Therapanacea SAS
% Bhairavi Ajachandra
QARA Manager
7 bis boulevard Bourdon
Paris, 75004
FRANCE

April 22, 2024

Re: K234068
Trade/Device Name: ART-Plan (v.2.2.0)
Regulation Number: 21 CFR 892.5050
Regulation Name: Medical Charged-Particle Radiation Therapy System
Regulatory Class: Class II
Product Code: MUJ
Dated: December 22, 2023
Received: December 22, 2023

Dear Bhairavi Ajachandra:

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,

Lora D. Weidner, Ph.D.
Assistant Director
Radiation Therapy 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: 07/31/2026
See PRA Statement below.

Submission Number *(if known)*

K234068

Device Name

ART-Plan (v.2.2.0)

Indications for Use *(Describe)*

ART-Plan's indicated target population is cancer patients for whom radiotherapy treatment has been prescribed. In this population, any patient for whom relevant modality imaging data is available.

ART-Plan is not intended to be used for patients less than 18 years of age.

The indicated users are trained medical professionals including, but not limited to, radiotherapists, radiation oncologists, medical physicists, dosimetrists and medical professionals involved in the radiation therapy process.

The indicated use environments are, but not limited to, hospitals, clinics and any health facility involved in radiation therapy.

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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510(k)#: K234068

510(k) Summary

Prepared on: 2024-04-18

Contact Details

Applicant Name: Therapanacea SAS

Applicant Address: 7 bis boulevard Bourdon Paris 75004 France

Applicant Contact Telephone: +33620604982

Applicant Contact: Mrs. Bhairavi AJACHANDRA

Applicant Contact Email: b.ajachandra@therapanacea.eu

Device Name

Device Trade Name: ART-Plan (v.2.2.0)

Common Name: Medical charged-particle radiation therapy system

Classification Name: System, Planning, Radiation Therapy Treatment

Regulation Number: 892.5050

Product Code: MUJ

Legally Marketed Predicate Devices

Predicate #	Predicate Trade Name (Primary Predicate is listed first)	Product Code
K232479	ART-Plan	MUJ

Device Description Summary

ART-Plan is a software platform allowing users with an account to contour regions of interest on 3D images, perform multi-model registration of images, and help in the decision for the need for replanning based on contours and doses on daily images. It includes several modules:

- Home,
- Annotate,
- SmartFuse,
- AdaptBox,
- Administration,
- About

ART-Plan asks the user to work by project. It is necessary to create a "project" entity in the Patient page by associating it to a reference volume (preferably the positioning CT or the positioning MR) in order to create the contours on this volume in the Annotate module or to use this image as reference to compare it with CBCT images in the AdaptBox module. It is possible to create several projects for a given patient.

The Home module allows the user to search for a patient already present in the software's database or to import it from the structure's imaging servers or from another external source and to manage the different projects of this patient.

The Annotate module allows the user to contour regions of interest on the reference volume. It also allows generation of pseudo-CTs from MRI images. Users are able to visualize, evaluate and modify the HU values of the associated structures on the pseudo-CT, if needed. After validation, manual and automatic contours can be generated on the pseudo-CT images. Registration can also be performed using the pseudo-CT either as a target or source image. All results can be exported upon approval.

The SmartFuse module allows the user to fuse the primary volume of a project with secondary volumes.

The AdapBox module helps the user to decide if a replanning is necessary. For this purpose, the module allows the user to generate a pseudo-CT from a CBCT image, to auto-delineate regions of interest on the pseudo-CT, to compute the dose on both planning CT and pseudo-CT and then define if there is a need for replanning by comparing volume and dose metrics computed on both images and over the course of the treatment. Those metrics are defined by the user.

The Administration module allows users with specific rights to manage the platform's usage parameters. Some more restricted rights are also accessible in the drop-down menu linked to the user account through the Settings menu.

The About module allows the user to obtain information about the software and its use, as well as to contact TheraPanacea.

ART-Plan offers deep-learning based automatic segmentation for the following localizations:

- head and neck (on CT and synthetic-CT from CBCT images)
- thorax/breast (for male/female and on CT and synthetic-CT from CBCT images)
- abdomen (on CT images and MR images)
- pelvis male(on CT images, on synthetic-CT from CBCT and on MR images)
- pelvis female (on CT images)
- brain (on CT images and MR images)

ART-Plan offers deep-learning based synthetic CT-generation from MR images for the following localizations:

- pelvis male
- Brain

ART-Plan offers deep-learning based synthetic CT-generation from CBCT images for the following localizations:

- pelvis male
- head and neck
- thorax/breast

Intended Use/Indications for Use

ART-Plan's indicated target population is cancer patients for whom radiotherapy treatment has been prescribed. In this population, any patient for whom relevant modality imaging data is available.

ART-Plan is not intended to be used for patients less than 18 years of age.

The indicated users are trained medical professionals including, but not limited to, radiotherapists, radiation oncologists, medical physicists, dosimetrists and medical professionals involved in the radiation therapy process.

The indicated use environments are, but not limited to, hospitals, clinics and any health facility involved in radiation therapy.

Indications for Use Comparison

The proposed device has the same indication for use as the predicate device.

Technological Comparison

The device has the same technological characteristics.

The similarities between the proposed device and the primary predicate are the following:

Both devices allow multi-modal vizualisation and rigid and deformable registration for the same modalities of images

Both devices allow displaying fused and non-fused images to facilitate the comparison and delineation of image data by the user

Both devices allow manual generation, modification and semi-automatic generation of contours for the regions of interest

Both devices allow automatic segmentation on medical images using AI algorithms

Both devices allow generation of synthetic-CT from CBCT and MR images

Both allow dose computation on CT and/or synthetic-CT images for external beam irradiation with photon beams

Both allow assisted CBCT-based off-line adaptation decision-making for supported anatomies

Both devices allow the import, manipulation, visualisation, generation and the export of DICOM images

- New anatomies for generation of synthetic CT from CBCT : Thorax, Breast, Head & Neck
- Addition of new structures to the already existing localizations for the segmentation feature

There are no differences between the proposed device and the primary predicate that represent an additional claim for the primary predicate.

Non-Clinical and/or Clinical Tests Summary & Conclusions

Within the primary predicate ART-Plan v2.1.0, for an auto segmentation model to be judged acceptable, every organ included in the model must pass at least one acceptance criterion with success across the different testings it has been submitted to. These criteria are as follows:

a) The Dice Similarity Coefficient (DSC) is equal to or superior to the acceptance criteria set by the AAPM: DSC (mean)≥ 0.8.

Or

b) The Dice Similarity Coefficient (DSC) is equal to or superior to inter-expert variability: DSC (mean)≥ 0.54 or DSC (mean) ≥ mean (DSC inter-expert) + 5%.

Or

c) The clinicians' s qualitative evaluation of the auto-segmentation is considered acceptable for clinical use without modifications (A) or with minor modifications / corrections (B) with a A+B % above or equal to 85% considering the following scale:

A: the contour is acceptable for a clinical use without any modification

B: the contour would be acceptable for clinical use after minor modifications/corrections

C: the contour requires major modifications (e.g. it would be faster for the expert to manually delineate the structure)"

Within the proposed device ART-Plan (v2.2.0), the same acceptance criteria were used. Moreover, in order to overcome the limitations of reporting DSC alone and to help establish that proposed device is functioning appropriately across each segmented structure, an additional quantitative metric was used: the Hausdorff Distance (95th percentile – HD95). This metric has been chosen as it is the second most used metric, after DSC. Based on litterature review, the acceptance criteria is set as the following: the Hausdorff distance 95th percentile (HD95) is equal to or inferior to the acceptance criteria set HD95 (mean) ≤ 5.75 mm.

Thus, in order to determine the substantial equivalence of ART-Plan v2.2.0, the following tests have been performed:

Non regression testing of autosegmentation of already existing organs at risk in the primary predicate ART-Plan v2.1.0 (previous version) - Validation of the performance of autosegmentation (on CT and MR images) of already existing structures after retraining or algorithm improvement was performed by comparison of the DSC between contours generated by the previous version of ART-Plan (v2.1.0) and manual contours performed by medical experts and the DSC between contours generated by the new version of ART-Plan (v2.2.0) and manual contours performed by medical experts. The evaluation was performed on a minimum sample size of 17 patients.

The contours are considered acceptable for clinical use if the following acceptance criterion is achieved:

- **Mean DSC should not regress negatively between the current and last validated version of Annotate beyond a maximum tolerance margin set to -5% relative error.**

Quantitative evaluation of autosegmentation of all organs at risk – Validation of the performance of autosegmentation of all organs at risk on CT, MR and synthetic-CT from CBCT images by comparison with manual performed by medical experts. The evaluation was performed on a minimum sample size

of 17 patients. The contours are considered acceptable for clinical use if the following acceptance criteria are achieved:

- The Dice Similarity Coefficient (DSC) is equal to or superior to the acceptance criteria set by the AAPM: DSC (mean)≥ 0.8.
- The Hausdorff distance 95th percentile (HD95) is equal to or inferior to the acceptance criteria set HD95 (mean) ≤ 5.75 mm.

Quantitative evaluation of autosegmentation of all organs at risk – Validation of the performance of autosegmentation of organs at risk on CT images **on US patient data compared to performance on non-US (nUS) patient data.** The comparison was assessed by comparing automatic contours with manual contours performed by medical experts. The evaluation was performed on a minimum sample size of 17 patients. The contours are considered acceptable for clinical use if the following acceptance criteria are achieved:

- The Dice Similarity Coefficient (DSC) is equal to or superior to the acceptance criteria set by the AAPM: DSC (mean)≥ 0.8.
- The Hausdorff distance 95th percentile (HD95) is equal to or inferior to the acceptance criteria set HD95 (mean) ≤ 5.75 mm.

or

- Mean DSC (US) ≥Mean DSC (nUS)

and/or

- Mean HD95(US) ≤ Mean HD95 (nUS)

Qualitative evaluation of autosegmentation of organs at risk - Validation of the performance of autosegmentation of all new organs at risk (or organs at risk not passing the non regression testing) on CT, MR and synthetic-CT from CBCT images was performed by qualitative evaluation of the contours by medical experts. This evaluation was performed on a minimum sample size of 15 patients.

The contours are considered acceptable for clinical use if the following acceptance criterion is achieved:

- **The clinicians' qualitative evaluation of the auto-segmentation is considered acceptable for clinical use without modifications (A) or with minor modifications / corrections (B) with a A+B % above or equal to 85% considering the following scale:**
    A. **the contour is acceptable for a clinical use without any modification**
    B. **the contour would be acceptable for clinical use after minor modifications/corrections**
    C. **the contour requires major modifications (e.g. it would be faster for the expert to manually delineate the structure)"**

Qualitative evaluation of contours propagation - Validation of the performance of propagation of target and organs at risk contours from the planning CT to the synthetic-CT from CBCT was performed by qualitative evaluation of the propagated contours on the synthetic-CT from CBCT. The evaluation was performed on a minimum sample size of 15 patients.

The propagation of contours is considered acceptable for clinical use if the following acceptance criterion is achieved:

- T**he clinicians' s qualitative evaluation of the propagated contours post-registration are considered acceptable for clinical use without modifications (A) or with minor modifications / corrections (B) with a A+B % above or equal to 85% for deformable and above or equal to 50% for rigid registration considering the following scale:**
    A. **the contour is acceptable for a clinical use without any modification**
    B. **the contour would be acceptable for clinical use after minor modifications/corrections**
    C. **the contour requires major modifications (e.g. it would be faster for the expert to manually delineate the structure)**

Dosimetric validation of synthetic-CT from CBCT - Validation of synthetic-CTs in terms of dosimetric endpoints was performed by a quantitative evaluation to evaluate the non-inferiority of synthetic-CTs compared to CT images. Treatment plans were optimised on the CT images and recalculated on the synthetic-CT of the same patient. The dose distributions of the CTs and the synthetic-CTs were compared to evaluate non-inferiority of sCTs in terms of dosimetric endpoints. The evaluation was performed on a sample size of 19 patients per supported anatomy.

The synthetic-CTs from CBCT are considered acceptable for clinical use if the following acceptance criteria are achieved:

- **DVH parameters (PTV): < 2%**
- **DVH Individual Pass Rates (PTV): > 76.7%**
- **Median Gamma Index 2%/2mm: ≥ 92%**
- **Median Gamma Index 3%/3mm: ≥ 93.57%**

Geometric and anatomic validation of the synthetic-CT from CBCT - Validation of synthetic-CTs in terms of anatomical and geometrical accuracy was performed by a quantitative evaluation. A deformable fusion was performed between the synthetic-CT from CBCT and original CBCT. The Jacobian determinant was calculated in order to determine if the synthetic-CT and the original CBCT are identical, thus meaning that the synthetic-CT reflects the anatomy of the CBCT. The evaluation was performed on a sample size of 19 patients per supported anatomy.

The synthetic-CTs from CBCT are considered acceptable for clinical use if the following acceptance criterion is achieved:

- **Jacobian Determinant = 1 +/- 5%**

Dosimetric validation of the dose engine - Validation of the dose engine was performed by quality evaluation based on the dosimetric quality evaluated from clinical dosimetric criteria in comparison with commercially available solutions. The evaluation was performed on a sample size of 45 patients per supported anatomy.

The dose engine is considered acceptable for clinical use if the following acceptance criteria are achieved:

- **Relative differences on DVH parameters (PTV/OARs): ≤ 4.4% (with some superior individual values); for Lungs ≤ 24.4%**
- **Median Gamma Index 2%/2mm (with different thresholds): ≥ 86.3%**
- **Median Gamma Index 3%/3mm (with different thresholds): ≥ 91.75%**

All validation tests were carried out using datasets representative of the worldwide population receiving radiotherapy treatments. Finally, all tests passed their respective acceptance criteria, thus showing ART-Plan v2.2.0 clinical acceptability.