Therefore, under the Federal Food, Drug, and Cosmetic Act, and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 73 is amended as follows:

PART 73—LISTING OF COLOR ADDITIVES EXEMPT FROM CERTIFICATION

■ 1. The authority citation for part 73 continues to read as follows:

Authority: 21 U.S.C. 321, 341, 342, 343, 348, 351, 352, 355, 361, 362, 371, 379e.

§ 73.2396 [Removed]

■ 2. Remove § 73.2396.

Dated: September 30, 2021.

Lauren K. Roth,

Acting Principal Associate Commissioner for Policy.

[FR Doc. 2021–21892 Filed 10–7–21; 8:45 am]

BILLING CODE 4164–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 878

[Docket No. FDA–2019–N–1250]

General and Plastic Surgery Devices; Reclassification of Certain Surgical Staplers

AGENCY: Food and Drug Administration, HHS.

ACTION: Final amendment; final order.

SUMMARY: The Food and Drug Administration (FDA or the Agency) is issuing a final order to reclassify surgical staplers for internal use (formerly regulated under the classification for ''manual surgical instrument for general use'' and assigned the product code GAG) from class I (general controls) into class II (special controls) and subject to premarket review. FDA is identifying the special controls for surgical staplers for internal use that the Agency believes are necessary to provide a reasonable assurance of the safety and effectiveness of the device. FDA is issuing this reclassification on its own initiative based on new information. As part of this reclassification, FDA is also amending the existing classification for ''manual surgical instrument for general use'' to remove staplers and to create a separate classification regulation for surgical staplers that distinguishes between surgical staplers for internal use and external use.

DATES: This order is effective October 8, 2021.

FOR FURTHER INFORMATION CONTACT: George Gibeily, Center for Devices and Radiological Health, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 66, Rm. 4660, Silver Spring, MD 20993, 301–796–0276, *george.gibeily@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

The Federal Food, Drug, and Cosmetic Act (FD&C Act), as amended, establishes a comprehensive system for the regulation of medical devices intended for human use. Section 513 of the FD&C Act (21 U.S.C. 360c) established three categories (classes) of devices, reflecting the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three categories of devices are class I (general controls), class II (special controls), and class III (premarket approval).

Under section 513(d)(1) of the FD&C Act, devices that were in commercial distribution before the enactment of the 1976 amendments (Medical Device Amendments of 1976, Pub. L. 94–295), May 28, 1976 (generally referred to as ''preamendments devices''), are classified after FDA has: (1) Received a recommendation from a device classification panel (an FDA advisory committee); (2) published the Panel's recommendation for comment, along with a proposed regulation classifying the device; and (3) published a final regulation classifying the device. FDA has classified most preamendments devices under these procedures.

Devices that were not in commercial distribution before May 28, 1976 (generally referred to as ''postamendments devices''), are automatically classified by section 513(f)(1) of the FD&C Act into class III without any FDA rulemaking process. Those devices remain in class III and require premarket approval, unless, and until: (1) FDA reclassifies the device into class I or II or (2) FDA issues an order finding the device to be substantially equivalent, in accordance with section 513(i) of the FD&C Act, to a predicate device that does not require premarket approval. The Agency determines whether new devices are substantially equivalent to previously marketed devices by means of premarket notification procedures in section 510(k) of the FD&C Act and part 807, subpart E of the regulations (21 CFR part 807).

On July 9, 2012, Congress enacted the Food and Drug Administration Safety and Innovation Act (FDASIA) (Pub. L. 112–144). Section 608(a) of FDASIA amended section 513(e) of the FD&C Act, changing the process for reclassifying a device from rulemaking to an administrative order. Section 513(e)(1)(A)(i) of the FD&C Act sets forth the process for issuing such a final order. Specifically, prior to the issuance of an administrative order reclassifying a device, the following must occur: (1) Publication of a proposed reclassification order in the **Federal Register**, (2) a meeting of a device classification panel described in section 513(b) of the FD&C Act, and (3) consideration of comments to a public docket. The proposed reclassification order must set forth the proposed reclassification and a substantive summary of the valid scientific evidence concerning the proposed reclassification, including the public health benefits of the use of the device, and the nature and incidence (if known) of the risks of the device.

Section 513(e)(1)(A)(i) provides that FDA may, by administrative order, reclassify a device based on ''new information.'' FDA can initiate a reclassification under section 513(e) or an interested person may petition FDA. The term ''new information,'' as used in section 513(e) of the FD&C Act, includes information developed as a result of a reevaluation of the data before the Agency when the device was originally classified, as well as information not presented, not available, or not developed at that time (See, *e.g., Holland-Rantos* v. *U.S. Dep't of Health, Educ. & Welfare,* 587 F.2d 1173, 1174 n.1 (D.C. Cir. 1978); *Upjohn Co.* v. *Finch,* 422 F.2d 944 (6th Cir. 1970); *Bell* v. *Goddard,* 366 F.2d 177 (7th Cir. 1966)).

Reevaluation of the data previously before the Agency is an appropriate basis for subsequent regulatory action where the reevaluation is made in light of newly available regulatory authority (see *Bell,* 366 F.2d at 181) or in light of changes in ''medical science'' (see *Upjohn,* 422 F.2d at 951). Whether data before the Agency are old or new, the ''new information'' to support reclassification under section 513(e) of the FD&C Act must be ''valid scientific evidence,'' as defined in section 513(a)(3) of the FD&C Act and 21 CFR 860.7(c)(2) (See, *e.g., Gen. Med. Co.* v. *FDA,* 770 F.2d 214 (D.C. Cir. 1985); *Contact Lens Mfrs. Ass'n* v. *FDA,* 766 F.2d 592 (D.C. Cir. 1985), cert. denied, 474 U.S. 1062 (1986)).

FDA relies upon ''valid scientific evidence'' in the classification process to determine the level of regulation for devices. To be considered in the reclassification process, the ''valid scientific evidence'' upon which the Agency relies must be publicly available. Publicly available information

excludes trade secret and/or confidential commercial information, *e.g.,* the contents of a pending premarket approval application (see section 520(c) of the FD&C Act).

Section 510(m) of the FD&C Act provides that a class II device may be exempted from the premarket notification requirements under section 510(k) of the FD&C Act if the Agency determines that premarket notification is not necessary to assure the safety and effectiveness of the device. FDA has determined that premarket notification is necessary to reasonably assure the safety and effectiveness of surgical staplers for internal use. Therefore, the Agency has not exempted this class II device from premarket notification (510(k)) submission as provided under section 510(m) of the FD&C Act.

On April 24, 2019 (84 FR 17116), FDA published a proposed order in the **Federal Register** to reclassify surgical staplers for internal use (the proposed order). FDA also proposed special controls and proposed amending the existing classification for ''manual surgical instrument for general use'' to remove staplers and to create a separate classification regulation for surgical staplers that distinguishes between surgical staplers for internal use and external use. The period for public comment on the proposed order closed on June 24, 2019. FDA received and has considered comments on the proposed order, as discussed in section III. FDA also held a meeting of the General and Plastic Surgery Devices Advisory Panel (the Panel) on May 30–31, 2019, in accordance with section 513(b) of the FD&C Act (21 U.S.C. 360c(b)) (Ref. 1). In publishing the proposed order, holding the Panel meeting, and considering comments to the docket, FDA has met the requirements for reclassification under section 513(e)(1)(A)(i) of the FD&C Act.

II. Panel Meeting

A. Panel Feedback

On May 30, 2019, the Panel met to discuss and make recommendations regarding the reclassification of surgical staplers for internal use from class I (general controls) to class II (special controls) (Ref. 1). At the Panel meeting, FDA presented the risks, mitigations, and special controls identified in the proposed order.

The Panel generally agreed that the list of risks and proposed mitigations proposed by FDA was accurate and agreed with FDA that the risk profile was consistent with class II devices. Some Panel members noted that adverse tissue reaction may not be a particular risk due to the minimal patient contact duration with body tissues. Some Panel members also stated that ''increased risk of cancer recurrence'' should be removed from the list of risks, and no Panel members disagreed with that position.

The Panel generally agreed that FDA's proposed special controls are reasonable and sufficient to support reclassification of surgical staplers for internal use to class II. Some members noted that biocompatibility testing may not be needed as a special control due to the limited contact duration with tissues.

The Panel also believed that usability testing should be required, but recommended revision of the term ''labeling comprehension study'' in the special controls, since the Panel felt that the study should focus on evaluation of the labeling rather than on the user. Some Panel members felt that certain warnings in the labeling special controls, such as ''establishing and maintaining proximal control of blood vessels prior to stapling'' and ''avoidance of use of the stapler on large blood vessels,'' should be removed, as they believed the labeling should allow the surgeon to exercise their own clinical judgement rather than dictating surgical practice. One Panel member additionally implied that the term ''large blood vessels'' is vague.

Some Panel members believed that a registry could be helpful as part of the special controls, but there was a divergence of opinion on the need for a registry as part of device reclassification and the ultimate utility of the data that would likely be collected.

The Panel also discussed unique sterility considerations regarding powered staplers. The Panel also discussed additional special controls that they believed were necessary for powered surgical staplers such as electrical safety and electromagnetic compatibility testing and software verification and validation. The Panel expressed the view that powered staplers should meet these requirements.

Based upon the available scientific evidence and risks to health posed by surgical staplers for internal use, the Panel unanimously recommended the reclassification of surgical staplers for internal use from class I (general controls) to class II (special controls), agreeing with FDA's conclusion that general controls by themselves were insufficient to provide reasonable assurance of safety and effectiveness.

B. FDA Response to Panel Feedback and Changes in the Final Order

The Panel agreed with FDA in recommending the reclassification of surgical staplers for internal use from class I (general controls) to class II (special controls). The Panel generally agreed with the risks to health identified by FDA and the applicable special controls associated with the identified risks. FDA's responses to the recommendations are detailed in this section. As discussed in detail in sections III and IV below, FDA also considered comments from industry, professional societies, and stakeholders in developing the special controls in this final order. However, here in section II, we specifically address the Panel recommendations and FDA's response.

1. Risks

The Panel recommended removing increased risk of cancer recurrence and adverse tissue reaction from the risks to health presented at the Panel meeting. While surgical stapler malfunctions have resulted in complications such as anastomotic leaks, which have been associated with an increased risk of cancer recurrence, FDA agrees that there is limited evidence directly linking surgical stapler failure or malfunction with an increased risk of cancer recurrence (Refs. 2- 4). Therefore, due to the limited evidence directly linking surgical stapler failure or malfunction with an increased risk of cancer recurrence, FDA agrees with removing increased risk of cancer recurrence from the list of complications associated with device failure/malfunction. FDA does not agree that adverse tissue reaction should be removed as a risk to health, as staplers for internal use contain patient-contacting materials that contact internal tissues, and these patient-contacting device materials may pose a risk of adverse tissue reaction if not adequately demonstrated to be biocompatible. The demonstration of biocompatibility for these devices is consistent with our approach for other devices with similar type and duration of contact; therefore, FDA has not removed the applicable special control regarding biocompatibility (Ref. 5).

The Panel had specifically been asked to consider additional risks posed by powered staplers that were not identified in the proposed order. The Panel noted that the risks associated with sterility are different for non-powered staplers, which are generally packaged sterile, and powered staplers, part of which must be reprocessed.

2. Special Controls

The Panel discussed and provided recommendations regarding the biocompatibility, labeling comprehension study, labeling, and sterility special controls identified in the proposed order. The Panel also discussed the possible addition of special controls regarding use of registries and powered staplers.

As discussed above in section II.B.1., FDA has not removed the special control regarding biocompatibility since surgical staplers for internal use contain patient-contacting device materials that may pose a risk of adverse tissue reaction if not adequately demonstrated to be biocompatible.

FDA acknowledges and agrees with the Panel's recommendation that ''labeling comprehension'' testing should focus on evaluation of the clarity of the labeling rather than on the user's comprehension of the labeling. In response to the Panel's recommendation to revise the term ''labeling comprehension study'' in the special controls, FDA notes that the term ''labeling comprehension study'' is commonly used when referring to a study assessing the extent to which the labeling conveys the intended message to the user, such that the user can understand and apply this information when making decisions regarding device selection and use. However, a labeling comprehension study may not be the only way to assess how well the labeling results in use of the device as intended, therefore we are revising this special control to use the term ''human factors testing'' in place of ''usability testing and labeling comprehension study.'' FDA continues to find that such human factors testing is necessary to mitigate the risk of complications associated with use error or improper device selection and use specifically related to device labeling.

Based, in part, on feedback from the Panel that the labeling should allow surgeons to exercise their own clinical judgement, FDA has made several edits to the labeling special controls. FDA has revised the warning regarding ''establishing and maintaining proximal control of blood vessels'' to state ''establishing proximal control of blood vessels prior to stapling where practical'' and to also include ''methods of blood vessel control in the event of stapler failure.'' FDA has revised the warning regarding ''avoidance of use of the stapler on large blood vessels, such as the aorta'' to state ''avoidance of use of the stapler on the aorta.'' FDA has also removed the requirement to include specific user instructions for evaluation of the resultant staple line from the labeling special controls.

While the Panel had a distinct discussion on the possible addition of registries as a special control, use of registries was not added as a special control due in part to the divergence of the Panel's opinion on the necessity for a registry as part of device reclassification. While FDA acknowledges that use of registries may be helpful in understanding the performance of these devices, FDA determines that mandating the use of registries is not needed to provide a reasonable assurance of the safety and effectiveness of surgical staplers for internal use.

Finally, the Panel did not disagree with FDA's request to consider the inclusion of specific special controls for powered surgical staplers for internal use. Special controls regarding electrical safety, electromagnetic compatibility, software verification, validation, and hazard analysis for powered staplers have been added accordingly. While FDA acknowledges that powered staplers may have unique sterility considerations as discussed by the Panel, FDA notes that all surgical staplers, both manual and powered, must be demonstrated to be sterile. Therefore, the special control regarding sterility (''Performance data must demonstrate the sterility of the device'') remains unchanged.

III. Comments on the Proposed Order and FDA Response to Comments

A. Introduction

In response to the April 24, 2019, proposed order (84 FR 17116), FDA received seven sets of comments to the docket for the proposed order (FDA–2019–N–1250), some of which contain one or more comments on more than one issue. In addition, FDA received two sets of public comments to the docket for FDA's draft guidance, ''Surgical Staplers and Staples for Internal Use—Labeling Recommendations'' (FDA–2019–D–1262) that contained one or more comments regarding the proposed order. Collectively, these comments originated from individual consumers, academia, healthcare professionals, healthcare associations, and industry. All commenters support the proposed reclassification of surgical staplers for internal use, and a few expressed concerns regarding specific special controls, which we address in section B. below.

Additionally, FDA received some comments to the docket for the proposed order that are regarding FDA's ''Draft Surgical Staplers and Staples for Internal Use—Labeling Recommendations'' guidance. Elsewhere in this issue of the **Federal Register**, FDA is publishing a notice of availability for the final ''Surgical Staplers and Staples for Internal Use—Labeling Recommendations'' guidance. These comments were considered in the finalization of this guidance. As discussed below, FDA intends for the ''Surgical Staplers and Staples for Internal Use—Labeling Recommendations'' guidance to provide recommendations to help manufacturers comply with the labeling special controls. As such, FDA has utilized the ''Surgical Staplers and Staples for Internal Use—Labeling Recommendations'' guidance to provide additional clarification, where appropriate.

The order of response to the commenters is purely for organizational purposes and does not signify the comment's value or importance nor the order in which comments were received. Certain comments are grouped together under a single number because the subject matter is similar.

B. Description of Comments and FDA Response

(Comment 1) Some commenters shared their own personal experiences with surgical staplers for internal use, such as adverse events experienced during surgeries, types of malfunctions encountered with surgical staplers, or best practices taken to help ensure safety of surgical staplers. One of these commenters encouraged FDA to put into effect whatever additional safety measures it sees fit to make surgical staplers for internal use safer.

(Response 1) FDA notes that, as discussed in the proposed order, malfunctions and misuse associated with surgical staplers for internal use have resulted in serious adverse events, including deaths. FDA determines that reclassifying surgical staplers for internal use from class I to class II, establishing special controls, and requiring premarket review will help ensure a reasonable assurance of safety and effectiveness for these devices.

(Comment 2) One commenter requested that FDA consider establishing requirements to make public announcements about large scale problems with medical devices.

(Response 2) Requiring public announcements about large scale problems with medical devices falls outside the scope of FDA's reclassification of surgical staplers for internal use described in this final order. Nonetheless, FDA routinely posts

Medical Device Safety Communications to describe FDA's analysis of a current issue or problem and provide specific regulatory approaches and clinical recommendations for patient management. FDA's publicly available Medical Device Reporting Database includes information on devices that may have malfunctioned or caused a death or serious injury. Likewise, FDA's publicly available Medical Device Recalls database provides information on medical device recalls. In addition, FDA posts consumer information about Class I and some Class II and III recalls on its website in order to ensure that patients are aware of the seriousness of the potential health hazard posed by exposure to the product.

(Comment 3) Some commenters discussed the benefits of surgical staplers for internal use, such as decreasing operative time, reducing surgical variability, and enabling more complex surgical procedures. Some commenters stated that the risks of the device need to be considered against these benefits, and that the number of adverse events need to be considered in the context of the large number of surgical procedures performed using these devices.

(Response 3) FDA agrees that surgical staplers for internal use offer many important benefits, and that the risks of these devices need to be considered against their benefits. As described in the proposed order, FDA set forth the proposed reclassification and a substantive summary of the valid scientific evidence, including the public health benefits of the use of the device, and the nature and incidence of the risks of the device. Based on our analysis of the benefits and risks posed by surgical staplers for internal use, FDA determines that general controls on their own are insufficient to provide reasonable assurance of safety and effectiveness. The special controls identified in this final order, together with general controls, are necessary to provide a reasonable assurance of safety and effectiveness for surgical staplers for internal use, and as such, class II is the more appropriate classification for these devices.

(Comment 4) Similar to the Panel's feedback, some commenters felt that increased risk of cancer recurrence should be removed from the list of risks to health due to lack of evidence associating surgical staplers for internal use with an increased risk of cancer recurrence.

(Response 4) As discussed above, in section II. B., while surgical stapler malfunctions have resulted in complications such as anastomotic leaks, and anastomotic leaks have been associated with an increased risk of cancer recurrence, FDA agrees that there is limited evidence directly linking surgical stapler failure/malfunction with an increased risk of cancer recurrence (Refs. 2–4). Therefore, FDA agrees with removing increased risk of cancer recurrence from the list of complications associated with device failure/malfunction in the risks to health.

(Comment 5) Similar to the Panel's feedback, some commenters felt that adverse tissue reaction should be removed as a risk to health associated with surgical staplers for internal use, as the stapler only has incidental contact with the patient.

(Response 5) As discussed above, in section II.B., FDA does not agree that adverse tissue reaction should be removed as a risk to health, as staplers for internal use contain patient-contacting materials that contact internal tissues, and these patient-contacting device materials may pose a risk of adverse tissue reaction if not adequately demonstrated to be biocompatible. The demonstration of biocompatibility for these devices is consistent with our approach for other devices with similar type and duration of contact, therefore the associated special control has also been maintained (Ref. 5).

(Comment 6) Some commenters requested that FDA work collaboratively with industry and professional societies to develop the special controls (*e.g.,* specific language for warnings) and to develop a uniform color coding system for all stapler reloads.

(Response 6) FDA has considered extensive comments from industry, professional societies, and other stakeholders in developing the special controls in this final order. While color coding is helpful and FDA would support development of a uniform color coding system if it came from a consensus body, FDA believes that the special controls in this final order, together with general controls, are sufficient to provide a reasonable assurance of safety and effectiveness for surgical staplers for internal use.

(Comment 7) One commenter stated that the special controls for surgical staplers for internal use should be established in accordance with least burdensome principles.

(Response 7) As stated in FDA's guidance, ''The Least Burdensome Provisions: Concepts and Principles,'' FDA defines ''least burdensome'' to be the minimum amount of information necessary to adequately address a relevant regulatory question or issue through the most efficient manner at the right time (Ref. 6). FDA used the least burdensome approach in weighing the risks of surgical staplers for internal use with their benefits. FDA finds that the special controls identified in this final order represent the minimum amount of information necessary to provide a reasonable assurance of the safety and effectiveness of these devices.

(Comment 8) One commenter felt that the proposed performance testing special controls represented a reasonable approach for evaluating the safety and effectiveness of surgical staplers for internal use, but that greater specifics regarding the standards, methods, and relevance of the proposed testing controls are needed to fully evaluate the proposed special controls.

(Response 8) FDA agrees that the performance testing special controls identified in this final order are necessary to provide a reasonable assurance of the safety and effectiveness for these devices. FDA notes that the performance testing special controls are stated broadly to allow flexibility in different approaches in complying with the special controls.

(Comment 9) Some commenters noted that firing force is an important parameter for manual surgical staplers for internal use, but is not applicable to powered surgical stapler devices.

(Response 9) FDA agrees that firing force is an important parameter applicable to manual surgical staplers for internal use and is not applicable to powered surgical staplers. Therefore, FDA has revised the performance testing special controls to include measurement of the worst-case deployment pressures on stapler firing force specifically for manual staplers.

(Comment 10) Similar to the Panel's feedback, some commenters noted the importance of ensuring that the product labeling and instructions for use do not interfere with clinical decision making and a physician's ability to exercise his or her professional judgement. The commenters noted that too much information in the product labeling can make the labeling difficult to read, reducing its value to physicians, and provided a general recommendation to make the labeling special controls less prescriptive.

(Response 10) As discussed above, in section II, regarding the Panel's discussion of the proposed special control for a labeling comprehension study, FDA acknowledges the concern that too much information in the product labeling can make the labeling difficult to read, and that it is important for the labeling to be clear for the user. However, FDA also notes that, as

discussed in the proposed order, there have been a large number of adverse events associated with use of both surgical staplers and staples for internal use; both device misuse and device malfunctions are root causes of these adverse events. Therefore, FDA finds it is essential to communicate specific information about the risks, limitations, and directions for use in the labeling for surgical staplers and staples for internal use to lower the risk of occurrence of these adverse events and to promote safe and effective use of these devices.

As discussed separately in the responses to the comments below in section IV, FDA has chosen to remove or revise certain labeling special controls in an effort to allow for physician discretion as discussed with the Panel, but we continue to conclude that other labeling special controls are necessary to provide a reasonable assurance of the safety and effectiveness of these devices.

(Comment 11) Some commenters felt that the contraindication that the device should not be used to staple tissues that are necrotic, friable, or have altered integrity should be removed from the stapler labeling as it extends into the realm of surgical practice and involves the application of medical judgement that should be left to trained surgeons.

(Response 11) FDA disagrees that the contraindication regarding stapling of tissues that are necrotic, friable, or have altered integrity should be removed from the labeling. FDA notes that application of staples to tissues that are necrotic, friable, or have altered integrity has resulted in complications such as, but not limited to, tissue damage, anastomotic leakage, bleeding, abscess, sepsis, peritonitis, and hemorrhage. To FDA's knowledge, there is no known benefit of applying surgical staples to tissues that are necrotic, friable, or have altered integrity. Therefore, FDA determines that the risk of stapling tissues that are necrotic, friable, or have altered integrity outweighs any reasonably foreseeable benefit due to known complications. FDA finds that this contraindication is necessary to mitigate the risks of complications associated with improper device use and to provide a reasonable assurance of the safety and effectiveness of these devices.

(Comment 12) One commenter felt that the warning to visually inspect for inclusion of unintended anatomic structures within the staple line should be removed from the stapler labeling as it extends into the realm of surgical practice and involves the application of medical judgement that should be left to trained surgeons.

(Response 12) FDA disagrees that the warning regarding avoidance of obstructions to the creation of the staple line and the unintended stapling of other anatomic structures should be removed from the labeling. As noted in the proposed order, obstructions to the creation of the staple line and unintended stapling of anatomic structures have been associated with known hazards. For example, FDA has received medical device reports where obstructions to the staple line and/or unintended stapling of anatomic structures have resulted in anastomotic leaks and other injuries. Therefore, FDA finds that this warning is necessary to mitigate the risks of complications associated with improper device use and to provide a reasonable assurance of the safety and effectiveness of these devices.

(Comment 13) Similar to the Panel discussion, some commenters felt that the warning to establish and maintain adequate proximal control of blood vessels prior to stapling should be removed from the stapler labeling as it extends into the realm of surgical practice and involves the application of medical judgement that should be left to trained surgeons.

(Response 13) FDA disagrees that the warning to establish and maintain adequate proximal control of blood vessels prior to stapling should be removed entirely, as it is important to have methods of blood vessel control in place in the event of stapler failure to prevent the risk of uncontrolled bleeding. However, FDA acknowledges there are situations where it may not be practical to establish proximal control of blood vessels prior to stapling. Therefore, FDA has revised the labeling special control to include a warning regarding the establishment of proximal control of blood vessels prior to stapling ''where practical'' and establishment of ''methods of blood vessel control in place in the event of stapler failure.'' FDA finds that this warning is necessary to mitigate the risks of complications associated with improper device use and to provide a reasonable assurance of the safety and effectiveness of these devices.

(Comment 14) One commenter felt that the warning that clamping and unclamping of delicate tissue structures, such as venous structures and bile ducts, may result in damage to tissue irrespective of stapler firing, should be removed from the stapler labeling as it extends into the realm of surgical practice and involves the application of medical judgement that should be left to trained surgeons.

(Response 14) FDA disagrees that the warning regarding avoidance of clamping and unclamping of delicate tissue structures should be removed from the labeling. As discussed in the proposed order, clamping and unclamping of delicate tissue structures have been associated with known hazards such as tissue damage. For example, FDA has received medical device reports where clamping of the stapler has resulted in tissue damage or bleeding. As also noted in FDA's Letter to Health Care Providers, ''Safe Use of Surgical Staplers and Staples,'' clamping of staplers on delicate tissue can cause injury even if no staples are fired (Ref. 7). Therefore, FDA finds that this warning is necessary to mitigate the risks of complications associated with improper device use and to provide a reasonable assurance of the safety and effectiveness of these devices.

(Comment 15) Some commenters felt that the warning regarding measures to take if a stapler malfunction occurs while applying staples across a blood vessel, including clamping or ligating the vessel before releasing the stapler, while the stapler is still closed on the tissue, should be removed from the stapler labeling as it extends into the realm of surgical practice and involves the application of medical judgement that should be left to trained surgeons.

(Response 15) FDA agrees that the warning regarding ''clamping or ligating the vessel before releasing the stapler, while the stapler is still closed on the tissue'' may be too prescriptive and has removed this from the labeling special controls. Nonetheless, FDA continues to find that it is important to have methods of blood vessel control in place in the event of stapler failure in order to prevent the risk of uncontrolled bleeding. Therefore, FDA has modified the remainder of the labeling special controls to add a warning regarding methods of blood vessel control in the event of stapler failure. FDA finds that this warning is necessary to mitigate the risks of complications associated with improper device use and to provide a reasonable assurance of the safety and effectiveness of these devices.

(Comment 16) Consistent with the Panel discussion, commenters requested revision or removal of the warning regarding ''avoidance of use of the stapler on large blood vessels, such as the aorta.'' Some commenters felt that the term ''large blood vessels'' is vague and recommended revising the statement to warn specifically against stapling the aorta. Some commenters noted that many surgical staplers are contraindicated for use on the aorta and felt that this statement should only be

included as a warning if it is not already included as a contraindication. Other commenters felt that this statement should be removed from the labeling, since it extends into the realm of surgical practice and involves the application of a surgeon's medical judgement.

(Response 16) FDA agrees that use of the term ''large blood vessels'' may be subject to interpretation and has revised the special control to remove ''avoidance of use of the stapler on large blood vessels'' to leave more room for surgeon judgement, which FDA believes is appropriate here. Nonetheless, FDA has retained the warning regarding ''avoidance of use of the stapler on the aorta.'' As discussed at the Panel meeting, FDA has received several medical device reports where stapling the aorta has resulted in serious adverse events, such as significant blood loss. Based on a benefit risk analysis, as well as information received from medical device reports, FDA finds that the risk of stapling the aorta outweighs the risk of stapling other large blood vessels. Therefore, FDA finds that a warning regarding avoidance of use of the stapler on the aorta is necessary to mitigate risks of complications associated with improper device use and to ensure a reasonable assurance of safety and effectiveness of these devices.

(Comment 17) One commenter noted that premarket testing for staple line integrity provides important information for assessing the safety and effectiveness of surgical staplers. Nonetheless, some commenters felt that the procedures for evaluating staple line integrity should not be included in the directions for use, as these procedures extend into the realm of surgical practice and may differ depending on different circumstances (*e.g.,* patient conditions, tissue types, surgeon's training and experience).

(Response 17) FDA agrees that premarket testing for staple line integrity provides important information for assessing the safety and effectiveness of surgical staplers for internal use. Therefore, confirmation of staple line integrity remains as a performance testing special control. FDA acknowledges that procedures for evaluating staple line integrity may differ depending on different circumstances. Therefore, FDA has removed the requirement to include specific user instructions for evaluation of the resultant staple line from the labeling special controls.

(Comment 18) One commenter felt that the warning to ensure stapler compatibility with staples is unnecessary, since the labeling of the device must include a list of staples with which the stapler has been demonstrated to be compatible.

(Response 18) Even with a list of compatible staples present in the labeling, it is possible that a user may still try to use the stapler with an incompatible staple if a warning to ensure stapler compatibility with staples is not present. Therefore, consistent with the proposed order, FDA continues to find that the warning to ensure stapler compatibility with staples is necessary to mitigate the risk of complications associated with improper device use and to ensure a reasonable assurance of safety and effectiveness of these devices.

(Comment 19) One commenter felt that the warning to ensure avoidance of obstructions to the creation of the staple line should not be included in the labeling, since clinical circumstances exist in which it may be necessary or appropriate to staple across an obstruction, *e.g.,* a prior staple line.

(Response 19) As noted in response 12 above, stapling across obstructions have been associated with risks such as anastomotic leaks and other injuries. While FDA acknowledges there may be clinical circumstances when a surgeon may deem it necessary or appropriate to cross staple lines, FDA notes that additional types of obstructions beyond prior staple lines exist (*e.g.,* clips, ligatures, drainage tubes), and that such obstructions should be avoided due to the associated risks. Therefore, FDA finds that the warning to ensure avoidance of obstructions to the creation of the staple line should be included in the labeling to mitigate the risk of complications associated with improper device use and to ensure a reasonable assurance of safety and effectiveness of these devices. As noted below, FDA has additionally revised the special controls to include a labeling requirement for a warning regarding risks of crossing staple lines in response to a comment recommending the addition of such a warning in the docket for FDA's draft guidance, ''Surgical Staplers and Staples for Internal Use—Labeling Recommendations'' (FDA–2019–D–1262).

(Comment 20) One commenter noted that premarket testing for staple line strength provides important information for assessing the safety and effectiveness of surgical staplers. Nonetheless, some commenters noted that there are no standardized test methods for evaluating staple line strength (*e.g.,* burst strength). These commenters felt that staple line strength (*e.g.,* burst strength) should not be included in the device labeling until standardized testing methodology is developed.

(Response 20) FDA agrees that premarket testing for staple line strength provides important information for assessing the safety and effectiveness of surgical staplers for internal use. Therefore, measurement of staple line strength remains as a performance testing special control.

For the reasons discussed in the proposed order, FDA finds that the labeling must include identification of key performance parameters and technical characteristics of the stapler and compatible staples needed for safe use of the device. The commenters' recommendations regarding removing staple line strength from product labeling due to lack of standardized methodology were considered in the finalization of FDA's ''Surgical Staplers and Staples for Internal Use—Labeling Recommendations'' guidance, which provides FDA's recommendations regarding key performance parameters and technical characteristics that should be included in the labeling for surgical staplers. At this time, due to the lack of standardized testing methodology for evaluating staple line strength, FDA revised the final guidance to remove staple line strength from the list of recommendations for labeling of key technical characteristics and performance parameters.

(Comment 21) One commenter noted that premarket testing for staple formation provides important information for assessing the safety and effectiveness of surgical staplers. Nonetheless, some commenters noted that there are no standardized test methods for evaluating the percentage of properly formed staples at the maximum and minimum tissue thickness. These commenters felt that percentage of properly formed staples at the maximum and minimum tissue thickness should not be included in the device labeling until standardized testing methodology is developed.

(Response 21) FDA agrees that premarket testing for staple formation provides important information for assessing the safety and effectiveness of surgical staplers for internal use. Therefore, evaluation of staple formation characteristics in the maximum and minimum tissue thicknesses for each staple type remains as a performance testing special control.

In addition, FDA finds that the labeling must include identification of key performance parameters and technical characteristics of the stapler and compatible staples needed for safe use of the device. FDA's ''Surgical Staplers and Staples for Internal Use—

Labeling Recommendations'' Guidance provides FDA's recommendations regarding key performance parameters and technical characteristics to include in the labeling for surgical staplers. The commenters' recommendations regarding percentage of properly formed staples were considered in the finalization of the guidance. Specifically, ''percentage of properly formed staples at the maximum and minimum tissue thickness'' was removed from the list of recommended key performance parameters and technical characteristics due to the lack of standardized test methodology for evaluating these parameters.

(Comment 22) One commenter asked FDA to clarify what is meant by ''safety mechanisms'' for surgical staplers for internal use.

(Response 22) FDA has provided examples and clarification for what is meant by ''safety mechanisms'' for surgical staplers for internal use in FDA's ''Surgical Staplers and Staples for Internal Use—Labeling Recommendations'' guidance. Specifically, the final guidance states that safety mechanisms include ''*e.g.,* identification of whether a stapler has built-in methods for assessing and/or limiting operation when the underlying tissues are outside of a predefined range.'' ''Lock-out'' and ''color firing zone'' are two examples of safety mechanisms for surgical staplers for internal use provided in the guidance.

(Comment 23) One commenter asked FDA to revise the labeling special control regarding inclusion of specific user instructions for ''evaluation of the appropriateness of the target tissue for stapling'' to include examples of procedures that may be used for determining that a tissue is appropriate for stapling, and to provide clarification for the types of target tissue. Another commenter requested that FDA remove this special control altogether, as it extends into the realm of surgical practice and involves the application of medical judgement that should be left to trained surgeons.

(Response 23) FDA does not agree that this special control should be removed, as FDA believes instructions for ''evaluation of the appropriateness of the target tissue for stapling'' are important to include within specific user instructions to reduce the risk of complications associated with improper device use. FDA has not included examples of procedures that may be used for determining that a tissue is appropriate for stapling or examples of types of tissue, since the examples of procedures and tissue types may vary depending on the design and intended use the stapler. Instead, manufacturers should identify appropriate procedures and tissue types based on the design and intended use of their own specific stapler.

(Comment 24) Some commenters requested that FDA clarify expectations for the evaluation of marketed surgical stapler products that were previously cleared. Some commenters felt that the special controls should not be retroactively applied to devices that already have been 510(k) cleared and have an established safety profile. Other commenters felt that FDA should evaluate previously cleared devices to determine if the devices and information contained in the previously cleared submissions meet the new special controls.

(Response 24) FDA finds that all surgical staplers for internal use, including previously cleared devices and new devices, must comply with the special controls identified in this final order to ensure a reasonable assurance of safety and effectiveness for these devices. Manufacturers should refer to section V (Implementation Strategy) of this final order for information on dates when FDA intends to enforce compliance with the final order. It is the manufacturer's responsibility to ensure compliance with applicable laws and regulations administered by FDA. Manufacturers should refer to FDA's guidance, ''Deciding When to Submit a 510(k) for a Change to an Existing Device'' (Ref. 8) to determine whether a new 510(k) is required for changes to an existing device.

IV. Changes in the Final Order

FDA is adopting the majority of our findings under section 513(e) of the FD&C Act, as published in the preamble to the proposed order (84 FR 17116). For the reasons described previously in sections II and III, FDA has made revisions in this final order in response to feedback from the Panel and comments regarding the proposed order that were submitted to public dockets.

Based, in part, on the Panel feedback and comments to the proposed reclassification order, FDA is issuing the following revised list of risks and Risks to Health and Risk Mitigation Table (table 1). The list reflects the addition of risks specific to powered staplers and the removal of ''increased risk of cancer recurrence'' as a risk:

- *Complications associated with device failure/malfunction.* Device failures or malfunctions may result in prolonged surgical procedures, unplanned surgical interventions, and other complications such as bleeding, sepsis, fistula formation, tearing of internal tissues and organs, and death. Additionally, for powered staplers, faulty hardware or software may cause electrical hazards or electromagnetic interference with other devices, such as the risk of interference with operating monitors, misfiring or locking of the stapler.
- *Complications associated with use error/improper device selection and use.* Use error may result from a device design that is difficult to operate and/or labeling that is difficult to comprehend. For example, user difficulty in firing the stapler may result in staples not being fully deployed, and misfiring may result in staples being inadvertently applied to the wrong tissue. Inadequate instructions for use may result in selection of incorrectly sized staples for the target tissue. When staples are applied to the wrong tissue or when incorrectly sized staples are applied, staples are unable to properly approximate the underlying tissue, resulting in tissue damage, anastomotic leakage, and bleeding. This in turn, may lead to more severe complications, such as abscess, sepsis, peritonitis, hemorrhage, or death.
- *Adverse tissue reaction.* If the patient-contacting materials of the device are not biocompatible, local tissue irritation and sensitization, cytotoxicity, or systemic toxicity may occur when the device contacts sterile tissue.
- *Infection.* If the device is not adequately reprocessed or sterilized, the device may introduce pathogenic organisms into sterile tissue and may cause an infection in a patient.

TABLE 1—RISKS TO HEALTH AND MITIGATION MEASURES FOR SURGICAL STAPLERS FOR INTERNAL USE

Identified risks to health	Mitigation measures
Complications associated with device failure/malfunction	Performance testing; Labeling; and for powered staplers only: Electrical, thermal, and mechanical safety testing; Electromagnetic compatibility testing; Software validation, verification, and hazard analysis.

TABLE 1—RISKS TO HEALTH AND MITIGATION MEASURES FOR SURGICAL STAPLERS FOR INTERNAL USE—Continued

Identified risks to health	Mitigation measures
Complications associated with use error/improper device selection and use.	Human Factors testing and Labeling.
Adverse Tissue Reaction	Biocompatibility evaluation.
Infection	Labeling, Sterility testing, and Shelf-Life Testing.

FDA modified the special controls to provide additional specificity regarding manual and powered staplers, where appropriate. Specifically, FDA modified the performance testing special controls to include clarification that measurement of worst-case deployment pressures on stapler firing force is applicable only to manual staplers (see § 878.4740(b)(2)(i)(B)). FDA added special controls for powered staplers regarding electrical safety, electromagnetic compatibility, software verification, validation, and hazard analysis (see § 878.4740(b)(2)(ii) and (b)(2)(iii)).

FDA also modified the special controls to refine certain labeling requirements. Specifically, FDA modified the requirement for a warning regarding ''establishing and maintaining proximal control of blood vessels prior to stapling'' to ''Establishing proximal control of blood vessels prior to stapling where practical'' (see § 878.4740(b)(2)(ix)(B)(*v*)). FDA replaced the requirement for a warning regarding ''appropriate measures to take if a stapler malfunction occurs while applying staples across a blood vessel, such as clamping or ligating the vessel before releasing the stapler, while the stapler is still closed on the tissue'' with the requirement for a warning regarding ''methods of blood vessel control in the event of stapler failure.'' (see § 878.4740(b)(2)(ix)(B)(*v*)). These edits were made for the reasons described above, including feedback from the Panel and commenters regarding instances where labeling should provide flexibility for a physician to exercise his or her professional judgement. FDA modified the requirement for a warning regarding ''avoidance of use of the stapler on large blood vessels, such as the aorta'' to a warning regarding ''avoidance of use of the stapler on the aorta'' (see § 878.4740(b)(2)(ix)(B)(i*v*)) in response to comments that use of the term ''large blood vessels'' is vague. FDA has also revised the special controls to remove the requirement for specific user instructions associated with ''evaluation of the resultant staple line'' (see § 878.4740(b)(2)(ix)(C)) in response to comments that procedures for evaluating staple line integrity may differ depending on different circumstances.

Elsewhere in this issue of the **Federal Register**, FDA is publishing a notice of availability for the final guidance, ''Surgical Staplers and Staples for Internal Use—Labeling Recommendations.'' FDA made additional revisions in this final order to reflect changes made during finalization of the guidance based on the feedback specifically on that document to the guidance docket. Specifically, FDA revised the special controls to include a labeling requirement for a warning regarding the risks of crossing staple lines (see § 878.4740(b)(2)(ix)(B)(*vii*)) in response to a comment recommending the addition of such a warning to the guidance. FDA notes that a risk of increased leak rates when staple lines are crossed has been commonly reported in the medical literature (Refs. 9 and 10). Therefore, FDA finds that this warning is necessary to mitigate the risks of complications associated with improper device use and to provide a reasonable assurance of the safety and effectiveness of these devices.

In response to a comment recommending removal of the contraindication for stapling of ''tissues outside the labeled limits of tissue thickness'' from the guidance, FDA revised the special controls to change this contraindication to a warning (see § 878.4740(b)(2)(ix)(B)(*i*)). FDA has changed the contraindication regarding stapling ''tissues outside the labeled limits for maximum and minimum tissue thickness'' to a warning instead of a contraindication so as not to impinge on surgeon judgement and since there is currently no standardized mechanism to accurately measure tissue thickness intraoperatively. Nonetheless, FDA notes that stapling of tissues outside labeled limits has been associated with serious adverse events, such as anastomotic leakage and bleeding, in medical device reports. Therefore, FDA finds that a warning regarding stapling tissues outside labeled limits is necessary to mitigate the risks of complications associated with improper device use and to provide a reasonable assurance of the safety and effectiveness of these devices.

FDA also modified the contraindication regarding ''stapling of necrotic or ischemic tissues'' to ''stapling of tissues that are necrotic, friable, or have altered integrity'' to promote consistency with the language used in the guidance (see § 878.4740(b)(2)(ix)(A)). FDA notes that ''necrotic or ischemic tissues'' are a subset of ''tissues that are necrotic, friable, or have altered integrity.'' As explained above, FDA has determined that the risk of stapling tissues that are necrotic, friable, or have altered integrity outweighs any reasonably foreseeable benefit due to known complications.

FDA is issuing this final order revising § 878.4800 by removing the classification of surgical staplers and codifying surgical staplers in the new 21 CFR 878.4740, under which surgical staplers for internal use is classified into class II with special controls and surgical staplers for external use remain in class I, exempt from premarket notification. In this final order, we have identified the special controls under section 513(a)(1)(B) of the FD&C Act that, together with general controls, provide a reasonable assurance of the safety and effectiveness for surgical staplers for internal use.[1]

FDA may exempt a class II device from the premarket notification requirements, under section 510(m) of the FD&C Act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the devices. FDA has determined that premarket notification is necessary to provide reasonable assurance of safety and effectiveness of surgical staplers for internal use, and therefore, this device type is not exempt from premarket notification requirements.

The device is assigned the generic name surgical stapler for internal use,

[1] FDA notes that the ''ACTION'' caption for this final order is styled as ''Final amendment; final order,'' rather than ''Final order.'' Beginning in December 2019, this editorial change was made to indicate that the document ''amends'' the Code of Federal Regulations. The change was made in accordance with the Office of Federal Register's (OFR) interpretations of the Federal Register Act (44 U.S.C. chapter 15), its implementing regulations (1 CFR 5.9 and parts 21 and 22), and the Document Drafting Handbook.

and it is identified as a specialized prescription device used to deliver compatible staples to internal tissues during surgery for resection, transection, and creating anastomoses.

V. Implementation Strategy

The order is effective on its date of publication in the **Federal Register**.

- Surgical staplers for internal use that have not been offered for sale prior to the effective date of the final order or have been offered for sale but are required to submit a new 510(k) under 21 CFR 807.81(a)(3): Manufacturers would have to obtain 510(k) clearance before marketing their devices after the effective date of the order. If a manufacturer markets such a device without receiving 510(k) clearance, then FDA would consider taking action against such a manufacturer under its usual enforcement authorities and policies.
- Surgical staplers for internal use that have been offered for sale prior to the effective date of the final order and do not already have 510(k) clearance: FDA does not intend to enforce compliance with the 510(k) requirement or special controls until 180 days after the effective date of the final order. After that date, if a manufacturer continues to market such a device but does not have 510(k) clearance or FDA determines that the device is not substantially equivalent or not compliant with special controls, then FDA would consider taking action against such manufacturer under its usual enforcement authorities and policies.

For surgical staplers for internal use that have prior 510(k) clearance, FDA would accept a new 510(k) and would issue a new clearance letter, as appropriate, indicating substantial equivalence and special controls compliance. These devices could serve as predicates for new devices. These clearance letters would be made publicly available in FDA's 510(k) database, and compliance with special controls at the time of clearance would also be stated in the publicly available 510(k) Summary posted in this database. FDA notes that our public database is a transparent tool allowing users to confirm that their devices have been submitted under a new 510(k) and demonstrated conformance to applicable special controls.

VI. Analysis of Environmental Impact

We have determined under 21 CFR 25.34(b) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VII. Paperwork Reduction Act of 1995

This administrative order establishes special controls that refer to previously approved collections of information found in other FDA regulations and guidance. Those collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501–3521). The collections of information in 21 CFR part 807, subpart E, have been approved under OMB control number 0910–0120; the collections of information in 21 CFR part 820 have been approved under OMB control number 0910–0073; and the collections of information under 21 CFR part 801 have been approved under OMB control number 0910–0485.

VIII. Codification of Orders

Prior to the amendments by FDASIA, section 513(e) of the FD&C Act provided for FDA to issue regulations to reclassify devices. Although section 513(e) as amended requires FDA to issue final orders rather than regulations, it also provides for FDA to revoke previously issued regulations by order. FDA will continue to codify classifications and reclassifications in the Code of Federal Regulations (CFR). Changes resulting from final orders will appear in the CFR as changes to codified classification determinations or as newly codified orders. Therefore, under section 513(e)(1)(A)(i), as amended by FDASIA, in the final order, we are revising 21 CFR 878.4800 to remove the classification of surgical staplers and codifying surgical staplers in the new 21 CFR 878.4740, under which surgical staplers for internal use would be reclassified into class II and surgical staplers for external use would remain in class I, exempt from premarket notification.

IX. References

The following references marked with an asterisk (*) are on display at the Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240–402–7500; and are available for viewing by interested persons between 9 a.m. and 4 p.m., Monday through Friday; they also are available electronically at *https://www.regulations.gov.* References without asterisks are not on public display at *https://www.regulations.gov* because they have copyright restriction. Some may be available at the website address, if listed. References without asterisks are available for viewing only at the Dockets Management Staff. FDA has verified the website addresses, as of the date this document publishes in the **Federal Register**, but websites are subject to change over time.

*1. FDA, May 30, 2019, Meeting of the General and Plastic Surgery Devices Panel Meeting Materials (available at *https://www.fda.gov/advisory-committees/advisory-committee-calendar/may-30-31-2019-general-and-plastic-surgery-devices-panel-medical-devices-advisory-committee-meeting*).

2. Folkesson, J., J. Nilsson, L. Påhlman, et al., ''The Circular Stapling Device as a Risk Factor for Anastomotic Leakage.'' *Colorectal Disease.* 2004 July; 6(4):275–9.

3. Ouchi, A., A. Masahiko, K. Aono, et al., ''Staple-Line Recurrence Arising 10 Years After Functional End-to-End Anastomosis for Colon Cancer: A Case Report.'' *Surgical Case Reports.* 2015 December; 1:7.

4. Hsu, T.C. and M.J. Chen, ''Presence of Colon Carcinoma Cells at the Resection Line May Cause Recurrence Following Stapling Anastomosis.'' *Asian Journal of Surgery.* 2018 November; 41(6):569–572.

*5. ''Guidance for Industry and Food and Drug Administration Staff: Use of International Standard ISO 10993–1, 'Biological Evaluation of Medical Devices—Part 1: Evaluation and Testing Within a Risk Management Process,' '' September 4, 2020, available at: *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-international-standard-iso-10993-1-biological-evaluation-medical-devices-part-1-evaluation-and.*

*6. ''Guidance for Industry and FDA Staff: The Least Burdensome Provisions: Concept and Principles,'' February 5, 2019, available at: *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/least-burdensome-provisions-concept-and-principles.*

*7. FDA, March 8, 2019, Letter to Health Care Providers, ''Safe Use of Surgical Staplers and Staples,'' available at: *https://www.fda.gov/medical-devices/letters-health-care-providers/safe-use-surgical-staplers-and-staples-letter-health-care-providers.*

*8. ''Guidance for Industry and Food and Drug Administration Staff: Deciding When to Submit a 510(k) for a Change to an Existing Device,'' October 25, 2017, available at: *https://www.fda.gov/regulatory-information/search-fda-guidance-documents/deciding-when-submit-510k-change-existing-device.*

9. Lee, S., B. Ahn, and S. Lee, ''The Relationship Between the Number of Intersections of Staple Lines and Anastomotic Leakage After the Use of a Double Stapling Technique in Laparoscopic Colorectal Surgery.'' *Surgical Laparoscopy, Endoscopy & Percutaneous Techniques.* 2017 August; 27(4):273–281.

10. Crafa, F., J. Megevand, G. Romano, and P. Sileri, ''New Double-Stapled

Anastomotic Technique to Avoid Crossing Staple Lines.'' *Techniques in Coloproctology.* 2015; 19: 319–320.

List of Subjects in 21 CFR Part 878

Medical devices.

Therefore, under the Federal Food, Drug, and Cosmetic Act, and under authority delegated to the Commissioner of Food and Drugs, 21 CFR part 878 is amended as follows:

PART 878—GENERAL AND PLASTIC SURGERY DEVICES

■ 1. The authority citation for part 878 continues to read as follows:

Authority: 21 U.S.C. 351, 360, 360c, 360e, 360j, 360*l,* 371.

■ 2. Add § 878.4740 to subpart E to read as follows:

§ 878.4740 Surgical stapler.

(a) Surgical stapler for external use.

(1) *Identification.* A surgical stapler for external use is a specialized prescription device used to deliver compatible staples to skin during surgery.

(2) *Classification.* Class I (general controls). The device is exempt from the premarket notification procedures in subpart E of part 807 of this chapter, subject to the limitations in § 878.9.

(b) Surgical stapler for internal use.

(1) *Identification.* A surgical stapler for internal use is a specialized prescription device used to deliver compatible staples to internal tissues during surgery for resection, transection, and creating anastomoses.

(2) *Classification.* Class II (special controls). The special controls for this device are:

(i) Performance testing must demonstrate that the stapler, when used with compatible staples, performs as intended under anticipated conditions of use. Performance testing must include the following:

(A) Evaluation of staple formation characteristics in the maximum and minimum tissue thicknesses for each staple type;

(B) For manual staplers only, measurement of the worst-case deployment pressures on stapler firing force;

(C) Measurement of staple line strength;

(D) Confirmation of staple line integrity; and

(E) In vivo confirmation of staple line hemostasis.

(ii) For powered staplers only, appropriate analysis/testing must demonstrate the electromagnetic compatibility and electrical, thermal, and mechanical safety of the device.

(iii) For powered staplers only, appropriate software verification, validation, and hazard analysis must be performed.

(iv) Human factors testing must demonstrate that the clinician can correctly select and safely use the device, as identified in the labeling, based on reading the directions for use.

(v) The elements of the device that may contact the patient must be demonstrated to be biocompatible.

(vi) Performance data must demonstrate the sterility of the device.

(vii) Validation of cleaning and sterilization instructions must demonstrate that any reusable device components can be safely and effectively reprocessed per the recommended cleaning and sterilization protocol in the labeling.

(viii) Performance data must support the shelf life of the device by demonstrating continued device functionality, sterility, and package integrity over the identified shelf life.

(ix) Labeling of the device must include the following:

(A) Unless data demonstrates the safety of doing so, contraindications must be identified regarding use of the device on tissues for which the risk of stapling outweighs any reasonably foreseeable benefit due to known complications, including the stapling of tissues that are necrotic, friable, or have altered integrity.

(B) Unless available information demonstrates that the specific warnings do not apply, the labeling must provide appropriate warnings regarding how to avoid known hazards associated with device use including:

(*1*) Avoidance of use of the stapler to staple tissue outside of the labeled limits for maximum and minimum tissue thickness;

(*2*) Avoidance of obstructions to the creation of the staple line and the unintended stapling of other anatomic structures;

(*3*) Avoidance of clamping and unclamping of delicate tissue structures to prevent tissue damage;

(*4*) Avoidance of use of the stapler on the aorta;

(*5*) Establishing proximal control of blood vessels prior to stapling where practical and methods of blood vessel control in the event of stapler failure;

(*6*) Ensuring stapler compatibility with staples; and

(*7*) Risks specifically associated with the crossing of staple lines.

(C) Specific user instructions for proper device use including measures associated with the prevention of device malfunction, and evaluation of the appropriateness of the target tissue for stapling.

(D) List of staples with which the stapler has been demonstrated to be compatible.

(E) Identification of key performance parameters and technical characteristics of the stapler and the compatible staples needed for safe use of the device.

(F) Information regarding tissues on which the stapler is intended to be used.

(G) Identification of safety mechanisms of the stapler.

(H) Validated methods and instructions for reprocessing of any reusable device components.

(I) An expiration date/shelf life.

(x) Package labels must include critical information and technical characteristics necessary for proper device selection.

■ 3. In § 878.4800, revise paragraph (a) to read as follows:

§ 878.4800 Manual surgical instrument for general use.

(a) *Identification.* A manual surgical instrument for general use is a nonpowered, hand-held, or hand-manipulated device, either reusable or disposable, intended to be used in various general surgical procedures. The device includes the applicator, clip applier, biopsy brush, manual dermabrasion brush, scrub brush, cannula, ligature carrier, chisel, clamp, contractor, curette, cutter, dissector, elevator, skin graft expander, file, forceps, gouge, instrument guide, needle guide, hammer, hemostat, amputation hook, ligature passing and knot-tying instrument, knife, blood lancet, mallet, disposable or reusable aspiration and injection needle, disposable or reusable suturing needle, osteotome, pliers, rasp, retainer, retractor, saw, scalpel blade, scalpel handle, one-piece scalpel, snare, spatula, disposable or reusable stripper, stylet, suturing apparatus for the stomach and intestine, measuring tape, and calipers. A surgical instrument that has specialized uses in a specific medical specialty is classified in separate regulations in parts 868 through 892 of this chapter.

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Dated: October 4, 2021.

Lauren K. Roth,

Associate Commissioner for Policy.

[FR Doc. 2021–22041 Filed 10–7–21; 8:45 am]

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