March 4, 2022

Pearl Inc.
% Zvi Ladin, Ph.D.
Principal
Boston MedTech Advisors
990 Washington Street, Suite #204
Dedham MA 02026

Re: K210365
Trade/Device Name: Second Opinion®
Regulation Number: 21 CFR 892.2070
Regulation Name: Medical Image Analyzer
Regulatory Class: Class II
Product Code: MYN
Dated: January 20, 2022
Received: January 24, 2022

Dear Zvi Ladin:

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,

Laurel Burk
Assistant Director
Diagnostic X-ray Systems Team
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

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)*
K210365

Device Name
Second Opinion®

Indications for Use *(Describe)*
Second Opinion® is a computer aided detection ("CADe") software to identify and mark regions in relation to suspected dental findings which include Caries, Discrepancy at the margin of an existing restoration, Calculus, Periapical radiolucency, Crown (metal, including zirconia & non-metal), Filling (metal & non-metal), Root canal, Bridge and Implants.

It is designed to aid dental health professionals to review bitewing and periapical radiographs of permanent teeth in patients 12 years of age or older as a second reader.

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.

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510(K) SUMMARY K210365

1. Submitter's Identification

Pearl Inc.
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Beverly Hills, CA, 90210
USA
(239) 450-8829

Contact Person: Bill Birdsall

Position: Chief Compliance Officer

Date Summary Prepared: March 2, 2022

2. Trade Name of the Device

Second Opinion®

3. Common or Usual Name

Analyzer, Medical Image

4. Classification Name, Regulatory Classification & Product Code

Classification Name: Analyzer, Medical Image
Regulatory Classification: 21CFR 892.2070, Class II
Product Code: MYN

5. Predicate Device Information

Predicate device: Logicon Caries Detection by Carestream Dental LLC. (P980025 & Supplements 1, 2, 3 & 4)

6. Device Description

Second Opinion® is a computer aided detection ("CADe") software device indicated for use by dental health professionals as an aid in their assessment of bitewing and periapical radiographs of permanent teeth in patients 12 years of age or older. *Second Opinion®* employs computer vision technology, developed using machine learning techniques, to detect and draw attention as second reader to regions on bitewing and periapical radiographs where distinct pathologic and/or nonpathologic dental features may appear.

Second Opinion® consists of three parts:

- In-office application or Client User Interface (“Client”)
- Application Programing Interface (“API”)
- Computer Vision Models (“CV Model”, “CV Models”)

The Client resides in the clinician’s office. The API and CV Models reside in a cloud computing platform, where image processing takes place.

The CV Models create and append to a metadata file information denoting pixel regions and other associated properties of each radiograph. Those associated properties include:

- Normal anatomy (e.g., Teeth)
- Nine radiological dental findings, which include five restorations (crowns, bridges, implants, root canals, fillings) and four pathologies (caries, margin discrepancy – MD, calculus, periapical radiolucency – PR)

The API delivers the metadata back to *Second Opinion*® via the cloud. The metadata information is displayed in graphical form to clinical users by way of the *Second Opinion*® Client’s user interface.

7. Indications for Use

Second Opinion® is a computer aided detection ("CADe”) software to identify and mark regions in relation to suspected dental findings which include Caries, Discrepancy at the margin of an existing restoration, Calculus, Periapical radiolucency, Crown (metal, including zirconia & non-metal), Filling (metal & non-metal), Root canal, Bridge and Implants.

It is designed to aid dental health professionals to review bitewing and periapical radiographs of permanent teeth in patients 12 years of age or older as a second reader.

8. Summary of Substantial Equivalence:

The predicate device and candidate device are similar CADe devices in the following ways:

1) *Intended use:* Both devices are intended to be used to aid dental clinicians in their detection of pathologic dental features in radiographs of permanent teeth.
2) *Technology characteristics:* Both devices employ computer vision and machine learning to output detections.
3) *Safety*: As both the candidate and predicate device are CADe systems, neither pose any direct safety hazard to the patient.
4) *Clinical Performance*: Both devices have undergone clinical studies which demonstrate statistically significant improvement in aided reader performance. However, due to technological differences (e.g., the need to mark the region of interest by the user of the predicate device), there are challenges for a direct technological and performance comparison with the predicate device.

For substantial equivalence comparison, the follow table is provided:

Item	**Candidate device:** **Second Opinion®**	**Predicate Device:** **Logicon Caries Detection (P980025)**	Comments
Manufacturer	Pearl Inc.	Carestream DentalLLC	N/A
Classification	892.2070	892.2070	Same
Product Code	MYN	MYN	Same (Productcode MYN wasrecently reclassified toclass II)
Image Modality	Radiograph	Radiograph	Same
Intended Use	To aid in clinical detection of pathologic and/or non-pathologic dental features in radiographs of permanent teeth, as a second reader, only after the initial read is completed	To aid in clinical detection of pathologic features in radiographs of adult teeth	Same indication as predicate device as both devices are intended to identify pathologic features in dental radiographs.
Indications for Use	Second Opinion® is a computer aided detection ("CADe") software to identify andmark regions in relation to suspected dental findings which include Caries, Discrepancy at the margin of an existing restoration, Calculus, Periapical radiolucency, Crown (metal, including zirconia & non-metal), Filling (metal & non- metal), Root canal, Bridge and Implants.It is designed to aid dental health professionals to review bitewing and periapical radiographs of permanent teeth in patients 12 years of age or older as a second reader.	The Logicon Caries Detector is a software device that is an aid in the diagnosis of caries that have penetrated into the dentin, on un- restored proximal surfaces of secondary dentition through the statistical analysis of digital intraoral radiographic imagery. The device provides additional information for the clinician to use in his/her diagnosis ofa tooth surface suspected of beingcarious. It is designed to work in conjunction with an existing Carestream DentalRVG digital x-ray radiographic system with Carestream Dental Imaging Software (DIS/CSI) for WINDOWS 7 or higher.	

Intended body part	Dental	Dental	Same as predicate device
Intended User	Dental Clinicians	Dental Clinicians	Same aspredicate device
Marker Type/Size	Bounding boxes / Fixed	User may mark ROI with V tool (to select a pie-wedge shape: narrow endat the center of thetooth, wide end extending through surface over the suspicious region) or the pencil tool todraw the ROIs.	
Prescription or OTC	For Prescription Use	For Prescription Use	Same
Algorithm	Utilizes computer vision neural network algorithms, developed from open-source models using supervised machine learning techniques.	Utilizes computer vision neural networkalgorithms developed using proprietary techniques.	Same
Reader workflow	Second reader workflow	The user can select specific regions of interest (ROI) to be analyzed by the program	

Clinical Study	Standalone study for pathological (Caries, discrepancy at the margin, calculus, and periapical radiolucency) and non-pathologic feature detection performance (Crowns, fillings, rootcanal, bridges, and Implants).
	• Multiple-Reader, Multiple-Case (MRMC) study for pathologic dental features
	• Analysis included:
	  • wAFROC-FOM analysis for primary endpoints
	  • Determination of the changes in sensitivity and change in number of false positive
		• MRMC study for two types of dental caries: approximal/enamel into dentin
		• Analysis included: ROC analysis for primary endpoints
			All devices included MRMC studies to assess effectiveness.

	dental pathologies of a given type per image (FPPI).		
Image Source	Accepts image formats from RVG, DICOM, JPEG, TIFF, and PNG and converts to JPEG.	Limited to Carestream proprietary radiography equipment.	Different
Type of Device	CADe	CADe	Same
Hardware Requirements	WINDOWS 7 or higher	WINDOWS 7 or higher	Same
Analysis of digital intraoral radiographic imagery	Bitewing & Periapical	Bitewing only	Similar

Table 1. Comparison of Second Opinion® with the predicate device

9. Technological Comparison to Predicate Device

The fundamental technological principle for both the candidate and predicate devices is theautomatic computerized lesion detection of the dental finding of interest, as an aid to dental health professionals to review patients' dental radiographs.

The candidate and predicate devices are technologically equivalent as follows:

- Both are software devices designed to run on Windows operating systems.
- Both devices are designed to process digital intraoral bitewing radiographs.
- Both devices use neural network-based computer vision algorithms for lesion detection.
- Both devices demarcate detections within the user interface with a graphical overlay on the radiograph.
- Both devices produce near-instantaneous detection results.
- Both devices are considered to be of "moderate" level of software concern.
- Both devices passed all verification and validation testing requirements.

The candidate and predicate devices are technologically different as follows:

- The candidate device includes computer vision algorithms capable of detecting other dental features in addition to carious lesions.
- The candidate device includes computer vision algorithms capable of making detections in periapical radiographs in addition to bitewing radiographs
- The candidate device uses a cloud-based rather than CD-ROM method of software installation
- The candidate device is capable of making detections in images captured on

radiography devices from a range of manufacturers, rather than in conjunction only with a Carestream digital imaging device.
- The candidate device outputs detections as a second reader only and physician needs to make final determinations. The user does not select specific regions of interest (ROI) to be analyzed by the program
- The candidate device does not predict lesion depth or severity.

10. Assessment of Benefit-Risk, Safety and Effectiveness, and Substantial Equivalence to Predicate Device:

Pearl has demonstrated the benefits of the device through a standalone and MRMC clinical studies of aided and unaided reader accuracy across the four pathologic features includedin *Second Opinion*®'s Indications for Use: caries, margin discrepancy, calculus, and periapical radiolucency. While detection accuracy improvement between aided and undead readers were seen to vary by pathologic feature, the results of the MRMC studiesshowed statistically significant aided-reader improvement in detection accuracy across all four pathologic features. When the probable benefits and probable risks of Second Opinion® are weighed against one another, the weight of benefits significantly exceeds that of risks. This judgement can be made based on review of the submitted materials showing that *Second Opinion*® meets the *design verification and validation* and *labeling* Special Controls required for clearance of Class II medical image analyzers. It is, thus, concluded that *Second Opinion*® can be considered safe and effective such that the devicewill aid users in the indicated user population in their radiographic detection of certain abnormal dental features.

11. Discussion of Non-Clinical Tests Performed

The device is a software-only device, so most testable characteristics common to other device types, including Biocompatibility/Materials, Shelf Life/Sterility, Electromagnetic Compatibility and Electrical Safety, Magnetic Resonance (MR) Compatibility, are not applicable to this device.

Software Verification and Validation Testing

Second Opinion® verification testing of software, unit testing, software integration testing, and software system testing were conducted. Verification and validation activities for *Second Opinion*® were conducted to provide evidence that the design meets user needs, intended use and application specification. The testing results support that all the software specifications have met the acceptance criteria and the claims of substantial equivalence.

12. Discussion of Clinical Tests Performed

Clinical evaluation of *Second Opinion*® was performed to validate the clinical efficacy of the system in helping dentists review four dental pathologies (caries, margin discrepancy, calculus, and periapical radiolucency) on intra oral radiographs. *Second Opinion*® was clinically tested as a standalone device and in a fully-crossed multi-reader multi-case (MRMC) reader study.

The Weighted Alternative Free-Response Receiver Operating Characteristic (wAFROC) paradigm was used as the metric of efficacy for all studies. The ground truth (GT) was assessed using the consensus approach (based on agreement among at least three out of

four expert readers). Each GT expert independently marked areas on any radiograph wherein they marked (using the smallest possible rectangular bounding box to encompass the entire region identified) and identified the pathologic and/or non-pathologic features. All experts went through the training and reading of the images over the same period of time. The studies were conducted as retrospective, unblinded open-label, multi-site trials that produced clinically useful information on the potential application of this device in a dental office setting. 2,010 images reviewed by all four GT readers were used for the standalone and MRMC studies:

Feature	Caries	MD	Calculus	PR
# of normal radiographs	1,640	1,741	1,766	1,887
# of lesion-containing radiographs	370	269	244	123
Number of lesions	655	355	467	144
Average # of lesions/image	1.77	1.32	1.91	1.17

Table 2. Images reviewed by all four GT readers

Standalone Testing

In the standalone study, the *Second Opinion*® CADe exhibited comparable performance to unaided readers in detecting four pathologic features and five restorations based on Jaccard Index (JI) of ≥ 0.4 for LL (Lesion Localization). This value of JI optimized lesion localization of unaided readers and was also used to process the Standalone performance of the candidate device. Use of other values of JI will clearly affect the overall performance of the product.

- Jaccard Index of 0.4 corresponds to an overlap area between the device's outputs and truth of 57% in theory. Using Jaccard Index of 0.4 leads to the device's standalone performance wAFROC-FOM 95% CI (0.73, 0.79), (0.71, 0.78), (0.78, 0.85) and (0.75,0.84) for Caries, MD, Calculus, and PR with consensus truthing method, respectively.

- Jaccard Index of 0.5 corresponds to an overlap area between the device's outputs and truth of 67% in theory. Using Jaccard Index of 0.5 leads to the device's standalone performance wAFROC-FOM 95% CI (0.61, 0.68), (0.62, 0.68), (0.75, 0.81) and (0.69,0.78) for Caries, MD, Calculus, and PR with consensus truthing method, respectively.

Product's standalone sensitivity and false positive rate were also assessed. Sensitivity is defined as the number of dental pathologies (of a given type) detected as a percentage of the same type GT pathologies on a given slide. The false positive rate is defined as the number of false positive findings of a given type identified on a given slide and expressed in terms of FPPI (false positive per image).

The standalone sensitivity of the product was in the range of 76.39% – 89.77% and the false positive rate was in the range of 0.46 – 4.85.

MRMC Testing and Results

Pearl conducted a fully-crossed multi-reader, multi-case (MRMC) retrospective reader study to determine the impact of Second Opinion® on reader performance in detecting fourdental pathologies. The primary objective of the study was to determine whether the detection accuracy of readers aided by Second Opinion® is superior to the detection accuracy of readers unaided by Second Opinion®.

Twenty-five readers were asked to determine the locations of all identified (i.e., classified) lesions, in a setting designed to increase user specificity in detection. Each reader reada total of 2,010 images – 1,005 images unaided and 1,005 images aided (using Second Opinion®).

The performance of readers aided by the use of Second Opinion® demonstrated statistically significant improvement over the performance of unaided readers for caries, margin discrepancy, calculus, and periapical radiolucency.

Moreover, the improvement in sensitivity of a single dental finding was in the range of 0.9%–11.7% and examination of the individual improvement in sensitivity documented that:

- 17/25 (68%) improved the sensitivity of detecting Caries
- 19/25 (76%) improved the sensitivity of detecting MD
- 22/25 (88%) improved the sensitivity of detecting Calculus
- 25/25 (100%) improved the sensitivity of detecting PR

The improvement in false positive rate of a single dental pathology was in the range of 0.08 – 0.136. Examination of the individual improvements in the rate of FPPI documented that:

- 23/25 (92%) improved the rate of FPPI for Caries
- 24/25 (96%) improved the rate of FPPI for MD
- 25/25 (100%) improved the rate of FPPI for Calculus
- 9/25 (36%) improved the rate of FPPI for PR

No statistically significant reductions in performance were observed when readers used *Second Opinion®* as an assistive aid. All pathologies met the pre-specified endpoints for the MRMC study.

The results have demonstrated that, in a significant portion of the target population, detection performances using the proposed device improved with statistical significance. Therefore, the proposed device could provide potential assistance for dentists in the reviewof dental pathologies found in intra oral radiographs when used as a second read.

13. Comparison to Predicate Clinical Outcomes

Predicate Device: Logicon Caries Detection by Carestream Dental LLC.

The predicate device's clinical study was based on a dataset of 175 tooth surfaces and

18 readers. The primary endpoint was to determine the device's effect on reader sensitivity (true positive identification), specificity (true negative), and accuracy (fraction of all correct diagnosis made by a dentist) as they pertain to detection of caries lesions into the dentin on proximal tooth surfaces. Truth was defined as the dentist's clinical assessment of the exposed lesion prior to restoration. Results from this study showed a significant increase in reader sensitivity and no significant change in reader specificity (slightly reduced when aided by Logicon) when readers used the device. Average reader accuracy, reported as the comparison of detection accuracy unaided readers to aided readers, were determined using the ROC paradigm and showed an improvement of 12.8 percent:

Unaided Reader Accuracy	Aided Readers Accuracy
0.756	0.883

Table 5. Logicon Caries Detector (predicate device) accuracy – Aided vs. Unaided

However, this observed median difference is not significant based on the Wilcoxon test (P=0.0537). Therefore, the improvement in diagnostic accuracy associated with the Logicon Caries device is mostly associated with the improvement in sensitivity.

The candidate device's clinical study was based on a dataset of 2010 radiographs which included 370 carious lesions. Three primary studies were performed: Standalone, MRMC, and CADe vs. Reader. The endpoints were designed to determine the candidate device's ability to identify dental features as a standalone system and to determine the device's effect on reader performance.

In comparison to the predicate device's clinical study, caries detection performance of the candidate device, measured based on wAFROC-FOM, for unaided and *Second Opinion®*-aided readers with *Second Opinion®* is:

Unaided Reader wAFROC-FOM	Aided Reader wAFROC-FOM
0.740	0.758

Table 6. Second Opinion® wAFROC-FOM – Aided vs. Unaided

This difference is significant with P=0.0062.

Therefore, similar to the predicate device, the candidate device also demonstrated improved detection accuracy in detecting carious lesions. Although candidate device performance was determined using a different statistical paradigm (wAFROC) than predicate device performance (ROC), the trend is the same: When aided by the device, readers' ability to detect carious lesions improves.

14. Conclusions

Based on the information presented above, *Second Opinion®* and its predicate device, Logicon Caries Detector, are deemed to have similar intended uses as devices which aid in

the detection of pathologic features that can appear in dental radiographic imagery. *Second Opinion*®'s clinical trial results demonstrate that like its predicate, the device effectively improves the performance of its intended users,as a second read CADe system.

As *Second Opinion*® raises no new or different questions of safety or effectiveness, performs in accordance with its specifications, meets user needs, meets the intended use and therefore was found substantially equivalent to the predicate device.