



June 28, 2024

Carl Zeiss Meditec AG
Chaitali Gawde
Senior Regulatory Affairs Specialist
5300 Central Parkway
Dublin, California 94588

Re: K240215

Trade/Device Name: BLUE 400; BLUE 400 S
Regulation Number: 21 CFR 882.4950
Regulation Name: Diagnostic Neurosurgical Microscope Filter
Regulatory Class: Class II
Product Code: QFX
Dated: January 25, 2024
Received: May 31, 2024

Dear Chaitali Gawde:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm> identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (<https://www.fda.gov/media/99812/download>) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (<https://www.fda.gov/media/99785/download>).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems>.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (<https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance>) and CDRH Learn (<https://www.fda.gov/training-and-continuing-education/cdrh-learn>). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (<https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice>) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

**Adam D.
Pierce -S** Digitally signed by
Adam D. Pierce -S
Date: 2024.06.28
14:17:06 -04'00'

Adam D. Pierce, Ph.D.
Assistant Director
DHT5A: Division of Neurosurgical,
Neurointerventional
and Neurodiagnostic Devices
OHT5: Office of Neurological

and Physical Medicine Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known)

K240215

Device Name

BLUE 400;

BLUE 400 S

Indications for Use (Describe)

BLUE 400 and BLUE 400 S are accessories to the surgical microscope and allow the fluorescence observation of fluorophores with an excitation peak between 400 nm and 410 nm and the fluorescence emission observation comprising the spectrum in a spectral band of 620 - 710 nm.

The ZEISS BLUE 400 and BLUE 400 S are surgical microscope accessories used in fluorescent visualization of suspected grade III and IV gliomas during neurosurgery.

Type of Use (Select one or both, as applicable)

☒ Prescription Use (Part 21 CFR 801 Subpart D)

☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRASStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

In accordance with 21 CFR 807.92 the 510(k) Summary for the Fluorescence Accessories is provided below.

1. SUBMITTER

Applicant:	Carl Zeiss Meditec AG Rudolf-Eber-Strasse 11D-73447 Oberkochen Germany
Primary Correspondent	Chaitali Gawde Senior Regulatory Affairs Specialist Carl Zeiss Meditec, Inc. 5300 Central Parkway Dublin, CA 94568 (224) 300-3992 Phone E-mail: chaitali.gawde@zeiss.com (preferred)
Secondary Correspondent	Paul Swift Head of Regulatory and Clinical Affairs, Americas Carl Zeiss Meditec, Inc. 5300 Central Parkway Dublin, CA 94568 (817) 925-8507 Phone E-mail: paul.swift@zeiss.com
Date Prepared:	June 27, 2024

2. DEVICE

Device Trade Name: BLUE 400; BLUE 400 S
Classification: 21 CFR 882.4950 Diagnostic Neurosurgical Microscope Filter
Regulatory Class: II
Product Code: QFX

3. LEGALLY MARKETED PREDICATE DEVICE

Predicate Device Name: BLUE 400 (K211346)
Classification: 21 CFR 882.4950 Diagnostic Neurosurgical Microscope Filter
Regulatory Class: II
Product Code: QFX

4. DEVICE DESCRIPTION SUMMARY

The BLUE 400 and BLUE 400 S are fluorescence accessories to qualified surgical microscopes, intended to allow intraoperative viewing of malignant glioma tissue grade III and IV under fluorescence. The overall system is comprised of excitation (illumination) and emission (observation) filters to detect fluorescence and are optimized in conjunction with the drug to pass light between 620 – 710 nanometers. The BLUE 400 and BLUE 400 S filters allow the surgical microscope to produce excitation light in a wavelength range covering at least 400 – 410 nanometers that excites an approved optical imaging agent and enables the surgeon to observe the emitted fluorescent signal in the oculars or on a display. Fluorescence of marked brain tissue helps visualization of tissue associated with Grade III & IV glioma during neurosurgeries.

Compared to the blue visualization of the surrounding non-fluorescent tissue in the BLUE 400 image, BLUE 400 S is designed to visualize the surrounding nonfluorescent tissue more similar to white light impression, while tumor visualization of grade III and IV glioma remains consistent. With the visualization of non-fluorescent anatomy in an almost white light impression, BLUE 400 S is expected to allow PpIX visualization with less frequent switching between fluorescence and white light imaging modes.

BLUE 400 and BLUE 400 S can be installed only into qualified ZEISS surgical microscopes. For these accessories to be used with a qualified ZEISS surgical microscope, the critical components of the surgical microscope need to fulfill the clinically relevant parameters for the Indications for Use of BLUE 400 and BLUE 400 S.

5. INDICATIONS FOR USE

BLUE 400 and BLUE 400 S are accessories to the surgical microscope and allow the fluorescence observation of fluorophores with an excitation peak between 400 nm and 410 nm and the fluorescence emission observation comprising the spectrum in a spectral band of 620 - 710 nm.

The ZEISS BLUE 400 and BLUE 400 S are surgical microscope accessories used in fluorescent visualization of suspected grade III and IV gliomas during neurosurgery.

6. SUBSTANTIAL EQUIVALENCE

Table 1. Subject to Predicate Device Comparison Table – Indications for Use

Attribute	Subject Device BLUE 400 / BLUE 400 S (K240215)	Predicate Device BLUE 400 (K211346)	Equivalence statement	Justification of equivalency
Indications for Use	BLUE 400 and BLUE 400 S are accessories to the surgical microscope and allow the fluorescence observation of fluorophores with an excitation peak between 400 nm and 410 nm and the fluorescence emission observation comprising the spectrum in a spectral band of 620 - 710 nm. The ZEISS BLUE 400 and BLUE 400 S are surgical microscope accessories used in fluorescent visualization of suspected grade III and IV gliomas during neurosurgery.	BLUE 400 is a surgical microscope accessory filter for viewing fluorescence of fluorophores with an excitation peak between 400 nm and 410 nm and the fluorescence emission observation comprising the spectrum in a spectral band of 620 - 710 nm. The ZEISS BLUE 400 is a surgical microscope accessory used in fluorescent visualization of suspected grade III and IV gliomas during neurosurgery.	Equivalent	Updated to include BLUE 400 S.
Patient Population	Patients undergoing neurological procedures who already have been diagnosed with grade III & IV glioma with the aid of further diagnostic procedures.	Patients undergoing neurological procedures.	Equivalent	The patient population remains the same, it is only described in more detail.
Configuration/Relationship to the device	<u>BLUE 400</u> consists of a HW module (specific filters). <u>BLUE 400 S</u> consists of a HW module (specific filters).	BLUE 400 consists of a HW module (specific filters).	Identical	N/A

Table 2. Subject to Predicate Device Comparison Table – Technical Characteristics

Attribute	Subject Device BLUE 400 / BLUE 400 S (K240215)	Predicate Device BLUE 400 (K211346)	Equivalence statement	Justification of equivalency
Manufacturer	Carl Zeiss Meditec AG Goeschwitzer Strasse 51-52 D-07745 Jena Germany	Carl Zeiss Meditec AG Goeschwitzer Strasse 51-52 D-07745 Jena Germany	Identical	N/A
Classification Product Code	QFX	QFX	Identical	N/A
Regulation Number	882.4950 (Diagnostic neurosurgical microscope filter)	882.4950 (Diagnostic neurosurgical microscope filter)	Identical	N/A
Review Panel	Neurology	Neurology	Identical	N/A
Fluorescence Excitation	<u>BLUE 400</u> : 400 nm to 430 nm (50% edges) <u>BLUE 400 S</u> : 398 nm to 457 nm (50% edges)	400 nm to 430 nm (50% edges)	Equivalent	Excitation wavelength range of PpIX is covered by both options (400 nm to 410 nm)
Fluorescence Detection	<u>BLUE 400</u> : > 450 nm (50% edge) <u>BLUE 400 S</u> : 540 nm to 728 nm (50% edges)	> 450 nm (50% edge)	Equivalent	Fluorescence light of PpIX between 620 nm and 710 nm is covered by both options.
Fluorescence Agent	5-Aminolevulinic acid hydrochloride (5-ALA HCl) Gleolan	5-Aminolevulinic acid hydrochloride (5-ALA HCl) Gleolan	Identical	N/A
Combination Device	No	No	Identical	N/A
Visualization Result	Fluorescent image of distribution of the accumulated protoporphyrin IX (PpIX) in malignant tissue during operation	Fluorescent image of distribution of the accumulated protoporphyrin IX (PpIX) in malignant tissue during operation	Identical	N/A
Visualization of Real Time Images	Yes	Yes	Identical	N/A
Visualization on Interface/ Display	Yes	Yes	Identical	N/A
Light Specifications – Type	White Light – Fluorescence	White Light – Fluorescence	Identical	N/A

Attribute	Subject Device BLUE 400 / BLUE 400 S (K240215)	Predicate Device BLUE 400 (K211346)	Equivalence statement	Justification of equivalency
Light Specifications – Light Source	Non-laser light source - Minimum Irradiance must be met (Brightness Ocular Image: ≥ 92 nW, Measured at a working distance of 250 mm)	300 Watt Xenon	Equivalent	Replaced by irradiance required for acceptable illumination

7. NON-CLINICAL AND/OR CLINICAL TESTS SUMMARY OF STUDIES

Sterilization and Shelf Life

The device is provided non-sterile. Shelf-Life is not applicable.

Biocompatibility

The device does not have patient-contacting materials; therefore, a biocompatibility assessment is not needed for this device.

Performance Testing – Bench

In order for BLUE 400 and BLUE 400 S to work, they must be installed onto a qualified ZEISS surgical microscope. A software license specific to BLUE 400 and BLUE 400 S must also be installed on the ZEISS microscope. Software verification testing (Documentation Level: Enhanced) has been performed in accordance with the FDA guidance document “Content of Premarket Submissions for Device Software Functions” to demonstrate that software is performing as intended. Cybersecurity concerns were addressed by providing cybersecurity documentation that included an assessment of the assets, threats, vulnerabilities, and controls in accordance with the FDA guidance document “Content of Premarket Submissions for Management of Cybersecurity in Medical Devices.”

Non-clinical system testing provided an evaluation of the performance of the system relevant to each of the system specifications. The functional and system level testing showed that the system met the defined specifications. To ensure that the clinically relevant parameters for the Indications for Use of the fluorescence accessories are fulfilled, the following parameters/specifications were tested:

Test	Test Method	Results
Brightness of the fluorescence ocular image	Measurement of the image brightness of the ZEISS fluorescence target at the ocular plane at a working distance of 250 mm.	Passed
Irradiance	Measurement of the excitation light density in the object plane.	Passed

Test	Test Method	Results
Excitation wavelength (of the microscope)	Excitation wavelength range of PpIX is covered by both options (400 nm to 410 nm).	Passed
Excitation filter	Check of optical filter specification of excitation filter	Passed
Emission wavelength (of the microscope – ocular image)	Design review via evaluation of component specifications or measurement of the spectrum at the ocular plane.	Passed
Emission wavelength (of the microscope – video image)	Design review via evaluation of component specifications or measurement of the spectrum at the ocular plane.	Passed
Emission filter	Check of optical filter specification of emission filter	Passed
Spatial resolution of the ocular image	Measurement of the spatial resolution with the spatial test target in white light mode. @min. magnification + working distance 200mm @max. magnification + working distance 200mm Values may vary depending on different working distances.	Passed
Non-mirrored video image	Visual inspection with a corresponding test target in white light mode.	Passed
Non-rotated video image	Visual inspection with a corresponding test target in white light mode.	Passed
Non-deformed video image	Visual inspection of the geometric distortions of a test target with a circle in white light mode	Passed
Centered video image	Visual inspection and measurement with a test target in white light mode.	Passed
Photometric resolution of video image	Grey value resolution test with a photometric resolution test target in white light mode.	Passed
Signal-to-noise ratio of the video image (sensitivity)	Measurement of the signal-to-noise ratio of a video image of a fluorescent target at a given signal value (pixel value).	Passed
Latency of the video image	Measurement of the video latency in white light mode.	Passed
Spatial resolution of the video image	Measurement of the spatial resolution with the spatial test target in white light mode.	Passed

Finally, special controls testing has also been performed and met the defined specifications. The following special controls testing has been conducted with and without cover glass:

Test	Test Method	Results
Spectrum of the Illumination Source (TS1)	The irradiance spectrum (250 nm – 1020 nm, mW/cm ²) of the illumination source was measured and verified with a spectrometer. These measurements were assessed prior to application of the excitation filter module.	Passed
Maximum Power and Irradiance of the Illumination Source (TS2)	The maximum output power and irradiance of illumination sources were measured and verified with a power meter at the end of the microscope light guide. These measurements were assessed prior to application of the excitation filter module.	Passed
Irradiance Spectrum of the Excitation Light and Spectral Response of the Excitation Filter (TS3)	The irradiance spectrum (250 nm – 1020 nm) of the illumination light, following passage through the excitation filter module, was measured at a working distance of 30 cm with a spectrometer. The edges at 50% decrease of the blue excitation peak were calculated respectively.	Passed
Maximum Excitation Power and Power Density (TS4)	The maximum power (mW) and power density (mW/cm²) of the excitation light was measured with a thermopile, at multiple different working distances and zoom settings, including the maximum and minimum zoom. The power density measurements of the subject device were compared to the predicate device.	Passed
Optical Path Loss (TS5)	To determine the overall detectable light output and the total losses in relation to device working distance and zoom setting, optical path loss was calculated by dividing the output signal measured at the microscope eyepiece (without emission filter) by the illumination signal measured with a spectrometer at the microscope focal plane for the same zoom setting. A reflection standard (white silicon remission disc) was used at a working distance of 35 cm.	Passed
Spectrum of the Emission Filter (TS6)	The spectrum (350 nm – 1050 nm) of the emission filter when integrated in the surgical operating microscope was measured with a spectroradiometer to include all the coating and optics that affects the spectrum of the observation path. For this test the excitation filter was	Passed

Test	Test Method	Results
	removed, and a reflection standard was used at the device focal plane with different zoom settings. To compare the light that passes the observation optics and emission filter, the 50% edge of the spectrum was calculated.	
Homogeneity of the Excitation Light at the Focal Point (TS7)	The reflected signal from a white sheet of paper positioned at 30 cm working distance was imaged by the surgical operating microscope camera and the intensity profile was calculated to demonstrate the homogeneity of the excitation light.	Passed
System Sensitivity (TS8)	BLUE 400: As a diffusely reflecting and fluorescent disc the ZEISS BLUE 400 fluorescent target was used and positioned at a microscope working distance of 22.5 cm. The zoom setting was chosen to lead to the same image size of the target for all devices. The fluorescence signal in the eyepiece of the subject device was compared to the predicate device. BLUE 400 S: The fluorescence light portion of the ZEISS BLUE 400 fluorescence target, measured with BLUE 400 is scaled to and subtracted from the spectrum measured with BLUE 400 S. This results in the BLUE 400 S remission spectrum. The integral of the reconstructed fluorescence signal is divided by the integral of the reconstructed remission spectrum, corresponding to the ratio of fluorescence to emission light.	Passed
Pre-Operative Phantom Test (TS9)	This test was conducted to demonstrate that the ZEISS BLUE 400 test phantom is suitable for the pre-operative checks of a surgical microscope. The phantom has one fluorescent area and was imaged by the surgical microscope camera. The same test was repeated by observation through the microscope eyepiece.	Passed
Spectrum of the Camera Filter (TS10)	The spectrum at the camera interface was measured with a spectroradiometer to demonstrate that camera filter can block near infrared and infrared leakage of excitation light to the camera.	Passed

No clinical tests were submitted.

8. CONCLUSION

Based on the similarities of the intended use/indications for use, device design, principles of operation, technological characteristics and the results of the non-clinical performance testing, the subject device, BLUE 400 and BLUE 400 S, is substantially equivalent to the legally marketed predicate device.