Summary of Safety and Effectiveness

I. General Information

A. Device Generic Name: Caries Removal System

B. Device Trade Name: Carisolv™ Non-invasive Dental Caries Removal System

C. U.S. Correspondent: B.A. Brown & Associates
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D. Premarket Approval Application (PMA) Number: P000005

E. Date of Panel Recommendation: None

F. Date of Notice of Approval to the Applicant: JUN 27 2001

II. Indication for Use:

Carisolv™ is indicated for the chemo-mechanical softening and removal of dentin caries when used in conjunction with a dental handpiece.

III. Warning and Precautions

See labeling for the list of warnings and precautions associated with the device.

IV. Device Description

The MediTeam Dental AB Carisolv™ Non-invasive Dental Caries Removal System is comprised of a 0.5 ml solution containing 0.5% sodium hypochlorite which is mixed with 0.5 ml solution containing amino acids, carboxymethylcellulose, sodium chloride, Erythrosine (E127B), purified water and sodium hydroxide with a pH 11. The two solutions are supplied in two separate syringes which are mixed together just before use. The two syringes have male and female connecting parts. These are attached and the solutions are mixed without air contact. After mixing the solutions form a gel substance that remains fully active for approximately 30 minutes. The mixed gel solution is then placed in a dappen glass and the gel is applied to the dental caries with the aid of a hand instrument or small forceps.

The Carisolv™ system also includes a set of hand instruments which aid in applying the caries removal gel solution and in the excavating of the carious material. The instrument set contains four different handles with eight different removable tips. The tips range in diameter from 0.3 – 2.0 mm and differ slightly in shape, and are designed for accessing the carious material once the gel solution is applied.

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V. Alternative Practices and Procedures

Alternative practices or procedures include the use of a spoon excavator and/or a rotary cutting instrument to remove the caries.

VI. Marketing History

On-going research and collaborative efforts between MediTeam and biochemists at Chalmers, Malmo and Huddinge have resulted in the development of Carisolv™. In January of 1998 Carisolv™ was approved for clinical use in the following countries:

Australia (approved 98)
Austria
Belgium (approved 99)
Canada (approved 2000)
Denmark
Finland
France
Germany
Great Britain
Greece
Iceland
Ireland
Italy
Liechtenstein
Luxembourg
Netherlands
Norway
Poland (approved 99)
Portugal
Spain
Switzerland

The device has not been removed from any market for reasons related to safety and effectiveness.

VII. Adverse Effects

None known.

VIII. Summary of Studies

A. Toxicity Studies

Dermal irritation study

Carisolv™ may come in contact with the skin during the clinical procedure and the dermal effect was therefore examined.
A single cutaneous application of Carisolv™ was administered to 30 Sprague Dawley rats in the following manner:

Group #	Group designation	Volume	Exposure time	Number of animals	
		(ml per animal)	(min)	Males	Females
1	Control article	0.5	10	5	5
2	Test article	0.5	1	5	5
3	Test article	0.5	10	5	5

An occlusive bandage was used for groups #1 and #3. Evaluation was performed at 15 minutes, 1, 2, and 4 hours after application, and then daily for 7 days.

There were no abnormal clinical signs in any of the treated animals during the observation period. Body weight changes in the treated animals were not influenced by treatment, and macroscopic findings were negative. The test article appeared to be non-irritating.

Buccal Mucosa Study

A similar study was performed to evaluate the effect of Carisolv™ on the buccal mucosa.

Carisolv™ was applied once to both sides of the buccal mucosa of 20 male albino Hartley guinea-pigs under anesthesia, in the following manner:

Group number	Exposure time (min.)	No. of animals	Substance administered	
			Left side (treated)	Right side (placebo)
1	1	10	Test article	Placebo
2	10	10	Test article	Placebo

The test article was placed on a cotton pellet and placed in contact with the buccal mucosa for one or ten minutes. A plain cotton pellet was placed contralaterally as a control.

The animals were weighed one day before and one day after application of Carisolv™. Evaluation of local reactions was performed 1 and 24 hours afterward. Macroscopic changes in appearance of the mucosa were noted and if necessary graded. Color photographs were taken of the control and treated sites during the observations. Histopathological examinations of the mucosa were performed at 24 hours.

No irritation was observed in any of the animals at 1 and 10 minutes. Minimal signs of irritation seen at histopathology were considered to be due mainly to the procedure of administration. Carisolv™ was considered to be well tolerated.

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Cutaneous Sensitivity Study

Delayed cutaneous hypersensitivity was performed in 40 albino Hartley guinea-pigs. One negative control group of 10 animals (induct-ion: water for injection – challenge: test article), one treated group of 20 animals (induction and challenge: test article) and one positive control group of 10 animals (induction and challenge: di-nitro chloro benzol, DNCB) were evaluated.

Examinations for morbidity/mortality were performed twice daily, at the beginning and at the end of the working day. The animals were weighed on day 1 and day 24.

Macroscopic examinations were performed at 24 and 48 hours. No mortality was observed during the study. Body weight changes in the treated animals were not influenced by treatment when compared to controls. Signs of irritations were noted during induction in both groups. Macroscopic examinations did not reveal any signs of delayed hypersensitivity. No cutaneous abnormality was noted in the negative control group. In the positive control group, DNCB induced signs of hypersensitivity.

The sensitizing potential of the test article dosing preparation for the skin of the albino guinea-pig may be expressed as weak (grade I). This demonstrated that Carisolv™ did not induce cutaneous sensitization in the animals examined.

Shelf Life Determination

Expiration dating for this device has been established and approved for 12 months when refrigerated or when stored for one month at room temperature.

IX. Summary of Clinical Investigations

Multi-center Study #1

This multi-center study was considered the pivotal evidence in support of the safety and effectiveness of the Carisolv™ System. The aim of the study was to evaluate the clinical efficacy and safety of a new method (Carisolv™) for chemo-mechanical caries removal. A study was conducted at four centers. A total of 137 consecutive patients (64 females and 73 males aged 3 – 85 years, mean 35) entered a prospective, controlled, randomized open study. One carious lesion with distinct dentine involvement and with an opening of more than 1.5 mm was selected per patient. A total of 116 lesions in permanent and 21 in deciduous teeth were treated. Caries were removed with a combination of using a dental handpiece and Carisolv™ gel. The gel was applied onto the carious dentine. The caries was gently removed with hand instruments. Additional applications of gel were applied and the procedure was repeated until no more debris could be removed. An independent examiner judged the cavity preparation, using the clinical criteria such as probing and visual inspection. One hundred thirteen patients were randomized for gel treatment and 24 for caries removal with a dental handpiece. Four patients selected for caries removal with a dental handpiece did not complete the treatment. Total caries removal was achieved in 108 cases with gel and in 19 from the handpiece group. Unsuccessful caries removal by the gel treatment was reported in 1 case. No adverse effects were reported with the

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use of Carisolv™. These results indicate that dentinal caries may be removed using a handpiece and Carisolv™ without adverse reactions. However, caries removal is not always complete, and use of the dental handpiece is frequently necessary.

Clinical Study #2

A clinical study was conducted at one center at Goteborg University, Faculty of Odontology. The objective of this study was to evaluate the safety and efficacy of the Carisolv™ method for removal of root caries by comparing it to the conventional method for removal of caries using a dental handpiece. This data represents a preliminary report of results.

Thirty-eight patients with 60 cavities were included in the study. Of the cavities, 34 were randomized for treatment with Carisolv™ and 26 for the handpiece group. Twenty-two of the patients were treated with both Carisolv™ and with the dental handpiece. The age distribution of the group corresponded well to a randomly selected patient population expected to have root surface caries, but the gender distribution was almost 2/3 male.

All of the cavities treated with Carisolv™ became caries free. All but one of the cavities in the handpiece group were judged to be caries free. All patients responded to treatment well. No negative reactions or complications were reported. Four patients asked for anesthesia in the Carisolv™ group compared to 6 patients in the control group. In the Carisolv™ group, none of the patients who did not receive dental anesthesia, experienced pain. Twelve of control group who did not use local anesthesia, experienced pain. The mean time for treatment with Carisolv™ was approximately 6 minutes, compared to 4 ½ minutes with drilling (excluding time for local anesthesia). An average of 6 drops of gel (~ 0.2 ml), with a maximum of less than 0.5 ml gel was used per cavity.

No severe side effects have been observed with the use of Carisolv™. This study supports safety claims for the use of Carisolv™ on root surface caries, as an adjunct to the traditional handpiece. The number of cases in the Carisolv™ group, where the handpiece was required, was not reported. In addition, failure to remove all caries in the handpiece group should be considered to be a clinician error, rather than a failure of the handpiece. Without reporting data on the extent of handpiece use in the Carisolv™ group, the ability of this study to evaluate of efficacy of using Carisolv™ with respect to caries removal, is limited.

Clinical Study #3

To evaluate the effect of contact of Carisolv™ on gingival tissues, a randomized clinical study was conducted to evaluate the effect of Carisolv™ on healthy oral mucosa of 34 healthy volunteers. Small pieces of blotting paper were soaked with either one drop of Carisolv™ or one drop of sodium hypochlorite (0.5%), and placed on the oral mucosa, on either side of the frenum of the lower lip. The blotting paper was left in place for three minutes.

The oral mucosa was inspected clinically and documented with photographs before treatment, and three minutes, 1 hour, and 24 hours after placement. If any signs or symptoms were documented at this time, the site was inspected again after 72 hours.

After three minutes, none of the oral mucosa at Carisolv™ sites demonstrated tissue changes. After one hour one patient had a slightly etched area with a slight blush on the test side. All other (33) patients were clinically symptom free. After 24 hours three persons had reactions on the Carisolv™ side. One person was somewhat swollen and two persons showed an erythemic blush. After 72 hours, none of the Carisolv™ subjects showed any symptoms.

The results demonstrate that Carisolv™ has minimal effect on the mucosa. The use of a rubber dam is also recommended when using this product to minimize the possibility of contact with oral tissues.

The following studies provided supplementary information in support of the safety and effectiveness of Carisolv™.

Clinical Study #4.

A voluntary patient follow-up survey with Swedish dentists was conducted. These dentists had used Carisolv™ during the autumn of 1997 and late summer of 1998. This is a report of the results from their first cases.

This survey consisted of 1305 teeth in 1075 patients, treated by 146 dentists. Eighty three percent of the patients were caries free after one Carisolv™ treatment session. Ten percent did not achieve a caries free status and in the remaining 7%, the results were uncertain or not reported. For those patients who did not achieve a caries free status, a step-by-step excav-ation of caries was performed using a dental handpiece.

In 55% of the cases, the handpiece was also used. The handpiece was used in the majority of these cases to gain access to the carious lesion, but a few used the handpiece to smooth the cavity preparation after Carisolv™ treatment or to achieve a caries free status. Before treatment, 24% (991 of 1305) of the patients asked for anesthesia. Another 22 patients (1.7%) asked for anesthesia during treatment. Eighty percent of Carisolv™ patients who did not receive anesthesia, reported little or no pain during the Carisolv™ treatment.

No adverse reactions were reported. Use of the dental handpiece was required in a higher percentage of cases than reported in Study #1.

Clinical Study #5

A voluntary follow-up patient survey was conducted in Germany by dentists who used Carisolv™ during 1998.

1003 teeth in 694 patients were treated by 91 dentists in the follow-up study. Eighty eight percent of the cases were successful, i.e. the patients achieved a caries free status after one treatment session, while 10% did not achieve a caries free status. Results of the remaining 2% of the cases in this survey were uncertain or not reported. In those

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cases where caries free status was not achieved, a step-by-step excavation was performed.

In 38% of these cases, the dentists reported using the dental handpiece to access the carious lesion, smooth the cavity after Carisolv™ treatment, or to remove caries. The survey did not report how removal of undermined dentin was accomplished. Before treatment, 18% of the patients asked for anesthesia, while 29 patients (2.9%) asked for anesthesia during treatment. More than 80% of the Carisolv™ patients reported little or no pain/discomfort, during the treatment. No adverse reactions, were reported.

X. Conclusions from Studies

From these studies it may be concluded that Carisolv™ appears to be safe as an adjunct to use of a dental handpiece in the removal of dental caries. Its efficacy in removing caries has been demonstrated in easily accessed areas where exposure to the dental pulp is not eminent.

Experimental studies with dermal application in rats and buccal administration in guinea pigs have demonstrated no local toxicity. Experimental sensitizing studies (Magnusson and Kligman test) have not revealed significant sensitization potential for Carisolv. The large clinical experience with Carisolv has not demonstrated any local toxicity.

Experimental and clinical studies with Carisolv™ have not shown any signs of pulpal toxicity. Considerable evidence for local pulpal tolerance has been achieved from studies with calcium hydroxide paste with similar pH.

Toxicity data for Carisolv™ included dermal buccal mucosa irritation and dermal sensitization. The results of the dermal irritation, buccal mucosa irritation and dermal sensitization (Guinea Pig Maximation Test) indicate that Carisolv™ is non-irritating and non-sensitizing.

XI. Panel Recommendation

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Dental Device Advisory Panel, an FDA advisory committee for review and recommendation because the information substantially duplicates information previously reviewed by the panel.

XII. FDA Decision

CDRH has concluded that the preclinical and clinical data provide reasonable assurance that that Carisolv™ Non-Invasive Dental Caries Removal System is safe and effective when used in accordance with the approved labeling.

FDA inspection of the applicant's manufacturing facilities determined the facilities to be in compliance with the Quality System Regulation.

CDRH issued an approval order on JUN 27 2001

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XIII. Approval Specifications

- Directions for use: See device labeling
- Hazards to Health from Device: See Indications, Contraindications, Precautions and Adverse Events in labeling.
- Postapproval Requirements and Restrictions: See Approval Order

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