Contains Nonbinding Recommendations

Surgical Staplers and Staples for Internal Use - Labeling Recommendations

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Guidance for Industry and Food and Drug Administration Staff

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Preface

Public Comment

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I. Introduction

The Food and Drug Administration (FDA) is issuing this guidance to provide labeling recommendations for surgical staplers and staples for internal use. These labeling recommendations are being issued because malfunctions and misuse associated with these devices have resulted in serious adverse events, including deaths.[1]

FDA believes that the labeling recommendations in this guidance would help promote the safe and effective use of surgical staplers and staples for internal use by helping manufacturers develop labeling with information about specific risks, limitations, and directions for use of the device.[2]

The contents of this document do not have the force and effect of law and are not meant to bind the public in any way, unless specifically incorporated into a contract. This document is intended only to provide clarity to the public regarding existing requirements under the law. FDA guidance documents, including this guidance, should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidance means that something is suggested or recommended, but not required.

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[1] See e.g., FDA Manufacturer and User Facility Device Experience (MAUDE) Database, search of the product codes GDW and GAG from January 1, 2011 – March 31, 2018.

[2] In addition, FDA has finalized the reclassification of surgical staplers for internal use from class I to class II with special controls. See the final order "Reclassification of Certain Surgical Staplers" issued October 8, 2021 (86 FR 56195) available at https://www.federalregister.gov/d/2021-22041.

II. Background

Surgical staplers for internal use are specialized prescription devices used to deliver compatible staples to internal tissues during surgery for resection, transection, and creating anastomoses. Surgical staplers and staples for internal use may be indicated for use in a wide range of surgical applications, including but not limited to gastrointestinal, gynecologic, and thoracic surgery.

FDA developed the draft of this guidance because we had become aware of a large number of adverse events associated with use of both surgical staplers and staples for internal use. Between January 2011 – March 2018, FDA received over 41,000 adverse event reports associated with surgical staplers and staples for internal use, including over 360 deaths associated with the use of surgical staplers and staples for internal use.[3] Some of the most commonly reported problems in these adverse event reports include an opening of the staple line or malformation of staples, misfiring, difficulty in firing, failure of the stapler to fire the staple, and misapplied staples (e.g., user applying staples to the wrong tissue or applying staples of the wrong size to the tissue).[4,5] Although the majority of the adverse events were reported under product code GDW (Staple, Implantable), FDA believes that many of the problems identified in these reports can be primarily attributed to surgical staplers for internal use, since proper staple formation is largely contingent on proper function and use of the stapler.[7]

Stapler and/or staple malfunctions may result in prolonged surgical procedures or unplanned, additional surgical interventions, and other complications such as bleeding, sepsis, fistula formation, tearing of internal tissues and organs, and death. Common causes for complications also include the use of incorrectly sized staples for the tissue, incorrect use of the device by the user and improper use of the device for the condition of the patient's tissues, which may result in reoperation or prolonged hospitalization.[6] For example, an early postoperative anastomotic leak due to such device issues may result in a septic patient with peritonitis, requiring immediate surgery with diversion of stool into a stoma. Minor or delayed anastomotic leaks due to such device issues may result in an intra-abdominal abscess requiring surgical or other invasive drainage procedures, temporary diversion of stool, and prolonged intravenous nutrition. These complications commonly result in prolonged hospital stays.[7]

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[3] FDA Manufacturer and User Facility Device Experience (MAUDE) Database, search of the product codes GDW and GAG from January 1, 2011 – March 31, 2018.

[4] U.S. Food and Drug Administration, "Safe Use of Surgical Staplers and Staples – Letter to Health Care Providers," March 8, 2019, available at https://www.fda.gov/medical-devices/letters-health-care-providers/safe-use-surgical-staplers-and-staples-letter-health-care-providers.

[5] 84 FR 17116 (See https://www.federalregister.gov/documents/2019/04/24/2019-08260/general-and-plastic-surgery-devices-reclassification-of-certain-surgical-staplers).

[6] Checkan E, Whelan RL. Surgical stapling device-tissue interactions: what surgeons need to know to improve patient outcomes. Med Devices (Auckl). 2014; 7:305-318.

[7] Betzold R, Laryea JA. Staple Line/Anastomotic Reinforcement and Other Adjuncts: Do They Make a Difference? Clin Colon Rectal Surg. 2014 Dec; 27(4): 156-161.

Both device misuse and device malfunctions are root causes of these adverse events.[8] Device misuse may be exacerbated by inadequate instructions for use, and insufficient warnings or precautions in the device labeling.[9] FDA believes that these problems will be mitigated by providing specific information about the risks, limitations, and directions for use in the labeling for the surgical staplers and staples for internal use. The inclusion of such information should also be helpful in developing labeling with adequate information for use under 21 CFR 801.109. For example, FDA believes the inclusion of important device technical characteristics and performance parameters in the labeling would inform end users on device limitations, thereby increasing the likelihood of appropriate device use and mitigate against device malfunctions. For these reasons, FDA recommends that the labeling of surgical staplers and staples for internal use contain the warnings, contraindications, instructions, and usage information identified below.

III. Scope

The scope of this document is limited to surgical staplers and staples for internal use with product codes listed in the table below:[10,11]

Product Code	Regulation Number	Name
GAG	21 CFR 878.4740	Stapler, Surgical
GDW	21 CFR 878.4750	Staple, Implantable
NLL	21 CFR 878.4750	Staple, Implantable, Reprocessed
NAY	21 CFR 876.1500	System, Surgical, Computer Controlled Instrument[12]

IV. Labeling Recommendations

Accurate labeling with clear communication will help mitigate the safety issues associated with surgical staplers and staples for internal use and help manufacturers develop labeling with adequate information. Based on FDA's review of the adverse event reports discussed above, the labeling for these devices may not contain all important information about the risks, limitations, and directions for use of the device, and therefore, may not contain adequate information for use

[8] Brown SL, Woo EK. Surgical stapler-associated fatalities and adverse events reported to the Food and Drug Administration. J Am Coll Surg. 2004; 199(3):374-381.

[9] Swayze S, Rich S. Promoting Safe Use of Medical Devices. The Online Journal of Issues in Nursing. 2011; 17(1).

[10] FDA has finalized the reclassification of surgical staplers for internal use from class I to class II with special controls that include specific labeling requirements cited in this section. See the final order "Reclassification of Certain Surgical Staplers" issued October 8, 2021 (86 FR 56195) available at https://www.federalregister.gov/d/2021-22041.

[11] Although the special controls under 21 CFR 878.4740 do not apply to product codes GDW, NLL, and NAY, the recommendations in this guidance are applicable to all product codes identified in this table.

[12] An analysis of adverse events for robotic surgical staplers for internal use (i.e., "robotic staplers"), which are class II devices and assigned the product code NAY, indicate that the same risks apply to robotic staplers as surgical staplers for internal use. Therefore, FDA believes that the labeling recommendations in this guidance should also apply to robotic staplers.

under 21 CFR 801.109.[13,14] FDA believes that accurate product labeling is important to make device users aware of the risks, limitations, and directions for use of surgical staplers and staples for internal use. As such, the contraindications, warnings, directions for use, technical characteristics and performance parameters identified below should help mitigate the safety issues associated with surgical staplers and staples for internal use and help manufacturers develop labeling with adequate information for use.[15]

In addition, FDA has established special controls that require specific labeling for surgical staplers for internal use (21 CFR 878.4740(b)(2)(ix) and 21 CFR 878.4740(b)(2)(x)). To help manufacturers develop labeling that complies with the required special controls (shown in *italic* font) and to mitigate the safety issues identified in surgical staplers for internal use, FDA is providing the following labeling recommendations. These recommendations are intended to supplement, and not replace, good clinical judgement. Although the special controls identified herein are only required for surgical staplers for internal use under 21 CFR 878.4740, the recommendations in this guidance are applicable to all surgical staplers and staples for internal use identified in Section III (Scope). We intend for the recommendations below to supplement and enhance the information that is often already included in labeling for these device types.

A. Contraindications

Special control 21 CFR 878.4740(b)(2)(ix)(A) states:

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.

Recommendation: A statement noting that the device should not be used to staple tissues that are necrotic, friable, or have altered integrity, e.g., ischemic or edematous tissues

B. Warnings

Special control 21 CFR 878.4740(b)(2)(ix)(B) states:

[13] See 21 CFR 801.109 for a complete list of the required information in device labeling. There are also other labeling requirements under the regulations and the Federal Food, Drug, and Cosmetic Act (FD&C Act), e.g., section 502(f)(2) of the FD&C Act.

[14] Moreover, a device shall be deemed misbranded if, among other things: its labeling is false or misleading or its labeling does not contain adequate warnings (see sections 502(a), 201(n), and 502(f) of the FD&C Act).

[15] While the recommendations are intended to help manufacturers develop labeling that contains adequate information for use under 21 CFR 801.109, the specific information required in device labeling to comply with this provision and other provisions in the regulations and the FD&C Act depends on the facts and circumstances regarding the particular device (e.g., the design of the device).

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:

- *Avoidance of use of the stapler to staple tissue outside of the labeled limits for maximum and minimum tissue thickness* (21 CFR 878.4740(b)(2)(ix)(B)(*i*))*;*

  Recommendation: A statement noting that the device should not be used to staple tissue outside of the labeled limits for maximum and minimum tissue thickness

- *Avoidance of obstructions to the creation of the staple line and the unintended stapling of other anatomic structures* (21 CFR 878.4740(b)(2)(ix)(B)(*ii*))*;*

  Recommendations:

  - A statement to visually inspect prior to firing for inclusion of unintended anatomic structures within the staple line
  - A statement to ensure that no obstructions, such as clips, are incorporated into the instrument jaws when positioning the stapler on the application site, and that firing over an obstruction may result in incomplete cutting action and/or improperly formed staples

- *Avoidance of clamping and unclamping of delicate tissue structures to prevent tissue damage* (21 CFR 878.4740(b)(2)(ix)(B)(*iii*))*;*

  Recommendation: A statement that clamping and unclamping of delicate structures, such as venous structures and bile ducts, may result in damage to tissue irrespective of stapler firing

- *Avoidance of use of the stapler on the aorta* (21 CFR 878.4740(b)(2)(ix)(B)(*iv*))*;*

  Recommendation: A statement to avoid use of the stapler on the aorta

- *Establishing proximal control of blood vessels prior to stapling where practical and methods of blood vessel control in the event of stapler failure* (21 CFR 878.4740(b)(2)(ix)(B)(*v*))*;*

  Recommendation: A statement that, where practical, proximal control of blood vessels is recommended prior to stapling, and that surgeons should have methods of blood vessel control in place in the event of stapler failure

- *Ensuring stapler compatibility with staples* (21 CFR 878.4740(b)(2)(ix)(B)(*vi*))*; and*

Recommendation: A statement to ensure that the staples are compatible with the stapler

- *Risks specifically associated with the crossing of staple lines* (21 CFR 878.4740(b)(2)(ix)(B)(*vii*)).

  Recommendation: A statement that there is a risk of increased leak rates when staple lines are crossed, even if there may be clinical circumstances when a surgeon may deem it necessary or appropriate to do so

C. Directions For Use

Consistent with the special controls identified below, the labeling of the device must include the following:

- *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* (21 CFR 878.4740(b)(2)(ix)(C)).

  Recommendation: FDA recommends that the product labeling for surgical staplers and staples for internal use contain clear instructions for use addressing the following:

  - The procedures for proper cartridge installation, removal/exchange, and preventing and mitigating the effects of the stapler jamming, locking, misfiring, or otherwise malfunctioning. Manufacturers should consider use of diagrams to help illustrate these procedures, when appropriate.
  - The procedures for determining that a tissue is appropriate for stapling
  - The time required for adequate pre-firing compression

- *Validated methods and instructions for reprocessing of any reusable device components* (21 CFR 878.4740(b)(2)(ix)(H)).

  Recommendation: For recommendations regarding the development and validation of reprocessing instructions in your proposed device labeling, refer to FDA's guidance "Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling."[16]

- *An expiration date/shelf life* (21 CFR 878.4740(b)(2)(ix)(I)).

[16] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/reprocessing-medical-devices-health-care-settings-validation-methods-and-labeling.

D. Technical Characteristics and Performance Parameters

Consistent with the special controls identified below, the labeling of the device must include the following:

- *List of staples with which the stapler has been demonstrated to be compatible* (21 CFR 878.4740(b)(2)(ix)(D)).

  Recommendation: Models of staples (e.g., identified by manufacturer, trade name, and model number) with which the stapler has been demonstrated to be compatible. (This need not be an exhaustive list of compatible staples, but should include at least one compatible model. The list should not preclude the use of staples that have independently demonstrated compatibility with the identified stapler.)

- *Identification of key performance parameters and technical characteristics of the stapler and the compatible staples needed for safe use of the device* (21 CFR 878.4740(b)(2)(ix)(E)).

  Recommendation: In identifying the key technical characteristics and performance parameters, the product labeling should do so clearly and should include the following, as applicable:

  - Maximum and minimum tissue thickness that can be comfortably compressed for each staple type based on their open and closed staple heights
  - Angle(s) of articulation (manufacturers should consider use of diagrams to illustrate angles of articulation when possible)
  - Cartridge size
  - Maximum number of consecutive firings the stapler can perform
  - Staple line reinforcing products with which the stapler is compatible (or include statement if no evaluation with staple line reinforcing materials has been completed)

- *Information regarding tissues on which the stapler is intended to be used* (21 CFR 878.4740(b)(2)(ix)(F)).

  Recommendation: Examples of types of tissues on which the stapler and staples may be used

- *Identification of safety mechanisms of the stapler* (21 CFR 878.4740(b)(2)(ix)(G)).

  Recommendation: Safety mechanism(s) for tissue thickness (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, etc.)

- *Package labels must include critical information and technical characteristics necessary for proper device selection* (21 CFR 878.4740(b)(2)(x)).

  Recommendation: Users should be able to easily look at the package label for surgical staplers for internal use and obtain critical information necessary for proper device selection.

  - For manual and powered linear cutting staplers for open/endoscopic surgery, and transverse approximator non-cutting open staplers, this information should include the following, as appropriate:

    - Cartridge color(s) and corresponding open and closed staple heights and intended tissues for approximation
    - Cartridge size
    - Shaft length
    - Tissue gap or distal jaw opening
    - Angle(s) of articulation
    - Total number of staple rows per cartridge
    - Staple pattern(s)
    - Maximum number of reloads
    - Pre-fire compression time
    - Number of incremental firings (e.g. trigger actualizations) required to complete a staple line
    - Safety mechanism(s) for tissue thickness
    - Type of ready-to-fire indicator (e.g., green window or illuminated LED)
    - Identification of compatible trocar sizes

  - For manual and powered circular staplers for open/endoscopic surgery, this information should include the following, as appropriate:

    - Cartridge color(s) and corresponding open and closed staple heights and intended tissues for approximation
    - Cartridge size (i.e., diameter)
    - Total number of staple rows per cartridge
    - Staple pattern(s)
    - Pre-fire compression time
    - Turns of handle knob counterclockwise required to remove the stapler after firing
    - Safety mechanism(s) for tissue thickness

- Type of ready-to-fire indicator (e.g., green window or illuminated LED)

Additionally, the package label for surgical staples for internal use should clearly identify the following technical characteristics and performance parameters:

- Cartridge color(s) and corresponding open and closed staple height(s) and intended tissues for approximation
- Number of staple rows per cartridge
- Models of staplers (e.g., identified by manufacturer, trade name, model number) with which the staple has been demonstrated to be compatible

Please see Appendix A for examples of package labels containing recommended technical characteristics and performance parameters for surgical staplers and staples for internal use.

Manufacturers of surgical staplers for internal use under 21 CFR 878.4740 should refer to Section V (Implementation Strategy) of FDA's Final Order, "General and Plastic Surgery Devices; Reclassification of Certain Surgical Staplers"[17] for information on dates when FDA intends to enforce compliance with the Final Order.

FDA also encourages manufacturers of all other surgical staplers and staples for internal use identified in Section III (Scope) (i.e., those that do not fall under 21 CFR 878.4740) to make any appropriate changes to their product labeling in a timely manner. FDA recommends that such labeling changes be made within 180 days from the publication of this document.

Manufacturers should evaluate their changes according to FDA's guidance "Deciding When to Submit a 510(k) for a Change to an Existing Device"[18] to determine whether a new 510(k) is required for changes to an existing device.

[17] See the final order "Reclassification of Certain Surgical Staplers" issued October 8, 2021 (86 FR 56195) available at https://www.federalregister.gov/d/2021-22041.

[18] https://www.fda.gov/regulatory-information/search-fda-guidance-documents/deciding-when-submit-510k-change-existing-device.

Appendix A. Examples of Package Labels

This section provides example package labels for different types of surgical staplers and staples for internal use containing the technical characteristics and performance parameters recommended for the package label, as described in Section IV.D.

Table 1. Example package label for an endoscopic linear cutting stapler.

Endoscopic Linear Cutting Stapler	
Cartridge color(s) and corresponding open and closed staple heights and intended tissues for approximation	Blue (3.5 mm open; 1.5 closed) – bowel White (2.5 mm open; 1.0 closed) – vascular Green (4.1 mm open; 2.0 closed) – stomach
Cartridge size	45 mm
Shaft length	38 cm
Tissue gap or distal jaw opening	12 mm
Angle(s) of articulation	90 degrees, 45 degrees, and 30 degrees in each set direction
Total number of staple rows per cartridge	Blue – 4 or 6 White – 4 Green – 6
Staple pattern(s)	Staggered, non-staggered
Maximum number of reloads	15
Pre-fire compression time	Blue: 15 – 20 seconds White: 5 - 10 seconds Green: 20 – 30 seconds
Number of incremental firings (e.g., trigger actualizations) required to complete a staple line	3
Safety mechanism(s) for tissue thickness	Lock-out, color firing zone
Type of ready-to-fire indicator	Illuminated LED
Compatible trocar sizes	5, 8, 12, and 15 mm

Table 2. Example package label for a circular stapler for open/endoscopic surgery.

Circular Stapler for Open/Endoscopic Surgery	
Cartridge color(s) and corresponding open and closed staple heights and intended tissues for approximation	Purple (3.5 mm open; 1.5 closed) – bowel
Cartridges size (i.e., diameter)	31 mm
Total number of staple rows per cartridge	2
Staple pattern(s)	Staggered, non-staggered
Pre-fire compression time	Purple: 1 – 2 minutes
Turns of handle knob counterclockwise required to remove the stapler after firing	1½ turn
Safety mechanism(s) for tissue thickness	Lock-out, color firing zone
Type of ready-to-fire indicator	Illuminated LED

Table 3. Example package label for surgical staples

Surgical Staples	
Cartridge color(s) and corresponding open and closed staple heights and intended tissues for approximation	White (2.5 mm open; 1.0 mm closed) – vascular
Number of staple rows per cartridge	2
Models of staplers (identified by manufacturer, trade name, model number) with which the staple has been demonstrated to be compatible	ABC Endoscopic Linear Cutting Stapler (Model # XYZ)