July 14, 2023

Brainlab AG
% Marc Bergenthal
Manager Regulatory Affairs
Olof-Palme-Str. 9
Munich, 81829
GERMANY

Re: K223106
Trade/Device Name: Brainlab Elements 6.0, Brainlab Elements Image Fusion, Brainlab Elements Image Fusion Angio, Brainlab Elements Contouring, Brainlab Elements BOLD MRI Mapping, Brainlab Elements Fibertracking
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical image management and processing system
Regulatory Class: Class II
Product Code: QIH, LLZ, JAK
Dated: June 23, 2023
Received: June 23, 2023

Dear Marc Bergenthal:

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 (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 located 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.

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 803) for devices or postmarketing safety reporting (21 CFR 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 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 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,

Daniel M. Krainak, Ph.D.
Assistant Director
Magnetic Resonance and Nuclear Medicine Team
DHT8C: Division of Radiological Imaging
and Radiation Therapy Devices
OHT8: Office of Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K223106

Device Name
Brainlab Elements 6.0, Brainlab Elements Image Fusion, Brainlab Elements Image Fusion Angio, Brainlab Elements Contouring, Brainlab Elements BOLD MRI Mapping, Brainlab Elements Fibertracking

Indications for Use *(Describe)*
Brainlab Elements are software applications indicated for the processing of medical image data to support the intended user group to perform image guided surgery and radiation treatment planning.

Brainlab Elements Contouring provides an interface with tools and views to outline, refine, combine and manipulate structures in patient image data. The generated 3D structures are not intended to create physical replicas used for diagnostic purposes.

Brainlab Elements Image Fusion is an application for the co-registration of image data within medical procedures by using rigid and deformable registration methods. It is intended to align anatomical structures between data sets.

Brainlab Elements Fibertracking is an application for the processing and visualization of cranial white matter tracts based on Diffusion Tensor Imaging (DTI) data for use in treatment planning procedures.

Brainlab Elements BOLD MRI Mapping provides tools to analyze task based blood oxygen level dependent data (BOLD MRI Data) to visualize the activation signal.
Brainlab Elements Image Fusion Angio is a software application that is intended to be used for the co-registration of cerebrovascular image data.

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.

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BRAINLAB

K223106

510(k) Summary

July 14, 2023

General Information	
Manufacturer	Brainlab AG; Olof-Palme Str.9; 81829, Munich, Germany
Establishment Registration	8043933
Trade Names	• Brainlab Elements Image Fusion • Brainlab Elements Image Fusion Angio • Brainlab Elements Contouring • Brainlab Elements BOLD MRI Mapping • Brainlab Elements Fibertracking
Classification Name	Medical image management and processing system
Product Code (primary)	QIH
Product Codes (secondary)	LLZ, JAK
Regulation Number	892.2050
Regulatory Class	II
Panel	Radiology
Primary Predicate Device	K212420 Brainlab Elements, Brainlab Elements Contouring (4.0), Brainlab Elements Fibertracking (2.0), Brainlab Elements Image Fusion (4.0), Brainlab Elements Image Fusion Angio (1.0)
Secondary Predicate Device	K113732 iPlan (iPlan Cranial, iPlan Stereotaxy, iPlan ENT, iPlan CMF, iPlan View, iPlan Spine)
Contact Information	
Primary Contact	Marc Bergenthal Manager Regulatory Affairs Regulatory Affairs Phone: +49 89 99 15 68 0 Email: regulatory.affairs@brainlab.com
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1. Indication for Use

Brainlab Elements are software applications indicated for the processing of medical image data to support the intended user group to perform image guided surgery and radiation treatment planning.

Brainlab Elements Contouring provides an interface with tools and views to outline, refine, combine and manipulate structures in patient image data. The generated 3D structures are not intended to create physical replicas used for diagnostic purposes.

Brainlab Elements Image Fusion is an application for the co-registration of image data within medical procedures by using rigid and deformable registration methods. It is intended to align anatomical structures between data sets.

Brainlab Elements Fibertracking is an application for the processing and visualization of cranial white matter tracts based on Diffusion Tensor Imaging (DTI) data for use in treatment planning procedures.

Brainlab Elements BOLD MRI Mapping provides tools to analyze task based blood oxygen level dependent data (BOLD MRI Data) to visualize the activation signal.

Brainlab Elements Image Fusion Angio is a software application that is intended to be used for the co-registration of cerebrovascular image data.

2. Device Description

The Brainlab Elements 6.0 are applications that transfer DICOM data to and from picture archiving and communication systems (PACS) and other storage media devices. They include modules for 2D & 3D image viewing, image processing, image co-registration, image segmentation and 3D visualization of medical image data for treatment planning procedures.

They consist of the following software applications:

1. Contouring 4.5
2. Image Fusion 4.5
3. Fibertracking 2.0
4. BOLD MRI Mapping 1.0
5. Image Fusion Angio 1.0

This device is a successor of the Predicate Device Brainlab Elements 5.0 (K212420).

Brainlab Elements Contouring provides an interface with tools and views to outline, edit, refine, combine and manipulate structures in patient image data. The output is saved as 3D DICOM segmentation object and can be used for further processing and treatment planning.

Brainlab Elements Image Fusion is an application for the co-registration of image data within medical procedures by using rigid and deformable registration methods.
The co-registration consists on providing spatial alignment/fusion of medical imaging data, which are derived from different or same imaging modalities (e.g. CT, MRI, PET, SPECT, US). Once two image sets are fused, they can be viewed simultaneously. All planned content (e.g. objects and trajectories) defined in one image set is visible in any other fused image set. The algorithm used in Image Fusion matches two image sets together with common anatomical structures for optimal fusion results. Therefore, the two image sets must share the same common anatomical area.

Brainlab Elements Fibertracking is an application for the processing and visualization of information based upon Diffusion Tensor Imaging (DTI) data, i.e. to calculate and visualize

cranial white matter tracts in selected regions of interest, which can be used for treatment planning procedures.
Diffusion Tensor Imaging (DTI) is a magnetic resonance technique, that allows the measurement of diffusion anisotropy in the brain using diffusion weighted images that were scanned with magnetic field gradients applied in several directions. The Fibertracking software uses the scans to calculate the diffusion direction of the water molecules along potential white matter fibers for the entire data volume.

Brainlab Elements Image Fusion Angio is a software application that is intended to be used for the co-registration of cerebrovascular image data. It allows to register digital subtraction angiographies to vascular images in order to combine flow and location information. In particular, 2D DSA (digital subtraction angiography) sequences can be fused to MRA, CTA and 3D DSA sequences.

AI Features:
Artificial Intelligence features included for the device refers to the identification of previously diagnosed lesions or tumors in T1-Weighted Contrast-Enhanced Magnetic Resonance (T1+C MR) volumetric images.

Such functionality was already present in previous versions of the devices, where it was based on a tumor segmentation algorithm without machine learning. As research has shown that tumor segmentation algorithms based on AI / ML can achieve better performance metrics than non-machine learning algorithms, the tumor segmentation algorithm is complemented with an AI / ML based algorithm that is preferred in case suitable T1+C MR volumes are provided to a device.

The AI/ML algorithm is a Convolutional Neuronal Network (CNN) developed using a Supervised Learning approach. The algorithm was developed using a controlled internal process that defines activities from the inspection of input data to the training and verification of the algorithm.
The training process begins with the model observing, learning, and optimizing its parameters based on the training pool data. The model's prediction and performance are then evaluated against the test pool. The test pool data is set aside at the beginning of the project.

3. Substantial Equivalence

The Subject Device has similar intended use and technological features as the predicate devices. An overview of the similarities and differences can be found in the tables below:

Predicate Device	Name
Subject Device	Brainlab Elements, Brainlab Elements Contouring (4.5), Brainlab Elements Fibertracking (2.0), Brainlab Elements Image Fusion (4.5), Brainlab Elements Image Fusion Angio (1.0), Brainlab Elements BOLD MRI Mapping (1.0)

Predicate Device	Name
Primary Predicate device (K212420)	Brainlab Elements, Brainlab Elements Contouring (4.0), Brainlab Elements Fibertracking (2.0), Brainlab Elements Image Fusion (4.0), Brainlab Elements Image Fusion Angio (1.0)
Secondary Predicate device (K113732)	iPlan (iPlan Cranial, iPlan Stereotaxy, iPlan ENT, iPlan CMF, iPlan View, iPlan Spine)

Brainlab Elements – Image Fusion 4.5

Topic/ Feature	Primary Predicate Device (Brainlab Elements Image Fusion 4.0 (K212420))	Subject Device (Brainlab Elements Image Fusion 4.5)	Comment
Indications for use	Brainlab Elements Image Fusion is an application for the co-registration of image data within medical procedures by using rigid and deformable registration methods. It is intended to align anatomical structures between data sets. The device itself does not have clinical indications.	Brainlab Elements Image Fusion is an application for the co-registration of image data within medical procedures by using rigid and deformable registration methods. It is intended to align anatomical structures between data sets. The device itself does not have clinical indications.	Same as the predicate.
Use Environment	The system shall be used in a hospital office environment or rooms appropriate for surgical interventions or radiotherapy planning.	The system shall be used in a hospital office environment or rooms appropriate for surgical interventions or radiotherapy planning.	Same as the predicate.
Computer Hardware Requirements	Brainlab Elements can be used on hardware that fulfills the defined minimum requirements: - Operating System: Windows 8.1 64bit - Minimum 4 logical cores - Minimum RAM: 6 GB - Graphics: Direct X compatible	Brainlab Elements can be used on hardware that fulfills the defined minimum requirements: - Operating System: Windows 8.1 64bit - Minimum 4 logical cores	Same as the predicate.

	- Display Resolution: 1920 x 1080 (Full HD)	- Minimum RAM: 6 GB - Graphics: Direct X compatible - Display Resolution: 1920 x 1080 (Full HD)	
Image Data Sets Format	DICOM 3D imaging Modalities, e.g. CT/XT, MRI, NM/PET, OT, are supported for automatic fusion. Other modalities are supported for manual fusion (alignment)	DICOM 3D imaging Modalities, e.g. CT/XT, MRI, NM/PET, OT, are supported for automatic fusion. Other modalities are supported for manual fusion (alignment)	Same as the predicate.
Rigid co-registration, rigid image fusion	Automatic rigid co-registration (rigid fusion) of 3D DICOM image data: CT (incl. low-dose CT), MR, OT (e.g. Perfusion), MR-DTI, MR-BOLD, NM/PET Manual rigid co-registration (rigid fusion) of other (unknown) 3D DICOM image data, e.g. US (ultrasound).	Automatic rigid co-registration (rigid fusion) of 3D DICOM image data: CT (incl. low-dose CT), MR, OT (e.g. Perfusion), MR-DTI, MR-BOLD, NM/PET, US (ultrasound). Manual rigid co-registration (rigid fusion) of other (unknown) 3D DICOM image data.	The subject device additionally provides functionality to automatically fuse US to MR images. Safety and efficacy of this feature was verified via Risk Management and Verification activities.

Brainlab Elements Contouring 4.5

Topic/ Feature	Primary Predicate Device (Brainlab Elements Image Fusion 4.0 (K212420))	Subject Device (Contouring 4.5)	Comment
Indications for Use	Brainlab Elements Contouring provides an interface with tools and views to outline, refine, combine and manipulate structures in patient image data. The generated 3D structures are not intended to create physical replicas used for diagnostic purposes.	Brainlab Elements Contouring provides an interface with tools and views to outline, refine, combine and manipulate structures in patient image data. The generated 3D structures are not intended to create physical replicas	Same as the predicate.

	The device itself does not have clinical indications	used for diagnostic purposes. The device itself does not have clinical indications	
Use Environment	The system shall be used in a hospital office environment or rooms appropriate for surgical interventions or radiotherapy planning.	The system shall be used in a hospital office environment or rooms appropriate for surgical interventions or radiotherapy planning.	Same as the predicate.
Automatic Segmentation of Objects	The application automatically creates segmentation objects provided by the Universal Atlas. Workflow relevant segmentation objects are created automatically or, if required by a workflow, on a single button click. The application also offers the possibility to define customized segmentation templates.	The application automatically creates segmentation objects provided by the Universal Atlas. Workflow relevant segmentation objects are created automatically or, if required by a workflow, on a single button click. The application also offers the possibility to define customized segmentation templates.	Same as the predicate.
Manual Creation and Refinement of Objects	The application provides tools for the manipulation of objects: The application provides tools for manual creation and refinement of segmentation objects: - SmartShaper - Brush 3D / Erase 3D - Brush 2D / Erase 2D - Smart Brush - Threshold Segmentation	The application provides tools for the manipulation of objects: The application provides tools for manual creation and refinement of segmentation objects: - SmartShaper - Brush 3D / Erase 3D - Brush 2D / Erase 2D - Smart Brush - Threshold Segmentation	Same as the predicate.
Object Manipulation	The application provides tools for the manipulation of objects: - Copy	The application provides tools for the manipulation of objects:	Same as the predicate.

	- Margins - Smoothing - Mirroring - Shifting and Rotation - Splitting - Automatic Object Fitting	- Copy - Margins - Smoothing - Mirroring - Shifting and Rotation - Splitting - Automatic Object Fitting	
Object Review	The application provides functionality to control the review state of objects. In case of leaving the application with unreviewed semi-automatically or automatically created objects, a message is displayed.	The application provides functionality to control the review state of objects. In case of leaving the application with unreviewed semi-automatically or automatically created objects, a message is displayed.	Same as the predicate.
Volumetric Report	It is possible to create a printable report for an object in a platform independent file format, giving information about the object's volume, its diameter according to the Macdonald criteria and its response evaluation criteria (RECIST). If multiple objects are selected and a volumetric report is created, it contains information about all objects.	It is possible to create a printable report for an object in a platform independent file format, giving information about the object's volume, its diameter according to the Macdonald criteria and its response evaluation criteria (RECIST). If multiple objects are selected and a volumetric report is created, it contains information about all objects.	Same as the predicate.

Brainlab Elements BOLD MRI Mapping

Topic/ Feature	Secondary Predicate Device (iPlan (K113732))	Subject Device (Brainlab Elements BOLD MRI Mapping)	Comment
Indications for Use	iPlan's indications for use are the viewing, presentation, and documentation of medical	Brainlab Elements BOLD MRI Mapping provides tools to analyze task based blood	Both devices contain highly generic product

	imaging, including different modules for image processing, image fusion, atlas assisted visualization and segmentation, intraoperative functional planning where the output can be used e.g. with stereotactic image guided surgery or other devices for further processing and visualization. The device itself does not have specific clinical indications.	oxygen level dependent data (BOLD MRI Data) to visualize the activation signal. The device itself does not have clinical indications	features that deal with data handling rather than specific indications for use. The BOLD MRI Mapping Element re-implements existing tools and functionality offered by iPlan BOLD MRI Mapping with regards to functional planning.
Preprocessing	- Brain Mask Filtering - Spatial Smoothing - Motion Correction (Optional) - Slice Time Correction (Optional) - Denoising (Low Pass Filtering)	- Brain Mask Filtering - Spatial Smoothing - Motion Correction - Optionally use of Distortion Correction from Brainlab Elements Image Fusion - Only for task-based analysis: Denoising (Low Pass Filtering)	The following preprocessing tools were added: - Optionally use of Distortion Correction from Brainlab Elements Image Fusion, These tools were evaluated for safety via risk management activities carried out validated via performance validation testing and literature review.

4. Performance Data

Software Verification:

Software verification was performed, verifying the software requirements through integration tests, and unit tests. Incremental test strategies have been set up after verification of the first release candidate for changes with limited scope. In this case, an impact analysis of the modifications is performed and tests to be performed are identified and planned

correspondingly. That means, not all tests have to be performed but only a subset, as some of the previous tests are not affected by the change and remain therefore valid.
Software verification verifies all specifications, including SOUP items and cybersecurity.
For newly added components, interoperability tests were carried out, in addition to the individual component verification.

Clinical Validation:
As a part of the design validation process, pre-clinical validation activities were carried out for the Subject Device pertaining to its indications for use.

The Clinical Validation activities concluded that the Subject Device:
- Provides state of the art features for the purposes of pre-planning for Cranial, ENT, CMF Surgery and Radiotherapy Planning.
- All applicable safety and performance requirements are fulfilled.
- Device does not pose significant levels of risk and adequate risk mitigation measures are implemented.
- Usability aspects have been considered during the development of the device and the device was found to be suitable for the user group stated.
- Clinical data collected establishes the performance and safety of the Subject Device and that the clinical benefits outweigh any potential risks associated with the product.

5. Conclusion

Verification and validation activities carried out established that the set requirements were met and that the device performs as claimed.
The Subject Devices' comparison with the Predicate Devices establishes that they have similar functionality, intended use and technological characteristics. Therefore, we believe that the Subject Device can be considered substantially equivalent to the predicate device.