Dear Yoram Levy:

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/cfpmm/pmm.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/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). 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 (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

For

Thalia T. Mills, Ph.D.
Director
Division of Radiological Health
OHT7: Office of In Vitro Diagnostics and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure
Indications for Use

Device Name
Brain Perfusion (BP) application

Indications for Use (Describe)
The Philips Medical Systems' Brain Perfusion (BP) application is a post processing software application intended to assist with the evaluation of an area of interest, to generate qualitative and quantitative information about changes in image intensity over time. It supports the analysis of dynamic/serial CT after injection of contrast agent, by calculating the parameters related to brain perfusion and displays the results as a composite (single image that is calculated from a set of time course images at a single location) images.

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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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.”
I. **Submitter’s name and address**

Establishment name: Philips Medical Systems Nederland B.V.

Establishment address: Veenpluis 4-6
5684 PC Best
The Netherlands

Establishment registration: 3003768277

Primary Contact person: Yoram Levy, Qsite
QA/RA Consultant
31 Haavoda Street
Binyamina, Israel 30500
Tel (972)4-638-8837
Fax (972)4-638-0510
Yoram@qsitemed.com

Alternative contact person: Anat Hersch
Regulatory Affairs Lead, ICAP
Philips Medical Systems Nederland B.V
anat.hersch@philips.com

II. **Device information**

Trade name: *Brain Perfusion (BP) application*

Device Classification Name: Computed tomography x-ray system,
System

Device Class: Class II

Classification Panel: Radiology

Product Code: JAK, LLZ

Regulation Number: 21 CFR 892.1750

Regulation Description: Computed tomography x-ray system

III. **Device Description:**

The Philips Medical Systems' Brain Perfusion (BP) application is a post processing software to be used as an advanced visualization application of CT brain perfusion images.
The BP application is used to support the analysis of dynamic and/or serial CT brain images after injection of contrast. The BP application is intended to assist with the evaluation of an area of interest, and to generate qualitative and quantitative information about changes in image intensity over time.

The BP application presents the results as a composite (single image that is calculated from a set of time course images at a single location) images and provides perfusion parameters maps. The following parameters related to brain perfusion are calculated: Cerebral Blood Flow (CBF), Cerebral Blood Volume (CBV), local bolus timing (Time to Peak (TTP)) and Mean Transit Time (MTT) and supports processing and visualization of Permeability maps.

The physician retains the ultimate responsibility for making the final diagnosis.

Key Features:

The Brain Perfusion (BP) application has the following key features:

1. Support visualization and processing of dynamic and/or serial brain CT scans with contrast agent injection.
2. Display the results as composite (single image calculated from a dynamic set of images at a single location) images (tMIP images).
3. Display time-density curves reflecting the HU contrast enhancement tracked for an ROI over time.
5. Supported option for 3D motion correction with anatomical alignment.
6. Provide Perfusion maps of Cerebral Blood Volume (CBV), Mean Transit Time (MTT), Cerebral Blood Flow (CBF) and Time to Peak (TTP).
7. Provide summary maps according to default thresholds. The user may manually adjust the summary maps thresholds and/or different parameters according to the physician's preference.
8. Provide colored warning strips (Traffic Lights), indicating the quality of the Brain Perfusion data (acquisition).
9. Support processing and visualization of permeability maps
10. Display pre-defined ROI templates for localized quantitative evaluation of perfusion information.
11. Support automatic workflow – Brain Perfusion application can generate and send automatic results to defined external destination.

IV. **Intended use and Indications for use:**
The Philips Medical Systems' Brain Perfusion (BP) application is a post processing software application intended to assist with the evaluation of an area of interest, to generate qualitative and quantitative information about changes in image intensity over time. It supports the analysis of dynamic/serial CT after injection of contrast agent, by calculating the parameters related to brain perfusion and displays the results as a composite (single image that is calculated from a set of time course images at a single location) images.

V. **Predicate Devices:**
The following table shows the predicate devices of proposed Philips Medical Systems Brain Perfusion (BP) application:

<table>
<thead>
<tr>
<th>Primary predicate</th>
<th>Device Name</th>
<th>Manufacturer</th>
<th>510k No</th>
<th>Date of Clearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain Perfusion</td>
<td>Brain Perfusion Option</td>
<td>Philips Medical Systems</td>
<td>K033677</td>
<td>November 24, 2003</td>
</tr>
<tr>
<td>Option</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Predicate</td>
<td>Olea Sphere V3.0</td>
<td>Olea Medical</td>
<td>K152602</td>
<td>March 3, 2016</td>
</tr>
</tbody>
</table>

The proposed Philips Medical Systems Brain Perfusion (BP) application and its predicate device, Brain Perfusion Option (K033677) are substantially equivalent in regards to their intended uses, clinical indications, principle of operation and fundamental technology principles.

VI. **Substantial Equivalence to Predicate Devices**

<table>
<thead>
<tr>
<th>Feature</th>
<th>The proposed device: Brain Perfusion (BP) Application</th>
<th>Primary Predicate: Philips Medical Brain Perfusion Option (K033677)</th>
<th>Predicate: Olea Medical Olea Sphere V3.0 (K152602)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Device Classification Name</td>
<td>Computed tomography x-ray system.</td>
<td>Computed tomography x-ray system</td>
<td>System, Image processing, Radiological</td>
</tr>
</tbody>
</table>

*Brain Perfusion (BP) application– Traditional 510k Submission*
<table>
<thead>
<tr>
<th>Feature</th>
<th>The proposed device: Brain Perfusion (BP) Application</th>
<th>Primary Predicate: Philips Medical Brain Perfusion Option (K033677)</th>
<th>Predicate: Olea Medical Olea Sphere V3.0 (K152602)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>System, Image processing, Radiological</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Device Class</td>
<td>Class II</td>
<td>Class II</td>
<td>Class II</td>
</tr>
<tr>
<td>Classification Panel</td>
<td>Radiology</td>
<td>Radiology</td>
<td>Radiology</td>
</tr>
<tr>
<td>Product Code</td>
<td>JAK, LLZ</td>
<td>JAK</td>
<td>LLZ</td>
</tr>
<tr>
<td>Regulation Description</td>
<td>Computed tomography x-ray system</td>
<td>Computed tomography x-ray system</td>
<td>Picture Archiving and communication system</td>
</tr>
<tr>
<td>Regulation Number</td>
<td>21 CFR 892.1750</td>
<td>21 CFR 892.1750</td>
<td>21 CFR 892.2050</td>
</tr>
<tr>
<td>Indications for Use</td>
<td>The Philips Medical Systems' Brain Perfusion (BP) application is a post processing software application intended to assist with the evaluation of an area of interest, to generate qualitative and quantitative information about changes in image intensity over time. It supports the analysis of dynamic/serial CT after injection of contrast, by calculating the parameters related to brain perfusion and displays the</td>
<td>The Philips Medical Systems CT Brain Perfusion Option is intended to assist the user by providing a diagnostic patient imaging tool to be included on a CT workspace. It is intended to assist the user-selected area of interest to generate qualitative and quantitative information about changes in image intensity over time. It supports the analysis of dynamic/serial CT after injection of contrast, by calculating the parameters</td>
<td>Olea Sphere V3.0 is an image processing software package to be used by trained professionals including, but not limited to, Physicians and medical technicians. The software runs on a standard &quot;off-the-shelf&quot; workstation and can be used to perform image viewing, processing, image collage and analysis of medical images. Data and images are acquired through DICOM compliant imaging devices and modalities. [...] The Dynamic Analysis Module is used for visualization and analysis of dynamic imaging data,</td>
</tr>
<tr>
<td>Feature</td>
<td>The proposed device: Brain Perfusion (BP) Application</td>
<td>Primary Predicate: Philips Medical Brain Perfusion Option (K033677)</td>
<td>Predicate: Olea Medical Olea Sphere V3.0 (K152602)</td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>-------------------------------------------------------</td>
<td>---------------------------------------------------------------</td>
<td>------------------------------------------------</td>
</tr>
<tr>
<td>results as a composite (single image that is calculated from a set of time course images at a single location) images.</td>
<td>related to brain perfusion and displays the results as a composite (single image that is calculated from a set of time course images at a single location) images. This software runs on the Philips Medical Systems Brilliance™ Workspace of a CT System.</td>
<td>showing properties of changes in contrast while repeating acquisitions (e.g., over time with or without variable Acquisition parameters) where such techniques are useful or necessary. This functionality is referred to as: Perfusion Module – the calculation of parameters related to tissue flow (perfusion) and tissue blood volume. Permeability Module— the calculation of parameters related to leakage of injected contrast material from intravascular to extracellular space. Arterial Spin Labeling (ASL) Module – the calculation of parameters related to tissue flow based on a MR technique using the water in arterial blood as endogenous tracer to evaluate the perfusion. Relaxometry module-the calculation of parameters related to</td>
<td></td>
</tr>
<tr>
<td>Feature</td>
<td>The proposed device: Brain Perfusion (BP) Application</td>
<td>Primary Predicate: Philips Medical Brain Perfusion Option (K033677)</td>
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</tr>
<tr>
<td>---------</td>
<td>--------------------------------------------------</td>
<td>--------------------------------------------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>the MR longitudinal and transversal relaxation time and rate. Metabolic module-the calculation of parameters related to the fat fraction based on a MR technique using opposed-phase imaging.</td>
<td></td>
</tr>
<tr>
<td>Intended users</td>
<td>Trained professionals including but not limited to physicians and medical technicians</td>
<td>Trained professionals including but not limited to physicians and medical technicians</td>
<td>Trained professionals including but not limited to physicians and medical technicians</td>
</tr>
<tr>
<td>Intended Body part</td>
<td>Brain</td>
<td>Brain</td>
<td>Brain</td>
</tr>
<tr>
<td>Type of scans</td>
<td>CT perfusion scans</td>
<td>CT perfusion scans</td>
<td>The Dynamic Analysis and Perfusion is for CT Perfusion scans.</td>
</tr>
<tr>
<td>Automatic motion correction</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>CBV parametric map</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>CBF parametric map</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>MTT parametric map</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Time to Peak Enhancement (TTP)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Feature</td>
<td>The proposed device: Brain Perfusion (BP) Application</td>
<td>Primary Predicate: Philips Medical Brain Perfusion Option (K033677)</td>
<td>Predicate: Olea Medical Olea Sphere V3.0 (K152602)</td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>------------------------------------------------------</td>
<td>-------------------------------------------------------------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>Visualization of permeability imaging map</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Support detection of reference artery</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Support detection of reference vein</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Volume calculation: marking the total volume of affected tissue (3D measurements)</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Region of Interest</td>
<td>Yes The user can select and draw the Region of Interest</td>
<td>Yes The user can select and draw the Region of Interest</td>
<td>Yes The user can select and draw the Region of Interest</td>
</tr>
<tr>
<td>Result</td>
<td>Display results in tabular and graphical format</td>
<td>Display results in tabular and graphical format</td>
<td>Display results in tabular and graphical format</td>
</tr>
<tr>
<td>Export image Option</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>DICOM format communication</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Support automatic workflow</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

The proposed Philips Medical Systems *Brain Perfusion (BP)* application and its predicate device, Brain Perfusion Option (K033677) are substantially equivalent in regards to their intended uses, clinical indications, principle of operation and fundamental technology principles.

In conclusion, Philips believes that the *Brain Perfusion (BP) application* does not introduce any new potential safety and/or effectiveness issues and is substantially equivalent to the identified predicate device, Brain Perfusion Option (K033677).
VII. Brief discussion of the nonclinical tests submitted, referenced or relied on

Non-clinical performance testing has been performed on Brain Perfusion (BP) application and demonstrates compliance with the following International and FDA-recognized consensus standards and FDA guidance document:

- ISO 14971 Medical devices – Application of risk management to medical devices
- IEC 62304 Medical device software – Software life cycle processes
- NEMA PS 3.1-3.20 - Digital Imaging and Communications in Medicine (DICOM) Standard
- IEC 62366-1 Medical devices - Part 1: Application of usability engineering to medical devices
- Guidance for Industry and FDA Staff – Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices
- Guidance for Industry and FDA Staff – Content of Premarket Submissions for Management of Cybersecurity in Medical Devices

Philips Medical Systems Brain Perfusion (BP) application was developed and tested in accordance with Philips design control measures including risk management, design review, performance evaluation, verification and validation processes.

Risk Management

Risk management activities were performed to identify, control, and monitor the hazards and hazardous situations related to the Brain Perfusion application and its intended use. Each risk has been individually assessed, and risk control measures were implemented in the product. Every risk has been reduced as far as possible and has been evaluated to have a probability of occurrence of harm of unexpected or inconceivable. It was concluded that the BP application is safe, and that the risks associated with its intended use constitute acceptable risks when weighed against the medical benefit.

Verification
Philips Medical Systems Brain Perfusion (BP) application verification was intended to ensure that the software fully satisfies the product requirements. Test cases were executed to verify product requirements and risk management mitigations. Design verification established the conformance of the design output to the design input requirements.

Performance Evaluation

Performance evaluation testing was conducted in order to validate the proper function of the perfusion and permeability parametric maps. The subject device’s perfusion parameters performance was evaluated in comparison with the predicate device according to pre-set acceptance criteria (assessment of correlation and agreement according to regression analysis characteristics). The perfusion parameters values were generated by utilizing a synthetic phantom. The performance of the perfusion parameters implemented in Brain Perfusion application has been demonstrated by meeting the acceptance criteria.

Internal performance evaluation of the Permeability maps calculation was conducted in two phases. In the technical validation, a quantitative validation using synthetic simulated data was performed in order to determine the appropriate permeability method. The Patlak analysis that was found to be most appropriate, was implemented in BP application for permeability maps. In the pre-clinical validation performed on rats, imaging during occlusion and after reperfusion were acquired. Histology was used to determine a ground truth for the status of the brain tissue and the BBB permeability. The images were compared to the histology and analyzed comparing the results of different methods. The implemented permeability method has successfully identified regions of increased permeability that correspond to ground truth permeability markers on histology. In external performance evaluations of the Permeability maps additional statistical analysis further demonstrated that areas of increased permeability measured in-vivo by imaging coincide with BBB disruption and hemorrhage area observed on gold standard histology.

Validation

Philips Medical Systems Brain Perfusion (BP) application validation was intended to ensure that the software conforms to its intended use and user needs. During the
validation of Brain Perfusion application, physicians evaluated if the features and the workflows fulfills the user needs and enables the intended use of the application. Based on the scores provided by the physicians, it has been established that the device meets the users’ needs and fulfils its intended use.

**Human Factors**

Philips Medical Systems Brain Perfusion (BP) application human factors validation activities was intended to minimize use errors and thereby reduce use-associated risks. Formative and Summative usability validation testing and the final usability engineering file analysis have found the Brain Perfusion application to be safe and effective for the intended use, intended users and the intended use environments.

**Cybersecurity**

The Brain Perfusion Application follows internal documentation on Cybersecurity which includes the information based on the FDA Guidance: Content of Premarket Submissions for Management of Cybersecurity in Medical Devices.

**Non clinical Test Conclusion**

The test results and design control activities described in this 510(k) premarket notification demonstrates that Brain Perfusion (BP) application:

- Complies with the aforementioned international and FDA-recognized consensus standards and FDA guidance documents, and
- Meets the acceptance criteria and is adequate for its intended use, users and specifications.

**VIII. Brief discussion of clinical tests submitted, referenced or relied on**

The subject of this premarket submission, Brain Perfusion (BP) application does not require clinical studies to support equivalence.

**IX. The conclusions drawn from the nonclinical and clinical tests**

Performance testing, verification and validation (V&V) activities required to establish performance and functionality of *Brain Perfusion (BP) application*
were performed. Testing performed demonstrated the *Brain Perfusion (BP) application* meets all defined functionality requirements and performance.

**X. Overall conclusion:**

The *Brain Perfusion (BP) application* is substantially equivalent to the identified predicate device, Brain Perfusion Option (K033677) in terms of design features, fundamental scientific technology, indications for use, and safety and effectiveness. Performance testing, verification and validation testing demonstrate that the device meets its intended use and specifications and is safe and effective.

Philips Medical believes that the proposed device, *Brain Perfusion (BP) application*, is substantially equivalent to its identified predicate device and is as safe and effective as its predicate device without raising different questions of safety and/or effectiveness.