FDA Executive Summary

Prepared for the
Fall 2021 Meeting of the
FDA's Pediatric Advisory Committee

H080005

ELANA Surgical Kit$_{HUD}$

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I. INTRODUCTION

In accordance with the Pediatric Medical Device Safety and Improvement Act, this review provides a status update regarding the post-marketing experience with the use of Elana Inc.'s ELANA (Excimer Laser Assisted Non-Occlusive Anastomosis) Surgical Kit_{HUD} in pediatric and adult patients since approval. The device was approved on March 10, 2011, by the Center for Devices and Radiological Health (CDRH) under Humanitarian Device Exemption (HDE) application H080005.

There were no sales or use of this device in the United States (US) since 2013. All patients with attempted treatments with the device prior to 2013 were all adult patients. Details are presented in section VII. Dated July 15, 2020, and received by the FDA on September 2, 2020, the sponsor requested in writing to withdraw the entire HDE H080005, removing the device from the US market. This withdrawal was acknowledged by FDA on May 20, 2021. Therefore, the ELANA Surgical Kit_{HUD} no longer has US marketing approval and this document will be the last Executive Summary prepared for the annual Pediatric Advisory Committee (PAC) meeting.

This memorandum will include summaries of the postmarket medical device reporting (MDR) for adverse events, post-approval studies, and the peer-reviewed literature associated with the device.

II. INDICATIONS FOR USE

The ELANA Surgical Kit_{HUD}, when connected to the Spectranetics Xenon-Chloride Laser Model CVX-300, is indicated for creating arteriotomies during an intracranial vascular bypass procedure in patients 13 years of age or older with an aneurysm or a skull base tumor affecting a large (> 2.5 mm), intracranial artery that failed balloon test occlusion, cannot be sacrificed, or cannot be treated with conventional means due to local anatomy or complexity.

III. DEVICE DESCRIPTION

Bypass grafting to large intracranial arteries is a complex surgery, generally performed on patients with tumors and intracranial aneurysms involving the large feeding arteries of the brain. The associated creation of a distal anastomosis using conventional bypass techniques carries the risk of severe complications related to temporary occlusion of the recipient artery and microvascular suturing. The patient is at high risk for ischemic stroke and peri-operative mortality, particularly during temporary occlusion of the recipient artery.

The ELANA operating technique was developed to create a large caliber anastomosis. For the steps of preparing and creating the arteriotomy, the ELANA operating technique requires two devices: the ELANA Catheter 2.0 and either one of the ELANA Rings 2.6 or 2.8. These devices are jointly called the ELANA Arteriotomy System and are included in the ELANA Surgical Kit_{HUD} together with the Medela Tubing.

The ELANA Surgical Kit_{HUD} does not create an anastomosis or bypass, it merely replaces the tools used to make a conventional arteriotomy. The arteriotomy site must be prepared with microsurgery techniques using an ELANA Ring before the arteriotomy is made with the ELANA Catheter. The ELANA Rings 2.6 and 2.8 are made of platinum, have an inner diameter of 2.6 mm and 2.8 mm and a material thickness of 0.25 mm.

The ELANA Catheter 2.0 is a laser-vacuum suction catheter consisting of a multitude of silica glass fibers suitable for the transmission of ultraviolet light arranged to form a plane circle with an outer diameter of 2.0 mm at the tip. Inside this circle, there is a vacuum lumen in a grid. The grid and its holder as well as the centering ring on the outside of the catheter near the tip are made from stainless steel. The remainder of the catheter consists of polymer materials. The catheter has a female luer lock connector for the connection to a vacuum source and a connector for connection to an excimer laser system.

The ELANA Rings 2.6 and 2.8 are designed to aid the surgeon in the preparation of a circular arteriotomy site. One Ring is to be connected to the recipient artery wall and the donor graft wall with conventional micro-neurosurgery suturing techniques to prepare an end-to-side anastomosis on a non-occluded recipient vessel.

The ELANA Catheter 2.0 is designed to perform a circular arteriotomy in the wall of an artery while blood is flowing through the artery's lumen at a site that is prepared by the attachment of a graft and an ELANA Ring 2.6 or 2.8. The ELANA Catheter is advanced through the donor graft, vacuum is applied to hold the wall, and the laser light is used to perform the arteriotomy. The diameter of the ring of fibers in the tip of the ELANA Catheter 2.0 is 2.0 mm. The arteriotomy will therefore have a diameter of 2 mm.

IV. REGULATORY HISTORY

The HUD designation (HUD #03-0108) was approved on September 26, 2003.
The HDE for the Elana Surgical Kit$_{HUD}$ (H080005) was approved on March 10, 2011.

File	Content	Status
H080005	HDE Original	Approved
H080005/S001	75-Day Supplement Location Change	Approved
H080005/S002	75-Day Supplement Location Change	Approved
H080005/S003	Special Changes Being Effected (CBE) Supplement Labeling Change	Approved
H080005/S004	75-Day Supplement Labeling Change	Approved
H080005/S005	75-Day Supplement Design Change	Withdrawn
H080005/S006	Special CBE Supplement Labeling Change	Withdrawn
H080005/S007	Special CBE Supplement Labeling Change	Approved
H080005/S008	30-Day Notice Process Change	Manufacturing Change OK (OK30)
H080005/S009	75-Day Supplement Location Change	Approved

H080005/S010	30-Day Notice Process Change	OK30
H080005/R001	Post-approval Study (PAS) Report	Report Acknowledged (RACK)
H080005/R002	Annual Report	RACK
H080005/R003	PAS Report	RACK
H080005/R004	PAS Report	Deficient Report (RDEF)
H080005/R004/A001	PAS Report	No Response Necessary (NORE)
H080005/R005	Annual Report	NORE
H080005/R006	PAS Report	RACK
H080005/R007	PAS Report	RDEF
H080005/R007/A001	PAS Report	NORE
H080005/R008	Annual Report	NORE
H080005/R009	Annual Report	NORE
H080005/R010	PAS Report	RDEF
H080005/R010/A001	PAS Report	NORE
H080005/R011	Annual Report	RACK
H080005/R012	PAS Report	RACK
H080005/R013	Annual Report	RACK
H080005/R014	Annual Report	RACK

V. POSTMARKET DATA: ANNUAL DISTRIBUTION NUMBER

Section 520(m)(6)(A)(ii) of The Food, Drug, and Cosmetic Act (FD&C) allows HDEs indicated for pediatric use to be sold for profit as long as the number of devices distributed in any calendar year does not exceed the annual distribution number (ADN). On December 13, 2016, the 21st Century Cures Act (Pub. L. No. 114-255) updated the definition of ADN to be the number of devices "reasonably needed to treat, diagnose, or cure a population of 8,000 individuals in the United States." Based on this definition, FDA calculates the ADN to be 8,000 multiplied by the number of devices reasonably necessary to treat an individual. The established ADN for this device is 8000. The last HDE Annual Report provided by the sponsor is dated August 2, 2019. The sponsor has stated in an email dated July 16, 2020, that there have been no sales in the US since the August 2019 HDE Annual Report. The device was withdrawn from the US market on May 20, 2021. Based on information from prior annual reporting and communication with the sponsor, there were no sales or use of the device in the US since 2013. All patients with attempted treatments with the device were all adult patients.

VI. POSTMARKET DATA: MEDICAL DEVICE REPORTS (MDRs)

The MDR database was searched on June 24, 2021, to identify any MDRs associated with the ELANA Surgical Kit_{HUD}. The database was searched by brand name, product code and manufacturer name with no date range. No MDRs associated with the ELANA Surgical Kit_{HUD} were identified.

VII. POSTMARKET DATA: POST-APPROVAL STUDY (PAS)

As a condition of approval, the sponsor was required to conduct a post-approval study (PAS) due to concerns about flap retention and post-market safety.

A. Overview of the Study

The aim of this PAS was to collect information about the ELANA Surgical Kit$_{HUD}$ performance in a post-approval setting with special attention to flap retention rate, mortality and stroke. The study was to be performed in the form of a registry that included all patients who received the procedure. This is an all-comers registry with no inclusion or exclusion criteria. The study was to be conducted only at sites that have a stroke unit and all necessary medical devices and equipment available. Furthermore, the neurosurgeons were required to have experience in micro-vascular surgery and underwent mandatory training on how to use the ELANA Surgical Kit$_{HUD}$.

The study was designed to collect information pre-operatively, during the operation and at one post-operative follow-up > 25 days. The latter follow-up was required to collect the modified Rankin Scale (mRS) score to be able to define non-fatal stroke.

Progress reports were required every six months during the first 2 years of the registry and annually thereafter. Due to the limited clinical indications for this device and the availability of new surgical alternatives, a limited number of patients was expected to be enrolled, treated, and reported in the progress reports every six months. The total number of patients reported every six months were anticipated to be not higher than 12-18 patients.

B. Endpoints

The primary endpoint was the ability of the ELANA Surgical Kit$_{HUD}$ to retrieve a flap on the tip of the ELANA Catheter while creating an arteriotomy. The flap retrieval was to be judged successful if the flap was retrieved on the tip of the ELANA Catheter. The flap retrieval was to be judged unsuccessful if the flap was either manually retrieved or not retrieved.

The total sample size for this registry was to be 80 device uses. A total of 80 device uses were to provide 80% power, for showing that the flap retention rate does not exceed 38% and with the assumption that the true rate is 22%. The true flap retention rate of 22% was based on the results of the Investigational Device Exemption (IDE) study with 37 device uses. It was expected that each site was to enroll between 3-5 patients on an annual basis. The total expected number of sites in the USA was 10 to 15 sites.

Mortality and non-fatal strokes were to be recorded as secondary measures, but no statistical analyses beyond summarization of these events was to be reported.

C. PAS Subject Data

Data collection summary per patient for the PAS included the following:

Data collection	Rationale
Name of hospital	To determine number of patients per hospital and to relate patient success to site.
Name of treating physician	To check if the physician is indeed trained and to evaluate if there is a difference between physicians if there is more than 1 treating physician per hospital.
Number of prior surgeries performed by physician	To help evaluate the potential learning curve effect.
Age and gender	Descriptive for patient population.
Indication for bypass	Descriptive for patient population.
Type of bypass (Extracranial/Intracranial)	Descriptive for procedure.
Location of lesion (anterior/posterior)	Descriptive for patient population.
Location of anastomosis and type of graft vessel	Descriptive for procedure.
Flap retention	Measure if a flap was retrieved on catheter, manually retrieved or not retrieved to determine the flap retention rate and corresponding learning curve.
Mortality	Measure of safety and mortality rates will be reported.
Non-fatal stroke	Measure of safety and total non-fatal stroke incidence will be reported.
Modified Rankin Scale (mRS) score	Scoring used in order to define stroke and patient outcome.

D. Study Status

The last PAS progress report was received on March 8, 2016. As of June 2020, a total of 21 devices were shipped to 8 sites and only one site used three devices (use occurred in April of 2013). No device has been shipped to any site or used in any patient since the PAC meeting in 2019. Three adult, non-pediatric, patients were enrolled in this PAS study from 2012 until 2016. In brief, of the three patients, the device was used successfully in only one patient. In the other two patients, the procedure was aborted, and the device was not used. A clinical summary of these three patients is provided in the table below.

	Subject 1	**Subject 2**	**Subject 3**
Pre-operative			
Demographic	Female, 66 yr old	Male, 52 yr old	Female, 56 yr old
Reason for bypass	Giant aneurysm of left internal carotid artery, partially thrombosed, symptomatic	Aneurysm - large calcified paraclinoid carotid aneurysm	Aneurysm, sacrifice of right posterior cerebral artery
mRS score pre-op	1	2	1
Surgery			
Bypass graft	Autologous Saphenous Vein	Autologous Saphenous Vein	Radial artery
Bypass type	Replacement	Replacement	Replacement
Distal Anastomosis			
Type of anastomosis	ELANA. Graft was inadvertently pulled. ELANA was aborted due to carotid laceration and conventional bypass was performed.	ELANA	Conventional
Arteriotomy successful?	n/a	Yes, retrograde flow from recipient	n/a
Flap retrieval	n/a	Yes, flap retrieved on catheter.	n/a
Complications in creating the arteriotomy	No	No	No
Proximal Anastomosis			
Type of anastomosis	Conventional	Conventional	Conventional. Elana ring was sewn but felt to be slightly too large. Therefore, a conventional bypass was performed.
Complications in creating the anastomosis	None	None	None
Post-OP Evaluation			
Follow-up 25-40 days post-op	mRS: 4 (3 weeks post-op); mRS: 6 (on Nov. 17, 2012)	mRS: 2 (on Feb. 25, 2013)	mRS: 0

Non-fatal stroke/death?	Non-fatal stroke, death due to mesenteric ischemia 4-weeks after surgery.	No	No new neurological deficit
Serious Adverse Events			
	Mesenteric Ischemia/Acute Abdomen. Definitely not device related	None	None

The sponsor has indicated that completing this PAS would be difficult due to recently available alternative options such as neurovascular flow diverting stents. High flow bypass surgeries, including bypass surgeries with the ELANA Surgical Kit$_{HUD}$, are essentially no longer performed. Approximately 90% of the limited number of cases that used to be treated with the ELANA technique are now being treated endovascularly. The sponsor stated that the use of the ELANA Surgical Kit$_{HUD}$ is at the end of the treatment ladder. Due to the availability of other treatment options, the sponsor stated their device will mainly be used as a last resort option.
Due to the reasons listed above and the limited sales and use within the US to date, the PAS was suspended by the FDA in 2016. The sponsor was informed in 2016 that the study status on the Post-Approval Studies webpage will be marked as "Other." However, the PAS would be reinstated if it is observed that the sale and use of the device increases in the future. Therefore, at this time, the sponsor is not required to submit PAS progress reports.

The PAS study included only the three subjects listed above. None were pediatric subjects.

VIII. POSTMARKET DATA: LITERATURE REVIEW

A. Methods

This systematic literature review aimed to examine the current body of literature on the use of the ELANA Surgical Kit$_{HUD}$ in the pediatric population following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The years of publication eligibility ranged from 2020 to 2021. These years were utilized to identify articles published since the previous ELANA Surgical Kit$_{HUD}$ literature review that was performed in 2020 by CDRH. The following search was initially conducted in PubMed and Embase:

Embase search criteria: (elana:ab,ti OR 'excimer laser-assisted non-occlusive anastomosis':ab,ti OR 'elana surgical kit':ab,ti) AND [2020-2021]/py. Search performed on June 14, 2021.

PubMed search criteria: ((ELANA) OR (Arteriotomy)) OR (Excimer Laser-Assisted Non-occlusive Anastomosis) and 2020:2021:[dp]. Search performed on June 14, 2021.

For Embase, this search identified 7 articles; and for PubMed, this search identified 101 articles.

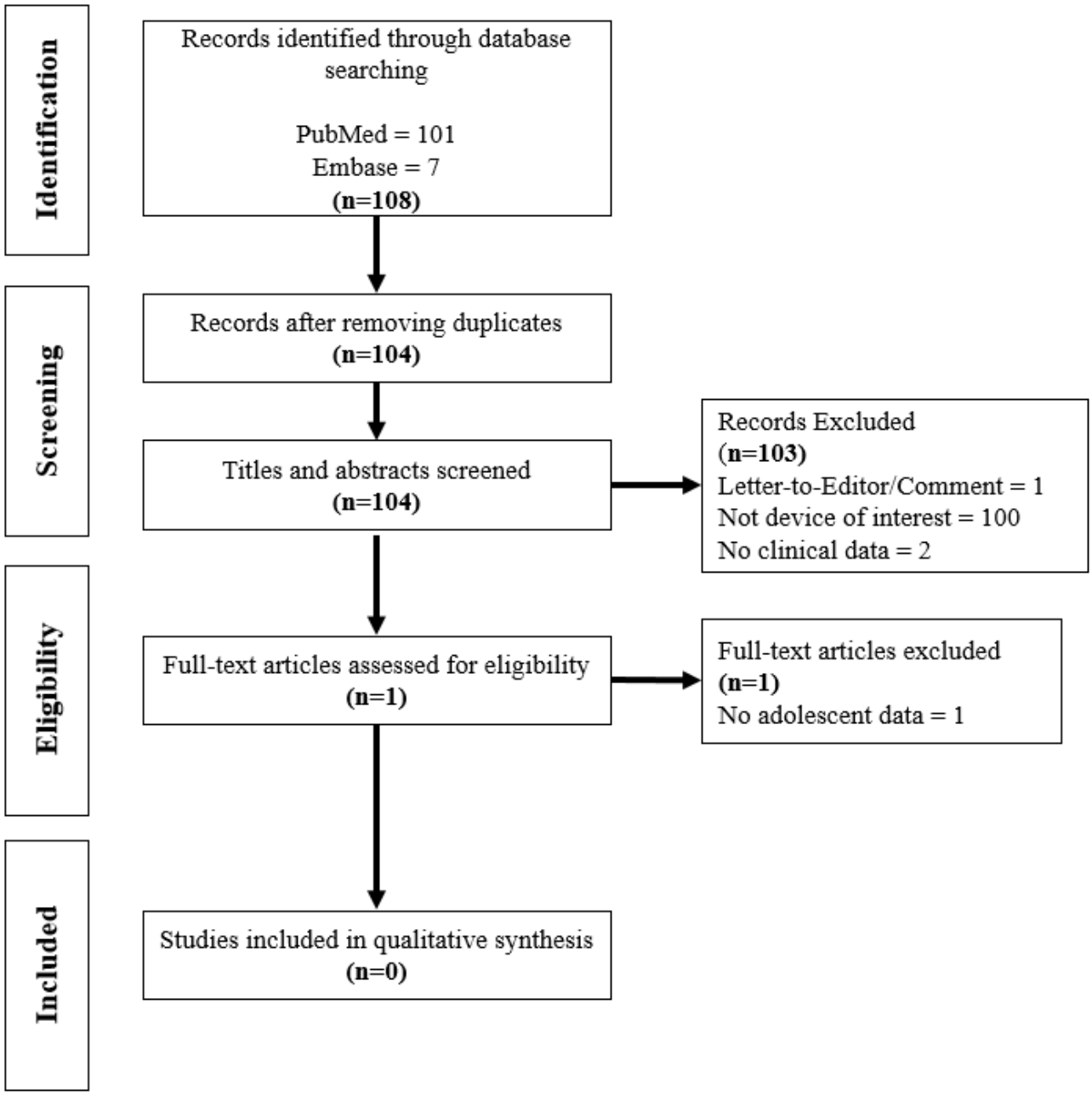
Exclusion Criteria and Accountability of Publications

After conducting these searches, a review of titles and abstracts was performed followed by full-text assessment. The full exclusion criteria included the following: duplicates, letters to the editor/commentaries/editorials, review articles, not the device of interest, no adolescent specific analysis, no humans in the study (e.g., animal study), and unrelated topic. Review articles were individually examined to check for other potential articles for inclusion. Review articles and articles therein were excluded if the ELANA Surgical Kit$_{HUD}$ was not mentioned, was not published

between January 1, 2020, to June 30, 2021, there were no relation to the treatment of neurological conditions or did not contain a pediatric population. This search was consistent with the search performed in 2020 (no results retrieved).

Figure 1 presents the article screening process. All 104 articles, after removing any duplicates, were excluded for the following reasons: letter-to-editor/commentary (1), not the device of interest (100), no humans in the study (2), and no adolescent data (1).

Figure 1. Search Strategy for Relevant Articles



B. Literature Review Conclusions

Given the current searches of the literature, we did not find any studies published on the ELANA Surgical Kit$_{HUD}$ that report results for the use of this device in the indicated pediatric population. Consequently, conclusions regarding the safety and probable benefit of the use of the ELANA Surgical Kit$_{HUD}$ in the indicated pediatric population cannot be obtained from the published literature.

IX. SUMMARY

The sponsor requested the withdrawal of the HDE in a formal letter dated July 15, 2020 and received on September 2, 2020. The FDA approved the withdrawal on May 20, 2021. FDA is unaware of any use of this device after 2013 in the US. Our current reviews continue to reveal no safety issues from review of MDRs and published literature.

The FDA recommends to cease the surveillance of the device following the PAC meeting in 2021 because the HDE, H080005, has been officially withdrawn and the device is no longer marketed in the US.