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Regulatory Considerations for Development of Wound Dressing Devices Used for Chemical and Radiation Injuries

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Editorial

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Wound Dressing Medical Devices and the 510(k) Regulatory Pathway

The US Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH) is responsible for the regulation of wound dressing medical devices. Depending on the wound dressing device's intended use and risk profile, these devices may require premarket review through premarket notification [510(k)] as outlined in 21 CFR 807 Subpart E, De Novo classification as outlined in 21 CFR 860 Subpart D, or premarket approval (PMA) as outlined in 21 CFR 814.

The 510(k)-review process determines whether a new device is substantially equivalent (or as safe and as effective) to a legally marketed device, known as a predicate device.[1] If an appropriate predicate device does not exist, a de novo classification request may be submitted to classify novel medical devices for which general controls alone (Class I), and/or general and special controls (Class II), provide reasonable assurance of safety and effectiveness for the intended use.[2] If a combination of general and special controls is not adequate to provide a reasonable assurance of safety and effectiveness for the intended use (Class III), a PMA application would be neded.[3]

If the intended use of a wound dressing device is limited to covering and protecting the wound, absorbing wound exudate, and maintaining a moist wound environment, the device is typically evaluated through the 510(k) pathway.

A determination of substantial equivalence of the new device and its predicate device is based on an evaluation of intended use and technological characteristics of the 2 devices, where:

- The **intended use** of a device refers to the general purpose of the device or its function, and is determined by an evaluation of the proposed labeling for the device as provided in the 510(k) submission[4]. A new device must have the same intended use as the predicate to support a determination of substantial equivalence[5].
- Technological characteristics include materials, design, energy source, and other device features[4]. To support a determination of substantial equivalence, any differences in technological characteristics as compared to the predicate must not raise different questions of safety and effectiveness. Differences in **technological characteristics** between a new device and its predicate may be addressed through performance data from bench, animal, and/or clinical testing. A different question of safety or effectiveness is a question raised by the technological characteristics of the new device that was not applicable to the predicate device, and poses a significant safety or effectiveness concern for the new device[6].

Animal, Clinical Data in Wound Dressing Medical Device Submissions

While many wound dressing devices cleared through the 510(k) pathway do *not* typically need to provide animal or clinical testing to demonstrate substantial equivalence to the predicate device, there are certain situations where such data may be necessary. For example, in vitro cytotoxicity testing may indicate that a newly proposed device is cytotoxic, and therefore, could theoretically impair wound healing. To help understand the potential implications of the in vitro cytotoxic effect and determine whether it may translate to delayed wound healing, a wound healing study in an animal model, which has similarities in wound healing between the proposed in vivo model and humans, may be requested to demonstrate substantial equivalence.

Another scenario which may arise warranting additional animal or clinical data is when bench testing alone is insufficient to demonstrate substantial equivalence. This may occur when a new device proposes an indication for use with a different patient population than the cited predicate device even though the overall intended use is the same as the cited predicate device. Here, we highlight a selection of examples where animal or clinical data were leveraged, in addition to bench testing, through the 510(k) submission pathway for wound dressing medical devices seeking indications for use including chemical or radiation injuries to the skin.

Example: Wound Dressing Indicated for Mustard-Induced Injuries

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There has been a growing interest in the utilization of in vitro wound healing models in recent years, but this remains an area of emerging research[7]. On the other hand, pigs have a long history of use as a model for wound healing due to the anatomical and physiological similarities between pig and human skin[8]. Mini-pigs in particular have been used in the literature to evaluate changes in skin tissue following exposure to sulfur mustard gas[9–11]. In July 2019, FDA relied upon data from a mini-pig animal study to clear a 510(k) for the first wound dressing device indicated for use on decontaminated, stable, unroofed, first and second degree mustard-induced vesicant injuries not requiring skin grafting.

Example: Wound Dressing Indicated for Radiation Injuries

FDA has cleared a limited number of wound dressing devices indicated for radiation dermatitis (RD) as a result of radiation therapy. However, radiation injuries may also occur from nontherapeutic exposure to a large external dose of radiation, referred to as cutaneous radiation injury (CRI)[12]. While the terms RD and CRI are used to describe similar injuries following exposure to ionizing radiation, signs and symptoms from CRI may be more severe and less controllable compared to RD[13]. In October 2022, FDA cleared the first wound dressing indicated for use on cutaneous radiation injuries through dry desquamation based on a clinical study in breast cancer patients undergoing radiation therapy[14].

Wound Dressing Development and Engagement with FDA

New device technologies and indications often present both scientific and regulatory challenges. As part of FDA's efforts to protect and promote the public health, the Agency facilitates the process of bringing innovative, safe, and effective medical products to market. Medical device sponsors considering seeking marketing authorization for a wound dressing for a new or specific indication should consider utilizing the Q-Submission program,[15] which provides an opportunity for FDA and sponsors to engage in early discussions on topics such as regulatory approach and study protocols prior to significant investments toward data collection. The Center for Devices and Radiological Health encourages these early interactions as they may help improve the quality of a future marketing submission and contribute to a more transparent review process.

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