June 5, 2025

ICU Medical, Inc.
Elizabeth Cozzi
Senior Manager, Global Regulatory Affairs
600 North Field Drive
Lake Forest, Illinois 60045

Re: K250616
Trade/Device Name: Clave™ Neutral-Displacement Needlefree Connectors
Regulation Number: 21 CFR 880.5440
Regulation Name: Intravascular Administration Set
Regulatory Class: Class II
Product Code: FPA
Dated: May 9, 2025
Received: May 9, 2025

Dear Elizabeth Cozzi:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

David Wolloscheck -S

David Wolloscheck, Ph.D.
Assistant Director
DHT3C: Division of Drug Delivery and
General Hospital Devices, and
Human Factors
OHT3: Office of Gastrorenal, ObGyn,
General Hospital, and Urology Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

Submission Number *(if known)*

K250616

Device Name

Clave™ Neutral-Displacement Needlefree Connectors

Indications for Use *(Describe)*

Clave Neutral-Displacement Connectors (MicroClave™/ NanoClave™/ Clave™Neutron) are intended for the aspiration, injection, or gravity/pump flow of IV fluids and blood upon insertion of a male luer connector. Clave Connectors may be used with power injectors at a maximum pressure of 400 psi and a maximum flow rate of 10ml/sec. Clave Connectors will prevent microbial ingress for seven (7) days.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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510(k) Summary

A summary of 510(k) substantial equivalence information in accordance with the requirements of 21CFR 880.5440 for Intravascular Administration Set.

Submitter Information	
Name	ICU Medical
Address	600 North Field Drive Lake Forest, IL. 60045
Phone number	847-363-3479
Fax number	N/A
Establishment Registration Number	3013319212
Name of contact person	Elizabeth M. Cozzi
Date prepared	06/05/2025
Name of device	
Trade or proprietary name	Clave ™ Neutral-Displacement Needlefree Connectors
Common or usual name	Intravascular Administration Set, Needleless Connector
Classification	II
Classification name	Intravascular administration set (21 CFR 880.5440)
Panel	General Hospital
Product Code(s)	FPA
Legally marketed device(s) to which equivalence is claimed	Predicate: Clave™ Neutron K100434
Trade or proprietary name	Clave ™ Neutron
Common or usual name	Needleless Connector, Closed Access
Classification	II
Classification name	Intravascular administration set (21 CFR 880.5440)
Panel	General Hospital
Product Code(s)	FPA
Reference Device	Microvolume Luer Access Device K212842
Trade or proprietary name	Microvolume Luer Access Device
Common or usual name	Luer Access Device, Needleless Connector; Needle-free Injection Site; Needle-free Luer Access Device; Needle-free connector; Valve

Classification	II
Classification name	Intravascular administration set (21 CFR 880.5440)
Panel	General Hospital
Product Code(s)	FPA
Reason for 510(k) submission	The purpose of the submission is to update the labeling for the Clave Neutral-Displacement Needlefree Connectors to add the results of a published CMS study, increase the psi for pressure infusion, and add a claim to prevent microbial ingress for seven days.
Device description	Clave Neutral-Displacement Connectors are needlefree, bi-directional connectors that utilize a pre-slit septum which prevents microbial ingress when in the un-activated state and allows access to the fluid path when activated with an ISO 80369-7 compliant male luer. The septum offers neutral displacement of fluid during connection or disconnection of a male luer and self-seals upon disconnection to prevent fluid loss or air ingress. The Neutron incorporates additional technology that will prevent fluid displacement resulting from syringe plunger compression; patient vascular pressure changes, such as coughing or sneezing; and IV solution container run-dry. The Clave Family of Connectors do not require a cap but may be used with disinfecting caps containing 70% isopropyl alcohol. A retrospective study published by the Journal of Vascular Access (Ryder and Battle, 2024) which analyzed 2019 CMS data determined that after adjusting for Hospital characteristics, acute-care Hospitals which utilized the Clave Family of Connectors (Clave, MicroClave, NanoClave, Clave Neutron) had a statistically significant lower relative risk (RR) of bloodstream infection and bloodstream infection-associated mortality when compared to acute-care Hospitals that did not utilize Clave Connectors. Connector representation is the study was 89.6% MicroClave; 6.3% Clave; 3.7% Clave Neutron; and 0.4% NanoClave, respectively. For the acute-care Hospitals that utilized Clave Connectors, the RR of CLABSI was 0.93, signifying a 7% decreased CLABSI risk (p=0.04) and for acute-care Hospitals that utilized the Clave Connectors in high volumes, the RR of CLABSI was 0.81 (p=0.04), representing a 19% decrease in CLABSI risk

Indications for Use	Clave Neutral-Displacement Connectors (MicroClave™/ NanoClave™/ Clave™ Neutron) are intended for the aspiration, injection, or gravity/pump flow of IV fluids and blood upon insertion of a male luer connector. Clave Connectors may be used with power injectors at a maximum pressure of 400 psi and a maximum flow rate of 10ml/sec. Clave Connectors will prevent microbial ingress for seven (7) days.
Intended Use	The intended use of the Clave Neutral-Displacement Connector is to provide a sterile needle-free fluid pathway for the administration or aspiration of blood, IV therapy, or medications as prescribed by the physician. Fluids are administered to the patient through a catheter or cannula. The device can be utilized as a conduit between two devices, in addition to being used to deliver contrast media via power injection. This is a general use device that may be used for any patient population with consideration given to the adequacy of vascular anatomy and appropriateness for the solution being infused and duration of therapy.

Table 1 provides a comparison of the subject Clave Neutral-Displacement Needlefree Connectors to the predicate Clave Neutron cleared under 510(k) K100434 and the reference connector Microvolume Luer Access Device under K212842.

Table 1: Comparison of Proposed and Predicate Devices

Feature	**Proposed Device**	**Predicate K100434**	**Comparison**
Product Code	FPA	FPA	Same
Common Name	Needleless Connector, Closed Access	Needleless Connector, Closed Access	Same as predicate
Manufacturer	ICU Medical	ICU Medical	Same as predicate
Indications for Use	Clave Neutral-Displacement Connectors (MicroClave™/ NanoClave™/ Clave™ Neutron) are intended for the aspiration, injection, or gravity/pump flow of IV fluids and blood upon insertion of a male luer connector. Clave Connectors may be used with power injectors at a maximum pressure of 400 psi and a maximum flow rate of 10ml/sec. Clave Connectors will prevent microbial ingress for seven (7) days.	CLAVE Neutron is a normally closed, bidirectional connector intended for use as an accessory to an intravascular catheter placed in the vein or artery. The device may be used for the administration of blood and fluids to patients, including pediatrics and immunocompromised patients. The device may also be used with power injector procedures up to 10mL per second of contrast media and a maximum pressure of 350psi. The device incorporates a technology that will prevent fluid displacement resulting from the following: Connection or disconnection of a luer; syringe plunger compression; patient vascular pressure changes, such as coughing or sneezing; and IV solution container run-dry. The CLAVE Neutron incorporates a pre-slit septum that does not require the use of needles and will therefore passively aid in the reduction of needlestick injuries.	Different - Maximum pressure infusion rating increased from predicate (350psi to 400psi) which also falls into the indication of use of the reference device. Prevention of microbial ingress over 7 days added for subject device.

Principle of Operation	Normally closed bi-direction valve with self-sealing pre-slit septum. ISO 80369-7 compliant male luer of device allows for connection to a vascular catheter, and ISO 80369-7 compatible female luer allows for fluid path access through the self-sealing pre-slit septum. Clave Neutron incorporates additional technology that will prevent fluid displacement resulting from syringe plunger compression; patient vascular pressure changes, such as coughing or sneezing; and IV solution container run- dry.	Normally closed bi-direction valve with self-sealing pre-slit septum. ISO 80369-7 compliant male luer of device allows for connection to a vascular catheter, and ISO 80369-7 compatible female luer allows for fluid path access through the self-sealing pre-slit septum. Neutron incorporates technology that will prevent fluid displacement resulting from syringe plunger compression; patient vascular pressure changes, such as coughing or sneezing; and IV solution container run-dry.	Same as predicate
Mechanism of Action	Self-sealing pre-slit septum activated with ISO 80369-7 compliant male luer to allow for bi-directional flow	Self-sealing pre-slit septum activated with ISO 80369-7 compliant male luer to allow for bi-directional flow	Same as predicate
Compatibility	IPA & CHG Compatibility. Disinfectant Caps, Infusate Compatibility (Standard IV Solutions), Blood	Standard IV solutions, IPA, Lipids, Alcohol, Blood	Similar to predicate Updated disinfectant compatibility to include CHG and disinfectant caps as in reference.
Materials of Construction	• Body / Luer: Polycarbonate • Septum: Silicone, Lubricated • Cannula / Luer: Polycarbonate • Base: Polycarbonate • Valve: Silicone, self-lubricating • Diverter: Nylon • Male Luer Cap: Polypropylene • Ring: Polypropylene	• Body /Luer: Polyester • Septum: Silicone, Lubricated • Cannula / Luer: Polycarbonate • Base: Polycarbonate • Valve: Silicone, self-lubricating • Diverter: Nylon • Male Luer Cap: Polypropylene	Similar to predicate The updated body is made of a material that is present in the predicate, but different than the predicate body material.
Biocompatibility	Conforms to ISO 10993-1	Conforms to ISO 10993-1	Similar to predicate

Sterilization	Irradiation	Irradiation	Same as predicate
Pyrogenicity	Non-pyrogenic	Non-pyrogenic	Same as predicate
Single Use	Single use	Single use	Same as predicate

Comparison Summary

Indications for Use

The intended use of the subject device and predicate device are similar. New testing also supports the additional claim that the Clave family (MicroClave™, NanoClave™, and Clave™ Neutron) prevents microbial ingress for seven days and the use with pressure infusion procedures up to 400 psi.

Principles of Operation

The subject devices principle of operation is the same as the previously cleared predicate device. Each device is a neutral displacement, normally closed, bi-directional connector with a shared self-sealing pre-slit septum. Each device incorporates an ISO 80369-7 compliant distal male luer that allows for connection to a vascular catheter or extension set. The female luer of each device is ISO 80369-7 compatible to mate with and allow access to the infusion system when activated using an ISO 80369-7 compliant male luer. When the male luer is removed from the pre-slit septum, the septum passively returns to self-seal and close the fluid path. Prior to access, disinfection of the septum is accomplished using a 70% isopropanol swab for three seconds and allow to dry, or with the application of a 70% isopropanol disinfecting cap. The subject device utilizes the same housing component and self-sealing pre-slit septum component as the predicate K100434 device. The predicate K100434 device Clave Neutron incorporates an additional design feature at the distal end of the connector to prevent fluid displacement resulting from syringe plunger rebound and patient-induced reflux. This design feature is separate from and in addition to the principles of operation which accomplish the bi-directional fluid flow and self-sealing nature of the pre-slit septum.

Intended Use

The subject devices intended use environments are the same as the previously cleared predicate and reference device. Devices are used externally to a patient as an accessory to an intravascular catheter placed in the vein or artery. The subject may be used for the administration of blood and fluids to patients. The subject device may be used for pressure infusion procedures up to 400 psi (10mL/sec), which is the same as the previously cleared predicate in K100434. The subject device has been evaluated for the prevention of microbial ingress for a worst-case simulated use protocol of seven (7) days, using Guidance for Industry and Staff: Intravascular Administration Sets Premarket Notification Submissions [510(k)], Section 8; Microbial Ingress Testing. The predicate devices evaluated microbial ingress using a three (3) day simulated use protocol. This difference in microbial ingress study duration does not raise new questions on safety and effectiveness as demonstrated by non-clinical performance testing and published clinical reports.

Technology

The subject devices have minor dimensional differences relative to the predicate that do not impact the Principles of Operation or Intended Use Environments. The difference in pressure infusion rating and microbial ingress is supported by testing in compliance with ANSI/AAMI CN 27. These differences do not raise new questions regarding safety and effectiveness of the subject devices.

Compatibility

The compatibility of the subject device and predicate device are similar. New testing supports the compatibility of the subject device with CHG based on methods described in ANSI/AAMI CN27 testing for isopropyl alcohol. Testing for compatibility with disinfectant caps is based on internal methodology.

Materials

The materials utilized in the subject device are similar to those of the predicate. The body of the subject devices has been updated to a polycarbonate material, rather than polyester as in the predicate body. The body is now made of the same material as the subject and predicate spike and base and presents no new issues of safety and effectiveness based on fully compliant ISO 10993 testing.

Summary of Non-Clinical Testing

Non-clinical verification has been conducted to evaluate the safety, performance and functionality. The results of these tests have demonstrated the overall safety of the subject device and ultimately supports a substantial equivalence determination to the predicate device. A summary of the testing conducted is presented below.

Biocompatibility Testing

Biocompatibility testing was conducted in accordance with ISO 10993-1 and FDA's September 2023 Guidance titled, "Use of International Standard ISO 10993-1, 'Biological Evaluation of Medical Devices Part 1: Evaluation and testing within a risk management process,'" as recognized by FDA. Testing included for Externally Communicating Device with Blood Path, Direct Contact, for a Prolonged Duration (>24hours to 30 days).

Performance Data: Non-Clinical Testing Summary

The following performance data supports the substantial equivalence of the Clave Neutral Displacement Needlefree Connectors:

Standard	Performance Testing
ISO 8536-4	• Particulate contamination • Leakage • Tensile strength • Flow rate of infusion fluid • Protective caps • Chemical Requirements • Pyrogenicity • Seal and Snap Tests • Seal Test • Seal Tests – Post Durability
ISO 8536-8	• Leakage
ISO 8536-10	• Avoidance of air bubbles

ISO 11607-1 ISO 11607-2	• Sterile Barrier System Validation
ISO 11137-1/A1 ISO 11137-2	• Radiation Sterilization Validation
ISO 80369-7	• Dimensional requirements for Luer connectors • Fluid leakage • Sub-atmospheric pressure air leakage • Stress cracking • Resistance to separation from axial load • Resistance to separation from unscrewing • Resistance to overriding
ANSI/AAMI CN27	• Non-interconnectability 4.1.1 Option A • Flow Rate • Test for exposure to IPA • Infusate Compatibility • Resistance to Separation from Axial Load • Resistance to separation from unscrewing • Resistance to overriding • Backpressure (unactivated) • Positive pressure fluid leakage (activated) • Subatmospheric pressure air leakage (unactivated) • Subatmospheric pressure air leakage (activated) • Duration of activation • Number of activations • Priming volume • Residual volume • Hemolysis • Power injection • Microbial ingress • Displacement volume
ANSI/AAMI ST72 & USP <85>	• Bacterial endotoxins

Particulates

Particulate contamination testing was performed by following USP <788> to demonstrate particulate levels on the subject devices meets USP <788> requirements.

Clinical Testing

The submission includes results of a published CMS study[1] which demonstrates a statistically significant lower relative risk of bloodstream infection and bloodstream infection-associated mortality when compared to non-Clave users in acute-care hospitals.

Conclusion

The subject device meets the functional claims and intended use as described in the product labeling. Test results from the performance testing conducted demonstrate the subject devices meet all acceptance criteria requirements. Therefore, the subject device is substantially equivalent to the predicate device cleared under K100434. The differences between the subject and predicate device do not raise any new or different questions of safety or effectiveness of the device and do not alter the intended use of the device.

Reference

Ryder, M., & Battle, J. (2024). Choice of needleless connector technology as a risk reduction strategy for catheter related bloodstream infection, mortality, and cost: A secondary data analysis. *The Journal of Vascular Access*. [https://doi.org/10.1177/11297298241261951]