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Attachment J

Repliderm™ Wound Dressing: 510(k) Summary

Date: August 16, 1996

Orphan Medical Inc. submits the following information as the **Summary**, under 21 CFR 807.92, for permission to market Repliderm™ Wound Dressing for wound healing, which is substantially equivalent to collagen powders now in commercial distribution. Information pertaining to this claimed substantial equivalency is as follows:

1. **Establishment Name and Address**

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2. **Device trade or proprietary name** Repliderm™ Wound Dressing
Common or usual name collagen wound dressing

3. **Indications for Use**

Repliderm™ Wound Dressing cartilage powder is a collagen based powder intended for use in the management of pressure ulcers (stages I - IV), stasis ulcers, 1st and 2nd degree burns, diabetic ulcers, foot ulcers, post surgical incisions, radiation dermatitis, cuts, abrasions, irritations of the skin, partial thickness wounds and skin conditions associated with peristomal care.

Repliderm™ Wound Dressing has also been shown to be useful for wound exudate absorption.

4. **Product Description**

Repliderm™ Wound Dressing is a collagen based product containing approximately 73% protein, 18% carbohydrates, and 5% other cartilage components. The particles, average particle size of approximately 35 microns, are composed of the natural three-dimensional network of macro-molecular chains of cross-linked collagen, which is large enough to allow substances with a molecular weight of less than 1,000 to freely enter. Substances with a molecular weight of 1,000 to 5,000 enter the particles less freely, while those substances with larger molecular weights remain in the interspaces between the particles.

Each gram of wound dressing powder can absorb approximately 3-4 ml of fluid. Its other wound healing properties derive from an average 35 micron particle size, combined with the materials biocompatibility and biodegradation characteristics.

5. **Substantial equivalency**

Repliderm™ Wound Dressing consists mainly of collagen powder, similar to Kollagen™ (Medifil™) particles from BioCore Inc.™ (K910944) and other collagen-based wound healing products in commercial distribution. Repliderm™ Wound Dressing can be used to absorb wound exudate similar to the prescribed use of Kollagen™ powder.

Repliderm™ Wound Dressing can also be used as a wound dressing, similar to Carrasyn™ Hydrogel wound dressing (Carrington Laboratories, K902345) and Comfeel® hydrogel powder (Coloplast Sween Corp., K834343).

Repliderm™ Wound Dressing is similar to the hydrogel wound dressings approved for commercial distribution, since it is derived from biological tissue (collagen versus gelatin), polysaccharides and other materials and exhibits general wound dressing characteristics.

Repliderm™ Wound Dressing can be compared to several predicate devices. These predicate devices include Kollagen™ (Medifil™) particles (BioCore Inc., K910944), Carrasyn™ Hydrogel wound dressing (Carrington Laboratories, K902345), Micro-Coll™ Collagen Dermal Wound Spray (K920642), Micro-Coll™ Collagen Wound Spray (K912565), and Comfeel® hydrogel powder (Coloplast Sween Corp., K834343).

6. **Safety and Efficacy**:

The safety and efficacy of Repliderm™ Wound Dressing are supported by the following:

a. *In vitro* study performed to evaluate wound exudate absorption

This *in vitro* study was designed to investigate the wound exudate absorption ability. Repliderm™ Wound Dressing was found to absorb 3½-4 times its weight of simulated wound exudate in an *in vitro* analytical study. This study shows that Repliderm™ Wound Dressing is an effective exudate absorbing material.

Summary: Wound exudate absorbed

b. Pig skin wound healing study performed to characterize wound healing properties

This pig study was designed to: (1) validate previously reported animal and clinical biocompatiblity studies and wound healing studies about this product, and (2) compare its wound healing capability to appropriate controls, including a predicate device (Carrasyn™ Hydrogel Wound Dressing).

No evidence of dermal irritation or dermal sensitivity was histologically observed in any skin sample associated with the cartilage powder treatment. No evidence of acute systemic toxicity was observed for any animal examined, during the post-wounding sampling period.

Summary: a. Wound healing/re-epithelization comparable to predicate device
b. No evidence of dermal irritation or dermal sensitivity was histologically observed in any skin sample associated with the Repliderm™ Wound Dressing treatment
c. No evidence of acute systemic toxicity was observed for any animal examined, during the post-wounding sampling period

c. Previously reported <u>animal</u> studies performed to characterize the wound healing properties of Repliderm™ Wound Dressing

Studies in rats using the bovine cartilage powder having an average 35 micron diameter was used for topical applications. These studies have shown that bovine tracheal cartilage powder has a positive effect in the wound healing process.

1.) Tensile Strength Evaluations in Rats

Three separate studies demonstrated that: (1) topical application of bovine cartilage powder (20-30 mg) resulted in greater wound tensile strength, (2) incisions treated with cartilage powder had statistically significantly greater tensile strength compared to control wounds, and (3) calf bovine cartilage powder with a particle size of 20 microns resulted in greater tensile strength as compared to 70 micron particles.

2.) Histological Evaluation of Wounds

A rat histologic study of the progress of wound healing that wounds treated with cartilage powder reached their maximum on the seventh day. Control wounds exhibited mature scar tissue by the eighth postoperative day while the cartilage wounds continued to show cellular activity until the twenty-first day. The initial acceleration of wound healing caused by cartilage powder is manifested histologically by earlier and greater endothelial and fibroblastic proliferation with concomitant production of reticulum fibers and collagen.

3.) Evaluation of the Time to Complete Healing

A study to evaluate the time to complete healing of 4-cm^2 excision wounds in rats showed that the mean time to complete healing was statistically significantly longer in the control group as compared to the cartilage powder group.

Summary: Wounds healed faster with higher tensile strength

d. Previously reported <u>human</u> clinical studies performed to characterize the wound healing properties of Repliderm™ Wound Dressing

Several human clinical studies were previously reported that characterized bovine tracheal cartilage powder wound healing. These studies utilized cartilage powder having an average 35 micron diameter for topical applications.

1.) Acute toxicity and surgical and non-healing chronic wound healing

Cartilage powder applied to chronic non-healing ulcers initiated the granulation process and formed a granulating bed over the wound in all but two cases. Once granulation was initiated, the healing process was self-sustaining in all instances. In surgical applications, after closure of the pleura or peritoneum, treated wounds healed without difficulty.

2.) Wound Healing, Human

Two wounds, one treatment site and one control site, per human volunteer were evaluated. The treated wounds were statistically stronger in 12 of 15 wound pairs as evidenced by the increased tensile strength.

3.) Histological Evaluation, Human

Biopsies samples from paired wounds in another volunteer study showed histologically evident increases wound healing rates were noted.

Summary: Wounds healed faster with higher tensile strength

e. Previously reported animal and clinical studies performed to characterize biocompatibility of Repliderm™ Wound Dressing

Several previously reported animal studies characterize the biocompatibility of cartilage powder wound dressing. Cartilage powder having an average 35 micron diameter was used for topical applications.

Collectively, the results of the testing, along with the absence of irritation or cytotoxicity in the porcine wound healing study, summarized above, demonstrate that Repliderm™ Wound Dressing meets the biocompatiblity requirements for a Wound Dressing (Draft Guidance for the Preparation of a Premarket Notification for a Wound Dressing, 1993).

Summary: Repliderm™ Wound Dressing meets the biocompatiblity requirements for a Wound Dressing