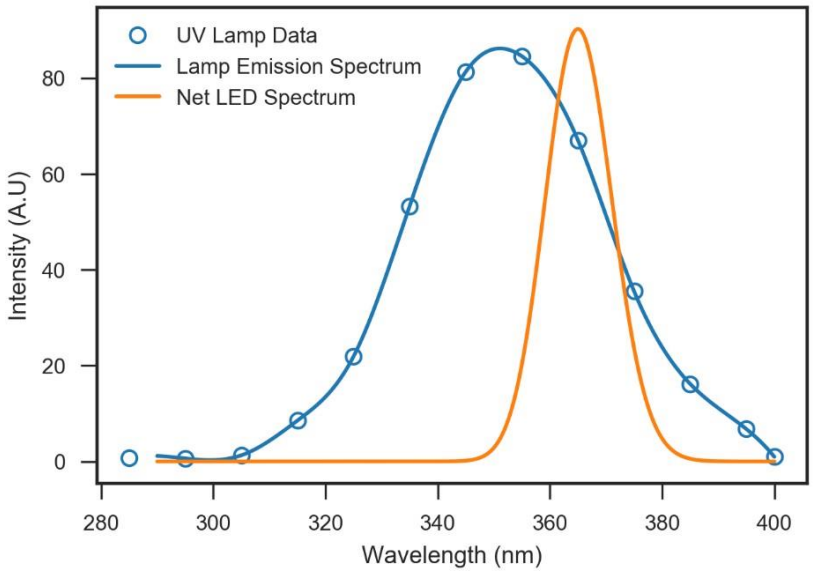


Figure 12: LED Concept 1 - emission spectrum for LED array composed of single wavelength LEDs

There are no high efficiency, high power LEDs currently available at the peak of UV gas lamp emission (λ =355 nm). The current market leader is Roithner (XSL-355-3E-R6, XSL-355-5E-R6) with a maximum power of 2.1 mW at 2.92% efficiency. Therefore, the concept is not likely to be a feasible option

Concept 2 – Array of Multiple Wavelength LEDs Matching Lamp Spectrum

The following UV Lamps were considered for the remaining concepts:

LED ID	Wavelength (nm)	Optical Power (mW)	FWHM (nm)	Efficiency (%)	Contribution (%)
Epigap LED (EOLS-340-697)	340	30	10	30.00	43.3
NS355L-3RLQ (Nitride Semiconductor)	353	2.4	5	3.33	10.3
SemiLEDs EV-D45A UA##	360	300	12	24.49	32.3
SBM-120-UV (Luminus Devices)	368	10600	17	35.16	14.2

Note that the LEDs below 340 nm have not been considered due to their unavailability. The spectrum can be evaluated against specifications using equation 1. The spectral ratio value for the LED array is given by,

$$R_{\text{spectral}} \approx 0.795$$

This falls within the specifications and compares well with the UV gas lamp ratio of

~0.76. However in order to meet the required energy requirements, an average of ~475 mW is required from each LED grouping (see Figure 16). Consequently many more LEDs are required from the 340 nm and 353 nm bands in comparison to the 360 nm and 368 nm bands, due to the much lower efficiencies at these wavelengths.

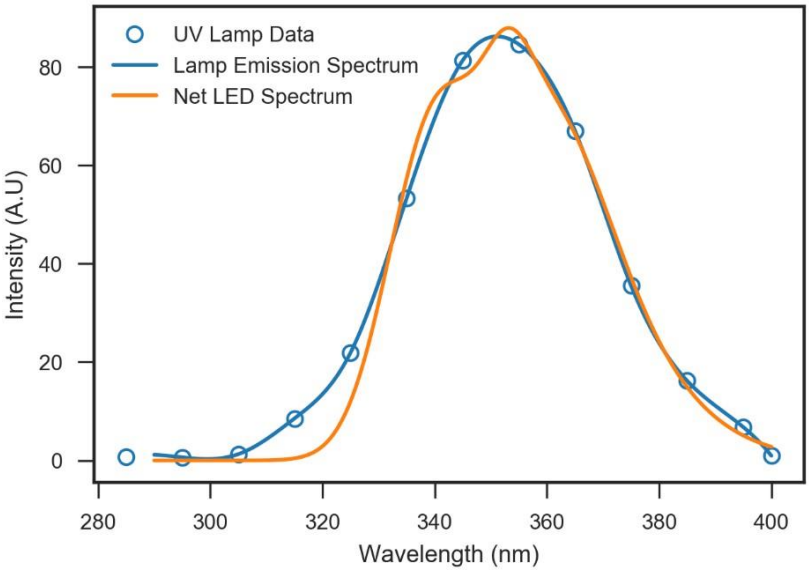


Figure 13: Net emission spectrum from multiple wavelength LEDs designed to fully replicate the UV gas lamp spectrum

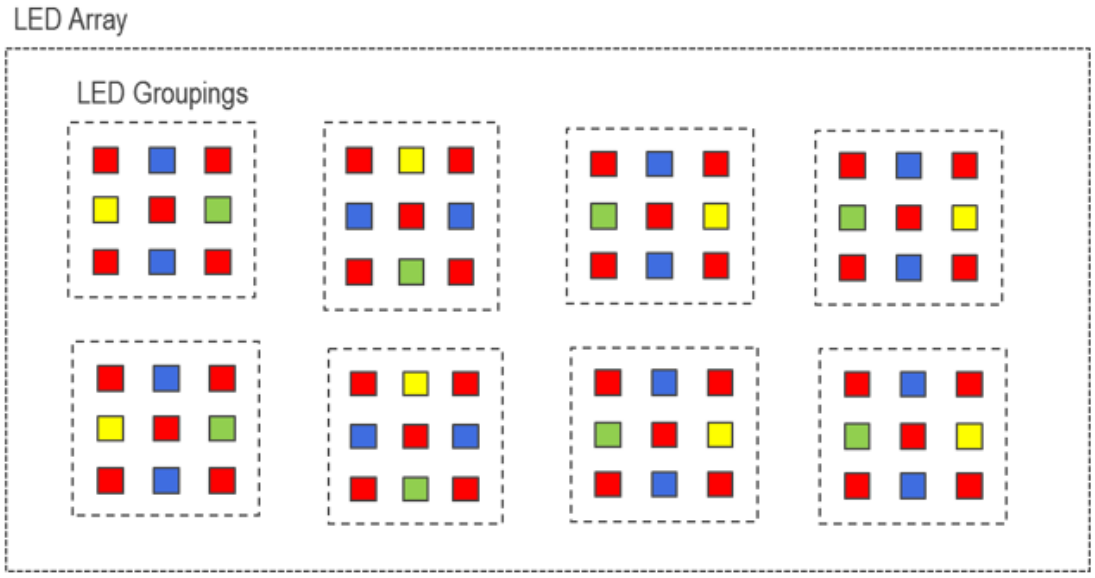


Figure 14: Schematic of multi-wavelength LED groupings arranged into an array to emulate both the spectral profile and irradiance of the UV gas lamp

The total number of LEDs necessary in order to support 475 mW of optical power, and their associated electrical power requirements are listed in Table 8. Unfortunately, while the spectrum satisfies the spectral specification, the number of LEDs required in the ~350 nm band is large due to the limited optical power. This would be difficult and costly to manufacture within the necessary pitch (~30 mm), requiring custom fabrication of multi-wavelength LED chips.

The low efficiency of the 353 nm LED will also require a large electrical power draw (total of ~3 W in comparison to 93 0mW for concept 1), and generating larger quantities of heat compared to the other concepts.

Based on these findings, it is perceived to better utilize LEDs of high efficiency and optical power, as discussed in Concept 3.

Concept 3 – Array of Multiple Wavelength LEDs for Partial Match of Lamp Spectrum

This concept partially matches the UV gas lamp emission spectrum with an array of LEDs at multiple wavelengths with pragmatic consideration for available efficient LEDs. The LEDs chosen are listed in the table below. Note only LEDs with efficiencies greater than 30%, and optical powers > 25 mW were considered in order to limit both the number of LEDs and their associated electrical power consumptions. The LED array emission spectrum is shown in Figure 15.

LED ID	Wavelength (nm)	Optical Power (mW)	FWHM (nm)	Efficiency (%)	Contribution (%)
Epigap LED (EOLS-340-697)	340	30	10	30.00	52.4
Marktech optoelectronics MTSM365UV-D5120	365	900	9	50.00	25.3
SBM-120-UV (Luminus Devices)	368	10600	17	35.16	22.3

LED Concept 3 - 3 LED wavelengths from 340-368 nm chosen to partially replicate UV gas lamp spectrum, whilst maintaining high electrical efficiencies in order to minimize the number of LEDs required overall and minimize thermal dissipation.

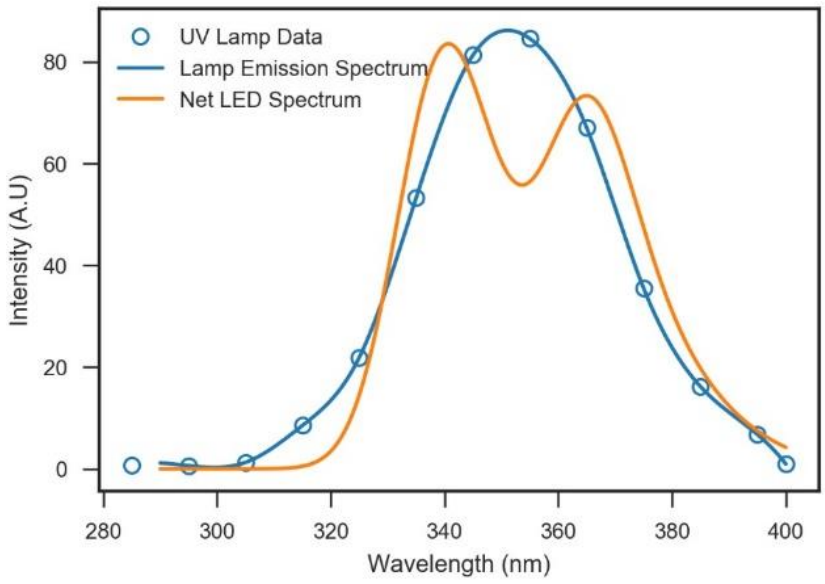


Figure 14: LED Concept 3 - emission spectrum for LED array for partial spectral coverage. Note the large dip in intensity at the lamp peak emission profile.

The spectral ratio of this composite spectrum is,

$$R_{\text{spectral}} \approx 0.742$$

Consequently, the spectrum lies on the boundary for the spectral ratio specification (0.74-0.8). However as illustrated by Figure 14, there is a significant decrease in relative intensity at the peak of the UV lamp emission. Due to this notable difference, while the spectrum qualifies for the spectral specification the spectra are not equivalent (unlike the spectra for concept 2). The clinical implications of this, if any, are not known.

The number of LEDs required in this case in order to replicate the necessary 475mW optical power per LED are listed in Table 10. The number of LEDs increases to 11 (from 1 in concept 1), but is significantly less than the 29 LEDs required for concept 2. In addition the necessary electrical power (per LED patch) increases to 1.37 W for concept 3, from 930mW for concept 1.

Conclusion of current LED technology:

Three main LED concepts were reviewed, which were conceived to potentially meet one or both of the following objectives:

- Maximize wall-plug efficiency in order to minimize thermal requirements and the total number of LEDs required, by means of selecting high efficiency LED wavelengths;
- Best match the spectral output of the current lamp system to be most equivalent to the current Cellex in terms of wavelengths.

Concept 1 (a single highly efficient LED at 365 nm) met this first objective, and found to be the simplest, most cost-effective solution, with the caveat that it is not known if additional or entirely different wavelengths are required for effective Photopheresis. This concept would require extensive CELLEX redesign and clinical evaluation to determine the feasibility of the light source that would be expected to be at least ten times greater than the current Cellex lamp.

Concept 2 best met the second requirement, was but not found to be practical due to the poor efficiencies of some the LEDs meaning a very large number of LEDs would be required overall, making manufacturing challenging or unfeasible.

Concept 3 was an iteration on Concept 2 that utilized only efficient LED types to reduce the total number of LEDs required, whilst still preserving the breadth of wavelengths emitted by the fluorescent lamp. This concept however exhibited a dip at around 350nm due to the availability of efficient LEDs in this region.

A key point of consideration moving forward is the true requirement for wavelengths of a new UV-A source for photopheresis. The broad spectral output (wide range of wavelengths) on the Cellex is due to the UV-A sources that were commercially available at the time of development of the Cellex, when UV-A LEDs, with narrower spectral outputs, were not an available option. It is not known whether all UV-A wavelengths contribute equally to the photopheresis treatment, and therefore which wavelengths are required from a new LED source. It could be that using any wavelength in the UV-A

band is acceptable, or that only a specific narrower wavelength band(s) is required. This obviously changes the acceptance criteria for the three proposed concepts. The only way to establish this would be to conduct an experimental study to investigate which wavelengths contribute to the photopheresis process.

As part of an on-going project, Mallinckrodt are investigating the effect of altering 8-MOP, UV dose and the influence of 8-MOP photoadducts on UV dosing. Recent studies (Buhimschi and Gasparro) have shown that the production of photoadducts is sensitive to the proportion of UVA and UVB emitted by the irradiation source, while other work by Galluzzi highlights the critical role of 8-MOP, specifically, in inducing immunogenic cell death. Until the influence of irradiation on 8-MOP photoadduct formation is clearly understood and this is further elucidated in the context of immunogenic cell death, the downstream impact of a spectral change on ECP efficacy will remain unknown.

- ***Other information***

Each lamp contains ~1 gram of phosphor material and this material contains ~0.7% lead as the dopant. Therefore each lamp will contain 7µg of lead. The estimated number of BSP lamps placed on the EU market in 2012 for photopheresis treatment is 4600.Therefore it is estimated that EU consumption of lead for this application is ~ 32g. Market usage is expected to grow to an equivalent of 74 grams of lead by 2020.

However, given the lamp lifetime and treatment time, the number of lamps required to support market growth is minimal compared to the number of treatments delivered.

- ***Life cycle assessment***

Extraction and refining: BSP lamp phosphors contain abundant and readily available elements, barium, silicon and lead. The phosphor types with spectra closest to BSP are $(Ba,Mg)Al_{11}O_{19}$:Ce which also contains mostly abundant elements. Cerium is a rare earth element which is not rare although currently its supply is restricted. Most rare earths are produced in China which restricts exports so that the supply of some is lower than demand although cerium is one of the most abundant and supplies are not too small.
Phosphor and lamp production: The production process used to make all types of lamp phosphors include similar process steps such as precipitation, milling and heating and so changing from one type of phosphor to another may not significantly change the manufacturing step. Lamp manufacture is the same irrespective of phosphor composition as only the internal coating material is changed.
Use phase: If the substitute lamps emit less UV light in the useful wavelength range, treatment times would need to be longer and so energy consumption would increase in proportion to the treatment time.

- ***Re-use and recycling of materials from waste EEE***

At end of life, fluorescent lamps should be collected and recycled as separate waste

streams because of the need to recover and dispose of safely the mercury content. BSP lamp packaging is marked to indicate that mercury is present and that it should be discarded in accordance with local regulation. EU WEEE Directive "Compliance Schemes" have been set up in all EU Member States to collect and safely dispose of all types of end of life electrical equipment and this includes fluorescent lamps and so suitable disposal procedures have been established and are available. It is probable that some consumers do not dispose of their household fluorescent lamps in an environmentally acceptable manner but businesses including hospitals and medical clinics that provide photopheresis treatments will generate a moderate number of used lamps and so are more likely to use waste disposal operators who are able to recover mercury safely.

The standard recycling process is to crush the lamps in a sealed vessel. This separates the metal end caps, the glass and the phosphor powder that also contains the majority of the mercury. Metal and glass can be reused and mercury is recovered from the phosphor by distillation. The remaining phosphor will be a mixture of phosphor types from all of the types of fluorescent lamp that were treated plus some glass powder. It is feasible to reuse phosphor powder to make new lamps but where mixtures of lamp types are recycled, the mixed phosphor cannot easily be used in this way[2]. Room lighting phosphors from the most common type of fluorescent lamp are based on rare earth phosphates, typically doped with europium, terbium and cerium and so contain scarce elements although rare earth recycling is very uncommon in the EU and elsewhere. The lead content of recovered phosphors will be extremely low as the lead content of BSP is <1% and BSP lamps will be an extremely small proportion of all fluorescent lamps that are recycled and so lead recovery would be impractical.

[2] Example processes http://www.hse.gov.uk/foi/internalops/sectors/manuf/03-11-01/appendix-3.htm http://www.recolight.co.uk/downloads/pdf/GUIDE%20FINAL.pdf

- ***Proposed plans to develop substitutes and timetable***

There are several medical treatments for cutaneous T-cell lymphoma (and the other disease states mentioned above) but the procedure using BSP lamps is the only option for now to be effective. Therefore the current viable option for a substitute would be an alternative UV lamp phosphor that does not contain lead. Use of a currently available UV phosphor such as one from table 1 could be evaluated for the medical treatment but as the spectra of all of the lamps are different, they cannot replace BSP without first carrying out extensive clinical trials and gaining approval under the medical devices and drug directives. It is noteworthy that this procedure requires both a device and drug approval to be able to market it. As all lamps are different and so pose a risk to patients who are already ill, trials will need to be carried out in several stages. For these trials only the lamps with similar wavelengths to BSP could be used as lamps with much shorter wavelengths are likely to be harmful.

- Before clinical trials could begin there would need to be extensive in-vitro (adduct formation, cell viability and PHA mitogen stimulation studies) and animal non clinical toxicology work to demonstrate the new lamp photoactivated the cells according to company specification.
- The instrument would require new software to control the photactivation time if a lamp with the correct spectral output could be found
- The instrument would need to be re-engineered and electrically safety tested.
- The redesigned instrument would then need to pass EMC emissions and susceptibility requirements to comply with EU legislation and to ensure that it does not interfere with other medical equipment.
- Given the orphan rare nature of the disease the first trial would be with a small group of patients over at least four years (time needed for finding suitable patients, treatment and follow up) to ensure that the alternative lamps are effective and do not cause undesirable side-effects. Finding suitable patients with this rare disease for these trials will take much longer than would be needed for common illness.
- If these trials show that the alternative lamp is equally effective, there are no serious side-effects and that treatment times do not need to be extended, then a larger trial can be carried out. This would be to confirm that the small-scale results are correct and to look for less common undesirable side-effects. This trial would establish whether any alternative lamps give the same medical benefit to the patient as BSP. Inferior treatments would not be acceptable and a medical device directive approval would be refused. These trials would last at least 5 years given the specific patient population that would be required to be enrolled i.e. new cases of CTCL.
- Once trials are complete and if an alternative lamp has been shown to give the same benefits to patients with no increase rate of harmful side-effects, then approval under the medical device and drug directives can be sought. This procedure can take a minimum one year and the treatment cannot be used until

regulatory approval is granted from both the device and drug regulatory authorities in the EU and other global markets.

Development of new phosphors – The development of lamp phosphors is very mature and it is very unlikely that a new phosphor with an emission spectrum identical to BSP could be found. The chances of success are extremely low as so many combinations of materials have already been prepared and evaluated. Research could be carried out but it is likely to be at least three years, the length of a PhD research project, before any alternatives are available for clinical trials.

- **Possible timetable**

Basic science and non-clinical studies	**2 years**
Preliminary clinical trial	4 years
Evaluation of results	6 months
Larger clinical trial	5 years
Evaluation of results	6 months
Medical Device Directive approval	1 year
Drug approval /can be concurrent with device approval	
1 year Total without development of a new type of phosphor	13 years

Once approval is granted, patients are monitored for a further 5 years (post treatment follow up) to ensure that the change to the treatment is safe and effective. If any evidence is found that it is not safe, the approval can be withdrawn.

LED Lamp technology will continue to be evaluated in parallel, although the development timetable is considered to be similar to that of new phosphors with greater risk for success.

- ***Proposed wording for exemption***

This exemption is required only for category 8 medical devices.
Lead as an activator in the fluorescent powder discharge lamps when used as photopheresis lamps containing phosphors such as BSP (BaSi2O5:Pb)

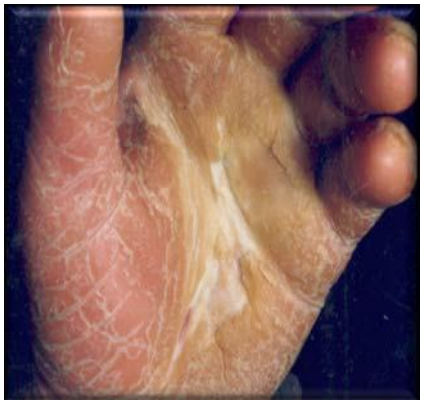
- **APPENDIX**

Therakos Photopheresis systems, which rely on BSP lamps, are used to treat individuals with immune-modulated diseases including those that have failed other therapies (Indications vary by region). This well-tolerated option offers an alternative to topical and pill-based solutions that may have serious side-effects including immune-suppression/secondary infections (a leading cause of death for immune-compromised patients), secondary malignancies or lipid or endocrine abnormalities.

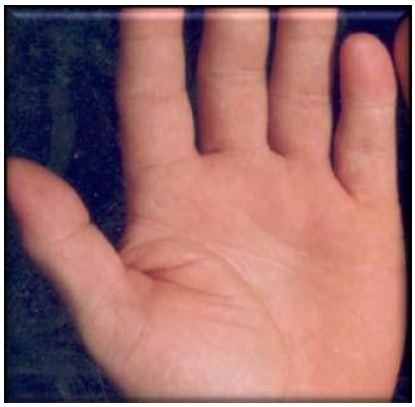
Therakos Photopheresis is a reliable and proven therapy used in over 700,000 treatments conducted across the world with a rare (<0.01%) incidence of serious adverse events in 25 years. The Therakos systems are the only regulatory approved integrated systems for ECP.

In the U.S., Therakos instruments are indicated for the palliative treatment of Cutaneous T-Cell Lymphoma (CTCL), to help patients manage the symptoms of this sometimes deadly disease. Patients with the disease suffer from patches and plaques covering large percentages of their bodies, and tumors may also develop. These debilitating skin symptoms frequently cause itching that cannot be relieved by topical or oral medications.

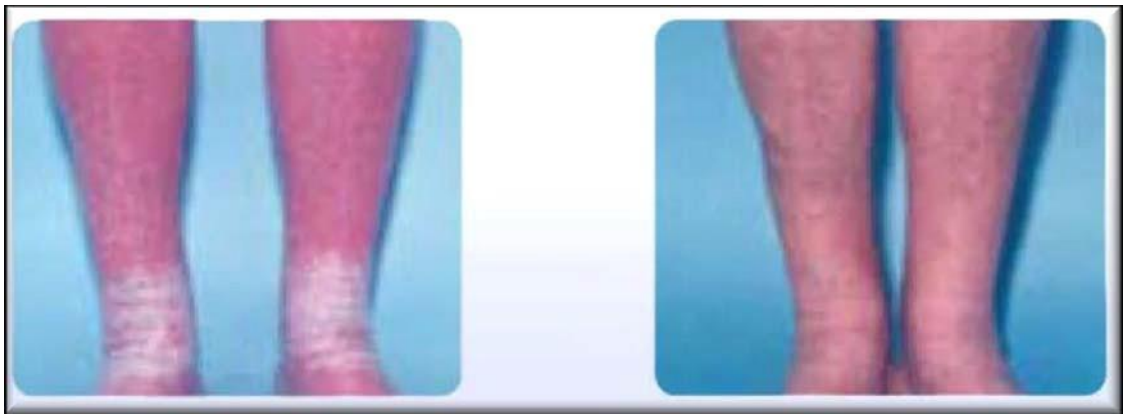
The photos below are of a patient with advanced-stage CTCL who was treated with the Therakos extracorporeal photopheresis (ECP) system. This patient developed severe cracks (fissures) in the skin which can be extremely painful and more importantly serve as a source of bacterial infection. After six months of treatment, normally twice a month, the photo on the right shows a significant reduction in skin fissures and a return of a functioning hand and reduced leg cracks.



Before



After



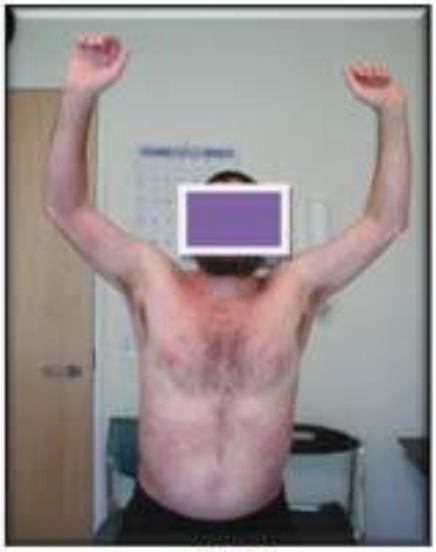
Before After

In Europe, Therakos instruments are indicated for Photopheresis. One of the disease states ECP is commonly used for is Graft-versus-host disease (GvHD) a serious and frequent complication of bone marrow transplantation that occurs partly due to the reaction of the donor cells. Both chronic and acute forms of the disease can occur.

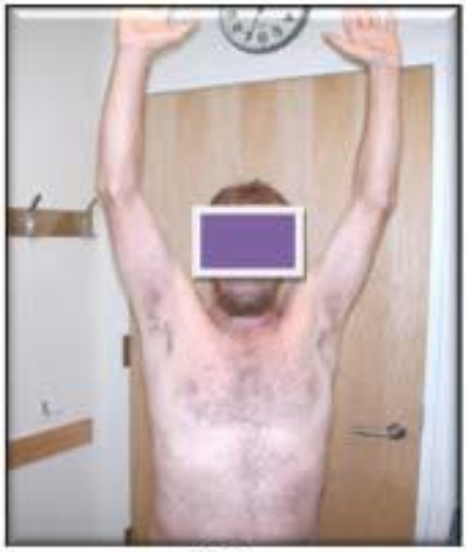
Symptoms of acute GvHD (aGvHD) can range from mild to severe. The first sign of aGvHD is typically a skin rash that appears on the palms of the hands and soles of the feet. Patients may complain of severe itching or tenderness in affected areas, and rash onset frequently correlates with engraftment of donor cells. The other two areas that are typically affected by aGvHD are the gastrointestinal (GI) tract and the liver. The severity of aGvHD is determined by the extent of involvement of the skin, GI tract and liver; and the disease can be graded (from I to IV) depending on severity. Steroids are the first-line treatment for aGvHD, but Photopheresis has also been shown to be useful as an adjunctive therapy when a patient stops responding to a previously-effective treatment. .

A chronic form of GvHD also can occur. Symptoms can range from mild to severe and commonly affect the skin, mouth, eyes and vaginal mucosa. Chronic GvHD can also affect the gut, nails, hair, liver, lungs, kidneys and heart, and may persist even when skin changes have resolved.

The photo below is a patient who has chronic GvHD following a bone marrow transplant. He has severe scleradermatous skin disease which has caused his skin to become so taut that he cannot lift his arms above his head. After not responding to other therapies he received approximately six months of photopheresis treatments and was able to recover almost complete range of motion.

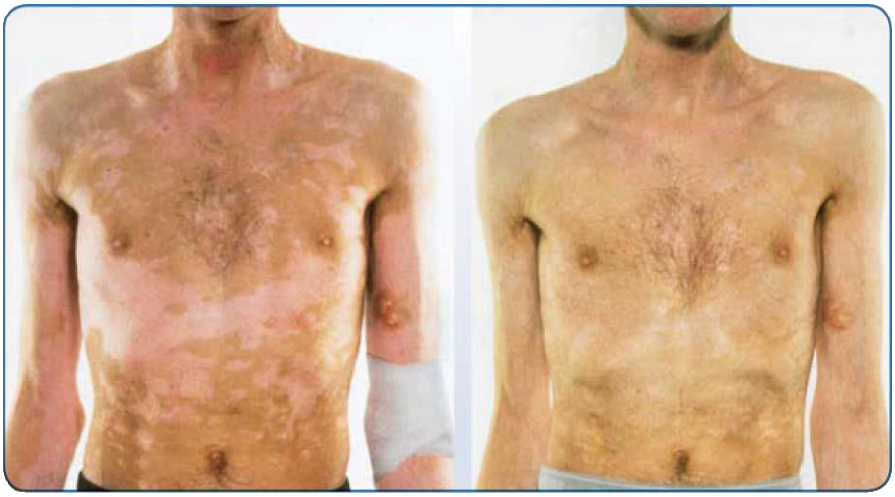


Before



After

The patient in these before-and-after photographs experienced skin lesions after a bone marrow transplant. After Photopheresis, the patient experienced skin lesion closure.



Before After