SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Caries detection product with drug or biologic
Device Trade Name:	CALCIVIS Imaging System
Device Procode:	QJX
Applicant's Name and Address:	CALCIVIS Limited Nine Edinburgh BioQuarter 9 Little France Road Edinburgh EH16 4UX United Kingdom
Date of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P170029/S003
Date of FDA Notice of Approval:	10/13/2023

The original PMA (P170029) for the CALCIVIS Imaging System was approved on 3/07/2023. The original device was intended to be used by dental healthcare professionals on patients (6 years and older) with, or at risk of developing, demineralization associated with caries lesions, on accessible coronal tooth surfaces to provide images of active demineralization on tooth surfaces, as an aid to the assessment, diagnosis and treatment planning of demineralization associated with caries lesions. The SSED to support the indication is available on the CDRH website and is incorporated by reference here (https://www.accessdata.fda.gov/cdrh_docs/pdf17/P170029B.pdf).
The current supplement was submitted to expand the indication for the CALCIVIS Imaging System to provide images of active demineralization on tooth surfaces as an aid to the monitoring of active demineralization associated with caries lesions.

II. INDICATIONS FOR USE

The CALCIVIS Imaging System is intended to be used by dental healthcare professionals on patients (6 years and older) with, or at risk of developing, demineralization associated with caries lesions, on accessible coronal tooth surfaces.

The CALCIVIS Imaging System is indicated for use to provide images of active demineralization on tooth surfaces, as an aid to the assessment, diagnosis, monitoring and treatment planning of demineralization associated with caries lesions.

III. CONTRAINDICATIONS

There are no known contraindications.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the CALCIVIS Imaging System labeling.

V. DEVICE DESCRIPTION

No design changes to the approved devices in the CALCIVIS Imaging System are required for the indication expansion.

The CALCIVIS Imaging System consists of two main components that are used in conjunction to enable a Dental Practitioner to obtain images of active demineralization on accessible coronal tooth surfaces: (1) CALCIVIS Imaging Device Kit and (2) CALCIVIS Imaging Kit.

The CALCIVIS Imaging Device Kit includes an intra-oral camera within the applicator main body of the Intra-oral Imaging Device and is used with associated software, which allows both video streaming of images and capture of still images. The Intra-oral Imaging Device contains a syringe applicator mechanism that dispenses a small amount (25µl) of CALCIVIS Photoprotein onto the tooth under investigation. As an accessory to the CALCIVIS Imaging Device Kit, the CALCIVIS Function Check Kit provides a gross check that the system is setup correctly to function for applicator dispensing and luminescent image capturing; it is not intended for calibration purposes.

The key component of the CALCIVIS Imaging Kit is the CALCIVIS Photoprotein that contains a non-therapeutic biologic component (recombinant photoprotein) to visualize luminescence of unbound calcium associated with active demineralization of caries lesions. When the photoprotein in the reconstituted CALCIVIS Photoprotein solution binds with free calcium ions, it emits light (in the visible spectrum) that is captured by the imaging system. The sequence of image capture and CALCIVIS Photoprotein application are controlled using the custom application software from the CALCIVIS Imaging Device Kit.

The overall CALCIVIS Imaging System comprises:

1) CALCIVIS Imaging Device Kit

Consists of:

- CALCIVIS Intra-oral Imaging Device
- CALCIVIS Device Cradle
- CALCIVIS (Imaging) Software on USB card

- CALCIVIS User Manual

a. Accessory - CALCIVIS Function Check Kit

Consists of:

- CALCIVIS Function Check Kit
- Instructions for use

2) CALCIVIS Imaging Kit

Consists of:

- CALCIVIS Photoprotein (freeze dried in vials)
- CALCIVIS Diluent for reconstitution (containing 0.9% anti-microbial preservative benzyl alcohol)
- Vial Adaptors to allow for needle-less reconstitution
- Device syringes
- Medical wipes used to clean the top of the multi-use vial adaptor
- CALCIVIS Applicator sheath single use components
- Instructions for use

Figure 1. CALCIVIS Imaging Device loading and fully assembled CALCIVIS Imaging Device on stand

Overall, the CALCIVIS Imaging System is intended to provide images of active demineralization on tooth surfaces, as an aid to the assessment, diagnosis, monitoring and treatment planning of demineralization associated with caries lesions. The CALCIVIS Imaging System is for use by trained dental healthcare professionals.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives used to detect tooth structure changes for clinician diagnosis of dental caries and treatment planning:

- Visual inspection with and without tactile exploration with a probe
- Radiograph images
- Caries detection dyes
- Transillumination
- Optically-based methodology (i.e., light induced fluorescence, laser induced fluorescence, near infrared)
- Use of electrical current to show existence of decay and carious lesions in a tooth

Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician and/or dentist to select the method(s) that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The CALCIVIS Imaging System has a CE mark, and it has been marketed in the United Kingdom since March 2018. The CALCIVIS Imaging System has never been withdrawn from marketing for any reason related to its safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the CALCIVIS Imaging System.

- Sensitivity or allergic reaction to photoprotein resulting in tissue irritation
- Sensitivity or allergic reaction to applicator plastic or Thermoplastic Elastomer (TPE) resulting in tissue irritation
- Not suitable for use if teeth cannot be accessed
- Not suitable if patient has limited ability to open their mouth or a small mouth opening that impacts the device intraoral placement and can result in risk of tissue trauma or patient discomfort
- Discomfort or jaw pain from prolonged usage
- Infection stemming from cross contamination if single use items are reused
- Choking hazard from patient biting down on applicator device components
- Unwanted shock due to malfunction of the electrical or power source components
- Risk from electromagnetic fields, which might interfere with the functions of implanted systems (such as pacemakers)

For the specific adverse events that occurred in the clinical study, please see Section X below.

IX. SUMMARY OF NONCLINICAL STUDIES

No additional nonclinical studies (bench and animal) were required to evaluate the safety and effectiveness of CALCIVIS Imaging System to expand the indication to provide images of active demineralization on tooth surfaces as an aid to the monitoring of active

demineralization associated with caries lesions. The nonclinical studies that were previously submitted to FDA in the original PMA (P170029) continue to support the safety and effectiveness of the CALCIVIS Imaging System for the proposed indication. For a summary of the nonclinical studies, please refer to the SSED of the original PMA P170029 (https://www.accessdata.fda.gov/cdrh_docs/pdf17/P170029B.pdf).

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness to provide images of active demineralization on accessible coronal tooth surfaces with the CALCIVIS Imaging System for use as an aid to the monitoring of active demineralization associated with caries lesions. Data from this clinical study were the basis for the PMA supplement approval decision. A summary of the clinical study is presented below. The primary clinical study was titled "CSR-04-2018, Version 1, 15 January 2019, Monitoring of Caries Lesion Activity in Orthodontic Patients with the Calcivis® System".

A. Study Design

Patients were treated between February 15, 2017, and May 01, 2018. The database for this PMA supplement reflected data collected through May 22, 2018, and included 36 patients. There was one investigational site.

The study was a prospective, single site, non-randomized clinical study to evaluate the use of the CALCIVIS Imaging System for monitoring active demineralization afer post bracket de-bond removal in orthodontic patients 12 years and older over a 12-week follow-up period. The study was conducted by four General Dental Practitioners at the one study site. The study investigators identified patients who had dental appliances consisting of metal brackets and orthodontic wires in place for a minimum of 12 months and had visible white spot lesions on the anterior surfaces (facial/labial) of upper incisors and/or canines at the time of bracket de-bonding. Following de-bonding of the brackets (but not removal of any underlying cement), images of the tooth surface were taken with the CALCIVIS Imaging System. Presence or absence of elevated luminescence on the images were evaluated to indicate active demineralization or not. Only patients with at least one tooth identified as having active demineralization associated with a white spot lesion using the CALCIVIS Imaging System continued in the study for the follow-up visits at 2, 4, 8, and 12 weeks after the de-bond. At each follow-up visit, the CALCIVIS Imaging System was used to capture additional images for comparison to the prior images taken of the facial/labial tooth surfaces of the same teeth. The percentage of teeth showing luminescence using the CALCIVIS Imaging System was calculated for all subjects for each post-baseline visit. If all lesions assessed as inactive, the patient was withdrawn from the study.

The study assessed the use of the CALCIVIS Imaging System for monitoring active demineratlization of clinically observed white spot lesions following the post-

orthodontic bracket de-bonding treatment per each patient. The study methodology involved capturing images of the same facial/labial tooth surfaces at relatively short intervals, paired with examiner assessment for the presence or absence of elevated luminescence on each tooth surface. Following the imaging procedures at both initial de-bond (baseline) and at the final study visit, patients completed a patient questionnaire. Additionally, at the end of both the initial de-bond (baseline) and final study visit, the investigators and dental nurses completed a user questionnaire. Adverse events were collected throughout the study.

There was no statistical hypothesis testing. All patients on whom the CALCIVIS Imaging System was used were included in the study population. For each subject, the percentage of teeth showing luminescence using the CALCIVIS Imaging System was calculated. This information was then summarized as descriptive statistics for all subjects after each visit. The descriptive statistics used continuous parameters and evaluated the results using standard summary statistics as appropriate (i.e., n, mean, standard deviation, minimum, median, and maximum). Summary statistics for categorical variables included frequency counts and percentages. Missing data were not imputed. All statistical analyses were performed using the validated statistical software of Statistical Analysis System (SAS) version 9.2 (or higher).

There was no core laboratory use, Data and Safety Monitoring Board (DSMB) or Independent Data Monitoring Committees (IDMC) for this study.

There was no control group for this study.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the CSR-04-2018 study was limited to patients who met the following inclusion criteria:

   - Patient must be ≥12 years old
   - Patient must have had orthodontic appliances placed on the upper incisors and/or canines for at least 12 months, and be ready for de-bond
   - Patient must have at least one white spot lesion examined by the CALCIVIS Imaging System immediately post de-bond and observed with elevated luminescence
   - Patient and/or parent or guardian must be willing and able to give written informed consent
   - Patient and/or parent or guardian must be willing and able to adhere to study schedule

   Patients were not permitted to enroll in the CSR-04-2018 study if they met any of the following exclusion criteria:

   - Any patient with recent tooth bleaching (within previous two weeks of imaging with the CALCIVIS Imaging System or within the follow-up period)

- Any patient currently taking part in a clinical research study, or has taken part in a clinical research study in the previous three months
- Pregnant and/or nursing mothers

2. Follow-up Schedule

All patients were scheduled for up to five visits after the initial screening – baseline (de-bond), then follow-up visits at 2, 4, 8, and 12 weeks post de-bond. Adverse events and complications were recorded at all visits after the initial screening.

Preoperatively, the initial screening and pre-imaging study procedures included:

- Investigators identifying patients meeting the inclusion and exclusion criteria during routine orthodontic appointments and were ready for de-bond.
- If interested in participating in the study, each patient and/or parent or guardian was explained the details of the study and given a copy of the Patient Information Sheet and Consent Forms.
- If agreeing to participate in the study, the patient and/or parent or guardian instructed to return to the clinic for the Visit 1 baseline appointment.

At baseline (de-bond) and postoperatively, the parameters collected or measured during the study included:

- Written informed consent (baseline only)
- Demographics – date of birth and gender (baseline only)
- Relevant medical history (baseline only)
- Relevant medications – calcium supplements and antacids (baseline only)
- Oral hygiene information – routine brushing regime, toothpaste and any other dental products used (baseline only)
- Orthodontic history – date braces applied, type of bracket, ligation used, and any other relevant information (e.g., re-mineralization products used) (baseline only)
- Tooth preparation by removing orthodontic appliances for de-bonding (baseline only)
- Record tooth identification and ICDAS (International Caries Detection and Assessment System) score
- Digital color photographs of the tooth or teeth taken with a digital camera for reference
- Imaging with CALCIVIS Imaging System according to the Instructions for Use
- Adverse events
- Patient Questionnaire (baseline and final study visits only)

- User Questionnaire by both dentists and dental nurses (baseline and final study visits only)

The key timepoints are shown below in **Table 1** summarizing safety and effectiveness.

Table 1. Schedule of Events

	Screening	**Visit 1 (de-bond) Baseline**		**Visits 2 – 3**	**Visit 4 – 5**
	Pre-Imaging	**Pre-Imaging**	**Imaging**	**2 & 4 weeks Post de-bond**	**8 & 12 weeks Post de-bond**
Identification of suitable patients / issue of Patient Information Sheet	**X**				
Written Informed Consent		**X**			
Demographics, Inclusion / Exclusion criteria		**X**			
Relevant medical history / medications		**X**			
Oral Hygiene information		**X**			
Orthodontic History		**X**			
Tooth ID (ICDAS score) and preparation		**X**		**X**	**X**
Reference color photographs		**X**		**X**	**X**
Calcivis System Imaging			**X**	**X**	**X**
Adverse Events		**X**	**X**	**X**	**X**
Patient Questionnaire			**X**		**X**
User Questionnaire			**X**		**X**

3. Clinical Endpoints
   There was one primary endpoint for this clinical study:

- EFFECTIVENESS: To assess the CALCIVIS Imaging System for monitoring the activity levels of post-orthodontic treatment white spot lesions. This was measured by luminescent output over time from baseline (de-bond) to 8 or 12 weeks post de-bond (presence or absence of luminescence).

There were two secondary endpoints for this clinical study:

- SAFETY: To assess the safety of the CALCIVIS Imaging System – measured by the collection of all adverse events.

- EFFECTIVENESS: To assess the value of feedback and/or communication with patients after using the CALCIVIS Imaging System – measured by Questionnaires for both the Patient and the User.

B. Accountability of PMA Cohort

A total of 36 patients were enrolled in the PMA supplement study and available for analysis at the time of database lock for the CSR-04-2018 clinical study. Of the 36 enrolled patients, 30 patients were eligible to have images taken with the CALCIVIS Imaging System at the baseline visit and consented to take part in the study. Of these 30 patients, 13 (36.1%) patients attended at two weeks, 21 patients (58.3%) attended at four weeks, 22 patients (61.1%) at eight weeks, and 8 patients attended at 12 (22.2%) weeks post de-bond. Therefore, data from a total of 30 out of 36 patients (83.3%) were included for analysis at the completion of the study in both the safety and effectiveness populations.

Table 2. Accountability Summary

	Overall (N=36)
Attended Baseline	36 (100%)
Attended Week 2	13 (36.1%)
Attended Week 4	21 (58.3%)
Attended Week 8	22 (61.1%)
Attended Week 12	8 (22.2%)
Completed Study	19 (52.8%)
Withdrew from Study	17 (47.2%)
Reason for Withdrawal	
No teeth show active demineralization	4 (11.1%)
Consent withdrawn by patient	2 (5.6%)
Investigator withdrew patient	0
Lost to follow-up	5 (13.9%)

Adverse Event	0	
Death	0	
Other	6	(16.7%)
Study Population	30	(83.3%)

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a caries detection study and considered a reasonable representation for use of the CALCIVIS Imaging System in the United States.

Data from a total of 30 patients were included in the safety and effectiveness populations of the clinical study. Patients were recruited between February 15, 2017, and May 01, 2018, with final patient follow-up on May 22, 2018. There were 14 males (46.7%) and 16 females (53.3%) included in the study population, with an age range of 13 to 39 years – mean 19.9 years, standard deviation (S.D.) 6.52.

From these 30 patients, a total of 119 teeth were imaged with 73 confirmed as having white spot lesions – in excess of the minimum 45 required per the clinical study protocol. The distribution of active teeth included in the imaging from the six upper anterior teeth of UR3, UR2, UR1, UL1, UL2, and UL3 (alpha-numeric system of dental notation[1]) is shown in **Table 3** below:

Table 3. Distribution of Teeth Imaged at Baseline with Identified Active White Spot Lesions

UR3	UR2	UR1	UL1	UL2	UL3
3 (4.11%)	12 (16.44%)	15 (20.55%)	20 (27.40%)	19 (26.03%)	4 (5.48%)

D. Safety and Effectiveness Results

1. Safety Results

   The analysis of safety was based on all 30 patients included in the safety population for the CSR-04-2018 clinical study that had images taken with the CALCIVIS Imaging System at the baseline visit.

   There were no patient related Adverse Events reported for the study associated to the CALCIVIS Imaging System.

   There was one patient related Adverse Event reported for the study for Patient 11-11, who experienced whiplash as the result of a car accident and withdrew from the study.

There were three Device Deficiencies (DD) reported:

- Patient 11-04 – the Investigator took images per the instructions for use, but reported the device was starting to separate at the joints. The device was removed from the site and replaced with another device. Internal investigations showed the screws holding the device parts together were no longer in place.

- Patient 11-32 – the Investigator reported the device was unable to focus, resulting in a blurry image. The device was removed from the site and replaced with another device. Internal investigations could not detect any issue with device.

- Patient 11-33 – the Investigator reported the device was unable to focus, resulting in a blurry image. The device was removed from the site and replaced with another device. Internal investigations could not detect any issue with device.

None of the above device deficiencies were considered serious. All three device deficiencies were also documented as part of Calcivis Quality Management System.

2. Effectiveness Results

The analysis of effectiveness was based on the 30 patients evaluated at the Visit 1, baseline time point. Key effectiveness outcomes are presented in **Table 4**, **Figure 2**, and **Figure 3**.

Primary Analysis

The primary objective of the study was to monitor white spot lesion activity as measured by the presence or absence of luminescence over time. From the 30 patients imaged with the CALCIVIS Imaging system, there were a total of 119 imaged teeth with 73 imaged teeth having clinically observed white spot lesions via elevated luminescence for the primary analysis.

The level of luminescence was shown at the baseline visit to be 61.7% and then reducing with time over the follow-up periods. At the 2 weeks post de-bond visit, luminescence for active teeth was down to 17.3%, at 4 weeks 6.0%, rising at 8 weeks to 10.2%, before reducing again to 6.3% at 12 weeks post de-bond.

The following **Table 4** provides the combined total numbers of patients imaged at each visit and the percentage of patients and active teeth with luminescence.

Table 4. Percentage of Patients and Imaged Teeth with Luminescence over Time

Visit	Number of patients imaged	% patients with luminescence	% teeth with luminescence
Baseline	30	61.7	61.3 (73/119)
2 weeks post de-bond	13	17.3	17.6 (9/51)
4 weeks post de-bond	21	6.0	6.0 (5/83)
8 weeks post de-bond	22	10.2	10.3 (9/87)
12 weeks post de-bond	8	6.3	6.5 (2/31)

As shown graphically, the results for all patients combined over time are shown in **Figure 2** below.

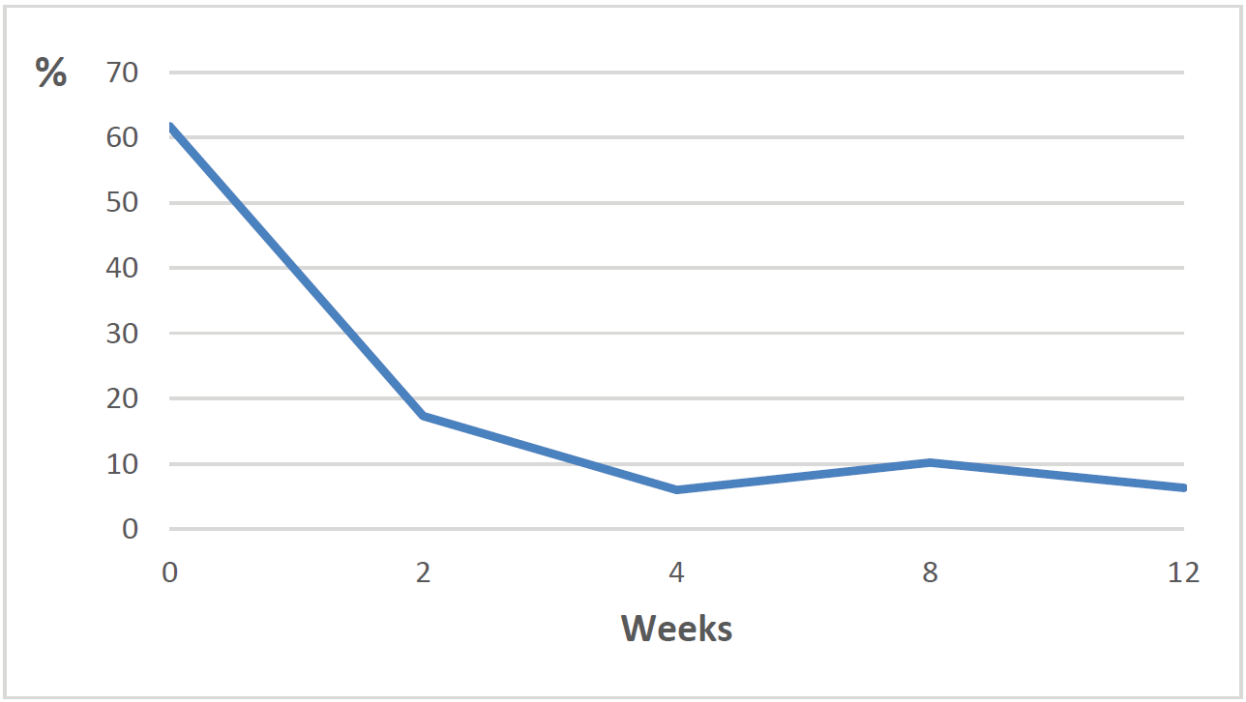

Figure 2. Percentage of Patients with Luminescence over Time

Accounting for the dropout rate experienced over the multiple reassessment visits, of the 30 patients imaged at the baseline visit, 22 patients had both baseline and week 8 images taken. As each patient could have up to 4 teeth imaged, this resulted in 87 teeth from the 22 patients being imaged at baseline and 8 weeks. Of the 87 teeth with baseline and week 8 images, 63 had a positive luminescence signal (indicating active demineralization) at the baseline visit, with 24 showing no signal to indicate inactivity. Of the 63 teeth showing active demineralization at baseline, 54 (86%) had no signal for luminescence after 8 weeks (indicating inactivity) as shown in **Figure 3**. There were 9 (13%) of the 63 teeth that

continued to show a signal at 8 weeks, indicating that these teeth were still showing active demineralization. From this study, the results showed that the levels of luminescence monitored at the baseline visits reduced with time over the follow-up periods. At 8 weeks post de-bond, a significant percentage of teeth showed loss of signal to indicate no active demineralization monitored at this time point.

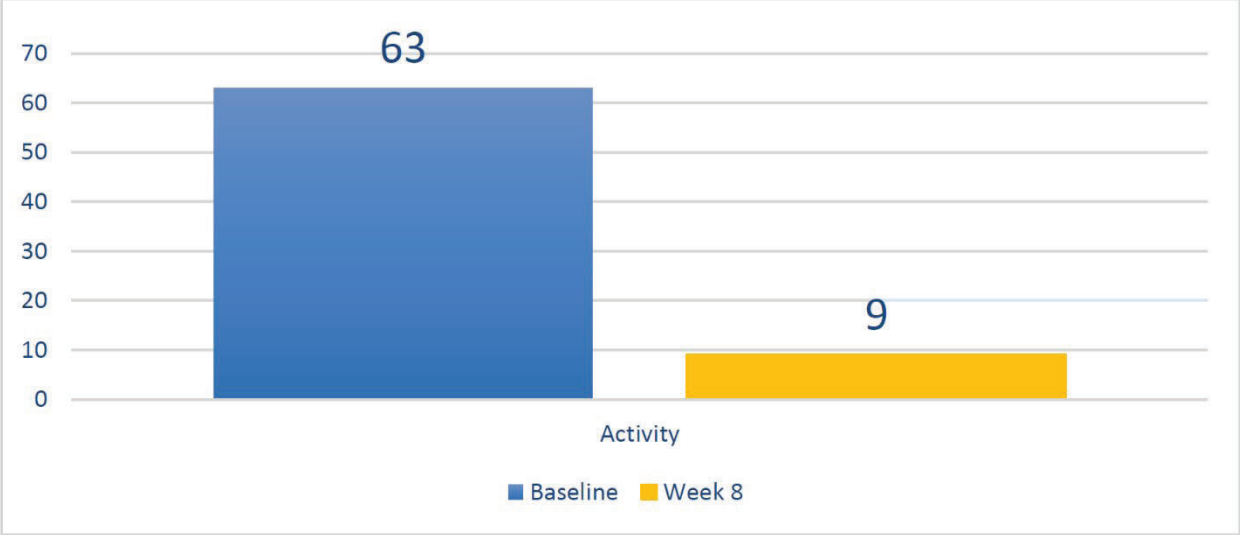

Figure 3. Number of Teeth Showing Active Demineralization at Baseline and 8 Weeks

The overall effectiveness study results were found to meet the primary analysis endpoint to show that the CALCIVIS Imaging System can identify and monitor active, white spot lesions over time.

Secondary Analysis

Patient Questionnaires showed positive feedback based on the two questions asked – with over 88% of patients rating their overall experience with CALCIVIS Imaging System as "Good", and 100% of patients rating seeing images of their teeth and having the dentist explain their situation as "Helpful".

User Questionnaires were completed at the end of the baseline and final study visits by both dentists and dental nurses. In response to four questions, 70% rated preparing the CALCIVIS Imaging System as "Easy", and 56.7% of responses rated using the CALCIVIS Imaging System as "Easy". Additionally, 80% of the user's responses rated their overall experience with the CALCIVIS Imaging System as "Good", and when asked if the instructions provided were sufficient to understand how to use the CALCIVIS Imaging System, 63.3% of the user's responses stated "Easy".

The patient and user questionnaire results were found to meet the secondary analysis endpoint to show the CALCIVIS Imaging System to be well accepted and generally easy to use.

3. Subgroup Analyses
   There was no subgroup analysis for the primary clinical study.

4. Pediatric Extrapolation
   In this premarket application, existing clinical data were found to support the reasonable assurance of safety and effectiveness of the proposed device in pediatric patients (≥ 6 yrs. old) primarily based on the Summary of Primary Clinical Study, see Section X above. The CSR-04-2018 primary clinical study conducted for the current PMA supplement evaluated the CALCIVIS Imaging System for monitoring caries lesion activity in orthodontic patients 12 years and older, and the study results are scientifically justified to be generalized and applicable to the full intended use population, including patients that are 6 years and older.

   There are several macro-morphological differences between primary and permanent teeth, such as the relative thickness of enamel and dentine, crown morphology (overall shapes of teeth, involving bulbosity of crowns), and pulp chamber and root morphology.[2,3] None of these macro-morphological differences impact directly the quality of the images captured by the CALCIVIS Imaging System because the system works by the application of a liquid containing the photoprotein to the outer surface of the tooth enamel, with the image capturing luminescence emitted within approximately 300 milliseconds. In addition, the photoprotein can only react with ionic calcium within the enamel pore fluid (and will not react with calcium from the solid enamel crystalline structure). Given this time limitation on the rate of diffusion of the photoprotein into the depth of the enamel nano- and micro-pores, the macro-morphological differences between primary and permanent tooth enamel will have no impact on the luminescent signal generated in the outer layer of the enamel to affect the images captured by the CALCIVIS Imaging System. Furthermore, although there are minor chemical content differences in the nano- and micro-structure (porosity) between primary and permanent tooth enamel, the fundamental physical chemistry and thermodynamics of the demineralization process in primary and permanent enamel are considered equivalent based on the involved hydroxyapatite and hydrogen ions.[4,5]

   Given all of the above, in addition to the previously demonstrated "CALCIVIS Photoprotein Activity Testing" referenced in the Summary of Nonclinical Studies section of the SSED for the original PMA P170029 (https://www.accessdata.fda.gov/cdrh_docs/pdf17/P170029B.pdf), the CALCIVIS Imaging System is justified as applicable for imaging active demineralization in primary teeth for pediatric extrapolation of the CSR-04-2018 primary clinical study to support the full intended use population for patients that are 6 years and older.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included four investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Dental Products Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The principal safety and effectiveness information for the CALCIVIS Imaging System is derived from the nonclinical studies that were previously submitted in the original PMA (P170029) and from the primary CSR-04-201 clinical study detailed for the current PMA supplement.

Nonclinical Data

The nonclinical studies that were previously submitted to FDA in the original PMA (P170029) continue to confirm the product design characteristics, specifications, and intended use of the CALCIVIS Imaging System for meeting the product specifications. For a summary of the nonclinical studies, please refer to the SSED of the original PMA P170029 (https://www.accessdata.fda.gov/cdrh_docs/pdf17/P170029B.pdf).

Clinical Data

Clinical study endpoints from the primary CSR-04-2018 clinical study were met, confirming that the CALCIVIS Imaging System is effective for use to provide images of active demineralization on tooth surfaces, as an aid to the assessment, diagnosis, monitoring, and treatment planning of demineralization associated with caries lesions on patients (6 years and older) with, or at risk of developing, demineralization associated with caries lesions, on accessible coronal tooth surfaces.

Primary Analysis

Table 5. Percentage of Patients and Imaged Teeth with Luminescence over Time

Visit	Number of patients imaged	% patients with luminescence	% teeth with luminescence
Baseline	30	61.7	61.3 (73/119)
2 weeks post de-bond	13	17.3	17.6 (9/51)
4 weeks post de-bond	21	6.0	6.0 (5/83)
8 weeks post de-bond	22	10.2	10.3 (9/87)
12 weeks post de-bond	8	6.3	6.5 (2/31)

From the 30 patients imaged with the CALCIVIS Imaging system, there were a total of 119 imaged teeth with 73 imaged teeth having clinically observed white spot lesions via elevated luminescence for the primary analysis.

The level of luminescence was shown at the baseline visit to be 61.7% and then reducing with time over the follow-up periods. At the 2 weeks post de-bond visit, luminescence for active teeth was down to 17.3%, at 4 weeks 6.0%, rising at 8 weeks to 10.2%, before reducing again to 6.3% at 12 weeks post de-bond.

The overall effectiveness clinical study results were found to meet the primary analysis endpoint to show that clinicians can use the CALCIVIS Imaging System to monitor active demineralization over time, thereby supporting the indication for use to provide images of active demineralization on tooth surfaces, as an aid to the assessment, diagnosis, monitoring and treatment planning of demineralization associated with caries lesions.

B. Safety Conclusions

The risks of the CALCIVIS Imaging System are based on nonclinical laboratory studies that were previously submitted in the original PMA (P170029) as well as data collected in the clinical study conducted to support this current PMA supplement approval as described above.

Nonclinical Data

The biocompatibility evaluation previously submitted to FDA in the original PMA (P170029) continues to demonstrate that the patient contacting components provide reasonable assurance of safety and acceptability for clinical use. For a summary of the nonclinical studies, please refer to the SSED of the original PMA P170029 (https://www.accessdata.fda.gov/cdrh_docs/pdf17/P170029B.pdf).

Clinical data

From the primary CSR-04-2018 clinical study, all 30 patients that had images taken with the CALCIVIS Imaging System at Visit 1 were included in the safety population.

There were no patient related Adverse Events reported for the clinical study associated to the CALCIVIS Imaging System.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in the clinical study conducted to support PMA approval as described above.

The study was intended to show the safety and effectiveness of the CALCIVIS Imaging System to provide and monitor images of active demineralization on tooth surfaces in a clinical setting. When used to characterize demineralization in teeth, it is anticipated that the CALCIVIS Imaging System will provide the following potential benefits:

- Aid in treatment planning of dental carious lesions.
- Aid in clinical decision making.
- Aid in communication between dentist and patients.

The probable risks of the device are also based on data collected in the clinical study conducted to support PMA approval as described above and on data derived from nonclinical laboratory and toxicology studies that were previously submitted in the original PMA (P170029).

All 30 patients that had images taken with the CALCIVIS Imaging System at Visit 1 are included in the safety population. There were no patient related Adverse Events reported for the study associated to the CALCIVIS Imaging System.

ISO 10993 compliant nonclinical toxicological studies on the CALCIVIS Photoprotein previously submitted to FDA in the original PMA (P170029) showed no signs of toxicity. The previous biocompatibility evaluations submitted in the original PMA (P170029) provide reasonable assurance of safety and acceptability of the patient contacting components for clinical use. For a summary of the nonclinical studies, please refer to the SSED of the original PMA P170029 (https://www.accessdata.fda.gov/cdrh_docs/pdf17/P170029B.pdf).

1. Patient Perspectives

Patient perspectives considered during the review included:

The CALCIVIS Imaging System has been designed and developed to support the practice of preventive dentistry. In the primary CSR-04-2018 clinical study, Patient

Questionnaires showed positive feedback based on two questions – with over 88% of patients rating their overall experience with CALCIVIS Imaging System as "Good", and 100% of patients rating seeing images of their teeth and having the dentist explain their situation as "Helpful".

In conclusion, given the available information above, the data support that for capturing images of active demineralization on accessible coronal tooth surfaces, as an aid to the assessment, diagnosis, monitoring and treatment planning of demineralization associated with caries lesions, the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of the CALCIVIS Imaging System when used in accordance with the indications for use.

The clinical study results demonstrate effectiveness in adult and pediatric patients with both primary and secondary effectiveness endpoints being met. Safety of the CALCIVIS Imaging System was established based on the relevant absence of device-specific patient related Adverse Events in the clinical studies.

XIII. CDRH DECISION

CDRH issued an approval order on 10/13/2023.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.

XV. REFERENCES

1. Grace M. Dental Notation. British Dental Journal 2000;188(5):229.

2. Lindén, LÅ, Björkman S, Hattab F. The Diffusion in vitro of Fluoride and Chlorhexidine in the Enamel of Human Deciduous and Permanent Teeth. Archives of Oral Biology 1986;31(1):33-57.

3. Wilson PR, Beynon AD. Mineralization Differences between Human Deciduous and Permanent Enamel Measured by Quantitative Microradiography. Archives of Oral Biology 1989;34(2):85-88.

4. Thylstrup A, Fejerskov O. Textbook of Cariology. Copenhagen, Munksgaard 1986; 186.

5. Fejerskov O, Nyvad B, Kidd EAM. Dental Caries: What is It. Dental Caries: The Disease and its Clinical Management 2015; 162.