MRIMath LLC
℅ Paul Dryden
Consultant
ProMedic Consulting LLC
131 Bay Point Dr NE
Saint Petersburg, Florida 33704

August 8, 2024

Re: K233822
Trade/Device Name: i2Contour
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical Image Management And Processing System
Regulatory Class: Class II
Product Code: QIH
Dated: July 9, 2024
Received: July 10, 2024

Dear Paul Dryden:

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,

Ningzhi Li -S

for
Daniel Krainak, Ph.D.
Assistant Director
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: 07/31/2026
See PRA Statement below.

Submission Number *(if known)*

K233822

Device Name

i2Contour

Indications for Use *(Describe)*

MRIMath i2contour is intended for the semi-automatic labeling, visualization, and volumetric quantification of WHO grade 4 glioblastoma (GBM) from a set of standard MRI images of male or female patients 18 years of age or older who are known to have pathologically proven glioblastoma. Volumetric measurements may be compared to past measurements if available. MRIMath i2contour is not to be used for primary diagnosis and is not intended to be the sole diagnostic metric.

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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7-Aug-24

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Subject Device
Name of Device: *i*2Contour
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical Image Management and Processing System
Product Code: QIH
Class: II

Predicate Device
Neosoma, Inc. NS-HGlio - K221738
Regulation Number: 21 CFR 892.2050
Regulation Name: Medical Image Management and Processing System
Product Code: QIH
Class: II

Device Description
The MRIMath *i*2Contour is a web-based software platform designed for the contouring and segmentation of the T1c and FLAIR sequences of the MRIs of patients already diagnosed with GBM. It combines AI with a user interface (UI) for review, manual contouring, and approval. The software is intended to be used by trained medical professionals as an aid in the tumor contouring process. Review by a trained professional is a requirement for completion.

The AI algorithm within MRIMath *i*2Contour generates an initial tumor contour, which serves as a starting point for medical professionals to complete the contouring process manually. It is important to note that the software does not alter the original MRI images and is not intended for tumor detection or diagnostic purposes. MRIMath *i*2Contour is specifically designed to generate tumor volume contours for GBM. It is not intended for use with images of other brain tumor types.

Indications for Use
MRIMath *i*2contour is intended for the semi-automatic labeling, visualization, and volumetric quantification of WHO grade 4 glioblastoma (GBM) from a set of standard MRI images of male or female patients 18 years of age or older who are known to have pathologically proven glioblastoma.

Volumetric measurements may be compared to past measurements if available. MRIMath *i*2contour is not to be used for primary diagnosis and is not intended to be the sole diagnostic metric.

Comparison to Predicate Device
We have selected the Neosoma – NS-HGlio, K221738 as the predicate. We have compared the features and performance in the table below.

Table 1 - Comparison of Subject vs. Predicate

	Subject Device i2Contour	Predicate Neosoma, Inc. - NS-HGlio	Comparison
K#		**K221738**	
Product Code	QIH	QIH	
CFR	21 CFR 892.2050	21 CFR 892.2050	
Classification	Medical image management and processing system	Medical image management and processing system	
Indications for Use	MRIMath *i*2contour is intended for the semi-automatic labeling, visualization, and volumetric quantification of WHO grade 4 glioblastoma (GBM) from a set of standard MRI images of male or female patients 18 years of age or older who are known to have pathologically proven glioblastoma. Volumetric measurements may be compared to past measurements if available. MRIMath *i*2contour is not to be used for primary diagnosis and is not intended to be the sole diagnostic metric.	NS-HGlio is intended for the semi-automatic labeling, visualization, and volumetric quantification of high-grade brain glioma (WHO grade 3 astrocytoma, WHO grade 4 astrocytoma and WHO grade 4 glioblastoma) from a set of standard MRI images of male or female patients 18 years of age or older who are known to have pathologically proven high-grade glioma. Volumetric measurements may be compared to past measurements if available. NS-HGlio is not to be used for primary diagnosis, and is intended to be used by qualified clinical personnel as an additional source of information and is not intended to be the sole diagnostic metric.	Similar except the subject device is specific for glioblastoma (GBM)
Patients	Male or female patients 18 years of age or older who are known to have pathologically proven glioblastoma	Male or female patients 18 years of age or older who are known to have pathologically proven high-grade glioma	Similar with the subject device is limited to GBM
Type of Scans Used	MRI: Acquired using two different MRI sequences either in 2D or 3D using a specified protocol: T1 post-contrast (T1c) or FLAIR.	MRI: Acquired using four different MRI sequences either in 2D or 3D using a specified protocol: T1, T2, T1 post-contrast (T1c) and FLAIR.	Different
Intended Anatomy	Brain	Brain	Similar
Lesion Review	2D and 3D	2D and 3D	Similar
Segmentation	Semi-automatic and manual segmentation of glioblastoma	Semi-automatic and manual segmentation of high-grade glioma	Similar
Quantification	Volumetric measurements of the combination of the enhancing and necrosis subcomponents of the T1c, and the combination of edema, tumor, and necrosis subcomponents in the FLAIR images of glioblastoma	Volumetric measurement of the edema, necrosis, and enhancing sub-components of high-grade glioma	Different

	Subject Device i2Contour	Predicate Neosoma, Inc. - NS-HGlio	Comparison
Output	- Provides volumetric measurements of glioblastoma and the tumor + edema + necrosis subcomponents in FLAIR and the enhancing + necrosis subcomponents in T1c series - Includes segmentation of the tumor + edema + necrosis subcomponents in FLAIR and the enhancing + necrosis subcomponents in T1c series - Automatically compares results to prior scans when available - Provides PDF Report of output data	- Provides volumetric measurements of glioblastoma and the enhancing, necrosis, and edema sub-components - Includes segmentation of sub-components - Automatically compares results to prior scans when available - Provides PDF Report of output data	Different
Image Format	DICOM	DICOM	Similar
Input	FLAIR or T1c Series	T1, T2, FLAIR and T1c Series	Different
Registration	NO	YES	Different
Skull Stripping	NO	YES	Different
Number of AIs	Two	One	Different
Report	YES	YES	Similar
Indications	Grade 4 GBM	Grade 3 astrocytoma, grade 4 astrocytoma, grade 4 GBM	Different
Evaluation of Accuracy	Using three US board certified neuroradiologists with expertise in measuring GBM	Using three US board certified neuroradiologists with expertise in measuring high grade gliomas	Similar

Comparison of Technological Characteristics with the Predicate Device

AI-powered segmentation of the magnetic resonance images (MRI) of patients diagnosed with glioblastoma multiforme is the technological principle for both the subject and predicate devices. At a high level, the subject and predicate devices are based on the following same technological elements:

- The input consists of MRI of patients diagnosed with GBM.
- AI-powered prediction of the pixels that correspond to the tumor.
- Computing a tumor volume.
- Review and manual revisions, if needed

The following technological differences exist between the subject and predicate device:

- The subject device includes two independent AIs, one for T1c and the other for the FLAIR series; the predicate device consists of a single AI.
- The subject device processes individual 2D slices. The predicate device requires a 3D set of images.
- The predicate device is semi-automated as it requires skull stripping and registration. The subject device is fully automated as it does need registration nor skull stripping.
- The predicate device requires all the four series, T1, T1c, FLAIR and T2 for a single AI. The subject device has two independent AIs for T1c and FLAIR; it does not require the T1 and T2 series.
- The subject device Flair AI output is equivalent to the sum of all the sub-components of the predicate device.
- The subject device T1c AI output is equivalent to the sum the enhancing lesion and necrosis subcomponents of the predicate device.

The Indications for use for the devices are as follows:

- Neosoma: grade 3 astrocytoma, grade 4 astrocytoma, and grade 4 GBM
- MRIMath: grade 4 GBM.

Performance Data

Like the predicate, the MRIMath *i*2Contour evaluated the accuracy of the subject device in the same manner.

The predicate evaluated using 33 subjects and 132 MRIs used for the evaluation of the machine learning model performance of males than females within the age range of 18 to 79. Three US board certified neuroradiologists with expertise in measuring high grade gliomas were used. The device achieved a mean DSC of 0.88 with 95% CI of 0.86-0.90 on preoperative imaging and 0.80 with 95% CI of 0.77-0.83 on postoperative imaging which is higher than the mean DSC of the average of the three experts for the same task, which was 0.84 on preoperative imaging and 0.74 for postoperative imaging respectively.

To evaluate the accuracy of the MRIMath i2Contour FLAIR and T1c AI contours, we compare their outputs with the manual segmentations by three board certified neuro-radiologists of 46 pre- and post-operative MRIs of patients diagnosed with glioblastoma multiforme. The manual contours were performed using the MRIMath smart manual contouring platform. The test MRIs were obtained at 19 centers in the United States located at 13 community hospitals and clinics, 4 imaging centers, and two university hospitals and clinics. The details are as follows: University of Alabama at Birmingham Hospital and Clinics, Birmingham, AL (n=25), MD Anderson Cancer Center, Houston, TX (n = 1), St Vincent Hospital, Birmingham, AL (n =2), Southwest Diagnostic Imaging Center, Dallas, TX (n = 1), Thomas Medical Center, Fairhope, AL (n=1), Carmichael Imaging Center, Montgomery, Alabama (n=1), East Alabama Medical Center, Opelika, AL (n=1), St Dominic, Jackson, MS (n=1), Mobile Infirmary, Mobile, AL (n=1), North Mississippi Medical Center Tupelo, MS (n=1), Sacred Heart Airport Medical Center, Pensacola, FL

(n=1), SHHP (n=2), LX DCH, Tuscaloosa, AL (n=1), Leeds Imaging Center, Leeds, AL (n=1), Black Warrior Medical Center, Tuscaloosa, AL (n=1), American Health Imaging, Birmingham, AL (n=1), Main (n=1), Floyd Medical Center, Rome, GA (n=1), Trinity Medical Center, Birmingham, AL (n=1), Jackson Hospital, Jackson, MS (n=1).

We evaluate the AI models developed by MRIMath for GBM T1c and fluid attenuation inversion recovery (FLAIR) images, by comparing their contours to three neuro-radiologists, who used the MRIMath smart manual contouring platform. We test the hypothesis that the proportion of overall AI DICE score (DSC) measurements that exceed the designated threshold of p_0=0.88 is different from 50%. The designated threshold is the best mean DSC achieved by the predicate device. The two-sided, one-sample Z-test shows that:

- For the FLAIR AI, the DSC proportions exceed p0, 85% of the time, with a confidence interval (CI) of (72%, 92%) and p-value of <0.001, implying that our proportion is significantly different than 50%.
- For T1C, the DSC proportions exceed p_0, 93% of the time, with a CI of (82%, 98%) and *p*-value of <0.001 of the time, implying that our proportion is significantly different than 50%.

The mean overall DICE scores for the post-contrast T1 (T1c) AI were 0.95 with a 95% confidence interval (C.I) of (93%, 96%), closely matching the radiologists' scores. For true positive T1c images, AI segmentation scored a mean DSC of 83%, versus radiologists' ranging from 76% to 86%. Sensitivity and specificity for T1c AI were 92.7% and 97.2%, respectively. The FLAIR AI mean DSC was 92% with a 95% CI interval of (90%, 94%), also matching the radiologists scores. The AI also achieved a mean DICE score of 80% for true positive FLAIR slices, against the radiologists' 75%-83%, and exhibited a median sensitivity and specificity of 93.4% and 98.6%, respectively. The T1C and FLAIR AI models also produced mean Hausdorff distances (< 5 mm), volume measurements, kappa scores, and Bland-Altman differences that align closely with measurements by radiologists. Finally, the inter-user variability between radiologists was < 5% and < 10% for the T1c and FLAIR images, respectively. These results highlight the low inter-user variability of the MRIMath smart manual contouring platform and the high accuracy of its T1c and FLAIR AI models.

Substantial Equivalence Conclusion

Based on the information submitted in this application, and based on the indications for use, technological characteristics, and performance testing, *i*2Contour raises no new questions of safety or effectiveness and is substantially equivalent to the predicate device in terms of safety, efficacy, and performance.