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Laser based devices: Key regulatory considerations

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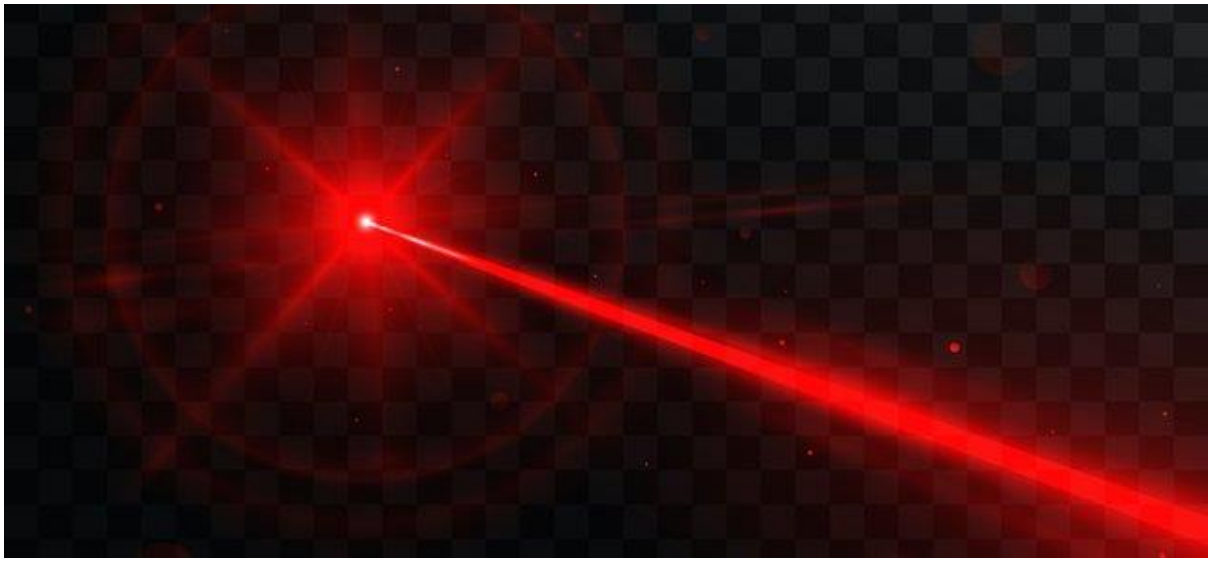
Light Amplification by the Stimulated Emission of Radiation, widely known as Laser technology, was first introduced in 1960 and it has far-flung applications in various industries including the medical field.



The laser-based products, available in various sizes, shapes and forms, have a laser system that stores and releases the energy from sources such as electrical charge or optical illumination or chemical reaction as light. Laser light in contrast to ordinary light has a specific wavelength, amplification of this specific wavelength and is a narrow beam of light focussed in one direction. All these features result in a light that is concentrated in a small area and can create a very high intensity light at farther distances from the source.

Its use in the medical industry varies from diagnosis of an underlying health condition for the treatment to life-threatening cancer disease. Its application in the fields of ophthalmology, cosmetics and dentistry has been resourceful for practitioners. Medical lasers are medical devices that use precisely focussed light sources to treat or remove tissues.

In the US, both medical and non-medical lasers are regulated by the FDA. The non-medical laser products are categorised and regulated under the radiological products category. Medical lasers are considered as medical devices and they comply with the requirements of both radiology products as well as devices. FDA recognises four major hazard classes (I to IV) of lasers, including three subclasses (IIa, IIIa, and IIIb). This nomenclature is different from the International Electrotechnical Commission classification system. However, in either of

them, the higher class corresponds to a more powerful laser and has greater potential to pose serious injury, if not used properly. Hence the labelling of Classes II-IV must include a warning symbol stating the class and output power of the LASER product. The medical lasers are categorised under Class IV and they are considered as high-risk radiological products by the US FDA.

Class FDA	Class IEC	Laser Product Hazard	Product Examples
I	1, 1M	Considered non-hazardous. Hazard increases if viewed with optical aids, including magnifiers, binoculars, or telescopes.	• laser printers • CD players • DVD players
IIa, II	2, 2M	Hazard increases when viewed directly for long periods of time. Hazard increases if viewed with optical aids	• bar code scanners
IIIa	3R	Depending on power and beam area, it can be momentarily hazardous when directly viewed or when staring directly at the beam with an unaided eye. The risk of injury increases when viewed with optical aids.	• laser pointers
IIIb	3B	Immediate skin hazard from direct beam and immediate eye hazard when viewed directly.	• laser light show projectors • industrial lasers • research lasers
IV	4	Immediate skin hazard and eye hazard from exposure to either the direct or reflected beam; may also present a fire hazard.	• laser light show projectors • industrial lasers • research lasers • medical device lasers for eye surgery or skin treatments

Table 1. The US FDA Classification of LASER Products as a Radiological Product

Various laws, regulations, and standards are applicable to the laser devices and mandate the manufacturer to ensure certain engineering controls and risk communication methodologies are applied to manage and mitigate possible biological hazards. The end-users must ensure proper use of the device as per the device labels issued by manufacturers as the failure of the same can lead to a lack of safety and effectiveness of the product.

Medical lasers have diversified applications and are used in various types of surgical procedures such as: –

- Cosmetic surgery: To remove tattoos, scars, stretch marks, sunspots, wrinkles, birthmarks, spider veins or hair
- Refractive eye surgery: To reshape the cornea to correct or improve vision as in LASIK or PRK)

- Dental procedures: Inclusive of endodontic/periodontic procedures, tooth whitening, and oral surgery
- General surgery: Inclusive of tumour removal, cataract removal, breast surgery, plastic surgery and most other surgical procedures.

Figure 1. Aesthetic Applications of LASER Devices

The laser surgical devices used in dermatology for general and plastic surgeries are regulated under 21 CFR Part 878.4810. There are various laser devices under different product codes used for aesthetic purposes.

Regulation Number	Device Name	Device Class	Product Code
§878.4810	Laser Assisted Lipolysis	Class 2	ORK
§878.5400	Laser for disruption of adipocyte cells for aesthetic use	Class 2	PKT
§878.5400	Fat Reducing Low Level Laser	Class 2	OLI
§878.4810	Laser, Cellulite Appearance	Class 2	OYW
§878.4810	Light-based, Over-the-Counter Wrinkle Reduction	Class 2	OHS
§878.4810	Light-based, Over-the-Counter Hair Removal	Class 2	OHT
§878.4810	Massager, Vacuum, Light Induced Heating	Class 2	NUV
§878.4810	Over-The-Counter, Powered Light-Based Laser for Acne	Class 2	OLP
§878.4810	Powered Laser Surgical Instrument	Class 2	GEX
§878.4810	Powered Laser Surgical Instrument with Microbeam\ Fractional Output	Class 2	ONG
§878.4810	Powered Light-based, Non-laser Surgical Instrument	Class 2	ONE
§878.4810	Powered Light-based, Non-laser Surgical Instrument with Thermal Effect	Class 2	ONF

Table 2. Product Codes for Aesthetic LASER Medical Devices

Manufacturers of aesthetic laser medical devices must comply with the regulations for Radiological Health i.e., Title 21 CFR (Subchapter J, Radiological Health) Parts 1000 through 1005 and the medical device regulations.

Regulation	Aspects
21 CFR Part 1000	General
21 CFR Part 1002	Records and reports
21 CFR Part 1003	Notification of defects or failure to comply
21 CFR Part 1004	Repurchase, repairs, or replacement of electronic products
21 CFR Part 1005	Importation of electronic products
21 CFR Part 1010	Performance standards for electronic products: General
21 CFR Part 1040.10	Performance standards for Light-emitting products - laser products
21 CFR Part 1040.11	Performance standards for Light-emitting products - Specific purpose laser products

Table 3. Applicable Regulations for Radiological Health

The aesthetic laser medical devices with medical applications must in addition to the above regulations, comply with the device regulations and consensus standards applicable for a given device product code.

Title		ORK, OYW, OHS, OHT, NUV, OLP	GEX, ONG, ONE, ONF	ONF*
12-102 ANSI IES RP-27.2-00/R17	Recommended Practice for Photobiological Safety for Lamps and Lamp Systems - Measurement Technique	X	X	NA
12-249 IEC 62471 First edition 2006-07	Photobiological safety of lamps and lamp systems	X	X	NA
12-297 ANSI IES RP-27.1-2015	Recommended Practice for Photobiological Safety for Lamps and Lamp Systems - General Requirements	X	X	NA
12-321 ANSI IES RP-27.3-17	Recommended Practice for Photobiological Safety for Lamps - Risk Group Classification and Labeling	X	X	NA
12-273 IEC 60825-1 Edition 2.0 2007-03	Safety of laser products - Part 1: Equipment classification, and requirements [Including: Technical Corrigendum 1 (2008), Interpretation Sheet 1 (2007), Interpretation Sheet 2 (2007)]	NA	X	NA

Table 4. Consensus Standards for LASER Devices

The majority of LASER devices used for aesthetic purposes are considered as moderate-risk devices, requiring compliance with special controls and a 510(k) clearance from the FDA for importing and marketing the device in the USA. Very few devices fall under Class I requiring compliance with general controls and few devices falling under Class III require a Pre-Market Approval (PMA) from the FDA. The labels of medical laser shall comply with 21 CFR 801 and 21 CFR 1040.10 & 1040.11, Performance Standard for Light Emitting Products.

It is critical to evaluate the intended use of the device and map them to the right regulations. For example, when not labelled or represented as sterile, laser for disruption of

adipocyte cells for aesthetic use, classified under PKT, is GMP exempt and 510(k) registration. The device, however, shall comply with general requirements concerning records (820.180) and complaint files (820.198).

The fat reducing low-level laser systems for aesthetic use are classified under product code OLI and regulated under 21 CFR 878.5400. They fall under Class II and shall comply with the special controls issued by the FDA for assured safety and effectiveness of the device and shall obtain the 510(k) approval for importation and distribution of the device within the US market. These are low-level laser systems for the disruption of adipocyte cells within the fat layer for the release of fat and lipids from these cells for non-invasive aesthetic use. The US FDA requirements for this device have been detailed below.

The manufacturer shall identify all the components of the device systems including system software and accessories. Photograph or drawing of the device, functional block diagram of the device along with its accessories, predicate comparison sheet; risk profile of the device covered in the risk assessment document shall be submitted to the FDA as a part of the 510(k) technical file. The ocular injury, electrical shock and unintended cell damage and use errors are the common risks involved in these devices used for fat reduction. The manufacturers can choose to justify the risk profile by adopting various mitigation measures such as bench testing, software validation, clinical testing, biocompatibility testing, labelling, and ensuring that the device is in compliance with IEC 60601-1 and IEC 60601-1-2.

Mitigation Strategy	Types of Risk	Objective
Bench or Preclinical Testing	• Ocular injury • Unintended cell damage	• It shall meet all design specifications and performance requirements • Assesses the probability of system failure, and possible mitigation measures, risk communication to the user
Software Validation	• Ocular injury • Unintended cell damage	• The software shall be developed in compliance with "IEC 60601-1-4: Medical electrical equipment – Part 1-4; "General Requirements for Safety; Collateral Standard: Programmable electrical medical devices" or equivalent methods • 510(k) content shall be in line with the US FDA's "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices" • The 510(k) shall detail the anticipated risks, level of concern for each of the identified risks
Electromagnetic Compatibility	• Electrical shock • Unintended cell damage	• The electromagnetic testing of the devices shall be conducted in compliance with IEC 60601
Clinical Testing	• Ocular injury • Unintended cell damage	• The clinical studies or trials, if required for establishing the substantial equivalence, shall comply with the IDE, IRB and informed consent regulations defined under 21 CFR 812, 21 CFR Part 56 and 21 CFR Part 50 respectively
Biocompatibility Studies	• Unintended cell damage	The studies shall be conducted either as per • ISO 10993-1, Biological Evaluation of Medical Devices Part 1: Evaluation and Testing for intermittent external contact with intact external body surfaces or • Shall compare with the predicate device the identical material of construction and material processing
Labeling	• Ocular injury • Electrical shock and unintended cell damage and use errors	• The labeling components of the 510(k) shall comply with 21 CFR 807.87(e) and the device labels shall comply with general labeling requirements defined under 21 CFR 801 • The device label must include directions for use, indications for use, contraindications, storage conditions, warnings, precautions as required by 21 CFR 801.109 • The device user manual shall include details on the device and all accessories; interconnectivity between the device and the other components or accessories; all features, functions, output modalities, and specifications; all user-accessible controls, indicators, markings, and/or labels on the device which provide information regarding the function or meaning of each control, display output jack, etc; illustrations of the device and accessories; summary of clinical testing

Table 5. Risk Mitigation Strategies for Fat Reducing, Low Level, Laser Aesthetic Device

Once the FDA approval/clearance is obtained, all the electronic products are subjected to achieve compliance for 21 CFR 1000-1050. Accordingly, the manufacturers of all the different classes of lasers must submit "Product Reports" (Also called as Radiation Safety Product Report) to the FDA, as per 21 CFR 1002, before the product is introduced into interstate commerce. Once a Product Report is submitted to the FDA, an Accession number is issued by the FDA for the device. Including the accession number is mandatory in the Customs Clearance Form and is usually verified by the US Customs during the importation of the product. If your product is made in another country for import into the United States, the import clearance process requests identification of the accession number on the import affirmation form, FDA 2877.

It is recommended by the FDA to submit the "Periodic Safety reports" at least one month before the product is imported into the US. The manufacturers have varied options to compile and submit the product reports. Product reports can be compiled using Form 3632 /one can compile the product reports using the e-submitter software available on the FDA website. Once an e-copy is generated, the e-copy of the file is usually exported as an XML document which can be submitted to the CDRH directly through ESG Gateway/alternatively the e-submitter can load the XML file onto a CD and can be mailed to CDRH or emailed to RadHealthCustomerService@fda.hhs.gov for processing and issuance of accession number. Reports prepared and submitted using e-submitter software may be acknowledged significantly faster than a traditionsal report submitted on paper. For faster acknowledgement of the receipt of the product report within 48 hours, the ESG Gateway can be used for product report submission.

In addition to product reports, the manufacturers shall submit duly filled Form 3636/use e-submitter tool to compile the annual reports on radiation safety testing of the devices by September 1st of each year.

Furthermore, EU MDR has broadened the definition of medical devices and more products such as epilation lasers are classified as medical devices. Products listed under Annex XVI make aesthetic claims or other non-medical purposes, but they are very similar to medical devices in terms of safety and risk profile. High-intensity electromagnetic radiation emitting equipment such as lasers and intense pulsed light equipment intended for skin resurfacing, tattoo or hair removal or other skin treatment are considered as medical devices. This might be overwhelming for the companies with medical device portfolios, as the EU MDR requirements could be all new to them. Such companies can start by appointing a Regulatory outsourcing partner and finding the right Notified Body for certification. The laser surgical instrument falls under Class IIb as per the classification rules defined in Chapter III rule 9 of the EU Medical Device Regulations. The manufacturers shall develop the EU MDR compliant device documentation, comply with ISO 13485:2016 followed by

conformity assessment of the device by the Notified Body and for CE certification of the device.

In China, powered laser surgical instrument used in dermatology and surgery and intended to remove unwanted brown spots, sun freckles, or tattoos from the skin is classified as Class III.

In a nutshell, the Laser products intended for medical use fall under the purview of multiple regulations and will be under the vigilance of various offices. Navigating through the regulations and framing the right regulatory strategy requires a thorough understanding of the device technologies as well as applicable regulations.