This guidance was written prior to the February 27, 1997 implementation of FDA's Good Guidance Practices, GGP's. It does not create or confer rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both. This guidance will be updated in the next revision to include the standard elements of GGP's.

DRAFT GUIDANCE FOR THE PREPARATION OF AN IDE SUBMISSION FOR AN INTERACTIVE WOUND AND BURN DRESSING*

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*Final comments from the FDA General and Plastic Surgery Devices Advisory Panel have not yet been received. Contents of this document are subject to change.

DRAFT GUIDANCE FOR THE PREPARATION OF AN IDE SUBMISSION FOR AN INTERACTIVE WOUND AND BURN DRESSING

This guidance document provides device manufacturers with a summary of the information which is to be contained in an Investigational Device Exemption (IDE) application for the group of products referred to as "interactive wound and burn dressings". This document is intended to supplement the IDE Manual which provides detailed information on preparing and submitting an IDE application. Although interactive or biologically active wound and burn dressings have not been finally classified, the General and Plastic Surgery Devices Advisory Panel proposed that these devices be classified as Class III devices (Federal Register, Vol. 54, No. 180, p. 38605). Furthermore, FDA is not aware of any preamendment devices to which these dressing could be found substantially equivalent. Currently, in order to market such a product, a manufacturer must supply valid scientific evidence of the safety and effectiveness of the dressing in a Premarket Approval Application (PMA) for the product. This would include extensive manufacturing information, preclinical studies, and clinical data. Because these products are considered by the FDA to present a significant risk to the patient, clinical data demonstrating the safety and effectiveness of the device must be gathered under the provisions of the IDE regulations (21 CFR 812). The information to be included in the submission of a IDE application is outlined below:

I. Name, address, and telephone number of the sponsor

II. Presentation and discussion of the relevant literature and reports of prior investigations, including data from preclinical studies and clinical trials conducted outside the United States

III. Complete description of the device, all significant components of the device, and the principle of action of each of the device components:

A. If collagen is a component of the dressing, the type of collagen as well as the tissue and species from which it was derived must be identified. In addition, if the collagen is derived from cattle in a herd outside the United States, certification that the herd is not infected with Bovine Spongiform Encephalopathy must be provided. Any processing/manipulation of the collagen must be described.

B. If cultured cells are incorporated into the device, a complete description of the origin of the cells, method of separation from the host tissue, the manner in which the cells will be handled and/or pooled, culturing techniques, culture media, and any agents such as growth factors used in the culturing must be provided.

Assurance that the cells are free of transmissible diseases and viruses must be provided. This should include testing of the donor's blood for $HTLV_{1+2}$, HIV_{1+2}, ALT, Hepatitis B, Hep non A / Hep non B, RPR, and CMV IgM at the time of cell donation. The test for HIV_{1+2} should be repeated at six months. Individual cell strains should be tested for infectious agents, including mycoplasma, sterility, HIV_{1+2}, $HTLV_{1+2}$, HSV_{1+2}, and CMV before pooling. HIV, CMV, mycoplasma, and an in-vitro viral assay should be repeated on the pooled cells before being placed in a Master Cell Bank if one is to be used. Final product testing should include sterility, mycoplasma, and endotoxin / pyrogenicity.

Individual cell lines should be tested to establish the normal human diploid karyotype. In addition, the number of population doublings permitted should be identified. Quality control procedures used to monitor the cells during the manufacturing process for unusual morphology or growth characteristics must also be described.

If the cells are to be plated onto a substrate, the methods used to monitor cellular viability and density should be described and the minimum levels of acceptability identified.

The validation process should also be described as well as the frequency with which it will be performed.

C. In accordance with the Tripartite Biocompatibility Guidance for Medical Devices, acceptable test results for any processed / manufactured materials must be supplied for the biological tests listed below. Standard protocols such as those identified by the USP or ASTM must be used in conducting the biocompatibility testing.

    a. Dermal Irritation
    b. Dermal Sensitization
    c. Cytotoxicity
    d. Acute Systemic Toxicity
    e. Hemocompatibility / Hemolysis
    f. Pyrogenicity
    g. Mutagenicity
    h. Subchronic Toxicity
    i. Chronic Toxicity

All of the above testing may not be needed in every case, such as when the material is being purchased from a manufacturer who has already completed the required biocompatibility testing and can provide support documentation.

IV. Complete investigational plan:

A. The name and intended use of the device;

B. The objectives of the study;

C. The number of patients to be enrolled and the number of investigational sites that will participate in the study. (Statistical justification for the patient population size should be presented);

D. The expected duration of the investigation;

E. A description of the design of the study (e.g. multi-centered, single-blinded, double-blinded, randomized, etc.);

F. The inclusion and exclusion criteria which will be used to determine patient eligibility for the study;

G. The methodology which will be used to assign patients to either the experimental or control groups;

H. The protocol to be followed, including;

1. The pretreatment regimen. This should include patient pre-screening for eligibility, baseline evaluations such as wound site photographs or measurements, wound biopsies or culturing, laboratory testing (hematologic, immunologic, urinary), hypersensitivity screening, blood samples for archiving, and preparation of the wound site (debridement, irrigation, etc.).

2. The treatment regimen for both the experimental and control groups. The treatment regimen must be described in detail and should include; descriptions of both the control and experimental treatments, the frequency of the treatments, and any other care the patients will receive such as wound debridement/irrigations, dressing changes, laboratory testing, application of topical agents, etc. The control treatment must be recognized as the current standard of care for this patient population. A description of how uniformity of the control and experimental treatments will be maintained across the investigational sites must be provided.

3. The post-treatment regimen. A description of the follow-up schedule must be provided. This should include the frequency of the follow-up visits as well as a description of all laboratory testing, dressing changes, and wound site evaluations such as photographs, tracings/molds, and biopsies to be performed at each follow up evaluation.

4. Wound assessment

a. Device effectiveness evaluation. The study endpoints should be clearly identified. These endpoints should be carefully considered since the labeling/claims for the device will be limited by the design of the study and the endpoints measured. The rationale for the selection of these endpoints should be presented. The parameters used to evaluate the effectiveness of the dressing in the management of the indicated wound must be presented. A description of the methodology to be used in making the assessments and the frequency with which they will be performed should also be included.

The submission of patient report forms is not required in the IDE application, however, inclusion of these forms is often helpful to both the submitter and the FDA in outlining the wound assessment program to be followed. Also, in developing the patient report forms, any potentially related data or variables which may be needed to justify pooling of the data and/or to help stratify the data for data analysis should be included.

b. Device safety evaluation. A description of the methodology and parameters which will be used to evaluate the safety of the device should be presented. This could include laboratory tests used to monitor systemic effects (hematology, blood chemistry profiles, urinalysis), assessment of local effects such as erythema, maceration, edema, etc., and monitoring of the severity and frequency of adverse events. The frequency of the assessments must also be stated.

5. An analysis of the protocol demonstrating its scientific soundness; and

6. A complete description of the statistical analysis to be performed on the data, including the level at which statistical significance will be asserted.

I. A description and analysis of all risks to the subjects; and

J. Written procedures for monitoring the investigation as well as the name(s) and address(es) of the individual(s) who will monitor the study.

V. Detailed description of the methods, facilities, and quality controls used in the manufacture, processing, packing, storing, transporting, and installation of the device

VI. Example of the agreements to be signed by the investigators and a list of the names and addresses of all investigators

VII. Certification that all investigators have signed the agreement, that the list of investigators includes all investigators participating in the study, and that new investigators will sign the agreement before being added to the study

VIII. A list of the names, addresses, and chairpersons of all IRBs that have or will be asked to review the investigation and certification of IRB action concerning the investigation

IX. The name and address of any institution (other than those above) where a part of the investigation may be conducted

X. The amount, if any, that will be charged for the device and an explanation of why sale does not constitute commercialization

XI. A claim for categorical exclusion (Section 25.24) or an environmental assessment (Section 25.31)

XII. Copies of all labeling for the device, including instructions for both storing the device and applying the device to the wound bed

XIII. Copies of all informed consent forms and all related information materials to be provided to the subjects

The attached "Checklist for an Interactive Wound and Burn Dressing IDE Submission" will be used in conjunction with the "Original IDE Checklist for Administrative Review" by FDA reviewers to determine if the IDE application for an interactive wound and burn dressing is sufficiently complete to permit an in-depth scientific review. Documents which lack important regulatory elements or are grossly deficient in scientific content may be returned to the sponsor without benefit of a scientific review. Therefore, before a sponsor submits an IDE application for an interactive wound and burn dressing, the contents of the document should be compared with both of these checklists. If further information is needed, please contact Charles Durfor, Ph.D. at (301) 594-3090.

CHECKLIST for an INTERACTIVE WOUND and BURN DRESSING IDE SUBMISSION

		Yes	No / NA
☞	Complete description of the device and all significant components?	☐	☐
	If collagen is a component, has all of the information specified in this guidance document (page 2) has been provided?	☐	☐
	If cultured cells are incorporated into the device, has all of the information specified in this guidance document been provided (e.g. origin of cells, culturing techniques, transmissible disease testing, sterility / contamination testing during the manufacturing process and of final end product, and description of the quality control and validation processes)?	☐	☐
☞	Biocompatibility test results for any processed / manufactured materials?	☐	☐
☞	Complete investigational plan including:		
	- patient inclusion / exclusion criteria?	☐	☐
	- methodology for assigning subjects to control / treatment groups?	☐	☐
	- all screening and treatment regimens?	☐	☐
	- all parameters to be used to assess device safety and effectiveness?	☐	☐
	- an analysis of the protocol demonstrating its scientific soundness?	☐	☐
☞	Copies of all labeling for the device, including instructions for string the device and applying the device to the wound bed?	☐	☐