**VOLTA MEDICAL**

**VX1+**

**Traditional 510(k) Premarket Notification**

**Volta Medical**
**65 Avenue Jules Cantini**
**13006 Marseille**
**France**

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## LIST OF APPENDICES

The following information is provided as required by 21 C.F.R. § 807.87 for Volta Medical's VX1+ 510(k) premarket notification:

## I. MEDICAL DEVICE USER FEE

The Company has remitted the Medical Device User Fee of $19,870 concurrent with this submission to the Food and Drug Administration, P.O. Box 956733, St. Louis, MO 63195-6733, by wire transfer under the reference TRN: YT29460911802811. A copy of the Medical Device User Fee Cover Page is provided below.

Form Approved: OMB No. 0910-0511 Expiration Date: October 31, 2024. See Instructions for OMB Statement.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
**MEDICAL DEVICE USER FEE COVER SHEET**

PAYMENT IDENTIFICATION NUMBER: **MD6133666**
Write the Payment Identification number on your check.

A completed cover sheet must accompany each original application or supplement subject to fees. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment and mailing instructions can be found at: https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/ucm370879.htm

1. COMPANY NAME AND ADDRESS (include name, street address, city state, country, and post office code)

SUBSTRATE HD
Volta Medical
65 avenue Jules Cantini
Marseille
13006
FR

1.1 EMPLOYER IDENTIFICATION NUMBER (EIN)

2. CONTACT NAME
Paola Milpied
2.1 E-MAIL ADDRESS
paola.milpied@volta-medical.com
2.2 TELEPHONE NUMBER (include Area code)
768025499
2.3 FACSIMILE (FAX) NUMBER (Include Area code)

3. TYPE OF PREMARKET APPLICATION (Select one of the following in each column; if you are unsure, please refer to the application descriptions at the following web site: http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm345263.htm

Select an application type:
[X] Premarket notification(510(k)); except for third party
[ ] 513(g) Request for Information
[ ] Biologics License Application (BLA)
[ ] Premarket Approval Application (PMA)
[ ] Modular PMA
[ ] Product Development Protocol (PDP)
[ ] Premarket Report (PMR)
[ ] 30-Day Notice
[ ] De Novo Request

3.1 Select a center
[X] CDRH
[ ] CBER

3.2 Select one of the types below
[X] Original Application

Supplement Types:
[ ] Efficacy (BLA)
[ ] Panel Track (PMA, PMR, PDP)
[ ] Real-Time (PMA, PMR, PDP)
[ ] 180-day (PMA, PMR, PDP)

4. ARE YOU A SMALL BUSINESS? (See the instructions for more information on determining this status)
[ ] YES, I meet the small business criteria and have submitted the required qualifying documents to FDA
[X] NO, I am not a small business
4.1 If Yes, please enter your Small Business Decision Number:

5. FDA WILL NOT ACCEPT YOUR SUBMISSION IF YOUR COMPANY HAS NOT PAID AN ESTABLISHMENT REGISTRATION FEE THAT IS DUE TO FDA. HAS YOUR COMPANY PAID ALL ESTABLISHMENT REGISTRATION FEES THAT ARE DUE TO FDA?
[X] YES (All of your establishments have registered and paid the fee, or this is your first device and you will register and pay the fee within 30 days after entering into an operation that requires you to register and submit device listing information.)
[ ] NO (If you currently market a medical device and your establishment is required to register and submit device listing information, FDA will not accept your submission until you have paid all fees due to FDA. See http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/RegistrationandListing/ucm053165.htm for additional information)

6. IS THIS PREMARKET APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCEPTIONS? IF SO, CHECK THE APPLICABLE EXCEPTION.
[ ] This application is the first PMA submitted by a qualified small business, including any affiliates
[ ] This biologics application is submitted under section 351 of the Public Health Service Act for a product licensed for further manufacturing use only
[ ] The sole purpose of the application is to support conditions of use for a pediatric population
[ ] The application is submitted by a state or federal government entity for a device that is not to be distributed commercially

7. IS THIS A SUPPLEMENT TO A PREMARKET APPLICATION FOR WHICH FEES WERE WAIVED DUE TO SOLE USE IN A PEDIATRIC POPULATION THAT NOW PROPOSES CONDITION OF USE FOR ANY ADULT POPULATION? (If so, the application is subject to the fee that applies for an original premarket approval application (PMA).
[ ] YES [X] NO

PAPERWORK REDUCTION ACT STATEMENT
Public reporting burden for this collection of information is estimated to average 18 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to the address below.

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff

PRAStaff@fda.hhs.gov

[Please do NOT return this form to the above address, except as it pertains to comments on the burden estimate.]

8. USER FEE PAYMENT AMOUNT SUBMITTED FOR THIS PREMARKET APPLICATION

$19,870.00 16-Oct-2022

Form FDA 3601 (07/22)

"Close Window" Print Cover sheet

## II. CDRH PREMARKET REVIEW SUBMISSION COVER SHEET

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

**CDRH PREMARKET REVIEW SUBMISSION COVER SHEET**

Form Approved : OMB No. 0910-0120
Expiration Date: June 30, 2023
*See PRA Statement on last page.*

| Date of Submission | User Fee Payment ID Number | FDA Submission Document Number *(If known)* |
|---|---|---|
| November 22, 2022 | MD6133666 | |

**SECTION A TYPE OF SUBMISSION**

**PMA& PDP**
- ☐ Original
- ☐ Modular Submission
- ☐ Amendment
- ☐ Report (annual or PAS)
- ☐ Report Amendment
- ☐ Other:
  - ☐ Premarket Report (reprocessed SUD)
  - ☐ Licensing Agreement

**PMA/PDP Supplement**
- ☐ 180 day - PAS protocol or labeling change, location change, trade name change
- ☐ 180 day - Design or labeling change
- ☐ Special CBE
- ☐ Panel Track
- ☐ 30-day Notice
- ☐ Real-time Review
- ☐ Amendment to PMA/PDP Supplement

**510(k)**
- ☒ Original Submission
  - ☒ Traditional
  - ☐ Special
  - ☐ Abbreviated
  - ☐ 3rd Party Traditional
  - ☐ 3rd Party Special
  - ☐ 3rd Party Abbreviated
  - ☐ Dual Track (Dual 510(k) and CLIA Waiver by Application)
- ☐ Amendment
- ☐ Supplement

**CLIA**

CLIA Categorization Record (CR)
- ☐ Original
- ☐ Amendment

CLIA Waiver by Application (CW)
- ☐ Original
- ☐ Amendment
- ☐ Supplement

**Q-Submission**
- ☐ Pre-Submission
- ☐ Informational Meeting
- ☐ Submission Issue Meeting
- ☐ Day 100 Meeting
- ☐ Agreement Meeting
- ☐ Determination Meeting
- ☐ Study Risk Determination
- ☐ Other (Specify below)

**IDE**
- ☐ Original IDE:
  - ☐ Amendment to Original IDE
- ☐ Supplement:
  - ☐ Amendment to Supplement
- ☐ Report:
  - ☐ Amendment to Report

**HDE**
- ☐ Original Submission
- ☐ Amendment to Original Report
- ☐ Report Amendment
- ☐ HDE Supplement:
  - ☐ 75-day Supplement
  - ☐ 30-day Notice
  - ☐ Special CBE
  - ☐ Amendment to Supplement

**Class II Exemption Petition**
- ☐ Original Submission
- ☐ Additional Information

**Emergency Use Authorization**
- ☐ Original
- ☐ Supplement
- ☐ Amendment
- ☐ Report

**De Novo**
- ☐ Original:
  - ☐ Direct
  - ☐ Post-NSE
- ☐ Amendment
- ☐ Supplement

**Pre-Emergency Use Authorization**
- ☐ Original
- ☐ Supplement
- ☐ Amendment

**Other Submission**
- ☐ 513(g)
- ☐ Appeal
- ☐ Other (Briefly describe submission below)

**Expanded Access to Devices**
- ☐ Compassionate Use Request **NOT associated with an IDE**
- ☐ Follow-up Report for Compassionate Use **NOT associated with an IDE**
- ☐ Emergency Use Follow-up Report **NOT associated with an IDE**

**SECTION B APPLICANT / SPONSOR**

| | | |
|---|---|---|
| Company/Institution Name<br>Volta Medical | | Establishment Registration Number/FEI *(if known)*<br>3017684005 |
| Street Address<br>65 Avenue Jules Cantini | | City<br>Marseille |
| State/Province | ZIP/Postal Code<br>13006 | Country<br>France |

| | |
|---|---|
| Contact Name<br>Paola MILPIED | Contact Title<br>VP Clinical & Regulatory Affairs |
| Division Name *(if applicable)* | Phone Number *(including area code)*<br>*+33 7 68 02 54 99* |
| Fax Number *(including area code)* | Contact Email Address<br>paola.milpied@volta-medical.com |

## SECTION C OFFICIAL CORRESPONDENT (e.g., may be a consultant and/or 510(k) Third Party) (if different from Section B)

| | | |
|---|---|---|
| Company/Institution Name<br>Hogan Lovells US LLP | | Establishment Registration Number/FE! *(if known)* |
| Street Address<br>555 13th Street NW | | City<br>Washington |
| State/Province<br>DC | ZIP/Postal Code<br>20004 | Country<br>USA |

| | |
|---|---|
| Contact 1 Name<br>Kristin Zielinski Duggan | Contact 1 Title<br>Partner |
| Contact 1 Division Name *(if applicable)* | Contact 1 Phone Number *(including area code)*<br>+1 202 637 8894 |
| Contact 1 Fax Number *(including area code)*<br>+1 202 637 5910 | Contact 1 Email Address<br>kristin.duggan@hoganlovells.com |
| Contact 2 Name | Contact 2 Title |
| Contact 2 Division Name *(if applicable)* | Contact 2 Phone Number *(including area code)* |
| Contact 2 Fax Number *(including area code)* | Contact 2 Email Address |
| Contact 3 Name | Contact 3 Title |
| Contact 3 Division Name *(if applicable)* | Contact 3 Phone Number *(including area code)* |
| Contact 3 Fax Number *(including area code)* | Contact 3 Email Address |

## SECTION D INTENDED USE POPULATION

*Check all that apply.*

☒ Adults Only (greater than 21 years of age)
☐ Adults and Pediatrics

☐ Neonate/Newborn (birth through 28 days)
☐ Infant (from 29 days to 2 years of age)
☐ Child (from 2 years to 12 years of age)
☐ Adolescent (from 12 years to 18 years of age)
☐ Transitional Adolescent A (18 through 21 years of age)
☐ Transitional Adolescent B (18 through 21 years of age)

☐ Other *(Specify below)*

## SECTION E PRODUCT INFORMATION – APPLICABLE TO ALL SUBMISSIONS

| | *Trade Name* |
|---|---|
| 1 | *VX1+* |
| 2 | |
| 3 | |
| 4 | |
| 5 | |
| | Common /Generic Name (*Include if no Trade Name*) |

## SECTION F PRIOR RELATED SUBMISSION FOR THIS DEVICE OR STUDY

FDA document numbers of all prior related submissions *(regardless of outcome)* or state no prior submission in box 1.

| | | |
|---|---|---|
| 1 None | 2 | 3 |
| 4 | 5 | 6 |
| 7 | 8 | 9 |
| 10 | 11 | 12 |

## SECTION G PRODUCT CLASSIFICATION – APPLICABLE TO ALL SUBMISSIONS

Product Code(s) *(when applicable) (If more than one, please separate with commas.)*

DQK

| | |
|---|---|
| C.F.R. Section *(If applicable)*<br>21 CFR. § 840.1245 | Classification Panel/Medical Specialty<br>Cardiovascular |

Device Class

☐ Class I ☒ Class II ☐ Class III ☐ Unclassified

## SECTION H1 REASON FOR APPLICATION – PMA, PDP, OR HDE

| | | |
|---|---|---|
| ☐ New Device<br>☐ STED | ☐ Change in Design, Component, or Specification:<br>☐ Software/Hardware<br>☐ Color Additive<br>☐ Material<br>☐ Specifications<br>☐ Other *(Specify below)* | ☐ Location Change:<br>☐ Manufacturer<br>☐ Sterilizer<br>☐ Packager |
| ☐ Post-approval Study Protocol | | ☐ Report Submission:<br>☐ Annual or Periodic<br>☐ Post-approval Study |
| ☐ HOE Request for Annual Distribution Number (AON) | | |
| ☐ Process Change:<br>☐ Manufacturing<br>☐ Packaging<br>☐ Sterilization<br>☐ Vendor/Supplier Change<br>☐ Other (Specify below) | ☐ Labeling Change:<br>☐ Indications<br>☐ Instructions<br>☐ PAS update<br>☐ Performance Characteristics<br>☐ Shelf Life<br>☐ Trade Name<br>☐ Other (Specify below) | ☐ Amendment:<br>☐ Withdrawal<br>☐ Change in Ownership<br>☐ Change in Correspondent<br>☐ Change of Address<br>☐ Request for Extension<br>☐ Response to FDA Correspondence<br>☐ Other *(Specify below)* |

☐ Bundle Submission - *If this* is *selected , list in the spaces below any PMAs in the Bundle.*

| | | |
|---|---|---|
| 1 | 2 | 3 |
| 4 | 5 | 6 |
| 7 | 8 | 9 |

## SECTION H2 REASON FOR APPLICATION – IDE

☐ Original IDE

☐ Supplement:
- ☐ New Study/New Protocol
- ☐ Change in Correspondent
- ☐ Change in Manufacturer
- ☐ Change in Sponsor
- ☐ Change in Design
- ☐ Change in Informed Consent
- ☐ Change in Manufacturing
- ☐ Change in Protocol
- ☐ 5-Day Notice - Device or Manufacturing
- ☐ 5-Day Notice - Protocol
- ☐ Compassionate Use Request (under an IDE)
- ☐ Live Case Request
- ☐ Request Deviation from Protocol
- ☐ Expansion of Study (Study/Sites)
- ☐ Extension of Time to Submit Annual Report or Respond to FDA Letter

Supplement *(Continued)*
- ☐ Request for Waiver
- ☐ IRB Certification
- ☐ Request for CMS Recategorization
- ☐ Study Resumed
- ☐ Study Suspension
- ☐ Other *(Specify below)*

☐ Report:
- ☐ Adverse Effect
- ☐ Final, Study Completed
- ☐ Annual Progress
- ☐ Interim Progress
- ☐ Semiannual Investigator List
- ☐ Failure to Obtain Informed Consent
- ☐ Compassionate Use Follow-up
- ☐ Emergency Use
- ☐ Live Case Follow-up
- ☐ Completion of Patient Enrollment ☐ Completion of Patient Follow-up
- ☐ Other *(Specify below)*

☐ Amendment to Original IDE:
- ☐ Amendment Before Final Decision
- ☐ Response to Refuse to Accept
- ☐ Response to Disapproval
- ☐ Response to Approval with Conditions
- ☐ Withdrawal
- ☐ Other *(Specify below)*

☐ Amendment to Supplement:
- ☐ Response to Disapproval
- ☐ Response to Approval with Conditions
- ☐ Withdrawal
- ☐ Amendment Before Final Decision (additional Information)
- ☐ Other *(Specify below)*

☐ Amendment to Report:
- ☐ Response to Deficiency Letter
- ☐ Withdrawal
- ☐ Amendment Before Final Decision (additional Information)
- ☐ Other *(Specify below)*

## SECTION H3 REASON FOR SUBMISSION – Q-SUBMISSION

☐ Pre-Submission:
- ☐ Request Face-to-Face Meeting
- ☐ Request Teleconference
- ☐ Request Email Response
- ☐ Submit Meeting Minutes
- ☐ Request Meeting Minutes Disagreement T-con

☐ Submission Issue Meeting:
- ☐ Request Face-to-Face Meeting
- ☐ Request Teleconference
- ☐ Request Email Response
- ☐ Submit Meeting Minutes
- ☐ Request Meeting Minutes Disagreement T-con

☐ Additional Information

☐ Change in Legal Entity:
- ☐ Change in Correspondent
- ☐ Change in Sponsors
- ☐ Change in Manufacturer
- ☐ Other *(Specify below)*

☐ Agreement Meeting:
- ☐ Request Face-to-Face Meeting
- ☐ Request Teleconference

☐ Determination Meeting:
- ☐ Request Face-to-Face Meeting
- ☐ Request Teleconference

☐ Informational Meeting:
- ☐ Request Face-to-Face Meeting
- ☐ Request Teleconference
- ☐ Submit Meeting Minutes
- ☐ Request Meeting Minutes Disagreement T-Con

☐ Other *(Specify)*:

**FORM FDA 3514 (8/20)**

## SECTION H4 REASON FOR SUBMISSION – 510(K)

| | | |
|---|---|---|
| ☒ Original<br>☐ Withdrawal of Original | ☐ Amendment Before Final Decision:<br>☐ Change in Ownership<br>☐ Change in Correspondent<br>☐ Withdrawal<br>☐ Amendment After Final Decision | ☐ Supplement:<br>☐ Response to Refuse to Accept (RTA)<br>☐ Response to Additional Information Request<br>☐ Withdrawal |
| ☐ Reprocessed SUD | ☐ Corrective Action | ☐ STED |
| ☐ Third Party *(Complete Section C)* | ☐ Other Reason *(Specify):* | |

Information on devices to which substantial equivalence is claimed *(If known)*

| | ***510(k) Number*** | ***Trade Name*** | ***Submitter*** | ***Product Code*** |
|---|---|---|---|---|
| **Primary Predicate (A)** | K201298 | VX1 | Volta Medical | DQK |
| **Predicate or Reference Device (B)** | | | | |

## SECTION H5 DE NOVO SUBMISSIONS

☐ Post NSE De Novo: Number of the 510(k) that was NSE'd in the past 30 days:
☐ Withdrawal

## SECTION H6 REASON FOR APPLICATION – CLIA

**Includes CLIA Parent Document number, CR number, or CW number.**

☐ **CLIA Categorization Record (CR):**
- ☐ CLIA Categorization of marketed device (include marketing submission number)
- ☐ CLIA Categorization of device exempt from premarket review
- ☐ Additional information regarding an open CR (include CR number)

☐ **CLIA Waiver by Application (CW):**
- ☐ Request for CLIA Waiver by Application for marketed device (include marketing submission number)
- ☐ Request for Dual 510(k) Clearance and CLIA Waiver by Application (include Pre-submission number)
- ☐ Response to FDA correspondence
- ☐ Additional information regarding an open CW (include CW number)

☐ **Other Reason** *(Specify)*

## SECTION I MANUFACTURING / PACKAGING / STERILIZATION SITES RELATING TO A SUBMISSION

**Applicable only to IDEs**

| | |
|---|---|
| *Note:* Submission of this information does not affect Registration and Listing. | FDA Document Number *(if known)* |

| | | |
|---|---|---|
| ☐ Original<br>☐ Add ☐ Delete | Facility Establishment Identifier **(FEI)** Number | ☐ Manufacturer ☐ Contract Sterilizer<br>☐ Contract Manufacturer ☐ Repackager/Relabeler |
| Company/Institution Name | | Establishment Registration Number/FEI *(if known)* |
| Street Address | | City |
| State/Province | ZIP/Postal Code | Country |
| Contact 1 Name | | Contact 1 Title |
| Contact 1 Division Name *(if applicable)* | | Contact 1 Phone Number *(including area code)* |
| Contact 1 Fax Number *(including area code)* | | Contact 1 Email Address |
| Contact 2 Name | | Contact 2 Title |
| Contact 2 Division Name *(if applicable)* | | Contact 2 Phone Number *(including area code)* |
| Contact 2 Fax Number *(including area code)* | | Contact 2 Email Address |

| | | |
|---|---|---|
| ☐ Original<br>☐ Add ☐ Delete | Facility Establishment Identifier **(FEI)** Number | ☐ Manufacturer ☐ Contract Sterilizer<br>☐ Contract Manufacturer ☐ Repackager/Relabeler |
| Company/Institution Name | | Establishment Registration Number/FEI *(if known)* |
| Street Address | | City |
| State/Province | ZIP/Postal Code | Country |
| Contact 1 Name | | Contact 1 Title |
| Contact 1 Division Name *(if applicable)* | | Contact 1 Phone Number *(including area code)* |
| Contact 1 Fax Number *(including area code)* | | Contact 1 Email Address |
| Contact 2 Name | | Contact 2 Title |
| Contact 2 Division Name *(if applicable)* | | Contact 2 Phone Number *(including area code)* |
| Contact 2 Fax Number *(including area code)* | | Contact 2 Email Address |

## SECTION J UTILIZATION OF STANDARDS

**Note** : Please see guidance document titled "Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices" for details on the Declaration of Conformity.

**Entries for Utilization of Standards**

| | Recognition Number | Declaration of Conformity or General Use | | Standards Development Organization (SDO), Designation Number-Year, and Title | Location |
|---|---|---|---|---|---|
| 1 | 2-282 | Declaration of Conformity | *If General Use*, Deviation? N/A | ISO 14155 – Third Edition 2020-07 Clinical Investigation of Medical Devices For Human Subjects – Good Clinical Practice | Sec. XXII |
| 2 | 5-125 | Declaration of Conformity | *If General Use*, Deviation? N/A | ISO 14971 - Third Edition 2019-12 Medical Devices – Application of Risk Management to Medical Devices | Sec. XII, XV, XVIII |
| 3 | 5-134 | Declaration of Conformity | *If General Use*, Deviation? N/A | ISO 15223-1 – Fourth Edition 2021-07 Medical Devices – Symbols to be used with information to be supplied by the Manufacturer – Part 1: General Requirements | Sec. XV |
| 4 | 19-46 | Declaration of Conformity | *If General Use*, Deviation? N/A | ANSI/AAMI ES60601-1:2005/(R)2012 AND A1:2012 C1:2009/(R)2012 AND A2:2010/(R)2012 (Consolidated Text) [Including AMD2:2021] Medical Electrical equipment – Part 1: General requirements for Basic Safety and Essential Performance (60601-1:2005, MOD) | Sec. XIX |
| 5 | 19-36 | Declaration of Conformity | *If General Use*, Deviation? N/A | IEC 60601-1-2 Edition 4.1 2020-09 (Consolidated Version) Medical Electrical Equipment – Part 1-2: General requirements for Basic Safety and Essential Performance – Collateral Standard: Electromagnetic Disturbances – Requirements and Tests | Sec. XIX |
| 6 | 5-132 | Declaration of Conformity | *If General Use*, Deviation? N/A | IEC 60601-1-6 Edition 3.2 2020-07 (Consolidated Version) Medical Electrical Equipment – Part 1-6: General requirements for Basic Safety and Essential Performance – Collateral Standard: Usability | Sec. XIX |
| 7 | 5-129 | Declaration of Conformity | *If General Use*, Deviation? N/A | IEC 62366-1 Edition 1.1 2020-06 (Consolidated Version) Medical Devices – Part 1 : Application of Usability Engineering to Medical Devices | Sec. XIX |
| 8 | 13-79 | Declaration of Conformity | *If General Use*, Deviation? N/A | IEC 62304 Edition 1.1 2015-06 (Consolidated Version) Medical Device Software – Software Life Cycle Processes | Sec. XIX |
| 9 | 15-135 | Declaration of Conformity | *If General Use*, Deviation? **N/A** | ISO 20417 First edition 2021-04 Corrected version 2021-12 Medical devices - Information to be supplied by the manufacturer | Sec. XV |

## SECTION K UTILIZATION OF CDRH GUIDANCE DOCUMENTS

**Entries for Utilization of CDRH Guidance Documents**

| | Title of Guidance Document |
|---|---|
| 1 | Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s |
| 2 | Guidance for Industry and FDA Staff: Refuse to Accept Policy for 510(k)s |
| 3 | Guidance for Industry and FDA Staff: Acceptance of Clinical data to Support Medical Device Applications and Submissions: Frequently Asked Questions |
| 4 | Guidance for Industry and FDA Staff: Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices |
| 5 | Guidance for Industry and FDA Staff: The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications (510(k)] |

| | |
|---|---|
| 6 | Guidance for Industry and FDA Staff: Medical Device Accessories – Describing Accessories and Classification Pathways |
| 7 | Guidance for Industry and FDA Staff: Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices |
| 8 | Guidance for Industry and FDA Staff: Unique Device Identification System: Form and Content of the Unique Device Identifier (UDI) |

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

***DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.***

The burden time for this collection of information is estimated to average .5 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
*PRAStaff@fda.hhs.gov*

*"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."*

## III. CERTIFICATION OF COMPLIANCE WITH CLINICALTRIALS.GOV DATA BANK

A completed copy of the Certification of Compliance with ClinicalTrials.gov Data Bank, FDA Form 3674, is provided on the following pages.

Form Approved: OMB No. 0910-0616. Expiration Date: 4/30/2024. See PRA Statement below.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

# Certification of Compliance

## Under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank

(For submission with an application/submission, including amendments, supplements, and resubmissions, under §§ 505, 515, 520(m), or 510(k) of the Federal Food, Drug, and Cosmetic Act or § 351 of the Public Health Service Act.)

## SPONSOR / APPLICANT / SUBMITTER INFORMATION

1. Name of Sponsor/Applicant/Submitter
Volta Medical

2. Date of the Application/Submission
11/22/2022

3. Address

Address 1 *(Street address, P.O. box, company name c/o)*
65 avenue Jules Cantini

Address 2 *(Apartment, suite, unit, building, floor, etc.)*

City
Marseille

State/Province/Region

Country
France

ZIP or Postal Code
13006

4. Telephone and Fax Numbers *(Include country code if applicable and area code)*

(Tel): +33 7 68 02 54 99

(Fax):

## PRODUCT INFORMATION

5. **For Drugs/Biologics:** Include Any/All Available Established, Proprietary and/or Chemical/Biochemical/Blood/Cellular/Gene Therapy Product Name(s).
**For Devices:** Include Any/All Common or Usual Name(s), Classification, Trade or Proprietary or Model Name(s) and/or Model Number(s)

VX1+, class II

Continuation Page for #5

## APPLICATION / SUBMISSION INFORMATION

6. Type of Application/Submission Which This Certification Accompanies

☐ IND ☐ NDA ☐ ANDA ☐ BLA ☐ PMA ☐ HDE ☒ 510(k) ☐ PDP ☐ Other

7. Include IND/NDA/ANDA/BLA/PMA/HDE/510(k)/PDP/ Other Number *(If number previously assigned)*

If BLA was selected in item 6, provide Supplement Number

8. Serial Number Assigned to Application/Submission Which This Certification Accompanies

## CERTIFICATION STATEMENT / INFORMATION

9. Check only one of the following boxes *(See instructions for additional information and explanation)*

☐ A. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act, including 42 CFR part 11, do not apply because the application/submission which this certification accompanies does not reference any clinical trial.

☐ B. I certify that the requirements of 42 U.S.C. § 282(j), Section 402(j) of the Public Health Service Act, including 42 CFR part 11, do not apply to any clinical trial referenced in the application/submission which this certification accompanies.

☒ C. I certify that the requirements of 42 U.S.C. § 282(j), section 402(j) of the Public Health Service Act, apply to one or more of the clinical trials referenced in the application/submission which this certification accompanies and that the requirements of 42 U.S.C. 282(j), including any applicable provisions of 42 CFR part 11, have been met.

*Certification Statement / Information section continued on page 2*

## CERTIFICATION STATEMENT / INFORMATION *(Continued)*

10. If you checked box C, in number 9, provide the National Clinical Trial (NCT) Number(s) for any "applicable clinical trial(s)," for which you (the sponsor/applicant/submitter) are the "responsible party" under 42 U.S.C. § 282(j)(1)(a)(i), section 402(j)(1)(a)(i) of the Public Health Service Act referenced in the application/ submission which this Certification accompanies. (Add continuation page as necessary.)

NCT Number(s): NCT05362656

Continuation Page for #10

The undersigned declares, to the best of her/his knowledge, that this is an accurate, true, and complete submission of information. I understand that the failure to submit the certification required by 42 U.S.C. § 282(j)(5)(B), section 402(j)(5)(B) of the Public Health Service Act, and the knowing submission of a false certification under such section are prohibited acts under 21 U.S.C. § 331, section 301 of the Federal Food, Drug, and Cosmetic Act.

**Warning:** A willfully and knowingly false statement is a criminal offense, U.S. Code, title 18, section 1001.

11. Name and Title of the Person who Signs Number 15

| Name | Title |
|---|---|
| Paola Milpied | VP of Clinical & Regulatory Affairs, Volta Medical |

12. Address

| | |
|---|---|
| Address 1 *(Street address, P.O. box, company name c/o)* | 65 avenue Jules Cantini |
| Address 2 *(Apartment, suite, unit, building, floor, etc.)* | |
| City | Marseille |
| State/Province/Region | |
| Country | France |
| ZIP or Postal Code | 13006 |

13. Telephone and Fax Numbers *(Include country code if applicable and area code)*

(Tel): +33 7 68 02 54 99

(Fax):

14. Date of Certification

11/21/2022

15. Signature of Sponsor/Applicant/Submitter or an Authorized Representative *(Sign)*

Sign

Paola Milpied Signature numérique de Paola Milpied
Date : 2022.11.21 22:28:29 +01'00'

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

*****DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.*****

The burden time for this collection of information is estimated to average 15 minutes and 45 minutes (depending on the type of application/ submission) per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
*PRAStaff@fda.hhs.gov*

*"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."*

## IV. 510(K) COVER LETTER

The cover letter for the submission is provided on the following pages.

Hogan Lovells US LLP
Columbia Square
555 Thirteenth Street, NW
Washington, DC 20004
T +1 202 637 5600
F +1 202 637 5910
www.hoganlovells.com

**November 22, 2022**

**By Messenger**

510(k) Document Mail Center (WO66-G609)
Center for Devices and Radiological Health
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Attention: Jessica Paulsen, Director Cardiac Ablation, Mapping, and Imaging Devices, Division of Health Technology 2 A (Cardiac Electrophysiology, Diagnostics, and Monitoring Devices)

**Re: Traditional Premarket Notification for Volta Medical's VX1+**

Dear Ms. Paulsen:

In accordance with Section 510(k) of the Federal Food, Drug, and Cosmetic Act ("FDC Act"), Volta Medical (or "the Company"), by its regulatory counsel, is submitting the attached premarket notification ("510(k) Notice") for its VX1+ device. This device is intended to assist operators in the real-time manual or automatic annotation of 3D anatomical and electrical maps of the human atria for the presence of multipolar intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion during atrial fibrillation or atrial tachycardia. The clinical significance of utilizing the VX1+ software to help identify areas with intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion for catheter ablation of atrial arrhythmias, such as atrial fibrillation, has not been established by clinical investigations.

The Volta Medical VX1+ is a Class II software device (21 C.F.R. § 870.1425, Product Code DQK) that operates in conjunction with existing 510(k) cleared catheters that meet certain designated characteristics and off-the-shelf components, including: a computer with an integrated analog-to-digital converter, a display monitor, and a connection cable that connects the data acquisition system to the analog-to-digital converter. The acquisition system determines which of two available types of connection cables is used.

In addition, the Volta Medical VX1+, intended to assist operators in the real-time manual or automatic annotation of 3D anatomical and electrical maps of human atria for the presence of multipolar intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion during atrial fibrillation or atrial tachycardia, is substantially equivalent to the Volta Medical VX1 that has already been cleared to assist operators in the real-time manual annotation of 3D anatomical and electrical maps of human atria for the presence of multipolar intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion during atrial fibrillation or atrial tachycardia, except for some minor technological

differences. The primary difference is VX1+'s ability to have a bidirectional digital communication with a compatible 3D mapping system, allowing automatic tagging of regions of interest and thus improving clinical workflow without affecting the device's diagnostic effects.

There have been no prior submissions regarding the subject of this submission.

To conform with the Food and Drug Administration's ("FDA" or the "Agency") September 13, 2019, *Guidance for Industry and FDA Staff: Format for Traditional and Abbreviated 510(k)s*, the principal factors concerning the design and use of the VX1+ are set forth in the following table of FDA questions.

| **Question** | **YES** | **NO** |
|---|---|---|
| Is the device intended for prescription use (21 CFR 801 Subpart D)? | x | |
| Is the device intended for over-the-counter use (21 CFR 807 Subpart C)? | | x |
| Does the device contain components derived from a tissue or other biologic source? | | x |
| Is the device provided sterile? | | x |
| Is the device intended for single use? | | x |
| Is the device a reprocessed single use device? | | x |
| If yes, does this device type require reprocessed validation data? | N/A | |
| Does the device contain a drug? | | x |
| Does the device contain a biologic? | | x |
| Does the device use software? | x | |
| Does the submission include clinical information? | x | |
| Is the device implanted? | | x |

As explained in more detail in the attached 510(k) notice, the VX1+ is substantially equivalent to VX1 (the "Predicate Device") that the Food and Drug Administration ("FDA") has already cleared to assist operators in the real-time manual annotation of 3D anatomical and electrical maps of human atria for the presence of multipolar intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion during atrial fibrillation or atrial tachycardia. The clinical significance of utilizing the VX1 software to help identify areas with intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion for catheter ablation of atrial arrhythmias, such as atrial fibrillation, has not been established by clinical investigations (K201298).

In accordance with the Medical Device User Fee Amendments of 2017 (MDUFA IV), Volta Medical has submitted the required application fee of $19,870. A copy of the User Fee Cover Sheet is provided with the attached premarket notification.

To conform to the agency's September 13, 2019, *Guidance for Industry and FDA Staff: Refuse to Accept Policy for 510(k)s*, **Section V** of this submission includes the agency's Refuse to Accept checklist and a guide to where in the submission the elements required for a complete 510(k) submission per 21 C.F.R. § 807.87 are located.

Volta Medical considers its intent to market the VX1+ as confidential commercial information. The Company has not disclosed its intent to market this device to anyone except its employees, others with a financial interest in the Company, its advertising or law firms, and its consultants. The Company, therefore requests that FDA not disclose the existence of this application until such time as final action on the submission is taken.

In addition, some of the material in this application may be trade secret or confidential commercial or financial information within the meaning of 21 C.F.R. § 20.61 and therefore not disclosable under the Freedom of Information Act even after the existence of this application becomes public. We ask that you consult with the Company as provided in 21 C.F.R. § 20.61(e) before making any part of this submission publicly available.

The information contained herein was provided by Volta Medical to Hogan Lovells US LLP for submission to FDA. Volta Medical is solely responsible for the completeness and accuracy of the submission.

We trust that the information provided in the 510(k) notice is sufficient for FDA to find the VX1+ substantially equivalent to the predicate device for the listed indication. If you have any questions regarding the information contained in this letter, please contact me at the phone number below.

Sincerely,

Kristin Zielinski Duggan
Partner
kristin.duggan@hoganlovells.com
D +1 (202) 637-8894

Attachments

ccs: Théophile Mohr Durdez, Co-Founder and CEO, Volta Medical
Jerome Kalifa, MD, PhD, Co-Founder and CMO, Volta Medical
Paola Milpied, PhD, Vice President of Clinical & Regulatory Affairs, Volta Medical
Janice M. Hogan, Partner, Hogan Lovells US LLP

## V. REFUSE TO ACCEPT CHECKLIST

***Contains Nonbinding Recommendations***

# Acceptance Checklist for Traditional 510(k)s

**(Should be completed within 15 days of DCC receipt)**

The following information is not intended to serve as a comprehensive review.

FDA recommends that the submitter include this completed checklist as part of the application.

**510(k)#:** **Date Received by DCC:**

**Lead Reviewer:**

**Center:** **Office:** **Division:**

**Decision: Accept_____ Refuse to Accept_____**

**If Accept, notify the submitter.**

**If Refuse to Accept, notify submitter electronically and include a copy of this checklist.**

**Is an Addendum attached?: Yes No**

Note: If an element is left blank on the checklist, it does not mean the checklist is incomplete; it means the reviewer did not assess the element during the RTA review and that the element will be assessed during substantive review.

| **Preliminary Questions**<br>**Answers in the shaded blocks indicate consultation with a Center advisor is needed.**<br>**(Boxes checked in this section represent FDAs preliminary assessment of these questions at the time of administrative review.)** | | | |
|---|---|---|---|
| | **Yes** | **No** | **N/A** |
| **1. Is the product a device (per section 201(h) of the FD&C Act) or a combination product (per 21 CFR 3.2(e)) with a device constituent part subject to review in a 510(k)?**<br>If it appears not to be a device (per section 201(h) of the FD&C Act) or such a combination product (per 21 CFR 3.2(e)), or you are unsure, consult with the CDRH Product Jurisdiction Officer or the CBER Product Jurisdiction Officer to determine the appropriate action, and inform management. *Provide a summary of* | ☒ | ☐ | |

| Preliminary Questions<br>**Answers in the shaded blocks indicate consultation with a Center advisor is needed.**<br>**(Boxes checked in this section represent FDAs preliminary assessment of these questions at the time of administrative review.)** | | | |
|---|---|---|---|
| | **Yes** | **No** | **N/A** |
| *the Product Jurisdiction Officer's determination/recommendation/action in the comment section below.*<br><br>If the product does not appear to be a device or such a combination product, mark "No."" | | | |
| **Comments:** | | | |
| **2. Is the submission with the appropriate Center?**<br>If the product is a device or a combination product with a device constituent part, is it subject to review by the Center in which the submission was received? If you believe the submission is not with the appropriate Center or you are unsure, consult with the CDRH Product Jurisdiction Officer or the CBER Product Jurisdiction Officer to determine the appropriate action and inform your management. *Provide a summary of the Product Jurisdiction Officer's determination/recommendation/action in the comment section below.*<br>If submission should not be reviewed by your Center mark "No." | ☒ | ☐ | |
| **Comments:** | | | |
| **3. If a Request for Designation (RFD) was submitted for the device or combination product with a device constituent part and assigned to your center, identify the RFD # and confirm the following:**<br>**(a) Is the device or combination product the same (e.g., design, formulation) as that presented in the RFD submission?**<br>**(b) Are the indications for use for the device or combination product identified in the 510(k) the same as those identified in the RFD submission?**<br>If you believe the product or the indications presented in the 510(k) have changed from the RFD, or you are unsure, consult with the CDRH Product Jurisdiction Officer or the CBER Product Jurisdiction Officer to determine the appropriate action and inform your management. *Provide summary of Product Jurisdiction Officer's determination/recommendation/action in the comment section below.*<br>If the answer to either question above is no, mark "No." If there was no RFD, mark "N/A." | ☐ | ☐ | ☒ |
| **Comments:** | | | |
| **4. Is the submission for a combination product that contains as a constituent part a drug that has the same active moiety as an approved drug with exclusivity as described in section 503(g)(5)(C)(ii)-(v) of the FD&C Act?**<br>If "Yes," then contact the CDRH Product Jurisdiction Officer or CBER Product Jurisdiction Officer to determine the appropriate action and inform your | ☐ | ☐ | ☒ |

| Preliminary Questions<br>**Answers in the shaded blocks indicate consultation with a Center advisor is needed.**<br>**(Boxes checked in this section represent FDAs preliminary assessment of these questions at the time of administrative review.)** | | | |
|---|---|---|---|
| | **Yes** | **No** | **N/A** |
| management. *Provide the summary of the Product Jurisdiction Officer's determination/recommendation/action in the comment section below.* | | | |
| **Comments:** | | | |
| **5. Is this device type eligible for a 510(k) submission?**<br>If a 510(k) does not appear to be appropriate (e.g., class III type and PMA required, or class I or II type and 510(k)-exempt), consult with the appropriate CDRH or CBER staff during the acceptance review, provide a summary of the discussion with them, and indicate their recommendation/action in the comment section below. If 510(k) is not the appropriate regulatory submission, mark "No." | ☒ | ☐ | |
| **Comments:** | | | |
| **6. Is there a pending PMA for the same device with the same indications for use?**<br>If "Yes," consult your management and CDRH Office of Product Evaluation and Quality/Office of Regulatory Programs/Division of Regulatory Programs 1 (Submission Support) (OPEQ/ORP/DRP1) or appropriate CBER staff to determine the appropriate action. | ☐ | ☒ | |
| **Comments:** | | | |
| **7. If clinical studies have been submitted, is the submitter the subject of an Application Integrity Policy (AIP)?**<br>If "Yes," consult with the CDRH Office of Product Evaluation and Quality/Office of Clinical Evidence and Analysis/Division of Clinical Science and Quality (OPEQ/OCEA/DCEA1) or CBER Office of Compliance and Biologics Quality/Division of Inspections and Surveillance/Bioresearch Monitoring Branch (OCBQ/DIS/BMB) to determine the appropriate action, provide a summary of the discussion with them, and indicate their recommendation/action<br>If no clinical studies have been submitted, mark "N/A." Check on the AIP list at https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/application-integrity-policy/application-integrity-policy-list. | ☐ | ☐ | ☒ |
| **Comments:** | | | |

- **If the answer to 1 or 2 appears to be "No," then stop review of the 510(k) and contact the CDRH Product Jurisdiction Officer or CBER Product Jurisdiction Officer.**
- **If the answer to 3a or 3b appears to be "No," then stop the review and contact the CDRH Product Jurisdiction Officer or CBER Product Jurisdiction Officer.**
- **If the answer to 4 is "Yes," then contact the CDRH Product Jurisdiction Officer or CBER Product Jurisdiction Officer, provide a summary of the discussion with them, and indicate their recommendation/action.**

Traditional RTA Checklist

- **If the answer to 5 is "No", the lead reviewer should consult division management and other Center resources to determine the appropriate action. Note that, for a device which is clearly ineligible for a 510(k) submission (such as a device type which is class III requiring PMA or class I/II and 510(k) exempt), this may be considered a basis for a refusal to accept the submission. A 510(k) submitted for a class I/II, 510(k)-exempt device that trips the limitations of the exemption would not be refused on this basis.**
- **If the answer to 6 is "Yes," then stop review of the 510(k), contact CDRH/OPEQ/ORP/DRP1, or appropriate CBER staff.**
- **If the answer to 7 is "Yes," then contact CDRH/OPEQ/OCEA/DCEA1 or CBER/OCBQ/DIS/BMB, provide a summary of the discussion with DCEA1 or BMB Staff, and indicate their recommendation/action.**

| **Organizational Elements**<br>Failure to include these items should not result in an RTA designation. | | | | |
|---|---|---|---|---|
| ***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.** | | **Yes** | **No** | ***Page #** |
| 1. | Submission contains a Table of Contents. | ☒ | ☐ | Table of Contents |
| 2. | Each section is labeled (e.g., headings or tabs designating Device Description section, Labeling section, etc.). | ☒ | ☐ | All |
| 3. | All pages of the submission are numbered.<br>*All pages should be numbered in such a manner that information can be referenced by page number. This may be done either by consecutively numbering the entire submission, or numbering the pages within a section (e.g., 12-1, 12-2...).* | ☒ | ☐ | All |
| 4. | Type of 510(k) is identified (i.e., Traditional, Abbreviated, or Special)<br>*If type of 510(k) is not designated, review as a Traditional 510(k).* | ☒ | ☐ | Section II, Section IV |
| **Comments:** | | | | |

| **Elements of a Complete Submission (RTA Items)**<br>**(21 CFR 807.87 unless otherwise indicated)**<br>Submission should be designated RTA if not addressed |
|---|
| • Any "No" answer will result in a "Refuse to Accept" decision; however, FDA staff has discretion to determine whether missing items are needed to ensure that the submission is administratively complete to allow the submission to be accepted or to request missing checklist items interactively from submitters during the RTA review.<br>• Each element on the checklist should be addressed within the submission. The submitter may provide a rationale for omission for any criteria that are deemed not applicable. If a rationale is provided, the criterion is considered present (Yes). An assessment of the rationale will be considered during the review of the submission. |

Traditional RTA Checklist

| Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.<br><br>*Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information. | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | **Yes** | **No** | **N/A** | ***Page #** |
| **A.** | **Administrative** | | | | | | |
| | 1. | All content used to support the submission is written in English (including translations of test reports, literature articles, etc.). | | ☒ | ☐ | | All |
| | | **Comments:** | | | | | |
| | 2. | Submission identifies the following (FDA recommends use of the CDRH Premarket Review Submission Cover Sheet form (Form 3514, available at https://www.fda.gov/media/72421/download)): | | | | | Section II |
| | | a. | Device trade/proprietary name | ☒ | ☐ | | Section II |
| | | b. | Device class and panel OR<br><br>Classification regulation OR<br><br>Statement that device has not been classified with rationale for that conclusion | ☒ | ☐ | | Section II |
| | | **Comments:** | | | | | |
| | 3. | Submission contains an Indications for Use Statement with Rx and/or OTC designated (see also 21 CFR 801.109, and FDA's final rule, "Use of Symbols in Labeling" (81 FR 38911), available at https://www.federalregister.gov/documents/2016/06/15/2016-13989/use-of-symbols-in-labeling). See recommended format (https://www.fda.gov/media/86323/download). | | ☒ | ☐ | | Section VI |
| | | **Comments:** | | | | | |
| | 4. | Submission contains a 510(k) Summary or 510(k) Statement.<br><br>*Refer to 21 CFR 807.92 and 21 CFR 807.93 for contents of 510(k) Summary and Statement, respectively. Adequacy of the content will be assessed during substantive review.* | | ☒ | ☐ | | Section VII |

| | | | | Yes | No | N/A | *Page # |
|---|---|---|---|---|---|---|---|
| **Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.**<br><br>***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.** | | | | | | | |
| | | **Comments:** | | | | | |
| | 5. | Submission contains a Truthful and Accuracy Statement per 21 CFR 807.87(l). See recommended format (https://www.fda.gov/medical-devices/premarket-notification-510k/premarket-notification-truthful-and-accurate-statement). | | ☒ | ☐ | | Section VIII |
| | | **Comments:** | | | | | |
| | 6. | Submission is a Class III 510(k) Device.<br><br>*Select "N/A" only if submission is not a Class III 510(k).* | | ☐ | | ☒ | Section IX |
| | | a. | Contains class III Summary and Certification per 21 CFR 807.87(k). See recommended content (https://www.fda.gov/medical-devices/premarket-notification-510k/premarket-notification-class-iii-certification-and-summary). Select "N/A" only if submission is not a class III 510(k). | ☐ | ☐ | ☐ | |
| | | **Comments:** | | | | | |
| | 7. | Submission contains clinical data.<br><br>*Select "N/A" if the submission does not contain clinical data. If "N/A" is selected, parts a, b, and c below are omitted from the checklist.* | | ☒ | | ☐ | Section XXII |
| | | a. | Submission includes completed Financial Certification (FDA Form 3454, available at https://www.fda.gov/media/70465/download) or Disclosure (FDA Form 3455, available at https://www.fda.gov/media/69872/download)) information for each covered clinical study included in the submission.<br><br>*Select "N/A" if the submitted clinical data is not a "covered clinical study" as defined in the guidance entitled "Financial Disclosures by Clinical Investigators," available at https://www.fda.gov/regulatory-information/search-fda-* | ☐ | ☐ | ☒ | Section X |

| Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.<br><br>*Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information. | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | Yes | No | N/A | *Page # |
| | | | guidance-documents/financial-disclosure-clinical-investigators. | | | | |
| | | b. | Submission includes completed Certification of Compliance with requirements of ClinicalTrials.gov Data Bank (see FDA Form 3674 which can be obtained at https://www.fda.gov/about-fda/reports-manuals-forms/forms) (42 U.S.C. 282(j)(5)(B)) for each applicable device clinical trial included in the submission. Select "N/A" if the submitted clinical data is not an "applicable device clinical trial" as defined in *Title VIII of FDAAA, Sec. 801(j)*. | ☒ | ☐ | ☐ | Section III |
| | | c. | Statements of Compliance for Clinical Investigations<br><br>*Select "N/A" if the submission does not contain any clinical data from investigations (as defined in 21 CFR 812.3(h)) to demonstrate substantial equivalence.*<br><br>*For multicenter clinical investigations involving both United States (US) and outside United States (OUS) sites, part (i) should be addressed for the US sites and part (ii) should be addressed for the OUS sites. 21 CFR 812.28 applies to all OUS clinical investigations that enroll the first subject on or after February 21, 2019.*<br><br>*Please refer to the guidance document entitled "Acceptance of Clinical Data to Support Medical Device Applications and Submissions - Frequently Asked Questions"* available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/acceptance-clinical-data-support-medical-device-applications-and-submissions-frequently-asked *for more information.* | ☒ | | ☐ | Section XXII |
| | | | i. For each clinical investigation conducted in the US, the submission includes a statement that the investigation was conducted in compliance with 21 CFR parts 50, 56, and 812 (or, with respect to part 56, that it was not | ☒ | ☐ | ☐ | |

| Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.<br><br>*Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information. | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | **Yes** | **No** | **N/A** | ***Page #** |
| | | | | subject to the regulations under 21 CFR 56.104 or 56.105).<br><br>**OR**<br><br>The submission includes a brief statement of the reason for noncompliance with 21 CFR parts 50, 56, and/or 812. *Select "N/A" if the clinical investigations were conducted solely OUS* | | | | |
| | | | ii. | For each clinical investigation conducted OUS, the submission includes a statement that the clinical investigations were conducted in accordance with good clinical practice (GCP) as described in 21 CFR 812.28(a)(1).<br><br>**OR**<br><br>The submission includes a waiver request in accordance with 21 CFR 812.28(c).<br><br>**OR**<br><br>The submission includes a brief statement of the reason for not conducting the investigation in accordance with GCP and a description of steps taken to ensure that the data and results are credible and accurate and that the rights, safety, and well-being of subjects have been adequately protected.<br><br>*Select "N/A" if the clinical investigations were conducted solely inside the US.* | ☒ | ☐ | ☐ | |
| | | **Comments:** | | | | | | |
| | 8. | The submission identifies prior submissions for the same device included in the current submission (e.g., submission numbers for | | | ☒ | ☐ | | Section II, Section IV |

| **Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.**<br><br>***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.** | | | | | | |
|---|---|---|---|---|---|---|
| | | | **Yes** | **No** | **N/A** | ***Page #** |
| | | a prior not substantially equivalent [NSE] determination, prior deleted or withdrawn 510(k), Q-Submission, IDE, PMA, etc.).<br><br>**OR**<br><br>States that there were no prior submissions for the subject device.<br><br>*Prior submissions (or no prior submissions) for this device should be included in Section F (prior related submissions) of the CDRH Premarket Review Submission Cover Sheet form (Form 3514 available at https://www.fda.gov/media/72421/download).*<br><br>*This information may also be included in the Cover Letter (i.e., as a statement that there were no prior submissions for the device or a listing of the number(s) of the prior submissions).* | | | | |
| | | a. If there were prior submissions, the submitter has identified where in the current submission any issues related to a determination of substantial equivalence from prior submissions for this device are addressed.<br><br>*To address this criterion, it is recommended that the submission include a separate section with the prior submission number(s), a copy of the FDA feedback (e.g., letter, meeting minutes), and a statement of how or where in the submission this prior feedback was addressed. Note that adequacy of how the feedback was addressed will be assessed during the substantive review.*<br><br>*Select "N/A" if the submitter states there were no prior submissions.* | ☐ | ☐ | ☒ | |
| | | **Comments:** | | | | |
| | 9. | The submission utilizes voluntary consensus standard(s) (See section 514(c) of the FD&C Act). *This includes both FDA-recognized and non-recognized consensus standards. Select* | ☒ | | ☐ | Section XI |

| Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.<br><br>*Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information. | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | **Yes** | **No** | **N/A** | ***Page #** |
| | | *"N/A" if the submission does not utilize voluntary consensus standards.* | | | | | | | | | |
| | | a. | The submission cites FDA-recognized voluntary consensus standard(s). | | | | | ☒ | | ☐ | Section XI |
| | | | i. | The submission includes a Declaration of Conformity (DOC) as outlined in FDA's guidance "Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/appropriate-use-voluntary-consensus-standards-premarket-submissions-medical-devices.<br><br>**OR**<br><br>If citing general use of a standard as noted in FDA's guidance "Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices," the basis of such use is included along with the underlying information or data that supports how the standard was used. | | | | | ☒ | ☐ | | Section XI |
| | | b. | The submission cites non-FDA-recognized voluntary consensus standard(s). | | | | | ☒ | | ☐ | Section XI |
| | | | i. | The basis of use is included along with the underlying information or data that supports how the standard was used. | | | | ☒ | ☐ | | Section XI |
| | | **Comments:** | | | | | | | | | |
| | **Combination Product Provisions – Per 503(g) of the FD&C Act.**<br><br>Select "N/A" if the product is not a combination product. 21 CFR 3.2(e). The remaining criteria in this section will be omitted from the checklist if "N/A" is selected. If you are unsure if the product is a combination | | | | | | | | | ☒ | |

| Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.<br><br>*Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information. | | | | | | |
|---|---|---|---|---|---|---|
| | | | **Yes** | **No** | **N/A** | ***Page #** |
| | product, consult with the CDRH Product Jurisdiction Officer or CBER Product Jurisdiction Officer. | | | | | |
| | 10. | Submission identifies the product as a combination product. | ☐ | ☐ | | |
| | 11. | The combination product contains as a constituent part an approved drug as defined in section 503(g)(5)(B) of the FD&C Act. Select "N/A" if the combination product does not contain as a constituent part an approved drug. Please also select "N/A" if a right of reference or use for the drug constituent part(s) is included with the submission. If "N/A" is selected, part a below is omitted from the checklist. | ☐ | | ☐ | |
| | | a. The submission includes appropriate patent statement or certification and a statement that the submitter will give notice, as applicable. See section 503(g)(5)(A)&(C) of the FD&C Act.. | ☐ | ☐ | | |
| | | **Comments:** | | | | |
| **B.** | **Device Description** | | | | | |
| | 12. | The device has a device-specific guidance document, special controls, and/or requirements in a device-specific classification regulation regarding the device description that is applicable to the subject device.<br><br>*If "N/A" is selected, parts a and b below are omitted from the checklist.* | ☐ | | ☒ | Section XIII |
| | | a. The submission addresses device description recommendations outlined in the device-specific guidance.<br><br>**OR**<br><br>The submission provides an alternative approach intended to address the applicable statutory and/or regulatory criteria. | ☐ | ☐ | ☒ | Section XIII |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.**<br><br>***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.** | | | | | | | |
| | | | | **Yes** | **No** | **N/A** | ***Page #** |
| | | | *Select "N/A" if there is no applicable device-specific guidance. Select "No" if the submission does not include a rationale for any omitted information or any alternative approach as outlined above. Note that the adequacy of how recommendations in a device-specific guidance, etc., have been addressed should be assessed during the substantive review.* | | | | |
| | | b. | The submission includes device description information that addresses relevant mitigation measures set forth in the special controls or device-specific classification regulation applicable to the device.<br><br>**OR**<br><br>The submission uses alternative mitigation measures and provides rationale why the alternative measures provide an equivalent assurance of safety and effectiveness.<br><br>*Select "N/A" if there are no applicable special controls or device-specific classification regulation. Select "No" if the submission does not include a rationale for any omitted information or any alternative approach as outlined above. Note that the adequacy of how such mitigation measures have been addressed should be assessed during the substantive review.* | ☐ | ☐ | ☒ | |
| | | **Comments:** | | | | | |
| | 13. | Descriptive information is present and consistent within the submission (e.g., the device description section is consistent with the device description in the labeling). | | ☒ | ☐ | | Section XIII |
| | | Comments: | | | | | |
| | 14. | The submission includes descriptive information for the device, including the following: | | | | | |

| Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.<br><br>*Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information. | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | **Yes** | **No** | **N/A** | ***Page #** |
| | | a. | A description of the principle of operation or mechanism of action for achieving the intended effect. | ☒ | ☐ | | Section XIII |
| | | b. | A description of proposed conditions of use, such as surgical technique for implants; anatomical location of use; user interface; how the device interacts with other devices; and/or how the device interacts with the patient. | ☒ | ☐ | | Section XIII |
| | | c. | A list and description of each device for which clearance is requested.<br><br>*Select "N/A" if there is only one device or model. "Device" may refer to models, part numbers, various sizes, etc.* | ☐ | ☐ | ☒ | |
| | | d. | Submission contains representative engineering drawing(s), schematics, illustrations, photos and/or figures of the device.<br><br>**OR**<br><br>Submission includes a statement that engineering drawings, schematics, etc. are not applicable to the device (e.g., device is a reagent and figures are not pertinent to describe the device).<br><br>*In lieu of engineering drawings, schematics, etc. of each device to be marketed, "representative" drawings, etc. may be provided, where "representative" is intended to mean that the drawings, etc. provided capture the differences in design, size, and other important characteristics of the various models, sizes, or versions of the device(s) to be marketed.* | ☒ | ☐ | | Section XIII, Appendix 13.1 |
| | | **Comments:** | | | | | |
| | 15. | Device is intended to be marketed with accessories, and/or as part of a system. | | ☒ | | ☐ | Section XIII |

| Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.<br><br>*Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information. | | | | Yes | No | N/A | *Page # |
|---|---|---|---|---|---|---|---|
| | | *Select "N/A" if the device is not intended to be marketed with accessories, and/or as part of a system. If "N/A" is selected, parts a-c below are omitted from the checklist.* | | | | | |
| | | a. | Submission includes a list of all accessories to be marketed with the subject device. | ☒ | ☐ | | Section XIII |
| | | b. | Submission includes a description (as detailed in item 14a., 14b., and 14d. above) of each accessory.<br><br>*Select "N/A" if the accessory(ies) has been previously cleared, or is exempt, and the proposed indications for use are consistent with the cleared indications.* | ☐ | ☐ | ☒ | |
| | | c. | A 510(k) number is provided for each accessory that received a prior 510(k) clearance<br><br>**AND**<br><br>A statement is provided that identifies accessories that have not received prior 510(k) clearance. | ☐ | ☐ | ☒ | |
| | | **Comments:** | | | | | |
| **C.** | **Substantial Equivalence Discussion** | | | | | | |
| | 16. | Submitter has identified a predicate device(s), including the following information: | | | | | |
| | | a. | Predicate device identifier provided (e.g., 510(k) number, De Novo number, reclassified PMA number, classification regulation reference if exempt (e.g., 21 CFR 872.3710) or statement that the predicate is a preamendment device).<br><br>For predicates that are preamendments devices, information is provided to document preamendments status.<br><br>*Information regarding documenting preamendment status is available online (https://www.fda.gov/medical-* | ☒ | ☐ | | Section XIV |

| Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.<br><br>*Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information. | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | Yes | No | N/A | *Page # |
| | | | devices/quality-and-compliance-medical-devices/preamendment-status). | | | | |
| | | b. | The identified predicate(s) is consistent throughout the submission (e.g., the predicate(s) identified in the Substantial Equivalence section is the same as that listed in the 510(k) Summary (if applicable) and that used in comparative performance testing. | ☒ | ☐ | | Section XIV |
| | | **Comments:** | | | | | |
| | 17. | Submission includes a comparison of the following for the predicate(s) and subject device and a discussion why any differences between the subject and predicate(s) do not impact safety and effectiveness [see section 513(i)(1)(A) of the FD&C Act and 21 CFR 807.87(f)].<br><br>*See the FDA guidance document "The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/510k-program-evaluating-substantial-equivalence-premarket-notifications-510k for more information on comparing intended use and technological characteristics.* | | | | |
| | | a. | Indications for use<br><br>*If there are no differences between the subject device and the predicate(s) with respect to indications and intended use, this should be explicitly stated.* | ☒ | ☐ | | Section XIV.A |
| | | b. | Technology, including technical specifications, features, materials, and principles of operation<br><br>*Examples of technological characteristics include, but are not limited to design, features, materials, energy source, and principle of operation.* | ☒ | ☐ | | Section XIV.B |

| Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.<br><br>*Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information. | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | **Yes** | **No** | **N/A** | ***Page #** |
| | | | *FDA recommends a tabular format for comparing technological characteristics. Any characteristic that is the same as the predicate(s) should be explicitly stated. Differences in technological characteristics should be identified and a rationale provided why they do not raise different questions of safety and effectiveness.* | | | | |
| | | **Comments:** | | | | | |
| **D.** | **Proposed Labeling (see also 21 CFR parts 801 and 809 as applicable)** | | | | | | |
| | 18. | Submission includes proposed package labels and labeling (e.g., instructions for use, package insert, operator's manual). | | ☒ | ☐ | | Appendices 15.1, 15.2, and 15.3 |
| | | a. | Indications for use are stated in labeling and are identical to Indications for Use form and 510(k) Summary (if 510(k) Summary provided). | ☒ | ☐ | | Appendices 15.1, 15.2, and 15.3 |
| | | b. | Labeling includes:<br><br>- Statements of conditions, purposes or uses for which the device is intended (e.g., hazards, warnings, precautions, contraindications) (21 CFR 801.5)<br><br>**AND**<br><br>- Includes adequate directions for use (see 21 CFR 801.5)<br><br>**OR**<br><br>- Submission states that device qualifies for exemption per 21 CFR 801 Subpart D | ☒ | ☐ | | Appendices 15.1, 15.2, and 15.3 |
| | | **Comments:** | | | | | |

| Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.<br><br>*Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information. | | | | | |
|---|---|---|---|---|---|
| | | | **Yes** | **No** | **N/A** | ***Page #** |
| | 19. | Labeling includes name and place of business of the manufacturer, packer, or distributor (21 CFR 801.1). | ☐ | ☐ | | Appendices 15.1, 15.2, and 15.3 |
| | | **Comments:** | | | | |
| | 20. | Labeling includes the prescription statement (see 21 CFR 801.109(b)(1)) or Rx Only symbol (see also Section 502(a) of the FD&C Act and FDA's final rule, "Use of Symbols in Labeling" (81 FR 38911), available at https://www.federalregister.gov/documents/2016/06/15/2016-13989/use-of-symbols-in-labeling).<br><br>*Select "N/A" if not indicated for prescription us* | ☒ | ☐ | ☐ | Appendices 15.1, 15.2, and 15.3 |
| | | **Comments:** | | | | |
| | 21. | The device has a device-specific guidance document, special controls, and/or requirements in a device-specific classification regulation regarding labeling that is applicable to the subject device.<br><br>*If "N/A" is selected, parts a and b below are omitted from the checklist.* | ☐ | | ☒ | |
| | | a. The submission addresses labeling recommendations outlined in the device-specific guidance.<br><br>**OR**<br><br>The submission provides an alternative approach intended to address the applicable statutory and/or regulatory criteria.<br><br>*Select "N/A" if there is no applicable device-specific guidance. Select "No" if the submission does not include a rationale for any omitted information or any alternative approach as outlined above. Note that the adequacy of how recommendations in a device-specific guidance, etc., have* | ☐ | ☐ | ☐ | |

| Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.<br><br>*Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information. | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | **Yes** | **No** | **N/A** | ***Page #** |
| | | | *been addressed should be assessed during the substantive review.* | | | | |
| | | b. | The submission includes labeling information that addresses relevant mitigation measures set forth in the special controls or device-specific classification regulation applicable to the device.<br><br>**OR**<br><br>The submission uses alternative mitigation measures and provides rationale why the alternative measures provide an equivalent assurance of safety and effectiveness.<br><br>*Select "N/A" if there are no applicable special document or device-specific classification regulation. Select "No" if the submission does not include a rationale for any omitted information or any alternative approach as outlined above. Note that the adequacy of how such mitigation measures have been addressed should be assessed during the substantive review.* | ☐ | ☐ | ☒ | |
| | | **Comments:** | | | | | |
| | 22. | If the device is an in vitro diagnostic device, provided labeling includes all applicable information required per 21 CFR 809.10.<br><br>*Select "N/A" if not an in vitro diagnostic device.* | | ☐ | ☐ | ☒ | |
| | | **Comments:** | | | | | |
| **E.** | **Sterilization**<br><br>*If an in vitro diagnostic (IVD) device and sterilization is not applicable, select "N/A." The criteria in this section will be omitted from the checklist if "N/A" is selected.* | | | | | ☐ | |

| **Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.**<br><br>***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.** | | | | |
|---|---|---|---|---|
| | **Yes** | **No** | **N/A** | ***Page #** |
| Submission states that the device and/or accessories, if applicable, are:<br><br>(*one of the below must be checked*)<br><br>☐ Provided sterile, intended to be single-use<br><br>☐ Requires processing during its use-life<br><br>☒ Non-sterile when used (and no processing required)<br><br>☐ Information regarding the sterility status of the device is not provided (if this box is checked, please also check one of the two boxes below)<br><br>☐ Sterility status not needed for this device (e.g., software-only device)<br><br>☐ Sterility status needed or need unclear<br><br>This information will determine whether and what type of additional information may be necessary for a substantial equivalence determination.<br><br>*If "non-sterile when used" or "not provided and not needed" is selected, the sterility-related criteria below are omitted from the checklist.*<br><br>*If information on sterility status is not provided, and it is needed or the need for this information is unclear, select "No."*<br><br>*The "Requires processing during its use-life" option refers to devices falling into one of the four categories below:*<br><br>• *Supplied sterile and requires reprocessing prior to subsequent patient use*<br><br>• *Supplied non-sterile and requires user to process the device for initial use, as well as to reprocess the device after each use* | ☐ | | | Section XVI |

| | | | | | | |
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| **Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.**<br><br>***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.** | | | | | | |
| | | | | **Yes** | **No** | **N/A** | ***Page #** |
| | • *Reusable medical device (single-user) reprocessed between each use*<br><br>• *Single-use medical devices initially supplied as non-sterile to the user, and requiring the user to process the device prior to its use*<br><br>*Please refer to the FDA guidance document "Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/reprocessing-medical-devices-health-care-settings-validation-methods-and-labeling, for additional information.* | | | | | | |
| | **Comments:** | | | | | | |
| | 23. | Assessment of the need for cleaning and subsequent disinfection or sterilization information. | | | | | |
| | | a. | Identification of device, and/or accessories, if applicable, that are provided sterile.<br><br>*Select "N/A" if no part of the device or accessories are provided sterile.* | ☐ | ☐ | ☒ | |
| | | b. | Identification of device, and/or accessories, if applicable, that are end user sterilized or disinfected.<br><br>*Select "N/A" if no part of the device are accessories, or components is end user sterilized or disinfected.* | ☐ | ☐ | ☒ | |
| | | c. | Identification of device, and/or accessories, if applicable, that are reusable.<br><br>*Select "N/A" if no part of the device or accessories are reusable.* | ☐ | ☐ | ☒ | |
| | | **Comments:** | | | | | |

| | | | | Yes | No | N/A | *Page # |
|---|---|---|---|---|---|---|---|
| **Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.**<br><br>***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.** | | | | | | | |
| | 24. | If the device and/or accessories, if applicable, are provided sterile:<br><br>*Select "N/A" if no part of the device or accessories are provided sterile, otherwise complete a-f below.* | | | | ☒ | |
| | | a. | Sterilization method is stated for each device (including dose for radiation sterilization) | ☐ | ☐ | | |
| | | b. | A description of method to validate the sterilization parameters is provided for each proposed sterilization method (e.g., half-cycle method and full citation of FDA-recognized standard, including date).<br><br>*Note: the sterilization validation report is not required.* | ☐ | ☐ | | |
| | | c. | For devices sterilized using chemical sterilants such as ethylene oxide (EO) and hydrogen peroxide, submission states maximum levels of sterilant residuals remaining on the device and sterilant residual limits.<br><br>*Select "N/A" if not sterilized using chemical sterilants.* | ☐ | ☐ | ☐ | |
| | | d. | Sterility Assurance Level (SAL) stated | ☐ | ☐ | | |
| | | e. | Submission includes description of packaging | ☐ | ☐ | | |
| | | f. | For products labeled "non-pyrogenic," a description of the method used to make the determination stated (e.g., limulus amebocyte lysate [LAL]).<br><br>*Select "N/A" if not labeled "non-pyrogenic."* | ☐ | ☐ | ☐ | |
| | | **Comments:** | | | | | |
| | 25. | If the device, and/or accessory, if applicable, is reusable or end user sterilized or disinfected: | | | | ☒ | |

| **Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.**<br><br>***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.** | | | | | **Yes** | **No** | **N/A** | ***Page #** |
|---|---|---|---|---|---|---|---|---|
| | | *Select "N/A" if no part of the device or accessories are reusable or end user sterilized or disinfected, otherwise complete a-d below.* | | | | | | |
| | | a. | Cleaning method is provided in labeling for each device and/or accessory, if applicable.<br><br>*Select "N/A" if not reusable and does not need cleaning prior to disinfection or sterilization.* | | ☐ | ☐ | ☒ | |
| | | b. | Disinfection method is provided in labeling for each device, and/or accessory, if applicable.<br><br>*Select "N/A" if not disinfected (i.e., undergoes terminal sterilization) prior to use* | | ☐ | ☐ | ☒ | |
| | | c. | Sterilization method is provided in labeling for each device and/or accessory, if applicable.<br><br>*Select "N/A" if not sterilized (i.e., undergoes disinfection) prior to use* | | ☐ | ☐ | ☒ | |
| | | d. | Device types in this submission are listed in the Federal Register (FR) Notice entitled "Validated Instructions for Use and Validation Data Requirements for Certain Reusable Medical Devices in Premarket Notifications" (Reprocessing FR Notice, available at https://www.federalregister.gov/documents/2017/06/09/2017-12007/medical-devices-validated-instructions-for-use-and-validation-data-requirements-for-certain-reusable).<br><br>*Device types identified in the Reprocessing FR Notice represent devices posing a greater likelihood of microbial transmission and represent a high risk of infection. Select "N/A" if the device type in the submission is not included in the Reprocessing FR Notice.* | | ☐ | | ☐ | |
| | | | i. | If device types in this submission are included in the Reprocessing FR Notice, the submission includes | ☐ | ☐ | ☒ | |

| **Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.**<br><br>***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.** | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | **Yes** | **No** | **N/A** | ***Page #** |
| | | | | protocols and test reports for validating the reprocessing instructions.<br><br>*Select "N/A" if the device type in the submission is not included in the Reprocessing FR Notice.* | | | | |
| | | **Comments:** | | | | | | |
| | 26. | The device has a device-specific guidance document, special controls, and/or requirement in a device-specific classification regulation regarding sterility and/or reprocessing that is applicable to the subject device.<br><br>*If "N/A" is selected, parts a and b below are omitted from the checklist.* | | | ☐ | | ☒ | |
| | | a. | The submission addresses sterility and/or reprocessing recommendations outlined in the device-specific guidance.<br><br>**OR**<br><br>The submission provides an alternative approach intended to address the applicable statutory and/or regulatory criteria.<br><br>*Select "N/A" if there is no applicable device-specific guidance. Select "No" if the submission does not include a rationale for any omitted information or any alternative approach as outlined above. Note that the adequacy of how recommendations in a device-specific guidance, etc., have been addressed should be assessed during the substantive review.* | | ☐ | ☐ | ☒ | |
| | | b. | The submission includes sterility and/or reprocessing information that addresses relevant mitigation measures set forth in the special controls or device-specific classification regulation applicable to the device.<br><br>**OR** | | ☐ | ☐ | ☒ | |

| | | | | | | | |
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| **Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.**<br><br>***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.** | | | | | | | |
| | | | | **Yes** | **No** | **N/A** | ***Page #** |
| | | | The submission uses alternative mitigation measures and provides rationale why the alternative measures provide an equivalent assurance of safety and effectiveness.<br><br>*Select "N/A" if there are no applicable special controls or device-specific classification regulation. Select "No" if the submission does not include a rationale for any omitted information or any alternative approach as outlined above. Note that the adequacy of how such mitigation measures have been addressed should be assessed during the substantive review.* | | | | |
| | | **Comments:** | | | | | |
| **F.** | **Shelf-Life** | | | | | | |
| | 27. | Proposed shelf life/ expiration date stated<br><br>**<u>OR</u>**<br><br>Statement that shelf-life is not applicable because of low likelihood of time-dependent product degradation. | | ☒ | ☐ | | Section XVI |
| | | **Comments:** | | | | | |
| | 28. | For a sterile device, submission includes summary of methods used to establish that device packaging will maintain a sterile barrier for the entirety of the proposed shelf-life.<br><br>*Select "N/A" if the device is not provided sterile.* | | ☐ | ☐ | ☒ | |
| | | **Comments:** | | | | | |
| | 29. | Submission includes summary of methods used to establish that device performance is maintained for the entirety of the proposed shelf-life (e.g., mechanical properties, coating integrity, pH, osmolality, etc.). | | ☐ | ☐ | ☒ | |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.**<br><br>***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.** | | | | | | |
| | | | **Yes** | **No** | **N/A** | ***Page #** |
| | | **OR**<br><br>Statement why performance data is not needed to establish maintenance of device performance characteristics over the shelf-life period. | | | | |
| | | **Comments:** | | | | |
| **G.** | **Biocompatibility**<br><br>*If an in vitro diagnostic (IVD) device, select "N/A." The criteria in this section will be omitted from the checklist if "N/A" is selected.* | | | | ☐ | Section XVII |
| | Submission states that there: *(one of the below must be checked)*<br><br>☐ Are direct or indirect tissue-contacting components<br><br>☒ Are no direct or indirect tissue -contacting components<br><br>☐ Information regarding tissue contact status of the device is not provided (if this box checked, please also check one of the two boxes below)<br><br>☐ Tissue contact information not needed for this device (e.g., software-only device)<br><br>☐ Tissue contact information is needed or need unclear<br><br>This information will determine whether and what type of additional information may be necessary for a substantial equivalence determination.<br><br>*If "are no" or "not provided and not needed" is selected, the biocompatibility-related criteria below are omitted from the checklist. If information on the tissue -contact status is not provided, and contact information is needed or its contact status is unclear, select "No."* | | | ☐ | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.**<br><br>***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.** | | | | | | |
| | | | **Yes** | **No** | **N/A** | ***Page #** |
| | *An example of a direct* tissue-*contacting device would be an implant that has direct contact with tissues during use. An example of an indirect* tissue-*contacting device would be fluid entering the body following passing through device/device components not in direct contact with the* tissue*.* | | | | | |
| | **Comments:** | | | | | |
| | 30. | Submission includes a list identifying each tissue-contacting device component (e.g., implant, delivery catheter) and associated materials of construction for each component, including identification of color additives, if present. | ☐ | ☐ | ☒ | |
| | | **Comments:** | | | | |
| | 31. | Submission identifies contact classification (e.g., surfacecontacting, less than 24 hour duration) for each tissue-contacting device component (e.g., implant, delivery catheter). | ☐ | ☐ | ☒ | |
| | | **Comments:** | | | | |
| | 32. | For a biocompatibility assessment of tissue-contacting components, submission includes:<br><br>• Each relevant endpoint for the device (as identified in device-specific guidance, or Attachment A of the FDA guidance document entitled "Use of International Standard ISO 10993- 1, 'Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process,'" 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), has been addressed.<br>• For any testing performed, test protocol (including identification and description of test article including whether the test article is the device in its final finished form using the recommended approach in Attachment F of "Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process,'" methods, and | ☐ | ☐ | ☒ | |

| Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.<br><br>*Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information. | | | | | |
|---|---|---|---|---|---|
| | | **Yes** | **No** | **N/A** | ***Page #** |
| | pass/fail criteria), and analysis of results (including tables with data points and statistical analyses, where appropriate), as described in Attachment E of the guidance document entitled "Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process'" provided for each completed test.<br>**OR**<br>A statement that biocompatibility testing is not needed with a rationale that considers all relevant endpoints (e.g., materials and manufacturing/processing are identical to the predicate) | | | | |
| | **Comments:** | | | | |
| **H.** | **Software** | | | | |
| | Submission states that the device: (*one of the below must be checked*)<br><br>☒ Does contain software/firmware<br><br>☐ Does not contain software/firmware<br><br>☐ Information on whether device contains software/firmware is not provided<br><br>(if this box checked, please also check one of the two boxes below)<br><br>☐ Software/firmware information not needed for this device (e.g., surgical suture, condom)<br><br>☐ Software/firmware information is needed or need unclear<br><br>This information will determine whether and what type of additional information may be necessary for a substantial equivalence determination.<br><br>*If "does not contain" or "not provided and not needed" is selected, the software-related criteria below are omitted from the checklist. If information on software* | | ☐ | | Section XVIII |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.**<br><br>***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.** | | | | | | |
| | | | **Yes** | **No** | **N/A** | ***Page #** |
| | *is not provided, and this information is needed or the need is unclear, select "No."* | | | | | |
| | **Comments:** | | | | | |
| | 33. | Submission includes a statement of software level of concern and rationale for the software level of concern | ☐ | ☐ | ☒ | |
| | | **Comments:** | | | | |
| | 34. | All applicable software documentation provided based on level of concern identified by the submitter, as described in Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices, " available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-content-premarket-submissions-software-contained-medical-device, or the submission includes information to establish that the submitter has otherwise met the applicable statutory or regulatory criteria through an alternative approach (i.e., the submitter has identified an alternate approach with a rationale).<br><br>*Note: This element is also applicable to non-internally generated or off-the-shelf (OTS) software used in the device.* | ☐ | ☐ | ☒ | |
| | | **Comments:** | | | | |
| **I.** | **Cybersecurity** | | | | | |
| | Submission states that the device: (*one of the below must be checked*)<br>Submission states that the device: (*one of the below must be checked*)<br><br>☒ Does contain any external wired and/or wireless communication interfaces (Wired: USB, ethernet, SD, CD, RGA, etc. or Wireless: Wi-Fi, Bluetooth, RF, inductive, Cloud, etc.)<br><br>☐ Does not contain external interfaces as described above | | | ☐ | | Section XVIII.K |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.**<br><br>***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.** | | | | | | |
| | | | **Yes** | **No** | **N/A** | ***Page #** |
| | ☐ Information on whether device has external interfaces is not provided (if this box is checked, please also check one of the two boxes below)<br><br>☐ Cybersecurity information not needed for this device (e.g., surgical suture, condom)<br><br>☐ Cybersecurity information is needed or need unclear<br><br>This information will determine whether and what type of additional information may be necessary for a substantial equivalence determination.<br><br>*If "does not require" or "not provided and not needed" is selected, the electrical safety criteria below are omitted from the checklist. If information on electrical safety is not provided, and it is needed or the need for this information is unclear, select "No."* | | | | | |
| | 35. | All applicable documentation identified by the submitter, as described in "Guidance for the Content of Premarket Submissions for Management of Cybersecurity in Medical Devices," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/content-premarket-submissions-management-cybersecurity-medical-devices-0.<br><br>**OR**<br><br>Submission includes information to establish that the submitter has otherwise met the applicable statutory or regulatory criteria through an alternative approach (i.e., the submitter has identified an alternate approach with a rationale). | ☒ | ☐ | | Section XVIII.K |
| | **Comments:** | | | | | |
| **J.** | **Electrical Safety and EMC** | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.**<br><br>***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.** | | | | | | |
| | | | **Yes** | **No** | **N/A** | ***Page #** |
| | Electrical Safety:<br><br>Submission states that the device: (*one of the below must be checked*)<br><br>☒ Does require electrical safety evaluation<br><br>☐ Does not require electrical safety evaluation<br><br>☐ Information on whether device requires electrical safety evaluation not provided (if this box checked, please also check one of the two boxes below)<br><br>☐ Electrical safety information not needed for this device (e.g., surgical suture, condom)<br><br>☐ Electrical safety information needed or need unclear<br><br>This information will determine whether and what type of additional information may be necessary for a substantial equivalence determination.<br><br>*If "does not require" or "not provided and not needed" is selected, the electrical safety criteria below are omitted from the checklist. If information on electrical safety is not provided, and it is needed or the need for this information is unclear, select "No."* | | | ☐ | | Section XIX |
| | **Comments:** | | | | | |
| | 36. | Submission includes evaluation of electrical safety (e.g., per IEC 60601-1, or equivalent FDA-recognized standard, and if applicable, a device-specific standard).<br><br>**<u>OR</u>**<br><br>Submission includes electrical safety evaluation using methods or standards that are not FDA-recognized and submission includes | ☒ | ☐ | | Section XIX |

| Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.<br><br>*Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information. | | | | | | |
|---|---|---|---|---|---|---|
| | | | Yes | No | N/A | *Page # |
| | | information to establish that the submitter has otherwise met the applicable statutory or regulatory criteria through this alternative approach (i.e., the submitter has identified alternate methods or standards with a rationale). | | | | |
| | **Comments:** | | | | | |
| | EMC:<br><br>Submission states that the device: (*one of the below must be checked*)<br><br>☒ Does require EMC evaluation<br><br>☐ Does not require EMC evaluation<br><br>☐ Information on whether device requires EMC evaluation not provided (if this box checked, please also check one of the two boxes below)<br><br>☐ EMC information not needed for this device (e.g., surgical suture, condom)<br><br>☐ EMC information needed or need unclear<br><br>This information will determine whether and what type of additional information may be necessary for a substantial equivalence determination.<br><br>*If "does not require" or "not provided and not needed" is selected, the EMC criteria below are omitted from the checklist. If information on EMC is not provided, and it is needed or the need for this information is unclear, select "No."* | | | ☐ | | Section XIX |
| | **Comments:** | | | | | |
| | 37. | Submission includes evaluation of electromagnetic compatibility (e.g., per IEC 60601-1-2 or equivalent FDA-recognized standard and if applicable, a device-specific standard). | ☒ | ☐ | | Section XIX |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.**<br><br>***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.** | | | | | | |
| | | | **Yes** | **No** | **N/A** | ***Page #** |
| | | **OR**<br><br>Submission includes electromagnetic compatibility evaluation using methods or standards that are not FDA-recognized and submission includes information to establish that the submitter has otherwise met the applicable statutory or regulatory criteria through this alternative approach (i.e., the submitter has identified alternate methods or standards with a rationale). | | | | |
| | | **Comments:** | | | | |
| **K.** | **Performance Data General**<br><br>*If an in vitro diagnostic (IVD) device, select "N/A." The criteria in this section will be omitted from the checklist if "N/A" is selected. Performance data criteria relating to IVD devices is addressed in Section K.* | | | | ☐ | Section XX |
| | **Comments:** | | | | | |
| | 38. | Summaries of the non-clinical laboratory studies and full test reports* are provided.<br><br>*Summary and full test report content recommendations can be found in FDA's guidance "Recommended Content and Format of Non-Clinical Bench Performance Testing Information in Premarket Submissions," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/recommended-content-and-format-non-clinical-bench-performance-testing-information-premarket.<br><br>If a submitter chooses to declare conformity to a voluntary consensus standard that FDA has recognized, submission of a full test report may not be necessary. Refer to 9a. See FDA's guidance "Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices," available at https://www.fda.gov/regulatory-information/search-fda- | ☒ | ☐ | ☐ | Section XX |

| Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.<br><br>*Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information. | | | | Yes | No | N/A | *Page # |
|---|---|---|---|---|---|---|---|
| | | guidance-documents/appropriate-use-voluntary-consensus-standards-premarket-submissions-medical-devices.<br><br>*Select "N/A" if the submission appropriately does not include performance data or there are no completed tests without a Declaration of Conformity.* | | | | | |
| | | a. | Submission includes an explanation of how the data generated from each test supports a finding of substantial equivalence (e.g., comparison to predicate device testing, dimensional analysis, etc.).<br><br>*Select "N/A" if the submission does not include performance data.* | ☒ | ☐ | ☐ | Section XX |
| | | **Comments:** | | | | | |
| | 39. | The device has a device-specific guidance document, special controls, and/or requirement in a device-specific classification regulation regarding performance data that is applicable to the subject device<br><br>*If "N/A" is selected, parts a and b below are omitted from the checklist.* | | ☒ | | ☐ | |
| | | a. | The submission addresses performance data recommendations outlined in the device-specific guidance.<br><br>**OR**<br><br>The submission provides an alternative approach intended to address the applicable statutory and/or regulatory criteria.<br><br>*Select "N/A" if there is no applicable device-specific guidance. Select "No" if the submission does not include a rationale for any omitted information or any alternative approach as outlined above. Note that the adequacy of* | ☒ | ☐ | ☐ | |

| Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.<br><br>*Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information. | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | **Yes** | **No** | **N/A** | ***Page #** |
| | | | *how recommendations in a device-specific guidance, etc., have been addressed should be assessed during the substantive review.* | | | | |
| | | b. | The submission includes performance data that addresses relevant mitigation measures set forth in the special controls or device-specific classification regulation applicable to the device.<br><br>**OR**<br><br>The submission uses alternative mitigation measures and provides rationale why the alternative measures provide an equivalent assurance of safety and effectiveness.<br><br>*Select "N/A" if there is are applicable special controls or device-specific regulation. Select "No" if the submission does not include a rationale for any omitted information or any alternative approach as outlined above. Note that the adequacy of how such mitigation measures have been addressed should be assessed during the substantive review.* | ☒ | ☐ | ☐ | |
| | | **Comments:** | | | | | |
| | 40. | If literature is referenced in the submission, submission includes:<br><br>*Select "N/A" if the submission does not reference literature. If "N/A" is selected, parts a and b below are omitted from the checklist.*<br><br>*Note that the applicability of the referenced article to support a substantial equivalence finding should be assessed during the substantive review; only the presence of a discussion is required to support acceptance.* | | | | ☐ | |
| | | a. | Legible reprints or a summary of each article. | ☒ | ☐ | | Sections XIII, XIV, and |

| Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.<br><br>*Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information. | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | **Yes** | **No** | **N/A** | ***Page #** |
| | | | | | | | XXIII, Appendix 23.1 |
| | | b. | Discussion of how each article is applicable to support the substantial equivalence of the subject device to the predicate. | ☒ | ☐ | | Sections XIII, XIV, and XXIII |
| | | **Comments:** | | | | | |
| | 41. | For each completed animal study, the submission provides the following:<br><br>*Select "N/A" if no animal study was conducted. If "N/A" is selected, parts a-c below are omitted from the checklist. Note that this section does not address biocompatibility evaluations, which are assessed in Section G of the checklist.* | | | | ☒ | |
| | | a. | Submission includes a study protocol which includes all elements as outlined in 21 CFR 58.120 | ☐ | ☐ | | |
| | | b. | Submission includes final study report which includes all elements outlined in 21 CFR 58.185 | ☐ | ☐ | | |
| | | c. | Submission contains a statement that the study was conducted in compliance with applicable requirements in the GLP regulation (21 CFR Part 58), OR, if the study was not conducted in compliance with the GLP regulation, the submission explains why the noncompliance would not impact the validity of the study data provided to support a substantial equivalence determination. | ☐ | ☐ | | |
| | | **Comments:** | | | | | |
| **L.** | **Performance Characteristics – In Vitro Diagnostic Devices Only**<br><br>**(see also 21 CFR 809.10(b)(12))** | | | | | | |

| | | | | Yes | No | N/A | *Page # |
|---|---|---|---|---|---|---|---|
| **Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.**<br><br>***Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information.** | | | | | | | |
| | Submission indicates that device: (*one of the below must be checked*)<br><br>☐ Is an in vitro diagnostic device<br><br>☒ Is not an in vitro diagnostic device<br><br>*If "is not" is selected, the performance data-related criteria below are omitted from the checklist.* | | | | | | |
| | 42. | Submission includes the following studies, as appropriate for the device type, including associated protocol descriptions, study results and line data: | | | | | |
| | | a. | Precision/reproducibility | ☐ | ☐ | ☐ | |
| | | b. | Accuracy (includes as appropriate linearity; calibrator or assay traceability; calibrator and/or assay stability protocol and acceptance criteria; assay cut-off; method comparison or comparison to clinical outcome; matrix comparison; and clinical reference range or cutoff. | ☐ | ☐ | ☐ | |
| | | c. | Sensitivity (detection limits, LoB, LoD, LoQ where relevant for the device type). | ☐ | ☐ | ☐ | |
| | | d. | Analytical specificity | ☐ | ☐ | ☐ | |
| | | Comments: | | | | | |
| | 43. | The device has a device-specific guidance document, special controls, and/or requirement in a device-specific classification regulation regarding performance data that is applicable to the subject device.<br><br>*If "N/A" is selected, parts a and b below are omitted from the checklist.* | | ☐ | ☐ | ☐ | |

| Check "Yes" if item is present, "N/A" if it is not needed and "No" if it is not included but needed.<br><br>*Submitters including the checklist with their submission should identify the page numbers where requested information is located. Use the comments section for an element if additional space is needed to identify the location of supporting information. | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | **Yes** | **No** | **N/A** | ***Page #** |
| | | a. | The submission addresses performance data recommendations outlined in the device-specific guidance.<br><br>**OR**<br><br>The submission provides an alternative approach intended to address the applicable statutory and/or regulatory criteria.<br><br>*Select "N/A" if there is no applicable device-specific guidance. Select "No" if the submission does not include a rationale for any omitted information or any alternative approach as outlined above. Note that the adequacy of how recommendations in a device-specific guidance, etc., have been addressed should be assessed during the substantive review.* | ☐ | ☐ | ☐ | |
| | | b. | The submission includes performance data that addresses relevant mitigation measures set forth in the special controls or device-specific classification regulation applicable to the device.<br><br>**OR**<br><br>The submission uses alternative mitigation measures and provides rationale why the alternative measures provide an equivalent assurance of safety and effectiveness.<br><br>*Select "N/A" if there iare no applicable special controls or device-specific classification regulation. Select "No" if the submission does not include a rationale for any omitted information or any alternative approach as outlined above. Note that the adequacy of how such mitigation measures have been addressed should be assessed during the substantive review.* | ☐ | ☐ | ☐ | |
| | | **Comments:** | | | | | |

| Digital Signature Concurrence Table | |
|---|---|
| Reviewer Sign-Off | |
| Management Sign-Off (digital signature optional)* | |

*Management review of checklist and concurrence with decision required.

## VI. INDICATIONS FOR USE STATEMENT

The Company's Indications for Use Statement for VX1+ is provided on the following page.

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

# Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
*See PRA Statement below*

510(k) Number *(if known)*

Device Name

VX1+

Indications for Use *(Describe)*

The VX1+ assists operators in the real-time manual or automatic annotation of 3D anatomical and electrical maps of human atria for the presence of multipolar intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion during atrial fibrillation or atrial tachycardia.

The clinical significance of utilizing the VX1+ software to help identify areas with intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion for catheter ablation of atrial arrhythmias, such as atrial fibrillation, has not been established by clinical investigations.

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.

***DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.***

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human
Services Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

*"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."*

## VII. 510(K) SUMMARY

The Company's 510(k) Summary is provided on the following pages.

**510(k) SUMMARY**

**VOLTA MEDICAL's VX1+**

**Submitter**

**Volta Medical**

**65 Avenue Jules Cantini**
**13006 Marseille**
**France**

Phone: +33 7 68 02 54 99

Contact Person: Paola MILPIED

Date Prepared: November 22, 2022

**Name of Device:** VX1+

**Common or Usual Name:** Cardiac Mapping System

**Classification Name:** Programmable Diagnostic Computer

**Regulatory Class:** 21 C.F.R § 870.1425

**Product Code:** DQK

**Predicate Devices**

Volta Medical, VX1 (K201298)

**Device Description**

The VX1+ is a machine and deep learning based-algorithm designed to assist operators in the real-time manual or automatic annotation of 3D anatomical and electrical maps of the human heart for the presence of electrograms exhibiting spatio-temporal dispersion, i.e., dispersed electrograms (DEs).

The VX1+ device is a non-sterile reusable medical device, composed of a computing platform and a software application. VX1+ works with all existing 510(k)-cleared catheters that meet specific dimension requirements and with one of the three specific data acquisition systems:

- two compatible EP recording systems (identical to VX1 (Volta Medical (K201298)): the *LabSystem Pro* EP Recording System (Boston Scientific) (K141185) or the *MacLab CardioLab* EP Recording System (General Electric) (K130626),
- a 3D mapping system (novelty compared to VX1): *EnSite X* 3D mapping system (Abbott) (K221213).

A connection cable is used to connect the corresponding data acquisition system to the VX1+ system, depending on the type of communication used:

- Unidirectional analog communication with the EP recording systems via a custom-made cable (two different variants: *DSUB, Octopus*) and an Advantech PCI-1713U analog-to-digital converter, which acquires analog data, digitizes it, and transmits the digital signals to the computer that hosts the VX1+ software.
- Bidirectional digital communication with the EnSite 3D mapping system via an ethernet cable (four different lengths: 20,10, 5 or 2m) which transmits the digital signals directly to the computer.

The computer and its attached display are located outside the sterile operating room area. The VX1+ software analyzes the patient's electrograms to cue operators in real-time to intra-cardiac electrograms of interest for atrial regions harboring DEs as well as a cycle length estimation from electrograms recorded with the mapping and the coronary sinus catheters. The results of the analysis are graphically presented on the attached computer display and/or on a secondary medical screen or on an operating room widescreen. The identified regions of interest are either manually (all configurations) or automatically (only available in digital bidirectional communication with the EnSite X 3D mapping system) tagged in the corresponding 3D mapping system.

**Intended Use / Indications for Use**

The VX1+ assists operators in the real-time manual or automatic annotation of 3D anatomical and electrical maps of human atria for the presence of multipolar intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion during atrial fibrillation or atrial tachycardia.

The clinical significance of utilizing the VX1+ software to help identify areas with intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion for catheter ablation of atrial arrhythmias, such as atrial fibrillation, has not been established by clinical investigations.

**Summary of Technological Characteristics**

The VX1+ device is a new device manufactured by Volta Medical, based on the same concept (identification of electrograms dispersion) than predicate VX1.

VX1 and VX1+ are both software programs that work with standard electrophysiology catheters to aid in mapping the heart. Both devices aid operators by assisting in annotating complex electrical maps of the heart, and both devices process and output information via a computer and display that are operated by use of a keyboard / mouse. VX1 and VX1+ have the same input (intra-cardiac multipolar signals) and the same output (associated dispersion), with the addition of the 3D position of the corresponding electrodes available in VX1+.

VX1 and VX1+ support Electrophysiologists in the manual annotation of dispersed areas using a unidirectional analog communication. In addition, VX1+ brings the ability to connect to a

specific 3D mapping system through a bidirectional digital communication, which enables the operator to use the automatic tagging function.

The VX1+ indications for use are the same as for the VX1, with the addition of automatic annotation. The VX1+ displays an analysis of dispersed electrograms, just as VX1 and therefore, the intended use of the VX1+ and the VX1 are essentially the same.

| | **Volta Medical VX1+** | **Volta Medical VX1 (K201298)** |
|---|---|---|
| **Regulation** | 21 C.F.R. § 870.1425 | 21 C.F.R. § 870.1425 |
| **Classification Name** | Programmable Diagnostic Computer | Programmable Diagnostic Computer |
| **Product Code** | DQK | DQK |
| **Indications for Use** | The VX1+ assists operators in the real-time manual or automatic annotation of 3D anatomical and electrical maps of human atria for the presence of multipolar intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion during atrial fibrillation or atrial tachycardia.<br><br>The clinical significance of utilizing the VX1+ software to help identify areas with intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion for catheter ablation of atrial arrhythmias, such as atrial fibrillation, has not been established by clinical investigations. | The VX1 assists operators in the real-time manual annotation of 3D anatomical and electrical maps of human atria for the presence of multipolar intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion during atrial fibrillation or atrial tachycardia.<br><br>The clinical significance of utilizing the VX1 software to help identify areas with intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion for catheter ablation of atrial arrhythmias, such as atrial fibrillation, has not been established by clinical investigations. |
| **System Type** | Signal processing based atrial mapping system | Signal processing based atrial mapping system |
| **Primary Feature** | Displays and analyzes electrical maps such as intra-cardiac electrograms in real-time using machine learning and signal processing techniques | Displays and analyzes electrical maps such as intra-cardiac electrograms in real-time using machine learning and signal processing techniques |

| | Volta Medical<br>VX1+ | Volta Medical<br>VX1<br>(K201298) |
|---|---|---|
| **3D Location Technology** | Electroanatomic location is performed by another commercially available navigation system.<br>In bidirectional digital communication, 3D Location is shared by the 3D Mapping System with VX1+. | Electroanatomic location is performed by another commercially available navigation system. |
| **Compatible Acquisition Systems** | • LabSystem Pro EP Recording System (Boston Scientific)<br>• CardioLab EP Recording System (GE)<br>• EnSite X 3D Mapping System (Abbott) | • LabSystem Pro EP Recording System (Boston Scientific)<br>• CardioLab EP Recording System (GE) |
| **Compatible Catheters** | Any compatible mapping and ablation catheter | Any compatible mapping and ablation catheter |
| **Display(s)** | Color monitor | Color monitor |
| **Multi-Display Support** | Yes, duplicate display on a secondary medical screen or on an operating room widescreen | Yes, duplicate display on a secondary medical screen or on an operating room widescreen |
| **Control** | Standard keyboard / mouse | Standard keyboard / mouse |
| **Display Timing** | Real-time | Real-time |
| **Inputs Required** | Analog or digital Intra-cardiac signals<br>In digital mode, 3D locations of corresponding electrodes bipoles | Analog Intra-cardiac signals |
| **Output** | Presence or absence of electrogram dispersion at each electrode bipole under consideration<br><br>In digital mode, 3D locations of corresponding electrodes bipoles<br><br>Computed values of mapping and reference cycle length | Presence or absence of electrogram dispersion at each electrode bipole under consideration<br><br>Computed values of mapping and reference cycle length |
| **Duration of Electrogram Recordings** | 1.5 Seconds | 1.5 Seconds |
| **Ouput Display** | The system generates color coded symbol(s) that indicates to the operator that the area under | The system generates color coded symbol(s) that indicates to the operator that the area under |

| | Volta Medical<br>VX1+ | Volta Medical<br>VX1<br>(K201298) |
|---|---|---|
| | investigation is one exhibiting dispersion<br><br>In bidirectional digital communication, validated dispersion area can also be automatically displayed in the 3D mapping system as tags in the 3D atrial shell | investigation is one exhibiting dispersion |
| **Signal Information Displayed** | Acquired patient signals, including body surface ECG and intra-cardiac EGMs. | Acquired patient signals, including body surface ECG and intra-cardiac EGMs. |
| **Computing Platform** | Computer with Intel Core i7-7700 CPU (8MB Cache, up to 4.20 GHz, RAM 32 GB),<br><br>with integrated analog/digital converter PCI card and TPM (Trusted Platform Module)<br><br>Debian-based Linux OS | Computer with Intel Core i5-6500 CPU (6MB Cache, up to 3.60 GHz, RAM 32 GB),<br><br>with integrated analog/digital converter PCI card<br><br>Windows 10 or higher OS |
| **Hardware Design and Materials** | Computing platform, proprietary software algorithm, monitor, mouse/keyboard, custom-made analog connection cable, ethernet cable, acquisition system | Computing platform, proprietary software algorithm, monitor, mouse/keyboard, custom-made analog connection cable, acquisition system |

**Performance Data – Nonclinical Tests:**

The Volta Medical VX1+ was subjected to non-clinical testing including electromagnetic compatibility and electrical safety tests, rigorous software verification and validation testing including unitary testing of the main algorithm modules of VX1+ application. Specifically the *Reader Study* described in VX1's 510(k) (K201298) and intended to show that the algorithm's adjudications acceptably correlate with unlimited-time expert visual analysis, was replayed with VX1+ dispersion algorithm.

A usability verification and validation study was launched in a simulated environment at Volta Medical headquarters and in a clinical environment in the scope of the AMPERE study. Usability evaluation did not raise any safety issues and confirmed the relevance of the related risks identified.

**Performance Data – Clinical Tests:**

Since a full set of tests was performed, including a non-regression analysis of VX1+ versus VX1 with respect to dispersion adjudication, additional clinical data is not required to demonstrate substantial equivalence of the VX1+. However; for completeness, the Company supplied data from an OUS clinical study of the VX1+. The study was aimed at evaluating the reliability of VX1+ detection of dispersed electrograms and automatic tagging function, and involved 1 center, 4 operators, and 22 patients. The results indicate that VX1+ reliably assists operators in the detection and auto-tagging of regions harboring dispersed electrograms during AF/AT, with no associated additional risks or procedure time.

**Conclusions**

The VX1+ is as safe and effective as the VX1. The VX1+ has the same intended uses and same indications, and substantially similar technological characteristics, and principles of operation as its predicate device. The introduction of the automatic tagging feature does not alter the intended use of the device as an electrophysiological evaluation tool and do not affect its safety and effectiveness when used as labeled. In addition, the minor technological differences (i.e., bidirectional communication with the acquisition system) between the VX1+ and its predicate device raise no new issues of safety or effectiveness. Performance data, as described above, demonstrate that the VX1+ device is as safe and effective as the VX1. Thus, the VX1+ device is substantially equivalent.

## VIII. TRUTHFUL AND ACCURATE STATEMENT

The Company's signed Truthful and Accurate statement is included on the following page.

**PREMARKET NOTIFICATION**

**TRUTHFUL AND ACCURATE STATEMENT**

**(As Required by 21 C.F.R. § 807.87(l))**

I certify that, in my capacity as Vice-President of Clinical and Regulatory Affairs of Volta Medical, I believe to the best of my knowledge, that all data and information submitted in this premarket notification for the VX1+ are truthful and accurate and that no material fact has been omitted.

(Signature)

Paola Milpied, VP Clinical & Regulatory Affairs
(Typed Name and Title)

Nov 21, 2022
(Date)

## IX. CLASS III SUMMARY AND CERTIFICATION

The VX1+ is a Class II device. Class III Summary and Certification is, therefore, not applicable.

## X. FINANCIAL DISCLOSURES

The Company has in **Section XXII** described a clinical study of the device which was conducted in France to evaluate the perioperative reliability of VX1+ in the real-time detection of electrograms in atrial fibrillation/tachycardia exhibiting spatio-temporal dispersion, and to validate the feasibility of automatic tagging of these dispersion areas on 3D electroanatomical maps. The Company does not, however, rely upon this study to demonstrate the safety or effectiveness of the VX1+ device or to establish substantial equivalence to an effective product. The VX1+ is not indicated for use, and the Company is making no claims regarding the use of the device, in directing treatment for or affecting the outcome of any particular heart arrhythmia. Accordingly, the study does not meet the definition of a “covered clinical study” found in 21 C.F.R. 54.2(e) for which financial disclosure is required.

## XI. DECLARATION OF CONFORMITY TO FDA RECOGNIZED STANDARDS

Consistent with FDA's guidance documents entitled, "Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices" (September 14, 2018), Volta Medical is including a declaration of conformity that the VX1+ complies with the following FDA recognized consensus standards:

- (Rec. No. 2-282) ISO 14155 Third Edition 2020-07 Clinical Investigation of Medical Devices For Human Subjects - Good Clinical Practice

- (Rec. No. 5-125) ISO 14971 Third Edition 2019-12 Medical Devices - Application of Risk Management to Medical Devices

- (Rec. No. 5-134) ISO 15223-1 Fourth Edition 2021-07 Medical Devices - Symbols to be used with information to be supplied by the Manufacturer - Part 1: General Requirements

- (Rec. No. 19-46) ANSI/AAMI ES60601-1:2005/(R)2012 AND A1:2012 C1:2009/(R)2012 And A2:2010/(R)2012 (Consolidated Text)[Including AMD2:2021] Medical Electrical Equipment - Part 1: General Requirements for Basic Safety and Essential Performance (IEC 60601-1:2005, MOD)

- (Rec. No. 19-36) IEC 60601-1-2 Edition 4.1 2020-09 (Consolidated Version) Medical Electrical Equipment – Part 1-2: General requirements for Basic Safety and Essential Performance – Collateral Standard: Electromagnetic Disturbances – Requirements and Tests

- (Rec. No. 5-132) IEC 60601-1-6 Edition 3.2 2020-07 (Consolidated Version) Medical Electrical Equipment - Part 1-6: General Requirements for Basic Safety and Essential Performance - Collateral Standard: Usability

- (Rec. No. 5-129) IEC 62366-1 Edition 1.1 2020-06 (Consolidated Version) Medical Devices – Part 1 : Application of Usability Engineering to Medical Devices

- (Rec. No. 13-79) IEC 62304 Edition 1.1 2015-06 (Consolidated Version) Medical Device Software – Software Life Cycle Processes

- (Rec. No. 15-135) ISO 20417 First edition 2021-04 Corrected version 2021-12 Medical devices - Information to be supplied by the manufacturer

The signed Declaration of Conformity is provided on the following page.

In addition, the design, development and production of VX1+ also complies with the following consensus standards:

- EN ISO 13485:2016 + AC:2016 Medical Devices – Quality Management Systems – Requirements for Regulatory Purposes

**Declaration of Conformity to Recognized Standards**

I certify that, in my capacity as VP of Clinical and Regulatory Affairs of Volta Medical, the subject of this Traditional 510(k) Notice, VX1+, classified under Product Code DQK, conforms to the following FDA-recognized standards:

| FDA Recognition Number | Standard / Guideline Name | Test Site |
|---|---|---|
| 2-282 | ISO 14155 Third Edition 2020-07 Clinical Investigation of Medical Devices For Human Subjects - Good Clinical Practice | **Volta Medical (Sponsor)**<br>65 Avenue Jules Cantini<br>13006 Marseille<br>FRANCE |
| 5-125 | ISO 14971 Third Edition 2019-12 Medical Devices - Application of Risk Management to Medical Devices | N/A |
| 5-134 | ISO 15223-1 – Fourth Edition 2021-07 Medical Devices – Symbols to be used with information to be supplied by the Manufacturer – Part 1: General Requirements | N/A |
| 19-46 | ANSI/AAMI ES60601-1:2005/(R)2012 AND A1:2012 C1:2009/(R)2012 AND A2:2010/(R)2012 (Consolidated Text) [Including AMD2:2021] Medical Electrical Equipment – Part 1: General requirements for Basic Safety and Essential Performance (60601-1:2005, MOD) | **LCIE Bureau Veritas**<br>ZI Centr'alp<br>170 rue de Chatagnon<br>38430 MOIRANS<br>France |
| 19-36 | IEC 60601-1-2 Edition 4.1 2020-09 (Consolidated Version) Medical Electrical Equipment – Part 1-2: General requirements for Basic Safety and Essential Performance – Collateral Standard: Electromagnetic Disturbances – Requirements and Tests | **LCIE Bureau Veritas**<br>ZI Centr'alp<br>170 rue de Chatagnon<br>38430 MOIRANS<br>FRANCE |
| 5-132 | IEC 60601-1-6 Edition 3.2 2020-07 (Consolidated version) Medical Electrical Equipment – Part 1-6: General requirements for Basic Safety and Essential Performance – Collateral Standard: Usability | **LCIE Bureau Veritas**<br>ZI Centr'alp<br>170 rue de Chatagnon<br>38430 MOIRANS<br>FRANCE |
| 5-129 | IEC 62366-1 Edition 1.1 2020-06 (Consolidated Version) Medical Devices – Part 1 : Application of Usability Engineering to Medical Devices | N/A |

| FDA Recognition Number | Standard / Guideline Name | Test Site |
|---|---|---|
| 13-79 | IEC 62304 Edition 1.1 2015-06 (Consolidated Version) Medical Device Software – Software Life Cycle Processes | N/A |
| 15-135 | ISO 20417 First edition 2021-04 Corrected version 2021-12 Medical devices - Information to be supplied by the manufacturer | N/A |

All requirements were met, alternative series of tests were not performed, all requirements were applicable to the device, and no deviations from applicable standards were applied.

In addition, there were no differences between the tested device and the finished device to be marketed.

Signed: 

**PAOLA MILPIED**
**VP OF CLINICAL & REGULATORY AFFAIRS**

Date: **November 21, 2022**

Address: **65 Avenue Jules Cantini**
**13006 Marseille**
**FRANCE**

## XII. EXECUTIVE SUMMARY

The VX1+ assists operators in the real-time manual or automatic annotation of 3D anatomical and electrical maps of human atria for the presence of multipolar intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion during atrial fibrillation or atrial tachycardia. The clinical significance of utilizing the VX1+ software to help identify areas with intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion for catheter ablation of atrial arrhythmias, such as atrial fibrillation, has not been established by clinical investigations.

As described in detail in **Section XIII**, the VX1+ is a machine and deep learning based-algorithm designed to assist in detecting multipolar electrograms exhibiting spatiotemporal dispersion, i.e., dispersed electrograms (DEs). The device works with all existing 510(k) cleared catheters that meet specific dimensional requirements, and with three compatible data acquisition systems: the *LabSystem Pro* EP Recording System (Boston Scientific) (K141185), the *MacLab CardioLab* EP Recording System (General Electric) (K130626) and a 3D mapping system *EnSite X* (Abbott) (K221213). One of the 3 types of connection cable is used to connect the corresponding data acquisition system to the VX1+ computer hosting the VX1+ software application. The input from the data acquisition system can be analog (use of an Advantech PCI-1713U analog-to-digital converter) or directly digital. The computer and its attached display are located outside the sterile operating room area during an ablation procedure. This computer is dedicated to (i) running the VX1+ software and (ii) showing the VX1+ interface on the connected display.

At the request of the electrophysiologist, the engineer present in the operating room, or an operating room nurse, initiates digital or analog acquisition of signals by VX1+.

In unidirectional analog communication, the analog signals from the EP recording system are routed to the PCI-1713U (A/D converter) through a dedicated 16-channel analog output. The PCI-1713U digitizes the electrograms and transfers them to the computer hosting the VX1+ software application, using an appropriate communication driver. In bidirectional digital communication, digital signals are directly sent by the 3D mapping system to the computer hosting the VX1+ software application

As the electrophysiologist moves a specific diagnostic multipolar catheter inside the heart, the system continuously collects data on the bipolar electrical activity of each pair of electrodes. Data incoming to the device is acquired and processed by several chained threads that provide for data extraction, analysis / classification of patient real-time data, and user interface display. The VX1+ algorithms evaluate the incoming data and displays a set of information to guide the operator in the detection of dispersions, including:

- A real-time identification of intra-cardiac electrograms of interest exhibiting dispersion (i.e., the same core machine learning algorithm in VX1 (Volta Medical) (K201298) trained on a database of 275,020 annotated electrogram samples). Operators are alerted to the presence of dispersion through auditory and visual notifications.
- A cycle length estimation from electrograms recorded with the mapping and coronary sinus catheters.

The catheter's schematic is shown on the VX1+ display surrounded by two half-circle-shaped symbols that depict the presence of dispersed electrograms among those of interest (upper half) and cycle length estimations as measured by the mapping and CS catheters (lower half). On the upper half-circle, 10 box sections correspond to the 10 dipoles of interest. When one or several dipole symbol(s) is / are blinking and is colored in orange / red on the catheter schematic, this indicates to the operator that the area under investigation is one exhibiting dispersion. For confirmation, the operator may stabilize the catheter in this region. Then, the operator must examine the corresponding multipolar electrograms to provide confirmation of the presence of dispersion. Further confirmation is given by the red / orange coloring of boxes on the upper half-circle.

The operator moves the catheter through both atria and may manually tag the location of any electrograms of interest, as confirmed by the VX1+ software, in the 3D shell of the 3D Mapping System.

In bidirectional analog communication, regions of interest are automatically tagged in the 3D mapping system, with the user able to remove the tags when not in agreement.

Testing performed in support of this submission is summarized below and described in more detail in **Sections XIX, XX, XXII**, and corresponding appendices.

- *Electromagnetic compatibility, safety and usability testing* of the finished device was performed in accordance with IEC 60601-1; 60601-1-2; and 60601-1-6 to ensure the basic safety and essential performance of the electrical device components.

- *Algorithm modules Unitary Tests* were performed for each of the algorithm modules: Dispersion, Local Cycle Length, Reference Cycle Length, and Automatic tagging to ensure that the performance of the different algorithms was similar to the performance of the predicate device VX1, including replaying the Reader Study performed as part of VX1 510(k) (K201298).

- *Usability Engineering testing,* including formative and summative evaluation performed in accordance with IEC 62366-1 to ensure usability.

Clinical Testing conducted outside of the US is presented in this submission for completeness even though the Company is making no claims for use of the device in directing treatment for, or affecting the outcome of, any particular heart arrhythmia and does not rely on these data to support substantial equivalence. The study was an interventional, monocentric, prospective, open-label, non-randomized clinical study designed to confirm the reliability of the VX1+ in dispersion detection and automatic tagging function. The results indicate that VX1+ reliably assists operators in the detection and auto-tagging of regions harboring dispersed electrograms during AF/AT, with no associated additional risks or procedure time.

As explained in detail in **Section XIV**, VX1+ is substantially equivalent to other legally marketed cardiac mapping software devices**.** Specifically, the VX1+ is substantially equivalent to the VX1 (K201298). VX1+ has the same intended use, indications for use, technological characteristics, and principles of operation as the previously cleared predicate VX1, except for the automatic annotation feature. For instance, both devices use color coded display cues to alert the operator to the presence of abnormal electrograms exhibiting dispersion (same definition and same algorithm used). The only

difference in the technological characteristics between the VX1+ and VX1, is the ability to communicate digitally in a bi-directional manner with the EnSite X (Abbott) 3D mapping system (K221213) to automatically tag areas of dispersion. This does not raise additional safety or effectiveness questions since both the VX1+ and VX1 successfully detect regions of dispersed electrograms and the performance testing demonstrates that the VX1+ is as safe and effective as its predicate device VX1.

A comparison table between the Volta Medical VX1+ and its predicate, Volta Medical VX1 can be found below.

| | **Volta Medical VX1+** | **Volta Medical VX1 (K201298)** |
|---|---|---|
| **Regulation** | 21 C.F.R. § 870.1425 | 21 C.F.R. § 870.1425 |
| **Classification Name** | Programmable Diagnostic Computer | Programmable Diagnostic Computer |
| **Product Code** | DQK | DQK |
| **Indications for Use** | The VX1+ assists operators in the real-time manual or automatic annotation of 3D anatomical and electrical maps of human atria for the presence of multipolar intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion during atrial fibrillation or atrial tachycardia.<br><br>The clinical significance of utilizing the VX1+ software to help identify areas with intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion for catheter ablation of atrial arrhythmias, such as atrial fibrillation, has not been established by clinical investigations. | The VX1 assists operators in the real-time manual annotation of 3D anatomical and electrical maps of human atria for the presence of multipolar intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion during atrial fibrillation or atrial tachycardia.<br><br>The clinical significance of utilizing the VX1 software to help identify areas with intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion for catheter ablation of atrial arrhythmias, such as atrial fibrillation, has not been established by clinical investigations. |
| **System Type** | Signal processing based atrial mapping system | Signal processing based atrial mapping system |
| **Primary Feature** | Displays and analyzes electrical maps such as intra-cardiac electrograms in real-time using machine learning and signal processing techniques | Displays and analyzes electrical maps such as intra-cardiac electrograms in real-time using machine learning and signal processing techniques |
| **3D Location Technology** | Electroanatomic location is performed by another commercially available navigation system. In bidirectional digital communication, 3D Location is shared by the 3D Mapping System with VX1+. | Electroanatomic location is performed by another commercially available navigation system. |

| | Volta Medical<br>VX1+ | Volta Medical<br>VX1<br>(K201298) |
|---|---|---|
| **Compatible Acquisition Systems** | • LabSystem Pro EP Recording System (Boston Scientific)<br>• CardioLab EP Recording System (GE)<br>• EnSite X 3D Mapping System (Abbott) | • LabSystem Pro EP Recording System (Boston Scientific)<br>• CardioLab EP Recording System (GE) |
| **Compatible Catheters** | Any compatible mapping and ablation catheter | Any compatible mapping and ablation catheter |
| **Display(s)** | Color monitor | Color monitor |
| **Multi-Display Support** | Yes, duplicate display on a secondary medical screen or on an operating room widescreen | Yes, duplicate display on a secondary medical screen or on an operating room widescreen |
| **Control** | Standard keyboard / mouse | Standard keyboard / mouse |
| **Display Timing** | Real-time | Real-time |
| **Inputs Required** | Analog or digital Intra-cardiac signals<br>In digital mode, 3D locations of corresponding electrodes bipoles | Analog Intra-cardiac signals |
| **Output** | Presence or absence of electrogram dispersion at each electrode bipole under consideration<br><br>In digital mode, 3D locations of corresponding electrodes bipoles<br><br>Computed values of mapping and reference cycle length | Presence or absence of electrogram dispersion at each electrode bipole under consideration<br><br>Computed values of mapping and reference cycle length |
| **Duration of Electrogram Recordings** | 1.5 Seconds | 1.5 Seconds |
| **Output Display** | The system generates color coded symbol(s) that indicates to the operator that the area under investigation is one exhibiting dispersion<br><br>In bidirectional digital communication, validated dispersion area can also be automatically displayed in the 3D mapping system as tags in the 3D atrial shell | The system generates color coded symbol(s) that indicates to the operator that the area under investigation is one exhibiting dispersion |
| **Signal Information Displayed** | Acquired patient signals, including body surface ECG and intra-cardiac EGMs. | Acquired patient signals, including body surface ECG and intra-cardiac EGMs. |

| | Volta Medical<br>VX1+ | Volta Medical<br>VX1<br>(K201298) |
|---|---|---|
| **Computing Platform** | Computer with Intel Core i7-7700 CPU (8MB Cache, up to 4.20 GHz, RAM 32 GB),<br><br>with integrated analog/digital converter PCI card and TPM (Trusted Platform Module)<br><br>Debian-based Linux OS | Computer with Intel Core i5-6500 CPU (6MB Cache, up to 3.60 GHz, RAM 32 GB),<br><br>with integrated analog/digital converter PCI card<br><br>Windows 10 or higher OS |
| **Hardware Design and Materials** | Computing platform, proprietary software algorithm, monitor, mouse/keyboard, custom-made analog connection cable, ethernet cable, acquisition system | Computing platform, proprietary software algorithm, monitor, mouse/keyboard, custom-made analog connection cable, acquisition system |

## XIII. DEVICE DESCRIPTION

VX1+'s intended use/indications for use, technological characteristics, and principles of operation are described below.

### A. Background

Over the last decades, multiple groups and technologies have offered approaches to localize regions of abnormal electrical activity in the heart based upon electrogram analysis. Some have focused on the frequency of activation of electrograms emanating from AF / AT drivers (Atienza, Almendral et al. 2009, Atienza, Almendral et al. 2014). Others have targeted driving regions localized after advanced signal processing, allowing for reentrant electrical source visualization (Narayan, Krummen et al. 2012, Miller, Kowal et al. 2014, Miller, Kalra et al. 2017). Also, some have simply ablated in areas where low voltage electrograms were suggestive of discontinuous impulse propagation (Narayan, Wright et al. 2011, Jadidi, Cochet et al. 2013, Jadidi, Lehrmann et al. 2016). Finally, some have chosen to target abnormal mono- or multipolar electrograms, named complex fractionated atrial electrograms (CFAEs) (Nademanee, McKenzie et al. 2004, Oral, Chugh et al. 2009). Spatio-temporal dispersion of electrograms is another electrogram abnormality described by Seitz, Bars et al. 2017. Multiple works have emphasized the usefulness of recognizing and targeting multipolar intra-cardiac electrograms exhibiting spatio-temporal dispersion (Nademanee, McKenzie et al. 2004, Kalifa, Tanaka et al. 2006, Lin, Scherlag et al. 2007, Zlochiver, Yamazaki et al. 2008, Narayan, Wright et al. 2011, Ashihara, Haraguchi et al. 2012, Jadidi, Cochet et al. 2013). Spatio-temporal dispersion is the focus of the Volta Medical technology.

Volta Medical has developed a first device VX1 (K201298) to aid in the identification of dispersion. Volta's VX1 software is based on machine and deep learning algorithms trained on a proprietary database and was designed to be used as an intra-operative device to reliably cue operators to detect atrial regions harboring dispersion. The result of the VX1 analysis (presence or absence of dispersion) is given exclusively on the dedicated VX1 graphical interface and is not communicated to any other existing EP system. The areas identified by VX1 must be then manually reported in existing 3D mapping systems.

VX1 has been clinically tested in a prospective, multicentric, nonrandomized study conducted in 85 de novo persistent AF patients, including 8 centers and 17 operators. VX1 allowed for robust center-to-center standardization of acute and long-term ablation outcomes after electrogram-based ablation (Seitz, Mohr Durdez et al. 2022, Deisenhofer 2022). Interestingly outcomes were compared to a comparable control group from the original paper from Seitz, Bars et al. 2017, in which dispersion-guided ablation was performed visually by trained operators, resulting in no statistical difference and confirming the relevance of the dispersion provided by VX1.

Following a technical collaboration between Volta Medical and Abbott, the company has developed a feature to exchange information with the EnSite X 3D mapping system using a digital interface called Live Export feature. Compatibility with future changes to EnSite X will be ensured through a specific process defined between Volta Medical and Abbott, ensuring that Volta is informed of changes in a timely manner for analysis and testing.

The VX1+ device has been developed by Volta Medical based on the same dispersion definition described by Seitz, Bars et al. 2017 (identical to previously cleared device VX1 (K201298)) and with the objective of improving clinical workflow by allowing areas with dispersed electrograms to be automatically tagged in the 3D electro-anatomical maps of the EnSite X mapping system.

### 1. Dispersion Definition

The Substrate HD study published in the Journal of the American College of Cardiology in 2017 described the visual criteria that may be used to identify intra-cardiac electrograms exhibiting spatio-temporal dispersion (Seitz, Bars et al. 2017).

As described in a previous submission by the Company for predicate device VX1 (K201298), the criteria used to recognize dispersed electrograms, as published in Seitz et al. 2017, have been utilized by the Company for:

- The annotation of the training database for the presence or absence of dispersion electrograms by two cardiac electrophysiologists.
- The evaluation of 28 cardiac electrophysiologists' performance within 17 seconds vs. the annotation of signals with virtually no limitation in time by two experts referred to as "annotating experts" or AEs, see Section XX.B.ii.b. of VX1 510(k) (K201298).
- The evaluation of inter-operator and VX1-operators agreement with virtually no limitation in time presented in the Reader Study, see Section XX.A. of VX1 510(k) (K201298).

In this current submission, the definition of dispersion, the training database and the VX1+ dispersion model are unchanged from previous submission for VX1 device (K201298).

### 2. Dispersion Annotation Criteria

Potentially dispersed electrograms should be analyzed both separately and together; with two electrograms displayed above and two electrograms displayed below. In that context, multipolar electrograms are considered as dispersed when one or several of the following criteria are present:

1) One continuously fractionated electrogram, with a cumulative duration longer than 80% of the 1.5 second window, i.e., 1.2 seconds;

2) Non-simultaneous activation of neighboring electrograms in such a way that 80% of the AF cycle length in the 1.5 second snippet may be present either consecutively (e.g., one second of dispersion and 0.5 sec. of non-dispersed electrogram), or non-consecutively (e.g.,0.5 sec of dispersion followed by 0.5 sec. of non-dispersion, followed by 0.5 sec. of dispersion);

3) In considering neighboring electrograms, both large deflections and small deflections should be noted at either of the neighboring locations. The visual effort consists of constructing from several neighboring electrogram locations a virtually "merged activation" and examining whether such a "merged activation" spans longer than 80% of the 1.5 sec. window either consecutively or non-consecutively.

### B. Intended Use/Indications for Use

The VX1+ assists operators in the real-time manual or automatic annotation of 3D anatomical and electrical maps of human atria for the presence of multipolar intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion during atrial fibrillation or atrial tachycardia.

The clinical significance of utilizing the VX1+ software to help identify areas with intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion for catheter ablation of atrial arrhythmias, such as atrial fibrillation, has not been established by clinical investigations.

### C. Technological Characteristics

The VX1+ device is a non-sterile reusable medical device, composed of a computing platform (including an analog/digital converter) and a software application designed to assist operators in detecting multipolar electrograms exhibiting spatiotemporal dispersion (Seitz, Bars et al. 2017).

The computer is manufactured by Advantech (external manufacturing site) and then assembled and configured (VX1+ software application installed) by Volta Medical (internal manufacturing site). VX1+ is supplied to the customer in a dedicated cardboard with appropriate medical/non-medical accessories (connection cables, screen, keyboard, mouse).

#### 1. VX1+ Software Application

VX1+ application is based on a machine and deep learning based-algorithm designed to assist in detecting multipolar electrograms exhibiting spatiotemporal dispersion and has been unchanged since VX1. The complete specifications of the core algorithm *vcore* can be found in **Appendix 13.1**. VX1+, similar to VX1, accomplishes this task with a real-time analysis of intra-cardiac signals in the operating room.

VX1+ also incorporates several other off-the-shelf algorithms, called the “external software” component. These algorithms, however, are fully enclosed within VX1+. They do not depend on external providers. They are fully accessible to our architecture and will not evolve. Importantly, the Company has total control of the external software component. Once these external code lines have been incorporated, there is no additional interaction with their provider.

The VX1/VX1+ dispersion-classifier algorithm is a blend of two distinct classifiers designed to analyze incoming data in real time. It uses a dual approach of: (i) machine learning and (ii) deep learning classifiers to analyze intra-cardiac signals recorded with a multipolar catheter. Both classifiers have been trained on a database of 275,020 annotated electrogram samples recorded in 110 procedures.

##### a) Machine Learning Classifier

The machine learning software relies on a mathematical approach called Extreme Gradient Boosting (XGBoost: A Scalable Tree Boosting System, Chen and Guestrin (https://arxiv.org/abs/1603.02754)). This approach is well-known to data scientists and is a core principle of state-of-the-art algorithms. It has notably been used for demanding use-cases in so-called “machine learning challenges”. The approach presents multiple operational advantages: mainly, its “sparsity awareness” helps to

circumvent impediments such as missing data. It also offers ways of running algorithms in a parallel mode, i.e., multiple sources of data may be processed simultaneously.

### b) Deep Learning Classifier

We use a deep convolutional neural network with the Tensorflow library within the framework of the recent 2015 architecture.

Both classifiers are unchanged from previous device VX1 (K201298).

### c) Software Architecture

The incoming data is acquired and processed by several chained threads as described in **Figure 1**. Threads are as follows: data extraction, analysis / classification of patient real-time data, and user interface display. Please note that the database is not included in the software and will remain in a dedicated data server.

The Feature extractor and classifier are unchanged from previous device VX1 (K201298).

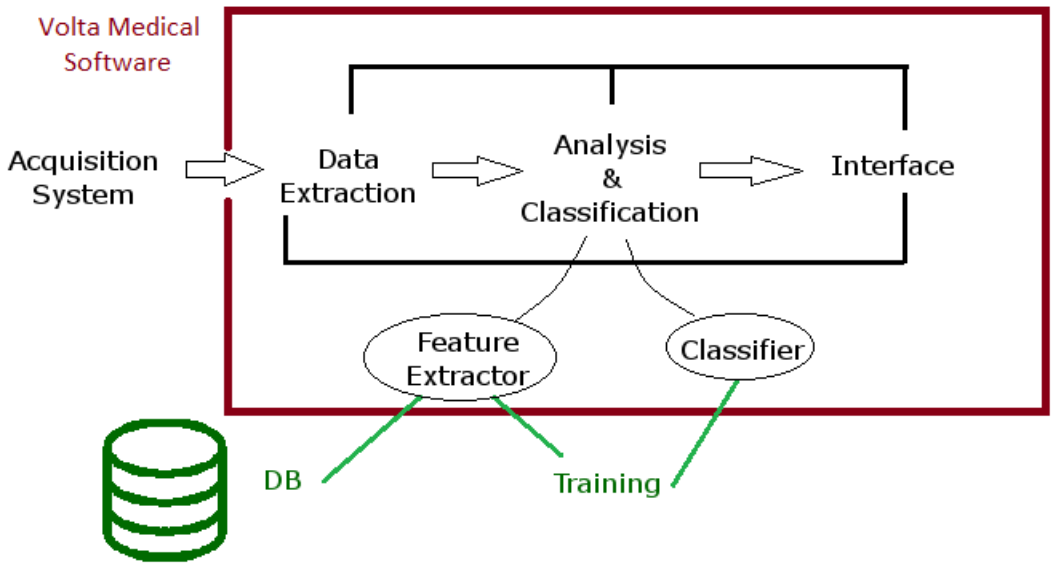



**Figure 1: Schematic highlighting the dataflow in the software and illustrating the DE-Classifier algorithm's functional chain.**

### d) Software Components

The detailed architecture of VX1+ application is described in **Section XVIII. D** and **Appendix 18.12**. It includes the main following components:

| Designation | Purpose |
|---|---|
| ***Daemon Application*** | This software component handles specific low-level operations such as shutdown, restart, mounting USB devices. It communicates with the FrontEnd component. |
| ***Processing Modules*** | This component includes the modules dedicated to to analyze incoming signal data and return outputs (likelihoods, estimations) to the User Interface. It contains the trained DE-classifier. |
| ***Driver*** | This software component is used to drive the acquisition system (connect, monitor the settings and launch acquisition), format incoming data and send it to the processing modules. |
| ***FrontEnd*** | This component produces the Graphic User Interface. |

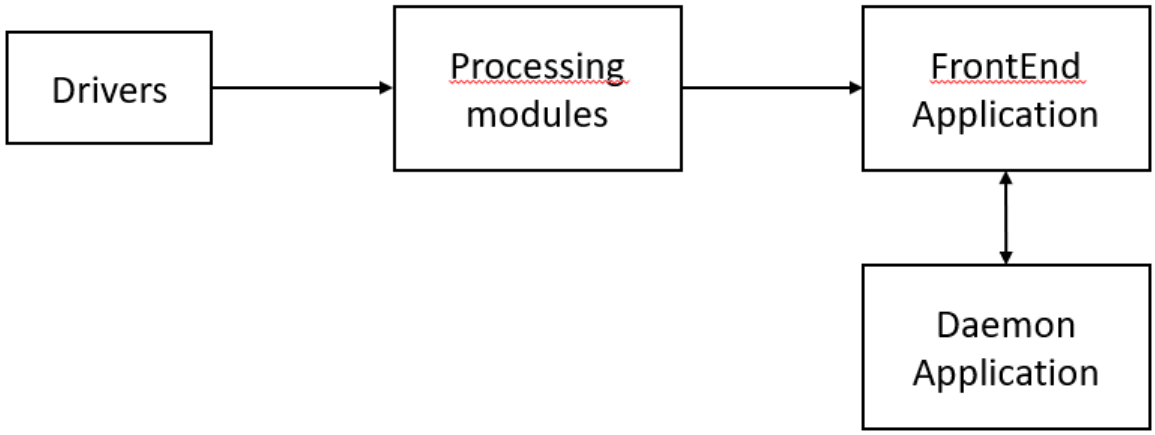



**Figure 2: Architecture diagram highlighting the software components and units**

## 2. Bidirectional Communication and Automatic Tagging Feature

VX1+, like VX1, operates in one-way (unidirectional) communication with the acquisition system. The analog EGMs are sent from the acquisition system to the VX1+ and the result of the dispersion analysis is provided only in the VX1+ interface. Tagging must be done manually in the 3D electro-anatomical map.

In addition, VX1+ brings the possibility to operate in a bidirectional communication with the EnSite X 3D mapping system:

EnSite X sends EGMs and electrodes position to VX1+ in real-time. EGMs are analyzed as they are received for the presence or absence of dispersion in the same manner as in unidirectional communication. The automatic tagging module (when activated) uses the 3D positions to send

relevant dispersion points of interest (mapping catheter dipoles) to the EnSite X system. Dispersion tags appear automatically in the 3D atrial shell of the EnSite X.

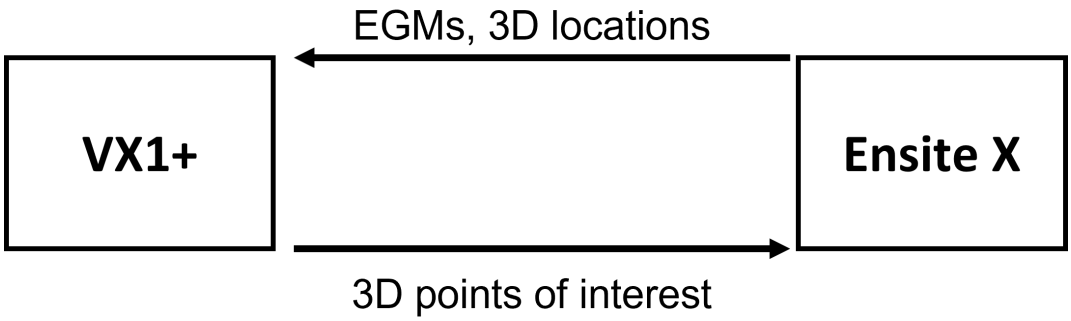
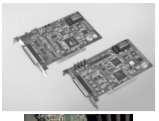



**Figure 3: Bidirectional communication schematic**

The digital interface is called Live Export and is a feature that is part of Abbott's EnSite X system, cleared by the FDA (K221213).

Color and size of the automatic dispersion tags coming through LiveExport were chosen such that they can be easily recognized by the user on the 3D atrial shell.

### 3. VX1+ Hardware Components

| Component Name | Description | Picture | VX1+ vs. VX1 comments |
|---|---|---|---|
| Computer<br>+<br>Analog/Digital Converter PCI Card<br>+<br>TPM | Computer with Intel Core i7-7700 CPU (8MB Cache, up to 4.20 GHz, RAM 32 GB), with VX1+ application installed.<br><br>Analog/digital 16 channels converter PCI card. Each channel provides a ±10 V measurement range at a 24-bit resolution. The converter has a maximum sample rate of 10 kS/s and features programmable hardware filters.<br><br>The TPM (Trusted Platform Module) is a security embedded ship in the computer which provides a cyber-security protection. |  <br>  <br>  | Minimum specifications are comparable between VX1 and VX1+. Both computers are manufactured by Advantech and have the same general reference. However the VX1+ computer has a more powerful CPU (Intel Core i7-7700 vs Intel Core i5-6500)<br><br>Same PCI card<br><br>Addition of TPM for cybersecurity protection in VX1+ |

| Component Name | Description | Picture | VX1+ vs. VX1 comments |
|---|---|---|---|
| | | | Operating system change (from Windows to Debian-based Linux) |
| Computer AC/DC switch converter | Computer power supply. AC/DC converter |  | Same converter |
| Computer AC/DC switch converter Power Cord | Computer power cord |  | Same power cord |
| Keyboard | QWERTY Keyboard with USB connection to computer |  | Equivalent standard keyboard |
| Mouse | Mouse with USB connection to computer |  | Equivalent standard mouse |
| Screen | 23.8” screen full HD 2560x1440, 75Hz. 16:9 ratio.<br>Speakers 2x2W, HDMI and DP outputs. |  | Equivalent standard screen |
| Screen Power Cord | Screen power cord |  | Equivalent power cord |
| DSUB Connection Cable | Connection cable between the analog output of an EP Recording System and the analog input of the computer.<br>Analog DB37 to DB37 Male/Male |  | Same custom-made analog connection cable |
| Octopus Connection Cable | Connection cable between the analog output of an EP Recording System and the analog input of the computer.<br>Analog DB37 to 16 pins Male/Male |  | Same custom-made analog connection cable |
| Ethernet Connection Cable | RJ-45 connection between ABBOTT EnSite X workstation and VX1+<br>Lengths: 20 / 10 / 5 / 2 meters |  | Addition of standard ethernet cable for digital bidirectional communication |

## 4. Compatibility and Interactions with Other Systems

VX1+ works with all existing 510(k)-cleared catheters that meet specific dimension requirements and with one of three compatible data acquisition systems. VX1+ supports both unidirectional analog communication and bidirectional digital communication, depending on the data acquisition system.

In unidirectional analog communication VX1+ is connected to one of the two compatible EP Recording System (identical to VX1 (Volta medical) (K201298): the *LabSystem Pro* EP Recording System (Boston Scientific) (K141185) and the *MacLab CardioLab* EP Recording System (General Electric) (K130626). Analog data are routed to the platform through a connection cable and converted to digital through an Analog-to-Digital (A/D) converter and transferred to the application.

In bidirectional digital communication (not available in VX1), VX1+ is connected to the *EnSite X* 3D Mapping System (Abbott) (K221213). Digital data are routed to the platform through an ethernet cable and transferred to the application.

Following configurations are available:

- Direct communication with the *MacLab CardioLab* EP Recording System (GE) (K130626):

Computer with VX1+ application installed and its power supply adapter and detachable power cord, and accessories: keyboard, mouse, screen with its detachable power cord, and the DSUB connection cable.

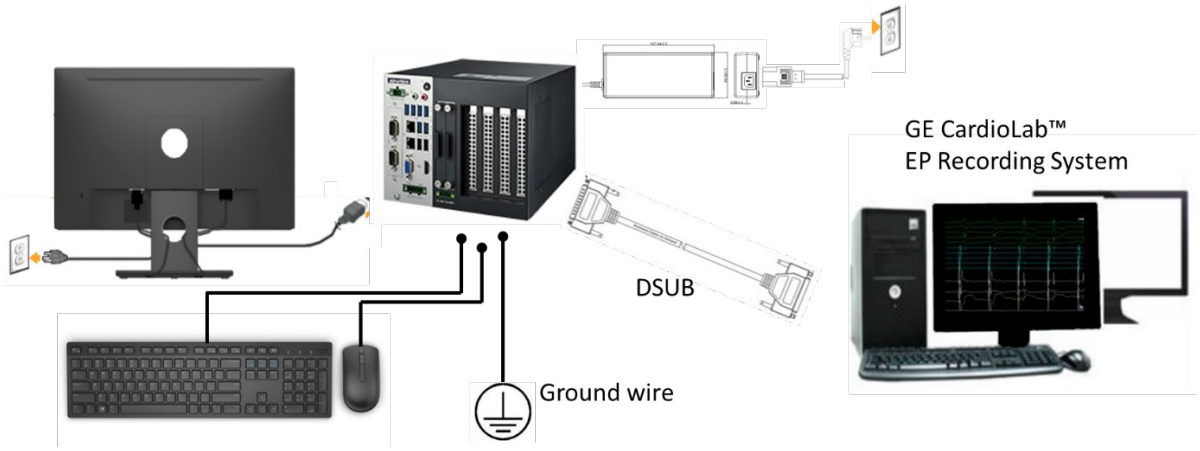



**Figure 4: Configuration #1 with GE CardioLab EP Recording System**

- Communication with the *MacLab CardioLab* EP Recording System (GE) (K130626) via analog output box:

Computer with VX1+ application installed and its power supply adapter and detachable power cord, and accessories: keyboard, mouse, screen with its detachable power cord, and the Octopus connection cable.
Analog output box 16 channels associated with the GE *CardioLab* EP recording system (sold separately, by GE representative or distributor).

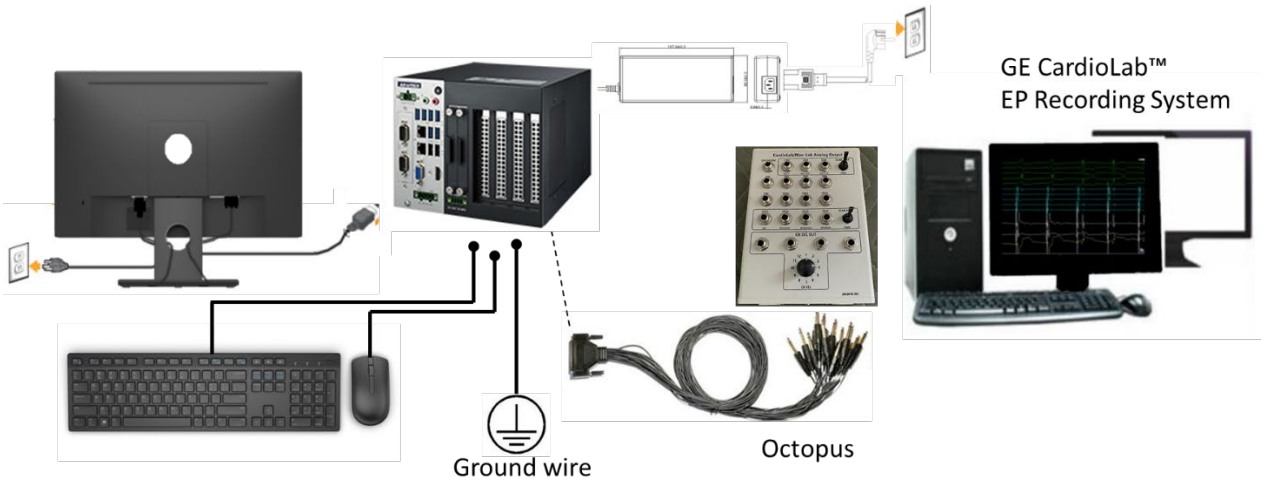



**Figure 5: Configuration #2 with GE CardioLab EP Recording System**

- Communication with the *LabSystem Pro* EP Recording System (Boston Scientific) (K141185):

Computer with VX1+ application installed and its power supply adapter and detachable power cord, and accessories: keyboard, mouse, screen with its detachable power cord and the Octopus connection cable.

Analog output box 16 channels associated with the Boston Scientific *LabSystem Pro* EP recording system (sold separately by Boston Scientific representative or distributor).

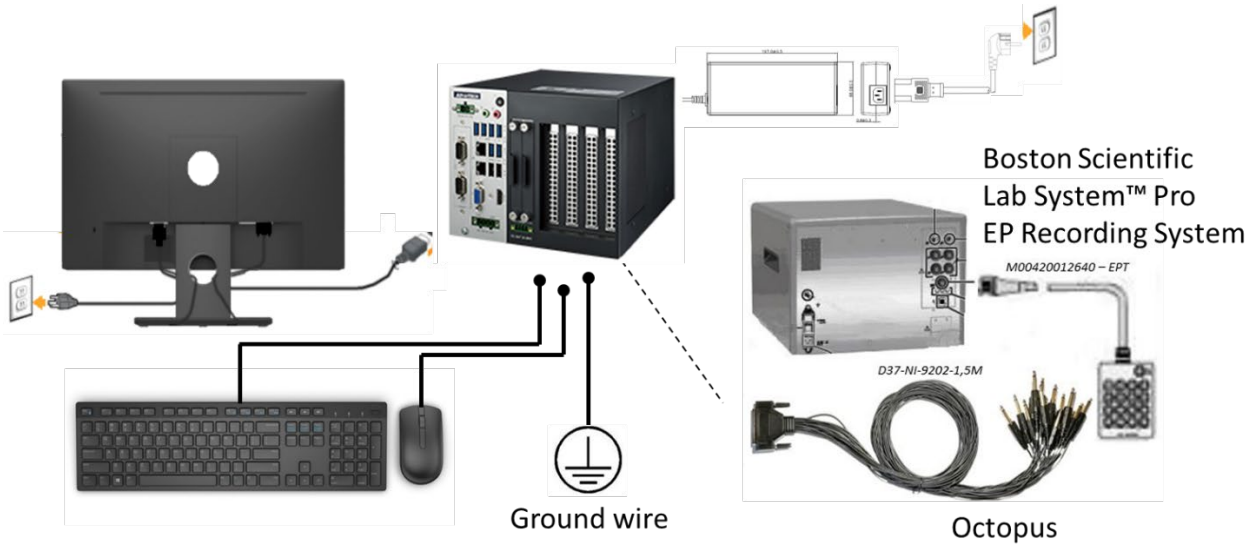



**Figure 6: Configuration with Boston Scientific LabSystem Pro EP Recording System**

- Communication with the *EnSite X* 3D mapping system (Abbott) (K221213):

Computer with VX1+ application installed and its power supply adapter and detachable power cord, and accessories: keyboard, mouse, screen with its detachable power cord and one ethernet cable.

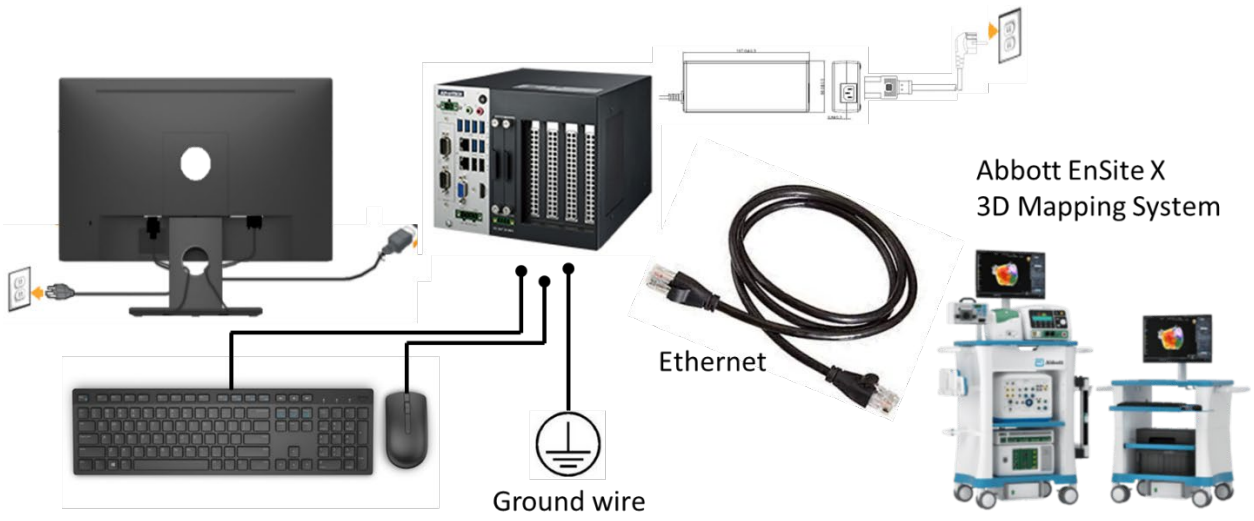



**Figure 7: Configuration with EnSite X 3D Mapping System**

In summary, VX1+ is compatible with the following devices:

| | |
|---|---|
| **Compatible EP Recording System** | VX1+ supports analog signals acquired from the following EP recording systems:<br>- LabSystem Pro EP Recording System (Boston Scientific)<br>- CardioLab EP Recording System (GE) |
| **Compatible 3D Mapping System** | VX1+ supports digital signals acquired from the following 3D mapping system:<br>- Ensite X (Abbott) |
| **Compatible 3D Mapping Catheters** | VX1+ supports compatible mapping catheters having the following specific characteristics:<br>- Electrodes with size (diameter for circular, length for rectangle/ square) between 0.4 mm and 1 mm (except distal electrode with size between 1-2 mm)<br>- Intra-bipoles spacing: 1 – 3 mm<br>- Number of selected dipoles: 10 |
| **Compatible CS Catheter** | VX1+ supports compatible CS catheter having specific properties:<br>- Electrode size: 1 mm<br>- Spacing: 2 – 3 mm<br>- Number of selected dipoles: 5 |

## D. Principles of Operation

### 1. General

The VX1+ application is installed on a computing platform and configured by a Volta Medical's representative on site during installation. The VX1+ application supports digital signal input from the platform and acquired either from an EP recording system (through an analog/digital converter) or from a 3D mapping system (directly in digital format).

VX1+ supports two configurations, unidirectional and bidirectional. In unidirectional mode, the tagging of regions of interest (ROI) is manual. In bidirectional mode, the tagging of ROI is either manual or automatic.

For each mapping catheter, the application displays which dipoles are of interest at a given time during the procedure.

The operating mode is the following:

1. While moving the mapping catheter, the user watches the display regularly.
2. If dipoles start to blink, the user stabilizes the mapping catheter.
3. If the dipoles of interest are confirmed as dispersed by the software, sound- and color- coded guidance on the upper hemicycle schematic are provided, and depending on the configuration:
    - The user may manually tag the associated locations on the 3D mapping system (available for both modes)
    - The associated locations are automatically tagged on the 3D shell of the atria in the 3D mapping system (only for bidirectional mode).

Ultimately, by repeating these 3 steps, the electrophysiologist may obtain a map of all dispersed areas in the mapping system.

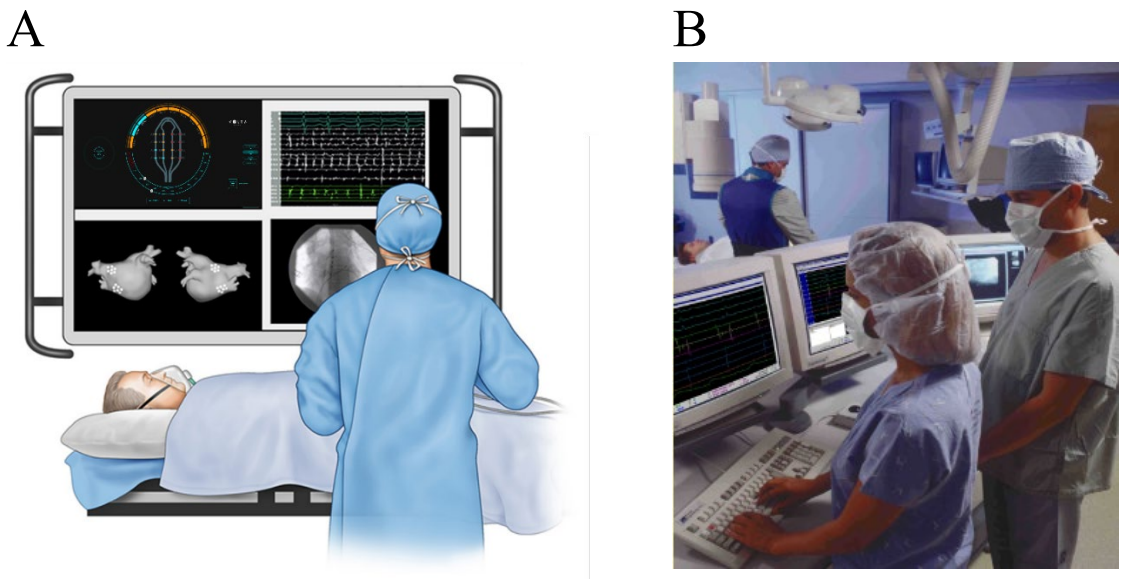



**Figure 8: Principle of Operation;** A) VX1+ interface (upper left corner of the widescreen) presents operators with a simple color coding of signals of interest: blue for no dispersion; orange for the high likelihood of dispersion; red for a very high likelihood of dispersion; B) After validation by the operator, the regions of interest can be tagged in commercially available 3D navigation systems, automatically or manually by the biomedical engineer.

### 2. User Interface (UI)

VX1+ displays a set of information to guide the operator in the detection of dispersion. The center of the screen displays a schematic representation of the catheter used for mapping. Around the catheter's schematic, two half-circle-shaped symbols depict the presence of dispersed electrograms

among those of interest (upper half) and cycle length estimations as measured by the mapping and coronary sinus catheters (lower half). On the upper half-circle, 10 box sections correspond to the 10 dipoles of interest. When one or several dipole symbol(s) is / are blinking and is colored in orange / red on the catheter schematic, this indicates to the operator that the area under investigation is one exhibiting dispersed electrograms. For confirmation, the operator may stabilize the catheter in this region. Then, the operator must examine the corresponding multipolar electrograms to provide confirmation of the presence of dispersion. Further confirmation is given by the red / orange coloring of boxes on the upper half-circle. Finally, the operator may tag this location (actively manually or confirmation of the automatic tag). The lower part of the frame displays (i) the average cycle length as recorded by the reference catheter (R) in the coronary sinus (surrogate for global cycle length of the arrhythmia); (ii) the average measurable local cycle length as recorded by the mapping catheter (M).

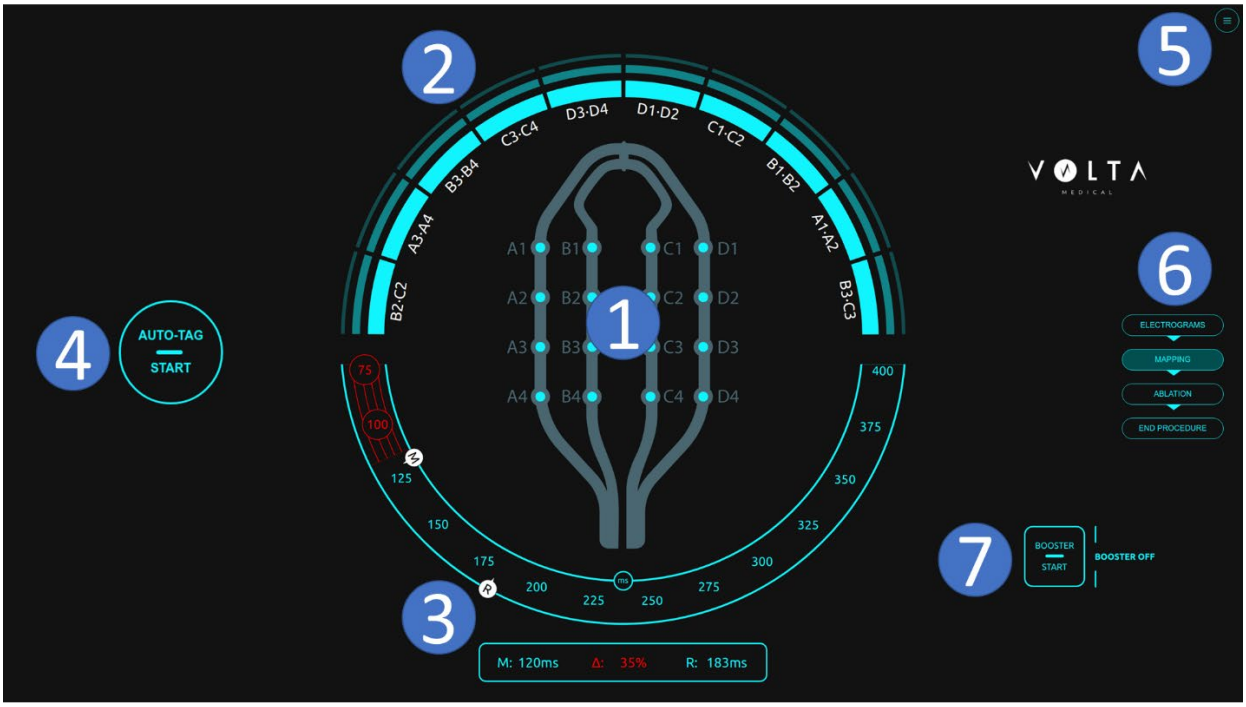



**Figure 9: HD Grid Catheter VX1+ UI <u>in digital communication mode</u>**. 1) The center of the screen displays a frame with a schematic representation of the catheter used for mapping. Catheter electrodes are numbered. If bipoles are blinking in orange / red, this indicates to the operator that the area under investigation is one exhibiting dispersed electrograms. For confirmation, the operator may stabilize the catheter in this region. 2) On the upper half-circle, 10 box sections correspond to the 10 bipoles of interest. When one or several bipole symbol(s) is / are blinking and is / are colored in orange / red, this indicates to the operator that the area under investigation is one that is confirmed as a region exhibiting dispersed electrograms. 3) The lower half-circle displays (i) the average global cycle length (GCL) as recorded by the reference catheter (R) and (ii) the average local cycle length (LCL) as recorded by the mapping catheter (M). In the lowest part of the interface, the exact values of the cycle lengths are given in miliseconds as well as the difference ratio in percentage computed as (R-M)/R. 4) Auto-tagging activation/deactivation button (only available in digital bidirectional communication with Abbott EnSite X and Abbott catheters).5) Main menu including Logout, Help Page, About, Shutdown and Restart. 6) Procedural stages buttons: Initialization replaced by Electrograms once initialized, Mapping, Ablation, End Procedure. 7) Booster mode activation/deactivation button.

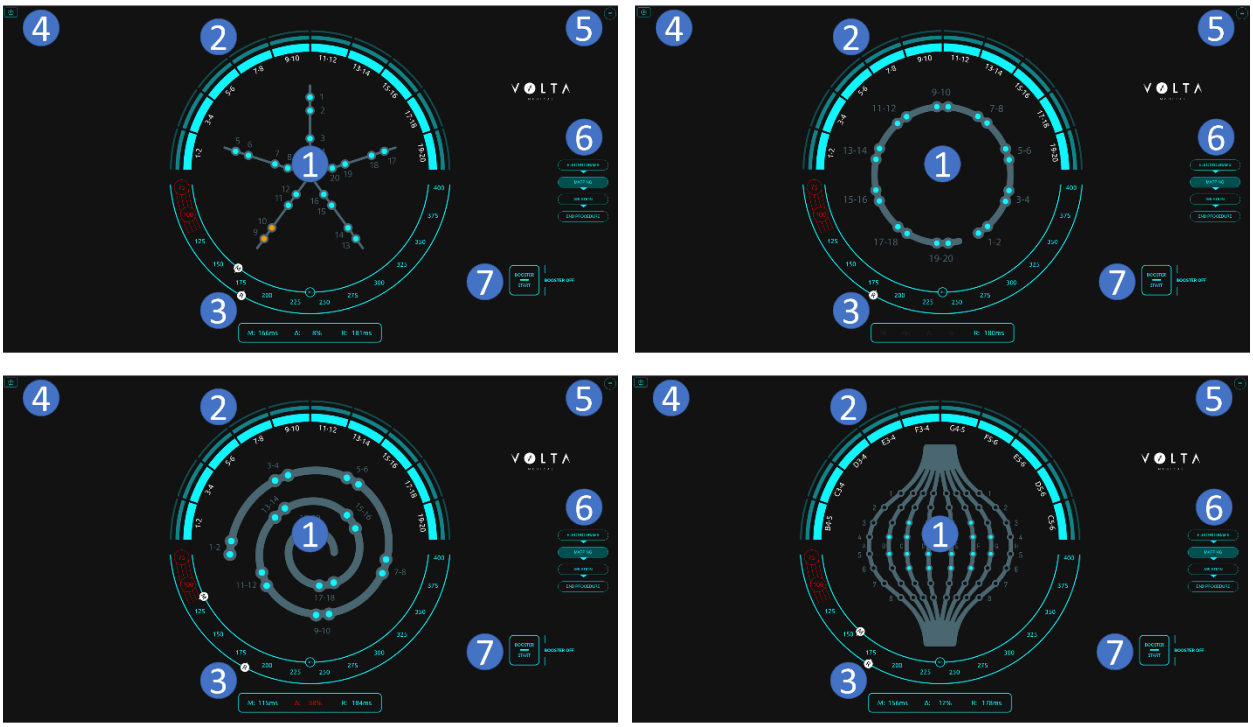



**Figure 10: Pentaray (top left), Circular 20 (top right), Reflexion HD (bottom left), Orion (botton right) Catheters VX1+ UI <u>in analog communication mode</u>**. 1) The center of the screen displays a frame with a schematic representation of the catheter used for mapping. Catheter electrodes are numbered. If bipoles are blinking in orange / red, this indicates to the operator that the area under investigation is one exhibiting dispersed electrograms. For confirmation, the operator may stabilize the catheter in this region. 2) On the upper half-circle, 10 box sections correspond to the 10 bipoles of interest. When one or several bipole symbol(s) is / are blinking and is / are colored in orange / red, this indicates to the operator that the area under investigation is one that is confirmed as a region exhibiting dispersed electrograms. 3) The lower half-circle displays (i) the average global cycle length (GCL) as recorded by the reference catheter (R) and (ii) the average local cycle length (LCL) as recorded by the mapping catheter (M). In the lowest part of the interface, the exact values of the cycle lengths are given in miliseconds as well as the difference ratio in percentage computed as (R-M)/R. 4) Analog Procedure settings page. 5) Main menu including Logout, Help Page, About, Shutdown and Restart. 6) Procedural stages buttons: Initialization replaced by Electrograms once initialized, Mapping, Ablation, End Procedure. 7) Booster mode activation/deactivation button.

## E. Device Versions

| VX1+ product version | VX1+ software version | Description of modifications | Release date | Testing performed |
|---|---|---|---|---|
| **1.0** | **1.0.0** | NA (initial version) | 24/MAY/2022 | 3 procedures in the scope of the Ampere study (see **Section XXII**) |
| | **1.0.1** | **Minor software updates** related to VX1+ blocked on the splash screen when changing gain during procedure & Ethernet cable error message update.<br><br>**Autotag algo**: no functional change | 07/JUN/2022 | 2 procedures in the scope of the Ampere study (see **Section XXII**) |
| | **1.0.2** | **Minor bug fixing** related to duplicated autotags sent to EnsiteX **& minor software updates** related to audit trail & PMS logs export button, Procedure start error message, & autotagging module configuration of its logger. | 22/JUN/2022 | 3 procedures in the scope of the Ampere study (see **Section XXII**) |
| | **1.0.3** | **Preprocessing module parameters updates** related to the signal received from Ensite without filter and filtered according to preprocessing module parameters from VX1+<br><br>**Minor bug fixing** related to GCL values sometimes not computed **& minor software updates** related to log files export, related to label information (language & SW version update) from About section, related to maintenance page confirmation message & update process launch, - user action logging into the audit trail logs**,** to USB device ejection, - to logs export. | 28/JUN/2022 | |
| | **1.0.4** | **Autotag algo update** related to a change of velocity filter from 3mm/s to 10mm/s: **functional change**<br><br>**Dispersion algo update** related to the display rules of the Log from INFO to DEBUG<br><br>**LCL algo update**: no functional change<br><br>**Minor software updates** related to upgrade vx-driver Abbott & SSL certificate, log Files archiving/deletion period, stability error message when exporting heavy logs, first/last names characters limitations, configuration/files update process, Help content page languages, maintenance page languages, | 06/JUL/2022 | First complete integration and verification test campaign.<br><br>1 procedure in the scope of the Ampere study (see **Section XXII**) |
| | **1.0.5** | **Minor code updates_** related to problems resolution.. | 11/JUL/2022 | Second complete integration and verification test campaign. |

| | | | | |
|---|---|---|---|---|
| | **1.0.6** | **Minor software updates** related to the label of the user interface. | 12/JUL/2022 | Third and final integration and verification test campaign.<br><br>All the other testing in **Sections XIX, XX, and XXII** |

## XIV. SUBSTANTIAL EQUIVALENCE

As explained in detail below, VX1+ is substantially equivalent to other legally marketed cardiac mapping software devices**.** Specifically, the VX1+ is substantially equivalent VX1 (Volta Medical) (K201298). As explained in more detail below, VX1+ has the same general intended use and indications, and substantially similar technological characteristics, and principles of operation as the previously cleared predicate VX1 (Volta Medical) (K201298). A substantial equivalence chart comparing the similarities and differences between the VX1+ and its predicate device is provided in pgs. 98-101 below. As also explained in more detail below, minor differences in the technological characteristics do not raise different questions of safety or effectiveness. Bench and clinical testing demonstrate that the VX1+ is as safe and effective as its predicate device VX1.

### A. Intended Use/ Indications for Use

The indications for use of the predicate device VX1 are:

> The VX1 assists operators in the real-time manual annotation of 3D anatomical and electrical maps of human atria for the presence of multipolar intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion during atrial fibrillation or atrial tachycardia.
>
> The clinical significance of utilizing the VX1 software to help identify areas with intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion for catheter ablation of atrial arrhythmias, such as atrial fibrillation, has not been established by clinical investigations.

Like the predicate device, the VX1+ assists operators in the real-time manual annotation of 3D anatomical and electrical maps of human atria for the presence of multipolar intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion during atrial fibrillation or atrial tachycardia.

The proposed indications for use of the VX1+ are:

> The VX1+ assists operators in the real-time manual or automatic annotation of 3D anatomical and electrical maps of human atria for the presence of multipolar intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion during atrial fibrillation or atrial tachycardia.
>
> The clinical significance of utilizing the VX1+ software to help identify areas with intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion for catheter ablation of atrial arrhythmias, such as atrial fibrillation, has not been established by clinical investigations.

The VX1+ device is a new device manufactured by Volta Medical, based on the same concept (identification of electrograms dispersion) than predicate VX1, from the same manufacturer. The core algorithm for dispersion detection is identical, no new electrogram adjudication, or new training of the database has been performed. Some minor modifications have been implemented to enhance the user experience: post-processing steps (specifically with the addition of 3D positions of the catheter electrodes and parameter adjustments), more accurate cycle length estimator, improved user interface. The main difference in the technological characteristics between the VX1+ and VX1, is

VX1+'s ability to have a bidirectional digital communication with a compatible 3D mapping system, allowing automatic tagging of regions of interest, resulting in the addition of "or automatic" in the indications for use of the VX1+. This alternative operating mode (areas of interest are automatically tagged instead of being manually added in the 3D mapping system) improves the clinical workflow without affecting the device's diagnostic effects. The intended use remains the same between VX1 and VX1+.

The VX1+ has the same intended use than its predicate device VX1. Thus, the VX1+ satisfies the first criterion for a finding of substantial equivalence.

### B. Technological Characteristics

Both the VX1+ and the predicate VX1 are machine and deep learning based-algorithm designed to assist in detecting cardiac multipolar electrograms exhibiting spatiotemporal dispersion (Seitz, Bars et al. 2017). They analyze in the same way intra-cardiac data from the patient's heart in real time and detect regions of interest.

#### 1. Components

Both the VX1+ and VX1 are comprised of the same following components:

- Software application
- Computer with Analog / digital converter
- Connection cable
- Display monitor
- Keyboard/mouse

VX1 and VX1+ computers are manufactured by same supplier Advantech and have the same general reference and capabilities. However, the VX1+ computer has a more powerful CPU (Intel Core i7-7700 vs Intel Core i5-6500). Also, the operating system has changed (from Windows to Debian-based Linux) and an additional Trusted Platform Module (TPM) for cybersecurity protection has been added in VX1+. All these differences allow for a more stable and fast processing but do not raise any questions about safety or effectiveness from the predicate.

The display monitor, keyboard and mouse are equivalent standard electronic control components with no effect on safety or effectiveness.

The only minor difference in the technological characteristics between the VX1+ and VX1, is the ability of VX1+ to have a bidirectional digital communication with the EnSite X 3D mapping system (Abbott) (K221213) via an additional ethernet cable (not available for VX1). The ethernet-based digital data acquisition chain has been optimized and validated to be equivalent to the analog data acquisition chain of VX1 device (where data is digitized by the A/D converter integrated in the computer). The complete system has also been tested for electromagnetic compatibility and electrical safety. The addition of a digital data acquisition chain via a standard ethernet cable therefore has no effect on the safety or effectiveness of the device.

## 2. Software Algorithm

The VX1+ application is a machine and deep learning based-algorithm designed to assist in detecting multipolar electrograms exhibiting spatiotemporal dispersion. The main algorithm, called *vcore,* has remained unchanged since VX1. The VX1+, similar to the predicate VX1, accomplishes this task with a real-time analysis of intra-cardiac signals in the operating room.

The *vcore* algorithm in VX1/VX1+ is a blend of two distinct classifiers designed to analyze incoming data in real time. It uses a dual approach of: (i) machine learning and (ii) deep learning classifiers to analyze intra-cardiac signals recorded with a multipolar catheter. Both classifiers have been trained on a database of 275,020 annotated electrogram samples recorded in 110 procedures.

The complete specifications of the core algorithm *vcore* can be found in the 510(k) for predicate device VX1 (K201298) and are attached here for completeness in **Appendix 13.1**.

VX1+ dispersion algorithm contains minor improvements while keeping the same level of clinical performance (i.e., obtaining substantially similar dispersion maps).

The improvement consists in parameters adjustment added to enhance the user experience, by reducing the "blinking" effect sometimes observed in dispersion display (e.g., when the catheter is moving). This “blinking effect” is naturally not considered by the operator during use with analog input and manual tagging (as in VX1). The adjustment of post-processing parameter is intended to mimic the natural visual filtering performed by the operator and thus to obtain similar dispersion maps. Thus, this parameter optimization does not raise any different question of safety or effectiveness.

The detailed algorithm design including specific changes to VX1 algorithm SPECDA-03-001 is provided in **Appendix 18.1**.

VX1+ cycle length estimators have also been improved compared to VX1 to reduce uncertainty and undesirable behavior (specifically the VX1 cursor may move a lot when estimation is not stable). The detailed algorithm design for the reference and mapping cycle length estimators SPECDA-03-002 and SPECDA-03-003 are provided in **Appendices 18.2** and **18.3**, respectively.

VX1+ also incorporates several other off-the-shelf algorithms, called the “external software” component. These algorithms, however, are fully enclosed within VX1+. They do not depend on external providers. They are fully accessible to our architecture and will not evolve. Importantly, the Company has total control of the external software component. Once these external code lines have been incorporated, there is no additional interaction with their provider.

With regard to the difference with the addition of the automatic annotation, VX1+ automatic tagging functionality was specifically designed to achieve at least as good performance as with the manual tagging workflow, by modeling the human decision making process. It means that with regard to the difference with the addition of the automatic annotation, the VX1+ performs similarly to the predicate VX1. Also, the automatic tagging function does not introduce any risks if the user were to rely on the automatic annotations, since they always have the ability to confirm and remove them in case of disagreement. Moreover, the bidirectional communication cannot negatively affect the performance of EnSite since the LiveExport data transfer uses a validated encrypted communication and each

connection to the EnSite is performed via specific authentication using a valid certificate for a predefined period of time. Therefore, the difference in additional automatic annotation does not affect the device performance or raise different questions of safety or effectiveness.

### C. Principles of Operation

The VX1 and VX1+ are installed on a computing platform and configured by a Volta Medical's representative on site at installation.

The VX1+ application supports digital signal input coming from the platform and acquired either from an EP recording system (through an analog/digital converter) or from a 3D mapping system (directly in digital format).

The unidirectional analog communication between VX1+ and the two compatible EP recording systems (the *LabSystem Pro* EP Recording System (Boston Scientific) (K141185) and the *MacLab CardioLab* EP Recording System (General Electric) (K130626)) remains unchanged from VX1.

However, a bidirectional digital communication with the *EnSite X* 3D Mapping System (Abbott) (K221213) constitutes a new feature of VX1+ along the possibility to have an automatic tagging directly in the 3D shell of the atria in the EnSite system.

For each mapping catheter, the application displays which dipoles are of interest at a given time during the procedure.

The operating mode of VX1+ is substantially the same than the one of VX1:

1. While moving the mapping catheter, the user watches the display regularly.
2. If dipoles start to blink, the user stabilizes the mapping catheter.
3. If the dipoles of interest are confirmed as dispersed by the software, sound- and color- coded guidance on the upper hemicycle schematic are provided, and depending on the configuration:
    - The user may manually tag the associated locations on the 3D mapping system (available for both VX1 and VX1+);
    - The associated locations may be automatically tagged on the 3D shell of the atria in the 3D mapping system (only for bidirectional mode, and thus only for VX1+).

Ultimately, by repeating these 3 steps, the electrophysiologist may obtain a map of all dispersed areas in the mapping system.

The practical difference in the mode of operation is that in manual tagging, the operator confirms the validity of the dispersion detection before the tagging, while in automatic tagging, the operator confirms the validity of the tagging a posteriori.

Both the subject and predicate devices consist of the same operational steps.

## D. Conclusion

The VX1+ and VX1 have strictly the same intended use and substantially similar indications, technological characteristics, and principles of operation. The introduction of automatic tagging feature does not alter the intended use of the device as an electrophysiological evaluation tool and do not affect its safety and effectiveness when used as labeled. In addition, the minor technological (i.e., bidirectional communication) differences and algorithm improvements between the VX1+ and its predicate device do not raise new issues of safety or effectiveness. Thus, the VX1+ device is substantially equivalent.

**Volta Medical's VX1+**

**Substantial Equivalence Comparison Chart**

| | Volta Medical VX1+ | Volta Medical VX1 (K201298) | Comments |
|---|---|---|---|
| **Regulation** | 21 C.F.R. § 870.1425 | 21 C.F.R. § 870.1425 | Same |
| **Classification Name** | Programmable Diagnostic Computer | Programmable Diagnostic Computer | Same |
| **Product Code** | DQK | DQK | Same |
| **Indications for Use** | The VX1+ assists operators in the real-time manual <u>or automatic</u> annotation of 3D anatomical and electrical maps of human atria for the presence of multipolar intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion during atrial fibrillation or atrial tachycardia.<br><br>The clinical significance of utilizing the VX1+ software to help identify areas with intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion for catheter ablation of atrial arrhythmias, such as atrial fibrillation, has not been established by clinical investigations. | The VX1 assists operators in the real-time manual annotation of 3D anatomical and electrical maps of human atria for the presence of multipolar intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion during atrial fibrillation or atrial tachycardia.<br><br>The clinical significance of utilizing the VX1 software to help identify areas with intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion for catheter ablation of atrial arrhythmias, such as atrial fibrillation, has not been established by clinical investigations. | Activation of the automatic tagging function does not alter the clinical use of VX1+. The VX1+ performs similar to the predicate VX1. Thus, there is no effect on safety or effectiveness. |
| **System Type** | Signal processing based atrial mapping system | Signal processing based atrial mapping system | Same |
| **Primary Feature** | Displays and analyzes electrical maps such as intra-cardiac electrograms in real-time using machine learning and | Displays and analyzes electrical maps such as intra-cardiac electrograms in real-time using machine learning and | Same |

| | Volta Medical VX1+ | Volta Medical VX1 (K201298) | Comments |
|---|---|---|---|
| | signal processing techniques | signal processing techniques | |
| **3D Location Technology** | Electroanatomic location is performed by another commercially available navigation system. In bidirectional digital communication, 3D location is shared by the 3D Mapping System with VX1+. | Electroanatomic location is performed by another commercially available navigation system. | In bidirectional digital communication, the EnSite X shares the 3D position of the electrodes with VX1+, VX1+ uses these positions for dispersion analysis but no processing is performed by the VX1+ on the 3D coordinates. Sharing the 3D electrode position does not affect the performance of the device and does not raise any safety or effectiveness issues. |
| **Compatible Acquisition Systems** | • LabSystem Pro EP Recording System (Boston Scientific)<br>• CardioLab EP Recording System (GE)<br>• EnSite X 3D Mapping System (Abbott) | • LabSystem Pro EP Recording System (Boston Scientific)<br>• CardioLab EP Recording System (GE) | Adding the EnSite X to the list of compatible acquisition systems does not affect the performance of the device. The VX1 and VX1+ can also be used with the Ensite X and corresponding compatible catheters via analog communication. |
| **Compatible Catheters** | Any compatible mapping and ablation catheter | Any compatible mapping and ablation catheter | Same |
| **Display(s)** | Color monitor | Color monitor | Same |
| **Multi-Display Support** | Yes, duplicate display on a secondary medical screen or on an operating room widescreen | Yes, duplicate display on a secondary medical screen or on an operating room widescreen | Same |
| **Control** | Standard keyboard / mouse | Standard keyboard / mouse | Same |
| **Display Timing** | Real-time | Real-time | Same |
| **Inputs Required** | Analog or digital Intra-cardiac signals | Analog Intra-cardiac signals | In bidirectional digital communication, the EnSite X digitally shares |

| | Volta Medical VX1+ | Volta Medical VX1 (K201298) | Comments |
|---|---|---|---|
| | In digital mode, 3D locations of corresponding electrodes bipoles | | electrograms and 3D electrode position with the VX1+. Appropriate filtering is performed to make the digital and analog inputs comparable. The performance of the device is not affected by this mode of operation and there are no safety or efficiency issues. |
| **Output** | Presence or absence of electrogram dispersion at each electrode bipole under consideration<br><br>In digital mode, 3D locations of corresponding electrodes bipoles<br><br>Computed values of mapping and reference cycle length | Presence or absence of electrogram dispersion at each electrode bipole under consideration<br><br>Computed values of mapping and reference cycle length | In bidirectional digital communication, VX1+ uses the 3D positions shared by EnSite for dispersion analysis and then sends back the dispersion result with the appropriate 3D coordinates. Sharing the 3D electrode position does not affect the performance of the device and does not raise any safety or effectiveness issues. |
| **Duration of Electrogram Recordings** | 1.5 Seconds | 1.5 Seconds | Same |
| **Output Display** | The system generates color coded symbol(s) that indicates to the operator that the area under investigation is one exhibiting dispersion<br><br>In bidirectional digital communication, validated dispersion area can also be automatically displayed in the 3D | The system generates color coded symbol(s) that indicates to the operator that the area under investigation is one exhibiting dispersion | Manual and automatic tagging provide comparable dispersion maps and do not alter the clinical use of VX1+. The performance of VX1+ with automatic tagging is similar to that of the VX1 predicate. Therefore, there is no effect on safety or effectiveness. |

| | Volta Medical VX1+ | Volta Medical VX1 (K201298) | Comments |
|---|---|---|---|
| | mapping system, as tags in the 3D atrial shell | | |
| **Signal Information Displayed** | Acquired patient signals, including body surface ECG and intra-cardiac EGMs. | Acquired patient signals, including body surface ECG and intra-cardiac EGMs. | Same |
| **Computing Platform** | Computer with Intel Core i7-7700 CPU (8MB Cache, up to 4.20 GHz, RAM 32 GB),<br><br>with integrated analog/digital converter PCI card and TPM (Trusted Platform Module)<br><br>Debian-based Linux OS | Computer with Intel Core i5-6500 CPU (6MB Cache, up to 3.60 GHz, RAM 32 GB),<br><br>with integrated analog/digital converter PCI card<br><br>Windows 10 or higher OS | The VX1+ computer has a slightly more powerful processor and an additional TPM. These differences allow for faster processing and cyber security protection, but do not change the performance of the device. There is no effect on safety or effectiveness. |
| **Hardware Design and Materials** | Computing platform, proprietary software algorithm, monitor, mouse/keyboard, custom-made analog connection cable, ethernet cable, acquisition system | Computing platform, proprietary software algorithm, monitor, mouse/keyboard, custom-made analog connection cable, acquisition system | The additional ethernet cable do not alter the performance of the device. The complete system has been tested for electromagnetic compatibility and electrical safety. The additional of a simple standard hardware component has no effect on safety or effectiveness. |

## XV. LABELING

The draft labeling of the VX1+, including the device's label, its Operator's Manual and its Service Manual, are provided in **Appendices 15.1**, **15.2**, and **15.3**, respectively. The Service Manual is provided specifically for hardware installation instructions, intended to be performed only by a Volta's representative.

## XVI. STERILIZATION AND SHELF LIFE

The VX1+ is supplied non sterile, is not intended to be sterilized by the user, and will not enter in the sterile area of the operating room.

The following instructions are provided in the Cleaning Section of the VX1+'s Instructions-For-Use available in **Appendix 15.2**:

- Clean the device with a soft cloth and non-flammable and non-explosive agents only. Make sure that moisture is prevented from entering the device.
- Do not clean the system components with disinfectants that contain surfactants.
- Do not clean system components with bleach.
- Do not apply cleaners while the system is warm to the touch.
- Do not sterilize system components.
- Do not immerse system components in liquid.

VX1+ is composed of common electronic components and is not subject to age-related degradation and has no specific shelf-life.

## XVII. BIOCOMPATIBILITY

The VX1+ does not come into contact with the patient. Therefore, biocompatibility testing is not required.

The control accessories (i.e., mouse and keyboard) which come into contact with a user's ungloved hands are made from materials in common use for other consumer products with a similar nature of contact. Therefore, according to ISO 10993-1:2018 Standard section 5.2.2 no further biological evaluation is needed for the control accessories.

## XVIII. SOFTWARE

As discussed in greater detail below, the controlling software for the VX1+ presents a "moderate" level of concern as defined in FDA's *Guidance for the Content of Premarket Submission for Software Contained in Medical Devices* (May 11, 2005) (Hereinafter *Guidance Document.*) According to the *Guidance Document*, software for a device has a "moderate" level of concern when "the operation of the software associated with device function directly affects the patient and/or operator so that failures or latent design flaws could result in non-serious injury to the patient and/or operator, or if it indirectly affects the patient and/or operator (e.g., through the action of a care provider) where incorrect or delayed information could result in non-serious injury of the patient and/or operator." Using FDA's "Approach to Deciding Level of Concern" as detailed in the *Guidance Document*, the VX1+ software has a moderate level of concern for the following reasons:

1. The software does not qualify as Blood Establishment Computer Software.

2. The software is not intended to be used in combination with a drug or biologic.

3. The software is not an accessory to a medical device that has a Major Level of Concern.

4. Prior to mitigation of hazards, a failure of the software could not result in death or serious injury, either to a patient or to a user of the device.

    a. The software does not control a life supporting or life sustaining function.

    b. The software does not control the delivery of potentially harmful energy that could result in death or serious injury.

    c. The software does not control the delivery of treatment or therapy such that an error or malfunction could result in death or serious injury.

    d. The software does not provide diagnostic information that directly drives a decision regarding treatment or therapy, such that if misapplied it could result in serious injury or death.

    e. The software does not provide vital signs monitoring and alarms for potentially life threatening situations in which medical intervention is necessary.

Accordingly, this software documentation includes the following information that is required for a software controlled device that presents a moderate level of concern: (1) a description of the software; (2) a hazard analysis; (3) the software requirements specification documentation; (4) an architectural design chart providing a detailed depiction of functional units and software modules; (5) the Software Design Specification document; (6) a traceability analysis (7) a summary of the software life cycle development plan; (8) a description of verification and validation activities at the unit, integration, and system level, and the system level test protocol, including pass/fail criteria, and tests results; (9) a revision level history log; and (10) a list of remaining software anomalies, annotated with an explanation of the impact on safety or effectiveness, including operator usage and human factors, and (11) documentation of cybersecurity information.

## A. Software Description

### 1. Brief Description of Device

The VX1+ includes both hardware and software. The software includes machine learning based-algorithms designed to assist in detecting cardiac multipolar electrograms exhibiting spatio-temporal dispersion. These algorithms analyze intra-cardiac data from the patient's heart in real time, detect regions of interest presenting electrical electrograms with specific characteristics, and measure arrhythmia cycle lengths. The information from these algorithms is then displayed on the user interface.

Compared to its predecessor VX1, VX1+ brings the ability to communicate bidirectionally with a 3D mapping system and therefore the ability to automatically tag the regions of interest in the 3D atria shell in the interface of the EnSite X 3D Mapping system (Abbott) (K221213).

In terms of hardware components, the VX1+ computer has a slightly more powerful processor than VX1 for faster processing. Also, VX1+ accounts for an additional TPM for cyber security protection, and an additional standard ethernet cable to allow for digital data transmission between VX1+ and the acquisition system.

The core algorithm for dispersion remains unchanged from VX1 and only post-processing parameters adjustment have been performed.

### 2. Purpose of Software

The VX1+ assists operators in the real-time manual or automatic annotation of 3D anatomical and electrical maps of human atria for the presence of multipolar intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion during atrial fibrillation or atrial tachycardia.

The clinical significance of utilizing the VX1+ software to help identify areas with intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion for catheter ablation of atrial arrhythmias, such as atrial fibrillation, has not been established by clinical investigations.

### 3. Specific Software Functions (e.g., User Interface, Hardware Control, Calibration, Data Acquisition, Data Presentation, Decision Making)

*User interface*

The device displays a set of information to guide the operator in the detection of dispersions. The center of the screen displays a schematic representation of the catheter used for mapping. Around the catheter's schematic, two half-circle-shaped symbols depict the presence of dispersed electrograms among those of interest (upper half) and cycle length estimations as measured by the mapping and CS catheters (lower half). On the upper half-circle, 10 box sections correspond to the 10 dipoles of interest. When one or several dipole symbol(s) is / are blinking and is colored in orange / red on the catheter schematic, this indicates to the operator that the area under investigation is one exhibiting dispersion. For confirmation, the operator may stabilize the catheter in this region. Then, the operator must examine the corresponding multipolar electrograms to provide confirmation of the

presence of dispersion. Further confirmation is given by the red / orange coloring of boxes on the upper half-circle. Finally, the operator may tag this location (actively manually or confirmation of the automatic tag). The lower part of the frame displays (i) the average cycle length as recorded by the reference catheter (R) in the coronary sinus (surrogate for global cycle length of the arrhythmia); (ii) the average measurable local cycle length as recorded by the mapping catheter (M).

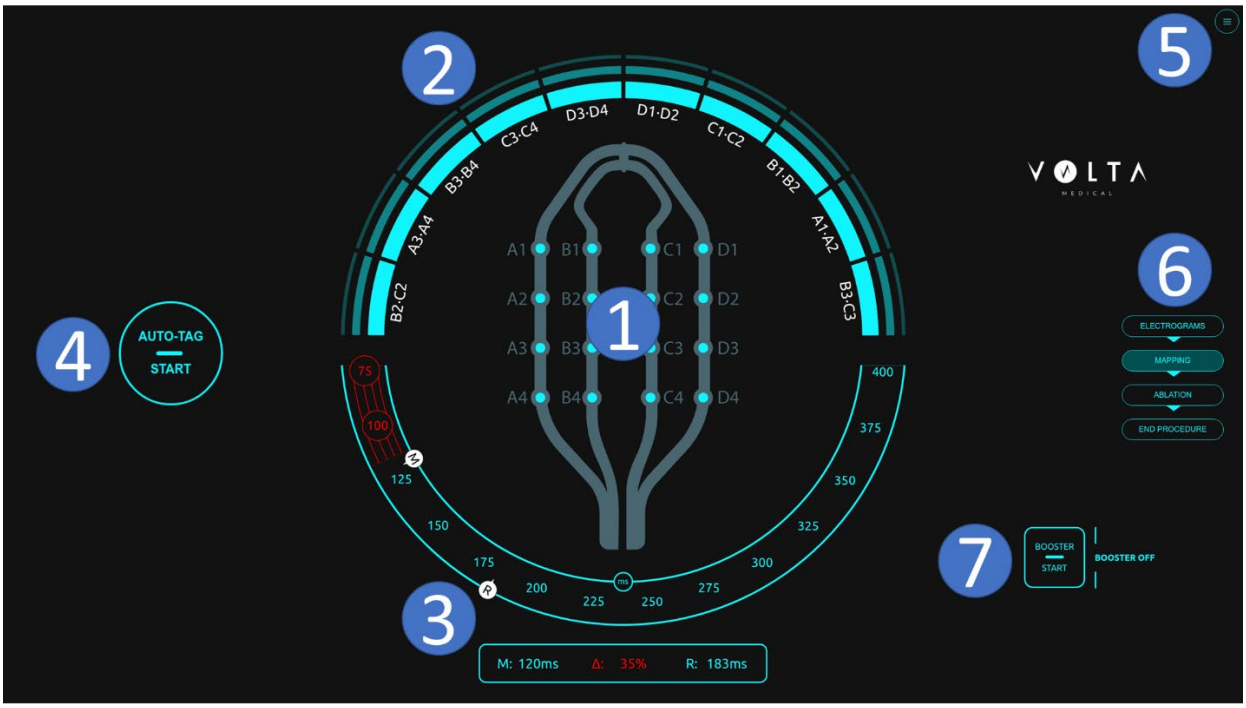



**Figure 11: HD Grid Catheter VX1+ UI <u>in digital communication mode</u>**. 1) The center of the screen displays a frame with a schematic representation of the catheter used for mapping. Catheter electrodes are numbered. If bipoles are blinking in orange / red, this indicates to the operator that the area under investigation is one exhibiting dispersed electrograms. For confirmation, the operator may stabilize the catheter in this region. 2) On the upper half-circle, 10 box sections correspond to the 10 bipoles of interest. When one or several bipole symbol(s) is / are blinking and is / are colored in orange / red, this indicates to the operator that the area under investigation is one that is confirmed as a region exhibiting dispersed electrograms. 3) The lower half-circle displays (i) the average global cycle length (GCL) as recorded by the reference catheter (R) and (ii) the average local cycle length (LCL) as recorded by the mapping catheter (M). In the lowest part of the interface, the exact values of the cycle lengths are given in miliseconds as well as the difference ratio in percentage computed as (R-M)/R. 4) Auto-tagging activation/deactivation button (only available in digital bidirectional communication with Abbott EnSite X and Abbott catheters).5) Main menu including Logout, Help Page, About, Shutdown and Restart. 6) Procedural stages buttons: Initialization replaced by Electrograms once initialized, Mapping, Ablation, End Procedure. 7) Booster mode activation/deactivation button.

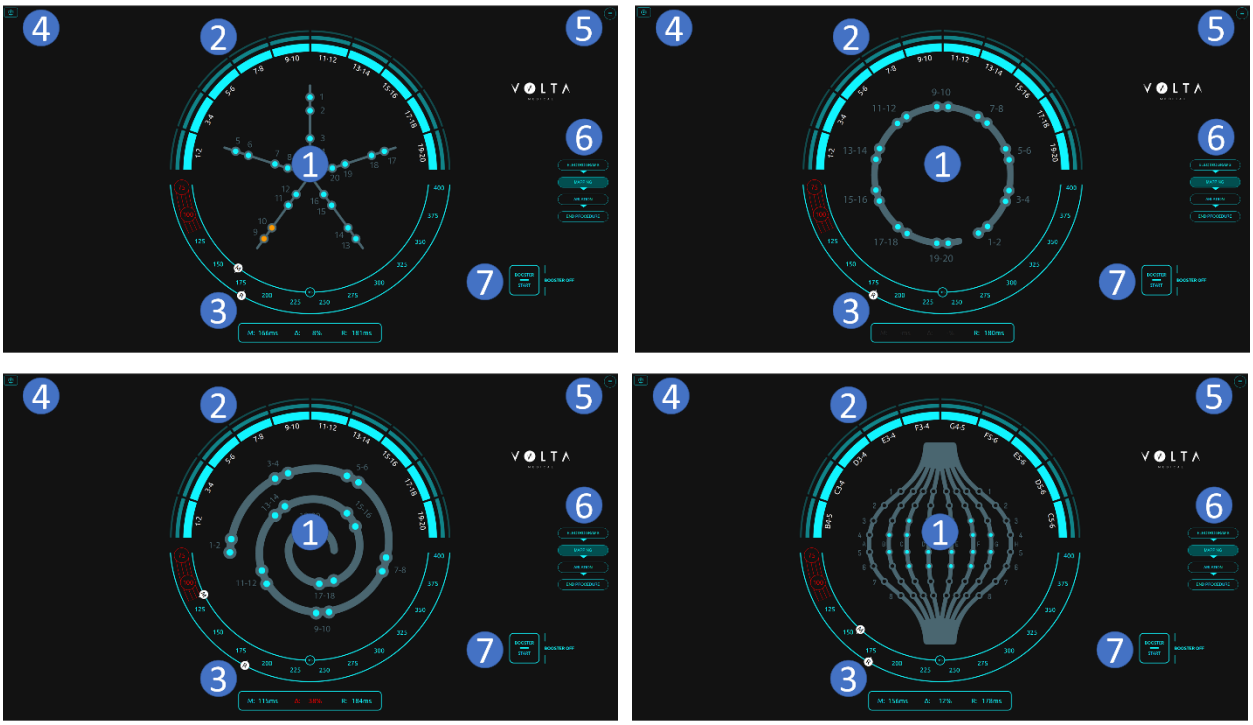


**Figure 12: Pentaray (top left), Circular 20 (top right), Reflexion HD (bottom left), Orion (botton right) Catheters VX1+ UI <u>in analog communication mode</u>**. 1) The center of the screen displays a frame with a schematic representation of the catheter used for mapping. Catheter electrodes are numbered. If bipoles are blinking in orange / red, this indicates to the operator that the area under investigation is one exhibiting dispersed electrograms. For confirmation, the operator may stabilize the catheter in this region. 2) On the upper half-circle, 10 box sections correspond to the 10 bipoles of interest. When one or several bipole symbol(s) is / are blinking and is / are colored in orange / red, this indicates to the operator that the area under investigation is one that is confirmed as a region exhibiting dispersed electrograms. 3) The lower half-circle displays (i) the average global cycle length (GCL) as recorded by the reference catheter (R) and (ii) the average local cycle length (LCL) as recorded by the mapping catheter (M). In the lowest part of the interface, the exact values of the cycle lengths are given in miliseconds as well as the difference ratio in percentage computed as (R-M)/R. 4) Analog Procedure settings page. 5) Main menu including Logout, Help Page, About, Shutdown and Restart. 6) Procedural stages buttons: Initialization replaced by Electrograms once initialized, Mapping, Ablation, End Procedure. 7) Booster mode activation/deactivation button.

*Algorithms*

VX1+ application is a machine and deep learning based-algorithm designed to assist in detecting multipolar electrograms exhibiting spatiotemporal dispersion. The main algorithm, called *vcore,* has remained unchanged since VX1. VX1+, as VX1, accomplishes this task with a real-time analysis of intra-cardiac signals in the operating room.

The *vcore* algorithm in VX1/VX1+ is a blend of two distinct classifiers designed to analyze incoming data in real time. It uses a dual approach of: (i) machine learning and (ii) deep learning classifiers to analyze intra-cardiac signals recorded with a multipolar catheter. Both classifiers have been trained on a database of 275,020 annotated electrogram samples recorded in 110 procedures.

The complete specifications of the core algorithm *vcore* can be found in the 510(k) for predicate device VX1 (K201298).

VX1+ dispersion algorithm contains minor improvements while keeping the same level of clinical performance (i.e., obtaining substantially similar dispersion maps). The detailed algorithm design including specific changes to VX1 algorithm SPECDA-03-001 is provided in **Appendix 18.1**.

VX1+ cycle length estimators have also been improved compared to VX1 to reduce uncertainty and undesirable behavior. The detailed algorithm design for the reference and mapping cycle length estimators SPECDA-03-002 and SPECDA-03-003 are provided in **Appendices 18.2** and **18.3**, respectively.

#### 4. Hardware Requirements

VX1+ software is designed to operate on an appropriate standard computing platform (cf. SPECF-04-001 provided in **Appendix 18.6**).

#### 5. Programming Language(s) Used

Following programming languages were used to develop VX1+ application:

- Typescript/JavaScript,
- python,
- C++

#### 6. Off-the-Shelf Software

Off the shelf software used are Ubuntu, Python and Nodejs. The full description of these software are available in documents VSOUP-03-001 – SOUP Monitoring, VSOUP-03-002 – NODEJS Libraries SOUP Monitoring and VSOUP-03-003 – Python Libraries SOUP Monitoring provided in **Appendices 18.8**, **18.9**, and **18.10**, respectively. The VX1+ software architecture is described in document SPECD-03-001 – VX1+ Application Architectural and detailed design provided in **Appendix 18.12**.

### B. Hazard Analysis

A software quality system risk assessment for VX1+ device demonstrated a moderate (medium) level of concern. The final hazard analysis for the VX1+ which was developed from the system and software requirements and was refined during the design process, is provided in **Appendix 18.14** in document ARISK-03-001 – VX1+ Risk Analysis. This hazard analysis includes potential, undesirable effects and identifies the hardware and software features or labeling that are designed to ensure that these potentially hazardous events do not occur.

VX1+ risks hazard analysis has been performed according to ISO 14971:2019 standard and the software class has been determined according to IEC 62304:2006 + A1:2015.

The full risk management activities performed for VX1+ device are provided in PLRSK-03-001 – VX1+ Risk Management Plan, ARISK-03-001 – VX1+ Risk Analysis and RPRSK-03-001 – VX1+ Risk Management Report, in **Appendices 18.13**, **18.14**, and **18.15**, respectively.

All risk reduction measures have been implemented and their effectiveness have been checked through verification and validation activities. The associated modes of evidence are recorded in the

risk management file. Their effectiveness has been verified by assessing residual risks. The effects of these measures were reviewed:

- new risks have been identified;
- the impact on the estimated risks has been considered (revaluation of the risks concerned).

The risk management plan defined has been implemented. Defined risk reduction measures have been implemented and their effectiveness verified, all residual risks are known and controlled. Information on these residual risks is contained in the accompanying documents (user manual and service manual).

The analysis of the benefit/risk balance was carried out for each individual risk and for all residual risks. The conclusion is that the medical benefits are greater than the residual risks. Given these results and based on the acceptability criteria defined in the risk management plan, the overall residual risk is acceptable and therefore in favor of the reliability of the product. This justifies the marketing and use of the VX1+ medical device.

### C. Software Requirements Specifications (SRS)

The software requirements for VX1+ were based on a value analysis approach, consisting of discussions with potential users, site visits, and a review of current, similar systems. The Software Requirements Specifications were developed based on these findings.

VX1+ Software Requirements Specifications have been declined in different levels according to IEC 62304:2006 standard as follow:

- Functional Use Requirements, provided in **Appendix 18.5** in document SPECF-03-001 – VX1+ Application Functional Use Requirements, based on users feedback and review of predicate VX1 (Volta Medical) (K201298).
- User Interface Requirements, provided in **Appendix 18.7** in document EXIU-03-001 – VX1+ User Interface Requirements, based on Functional Use Requirements.
- Technical Specification, provided in **Appendix 18.11** in document SPECT-03-001 – VX1+ Technical Specification, based on functional use requirements and user interface requirements.

### D. Architecture Design Chart

The VX1+ software architecture design chart can be found in **Appendix 18.12**.

The diagram below shows the different software units involved (the yellow and pink boxes) and their interactions. All of these software units are processes that communicate with each other. We differentiate two types of software units: the modules (depicted in yellow) and the applications (depicted in pink).

- The green arrows represent the asynchronous streams used to transfer the EGM signals.
- The blue arrows represent the asynchronous streams of control messages between modules and applications.

- The red arrows represent the synchronous stream of messages between frontend and daemon applications.

The VX1+ software is comprised of the following software units separated as modules and applications):

**Modules**

- Dispersion Module described in document SPECDA-03-001 – Detailed Algorithm Design (Dispersion) provided in **Appendix 18.1**
- Reference Cycle Length module described in document SPECDA-03-002 – Detailed Algorithm Design (Reference Cycle Length) provided in **Appendix 18.2**
- Local Cycle Length module described in document SPECDA-03-003 – Detailed Algorithm Design (Local Cycle Length) provided in **Appendix 18.3**
- Auto-tagging module described in document SPECDA-03-004 – Detailed Algorithm Design (Auto-tagging) provided in **Appendix 18.4**
- Recorder module
- Preprocessing module
- Abbott driver module
- Advantech driver module
- Replay driver module
- Application graph module

**Applications**

- frontend application
- daemon application

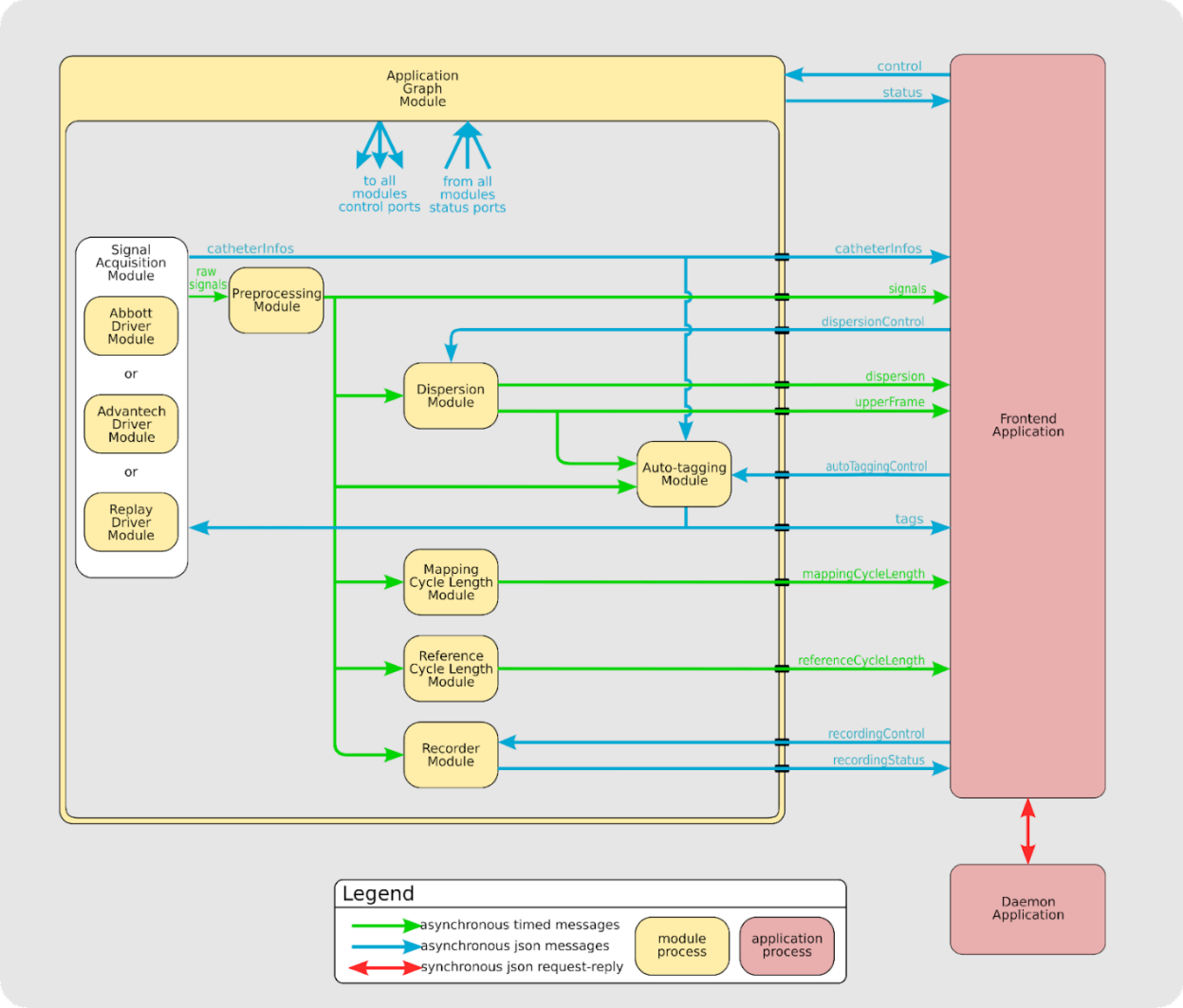



**Figure 13: VX1+ Software Architecture Diagram**

### E. Software Design Specification

The **VX1+** software design specification can be found in document SPECD-03-001 – VX1+ Application Architectural and Detailed Design provided in **Appendix 18.12**.

VX1+ performs real-time analysis of intra-cardiac atrial EGMs and proceeds to the identification of dispersed EGMs during a cardiac electrophysiology procedure. Those EGM signals can be acquired from multiple possible sources:

- from the electrophysiology acquisition system, via an analog to digital converter card,
- from the 3D mapping system, via a dedicated network, or
- from pre-recorded signal files (only in "test" mode).

Those signals are then processed, and the result of the different analyses is displayed to the physician. The application performances should allow the smooth use of the product. In case this requirement is not met, an error will be raised.

### F. Traceability Analysis

Software verification and validation tests were performed. A software verification test campaign was conducted during the dedicated design phase. All of the technical specifications were tested during verification test campaign. The related test plan and test report are provided in documents TSPLVE-03-001 – VX1+ Application Verification Test Plan and RPTSVE-03-001 – VX1+ Application Verification Test Report, provided in **Appendices 18.16** and **18.17**, respectively. The complete traceability matrix is provided in **Appendix 18.18**.

### G. Summary of the Software Life Cycle Development Plan

As stated above, the requirements for the **VX1+** were based on a value analysis approach, consisting of discussions with potential users, site visits, and a review of the currently available devices. Once the system requirements were formulated, a system test plan was drafted to list what would be tested during the initial system verification and validation and how testing would be conducted. These test plans are provided in **Appendices 18.16** and **18.19**, in documents TSPLVE-03-001 – VX1+ Verification test Plan and TSPLVA-03-001 – VX1+ Validation test Plan.

After the system requirements phase, a preliminary hazard analysis was conducted (1) to identify the potential hazards, such as associated with the VX1+; and (2) to determine how each risk will be addressed. Additional hazard analyses were conducted throughout the design process and new safety features were incorporated into the software program to avoid these additional risks. The final hazard analysis is included in **Section XVIII.B**.

According to the system requirements, the software requirements were developed prior to the software development stage. As discussed in the previous section, during the software design, the different software modules were defined using a V Cycle approach as defined in the 62304 standard, during development phase iterative cycles were used with respect to V cycle requirements. **I**n order to make the product evolve faster a modular approach was defined**.** The resulting software modular structure was presented to other engineering team members working on the project. After modification, the software modular structure was accepted by all of the software team members.

The coding then began. The coding of the structural level routines were made prior to those of the functional level modules. Code “walk-throughs,” whereby software programmers check the codes written by another programmer, were conducted by the software developers with other programmers. The purpose of the “walk-throughs” is (1) to review the code for consistency, error handling and correctness; (2) to check the fulfillment of design goals; and (3) to detect problems with the software design early in the development process.

Automatic unit tests were coded for each software unit with the same pair review approach. After the coding was completed, unit testing was conducted thanks to continuous integration. For example, dispersion module was tested in isolation. The unit testing was deemed complete only when the results corresponded to the expected results. The expected results were defined by related test plan

TSPLUN-03-001 – Unitary Test Plan (Dispersion) provided in **Appendix 18.22**, the software which performs the dispersion computation was first tested separately from the rest of the controlling software before integration testing was conducted. As explained below, this software was subsequently integrated and tested on the system as a whole.

After the unit testing was completed, the modules of the software were integrated and tested on a module per module basis in order to obtain the final software package. For example, by playing a well-known signal file, we ensured that the final user interface displayed correct values**.** The integration testing was deemed complete only when all the modules worked correctly on this simulation system.

All of the software modules were then tested on the mechanical, electrical, and hardware system to perform the software system level testing. All of the functions of the software, (*i.e.*, the functions described in Section 3) were tested. All of the variations of the user inputs were also tested to detect unexpected conditions. The software safety features resulting from the hazard analysis were also tested.

The final system verification and validation was conducted in-house, following the final system test plan. The test results were recorded in the system validation test report.

Finally, an acceptance review, in which the management, Quality Assurance Personnel, and engineering team take part, was held both to present the results of the final system verification and validation and to decide whether design changes were needed before pre-production begins. See below for information on Verification and Validation and Conformity Assessment.

The overall Development Plan PLD-03-001 can be found in **Appendix 18.21**.

### H. Verification and Validation Documentation

Based on the Software Requirements Specification (SRS) found in **Section XVIII.C**, a software validation test plan was devised to verify that the software meets the requirements. Each element of the SRS was tested and found to meet the requirements.

A software verification test campaign has been conducted during the dedicated design phase. Related test plan and test report are provided in **Appendices 18.16** and **18.17** in documents TSPLVE-03-001 – VX1+ Application Verification Test Plan and RPTSVE-03-001 – VX1+ Application Verification Test Report.

A validation test campaign has been conducted during the dedicated design phase. Related test plan and report are provided in **Appendices 18.19** and **18.20** in documents TSPLVA-03-001 – VX1+ Validation Test Plan and RPTSVA-03-001 – VX1+ Validation Test Report. Validation test campaign has been performed trough Usability Evaluation provided in **Appendix 20.3** in document APTIU-03-001 – VX1+ Usability Engineering File to validate user interface usability and ensure its safe use. In addition to the usability evaluation, software validation has been performed in the scope of Ampere Study, clinical investigation conducted in Marseille (France) to assess and validate software performance and safety in clinical conditions (see **Section XXII**).

All these verification & validation results have been compiled and analyzed in document RPCRP-03-001 – VX1+ Project Conformity Report provided in **Appendix 18.34**.

An assessment of compliance with the requirements of IEC 62304 has been performed for the VX1+ software and is provided in **Appendix 18.35**, SWLCP-03-001 – 62304 Evaluation.

Each software requirements have been tested during verification and validation test campaigns.

### I. Revision History Log

A software history revision log is provided below. Clearance is being sought for version **V1.0.6,** which is the most recent version of the VX1+ software.

| File name/ Revision number | Creation date | Notes |
|---|---|---|
| SWRLN-03-001-B – VX1+ Software Release Note / V1.0.6 | 26/AUG/2022 | Known bugs and fixed bugs are listed in the software release note SWRLN-03-001-B – VX1+ Software Release Note provided in **Appendix 18.36**. |

### J. Unresolved Anomalies

| Ticket Number | Description | Affected Version | Comment |
|---|---|---|---|
| VX2-1698 | VX1+ is stuck on update dialog if the update process fails | V1.0.6 | This anomaly does not impact the user. It can only affect service engineers during the update process in rare situations. Workaround is to relaunch the update process. |
| VX2-1490 | Cursor is displayed as "X" in the right and bottom borders of the application | V1.0.6 | Purely cosmetic issue with no impact on user workflow (mouse cursor shape). |
| VX2-1515 | Electrogram bar sometimes rolls back | V1.0.6 | Purely cosmetic issue with the electrogram bar display with rare occurrence and no impact on user workflow. Visualization of electrograms during initialization and during procedure is not impacted by the defect. |

| | | | |
|---|---|---|---|
| VX2-1793 | Signal loss on VX1+ during Digital procedure | V1.0.6 | The problem is due to an interruption in the input digital signals sent by the mapping system (Ensite X) which can happen in some occurrences at the end of the procedure. In this situation, the workaround is to relaunch VX1+ application in analog mode with no risk of significantly extending the procedure time (e.g. quick reboot of the system and selection of analog mode on the start page). If no analog cable is connected, the operator can still continue the procedure without VX1+ with no consequence on the procedure time. |

All these unresolved minor anomalies have been considered for the VX1+ risk analysis provided in **Appendix 18.14** and IFU updates ("Troubleshooting" section) provided in **Appendix 15.2**.

### K. Cybersecurity Information

Volta Medical has addressed potential cybersecurity risks by providing the documentation requested within the FDA Guidance "Content of Premarket Submissions for Management of Cybersecurity in Medical Devices", 2018. Specifically, the Volta Medical software mitigates or prevents the unauthorized access, modification, misuse and unauthorized use of information that is stored, accessed or transferred.

Hazard Analysis: A hazard analysis, which includes cybersecurity risks assessed during the development of the device, was developed from the software requirements and was refined during the design process. This hazard analysis includes potential, undesirable effects and identifies the hardware and software features or labeling mitigations designed to ensure that these potentially hazardous events do not occur.

A specific list of all cybersecurity risks is provided in **Appendix 18.14** in the Risk Analysis document ARISK-03-001 – VX1+ Risk Analysis (tab cybersecurity), as well as implemented risk mitigation measures.

Penetration tests have been performed by an independent laboratory to guarantee VX1+ software is protected against unauthorized access. The test report is provided in **Appendix 18.37**. Verification test campaign conducted for VX1+ also covers cybersecurity requirements, related

test plan TSPLVE-03-001 – VX1+ Application Verification Test Plan and test report RPTSVE-03-001 – VX1+ Application Verification Test Report are provided in **Appendices 18.16** and **18.17**.

Traceability Matrix: The traceability analysis aligning the SRS, requirement ID, design output and design verification documents is attached in **Appendix 18.18**.

Software Validation and updates: Volta Medical controls deployment of software updates as per change control and procedures within the Project Management Plan (S*ee* **Appendix 18.21** PLD-03-001 – VX1+ Project Development Plan).
Software Updates or Patches: All potential software updates are reviewed against the most recent versions of the SRS. Additionally, a validation and risk analysis/mitigation is conducted to determine the extent and impact of the change to the device. Following the modification and appropriate validation tasks (including verification test campaign) for the change, the device documentation is updated as part of the lifecycle process. Volta Medical does not release software updates through a network. In case of any software updates, the Service Technician updates the devices during service.

Off- the-Shelf Software: All OTS software versions and configurations are documented in the SRS (SPECT-03-001 – VX1+ Technical Specification provided in **Appendix 18.11**) and SDS (SPECD-03-001 – VX1+ Application Architectural and Detailed Design provided in **Appendix 18.12**). Per Volta Medical change control procedures, any updates to the OTS software will undergo a risk analysis and mitigation, which will be documented in the design history file. Any modifications to the OTS software will be documented in the SDS.

Integrity Controls: Volta Medical controls the integrity of the software by limiting access to trusted users and ensuring trusted content through software controls as defined within the Cybersecurity section of the SDS (*See* **Appendix 18.12** SPECD-03-001 – VX1+ Application Architectural and Detailed Design).

Instructions For Use and Product Specification Security Controls: instructions for use provided to users gives information related to authentication process with a specific note explaining how the device behaves in case of wrong password to protect from unauthorized access. VX1+ IFU is provided in **Appendix 15.2**.

## XIX. ELECTROMAGNETIC COMPATIBILITY AND ELECTRICAL SAFETY

The Volta Medical VX1+ was tested by an independent lab and found to comply with the requirements set for Electrical Safety and Electromagnetic Compatibility (EMC) per FDA recognized consensus standards. The full test reports are provided in **Appendices 19.1, 19.2** and **19.3**.

The electromagnetic compatibility, electrical safety, and usability testing were prepared by the following external safety testing laboratory:

LCIE Bureau Veritas
ZI Centr'alp
170 rue de Chatagnon
38430 Moirans
France

### A. Electromagnetic Compatibility

The Volta Medical VX1+ was tested and found to be in compliance with IEC 60601-1-2 edition 4.1 (2020). There were no deviations from the standard and the full test report can be found in **Appendix 19.1**.The setup included the complete device setup consisting of the central unit, power supply, connection cable, screen, keyboard, and mouse, meeting the IEC 60601-1-2 requirement.

### B. Electrical Safety

The Volta Medical VX1 was also tested and found to be in compliance with IEC 60601-1 edition 3.2 (2020). There were no deviations from the standard and the full test report can be found in **Appendix 19.2**.

### C. Usability

The VX1+ was also tested and found to be in compliance with IEC 60601-1-6 edition 3.2 (2020). There were no deviations from the standard and the full test report can be found in **Appendix 19.3**.

The VX1+ is labeled in accordance with the labeling requirements of IEC 60601-1 and IEC 60601-1-2 standards. Device labeling is provided in **Appendix 15.1**.

## XX. PERFORMANCE TESTING - BENCH

### A. Preclinical Testing on the VX1 Algorithm Model

The preclinical testing on the VX1 algorithm model found in Section XX. Performance Testing – Bench of the VX1 510(k) (K201298), also applies to VX1+ due to model equivalence. These documents are provided in **Appendices 20.1** and **20.2** for completeness.

- Evaluation of the inter-reliability/concordance of adjudications of dispersed vs non-dispersed EGMs between 2 operators in comparison with a random association (*The Reader Study*).
  All kappa values pertaining to readers to VX1 comparisons and inter-reader comparisons were larger than 0.50 (range: 0.63-0.79) with corresponding concordance values ranging from 0.91 to 0.94. This study showed that three independent experts may strongly agree upon the presence or absence of dispersion in a multipolar electrogram recording. It also showed that the expert readers independently agree with VX1's adjudications of the presence or absence of dispersion.
- Evaluation of the performances of VX1 vs. 28 expert electrophysiologists with limited time for Annotation (ROC curve).
  The results suggested that with limited time the algorithmic performance exceeds the one of experts. VX1 also allows for a faster and more reproducible analysis in a real-time configuration.

Additional preclinical testing has been performed on VX1+ and are described below.

### B. Unitary Tests Campaign During Verification Phase of VX1+ Algorithm Modules

#### 1. Dispersion Algorithm Unit

The Dispersion algorithm unit described in SPECDA-03-001 (provided in **Appendix 18.1**) was tested according to test plan TSPLUN-03-001 (provided in **Appendix 18.22**).

**Method:**

The *Reader Study* described in VX1's 510(k) (K201298), was intended to show on a similar patient electrogram dataset that VX1 algorithm's adjudications acceptably correlate with unlimited-time expert visual analysis.

As mentioned above, VX1+ algorithm relies on the same core algorithm as VX1, and has some parameters adjustment to enhance the user experience, in order to reduce the "blinking" effect sometimes observed in dispersion display. This *Reader Study* was used here as a non-regression test: no deprecation on the reader study metrics is allowed with the modified version of the algorithm embedded in VX1+.

For general kappa results endpoints, a score that is within the confidence interval or above the previously recorded VX1 reference is the acceptance criteria.

Metrics:

- *Kappa Scores (*agreement between VX1+ and readers vs VX1 reference mean): This indicator aims at measuring the concordance between VX1+ and the readers.
- *Kappa Score* (agreement between VX1+ and VX1): This indicator aims at measuring the raw concordance in space and time between the previous and the new upper-frame computation. This indicator is linked to the activity indicator, there is an expected discrepancy between VX1 and VX1+ but the kappa score is expected to be more than the VX1 reader study inter-operator average kappa score for the upper-frame (0.71) and the average VX1 and operators average kappa score (0.68).
- *Corrected Activity Indicator*: this indicator aims at controlling the activation behavior of the upper-frame, which is linked to the extent of dispersion maps. This indicator is expected to be less than 1 (meaning less activations than VX1), but at least comparable. This indicator is computed as the ratio of the number of activation of VX1 and the number of activation of a new algorithm candidate on the whole dataset. Meaning that VX1 has an indicator of 1, an algorithm with an indicator below 1 tends to activate, overall, less than VX1 and an algorithm with an indicator over 1 tends to activate, overall, more than VX1.
- *Temporal Coherence Indicator*: this indicator aims at controlling the reproducibility of a dispersion map and activation. That is to say that the activation of the upper-frame does not depend on when the procedure starts. That indicator was computed by shifting the signal input of each mapping of the dataset by 100 ms, 200 ms… up to 1400 ms and computing the Cohen kappa score between each response of the same algorithm. The acceptance criteria for this indicator is to be at least better, meaning better reproducibility between mapping, than the VX1 computed indicator.
- *Blinking indicator*: this indicator aims at measuring the improvement over the “blinking” effect that was sometimes observed on the VX1 upper-frame computation. The acceptance criteria for this indicator is to be at least better, meaning less blinking behavior, than the VX1 computed indicator. One activation was considered a blinking if there was no activation 3 times before and 3 times after (with an activation each 1.5 seconds). The indicator is the number of occurrences of this pattern on the whole dataset.

**Results:**

*Kappa Score* (agreement between VX1+ and readers vs VX1 reference mean) : “Mean” Kappa scores for VX1+ (range: 0.68-0.79) are all within the confidence interval or above the previously recorded Kappa scores with VX1 (“VX1 reference mean”). These results indicate a strong agreement between VX1+ and the readers in either Mode (Default or Booster).

*Blinking indicator*: VX1 behavior results in 1062 ± 25 (with the value and interval being the mean and standard deviation over all the algorithm runs) occurrences of blinking whereas VX1+ algorithm count is 690 ± 23 (with the value and interval being the mean and standard deviation over all the algorithm runs), meaning a reduction of blinking behavior by ~ 30 %.

*Kappa Score* (agreement with VX1): We can see a good concordance between VX1 and VX1+ algorithm, with a Cohen kappa score of 0.742 ± 0.001 (with the value and interval being the mean and standard deviation over all the algorithm runs).

*Activity Indicator*: VX1+ algorithm has an activity indicator of 0.746 ± 0.001 (with the value and interval being the mean and standard deviation over all the algorithm runs). The corrected activity indicator for the relative neighborhood is 0.935 ± 0.001 (with the value and interval being the mean and standard deviation over all the algorithm runs), which is close to 1 meaning that the new algorithm activity can be considered faithful to VX1.

*Temporal coherence indicator:* We can conclude that the VX1+ algorithm is a major improvement regarding reproducibility and temporal coherence of the upper-frame responses.

The non-regression test (VX1 Reader study replayed with VX1+) concluded that Kappa scores were all within the confidence interval or above the previously recorded VX1 reference. Therefore, the VX1 reader study conclusions are still valid with the modified VX1+ algorithm The test results are available in RPTSUN-03-001 (provided in **Appendix 18.23**).

### 2. Reference Cycle Length Algorithm Unit

The Reference or Global Cycle Length (GCL) algorithm unit described in SPECDA-03-002 (provided in **Appendix 18.2**) was tested according to test plan TSPLUN-03-002 (provided in **Appendix 18.24**).

**Method:**

The expected results are to demonstrate that the new VX1+ reference cycle length algorithm provides comparable results than the previous VX1 reference cycle length algorithm. Both a quantitative evaluation process and a qualitative evaluation process were performed.

The quantitative evaluation measured the performance of GCL estimations in terms of different metrics: MAE (mean absolute error), MAPE (root mean squared error), RMSRE (root mean squared relative error), % outliers.

The expected scores had to be as low as possible. A RMSRE less than 10 % is expected (that is to say, the mean error on the annotated segment is less than 10 % of the actual cycle length for each annotated procedure).

A qualitative validation (on pre-recorded videos) was also performed to meet the following expectations:

- The algorithm should provide a CL value correctly representing the studied electrical activity.
- The algorithm should know when its estimation is uncertain.
- The algorithm cycle length estimation should be stable.

**Results:**

The tests performed showed that the results of the VX1+ GCL algorithm are closer to expert annotations and are at least as good as those of the previous VX1 GCL algorithm. The test results are available in RPTSUN-03-002 (provided in **Appendix 18.25**).

Results for the previous algorithm (VX1):

| Rhythm | % of uncertain on the whole run | MAE | MAPE | RMSRE | % Outliers | % of uncertain on annotated batches |
|---|---|---|---|---|---|---|
| **AF** | 33 % | 17.0 ms | *Not computed* | | 6.9 % | 45.7 % |
| **AT** | 23.1 % | 16.7 ms | | | 9.0 % | 23.1 % |
| **SR** | 61.2 % | 412.6 ms | | | 55.1 % | 66.9 % |
| **Overall** | 32.8 % | 69.6 ms | 10.1 % | 12.5 % | 14.8 % | 42.8 % |

Results for GCL 0.4.2:

| Rhythm | % of uncertain on the whole run | MAE | MAPE | RMSRE | % Outliers | % of uncertain on annotated batches |
|---|---|---|---|---|---|---|
| **AF** | 1.6 % | 8.6 ms | *Not computed* | | 8.0 % | 2.2 % |
| **AT** | 9.8 % | 7.0 ms | | | 5.9 % | 5.9 % |
| **SR** | 47.5 % | 62.4 ms | | | 23.4 % | 36.1 % |
| **Overall** | 15.7 % | 14.6 ms | 2.9 % | 3.5 % | 8.5 % | 18.6 % |

### 3. Mapping Cycle Length Algorithm Unit

The Mapping or Local Cycle Length (LCL) algorithm unit described in SPECDA-03-003 (provided in **Appendix 18.3**) was tested according to test plan TSPLUN-03-003 (provided in **Appendix 18.26**).

**Method:**

The expected results are to demonstrate that the new candidate VX1+ mapping cycle length algorithm provides comparable results than the previous VX1 mapping cycle length algorithm. Both a quantitative evaluation process and a qualitative evaluation process were performed.

The quantitative evaluation measured the performance of LCL estimations in terms of different metrics: confusion matrix by class, accuracy/F1, MAE (mean absolute error), RMSE (root mean squared error), RMSRE (root mean squared relative error), errors by rhythm/velocity/amplitude.

For classification task, we expected the accuracy to be at least equal or higher than 0.85 (reference VX1 score). If less, the misclassification could be accepted only in hardly identifiable periodic examples (that is to say, annotated as non-periodic but correctly predicted as potentially periodic) or errors of annotation. F1 score for each class (periodic and non-periodic) comparable with those for VX1 and similarly, with errors related to errors of annotation.

For errors on estimation: we expected results as least as good as those of VX1. As both algorithms perform the classification task differently, the comparison should be done only on periodic samples classified as periodic by both algorithms. We provide metrics of refactored VX1 algorithm on the dataset of 18 patients.

A qualitative validation (on pre-recorded videos) was also performed to meet the following expectations:

- The algorithm should provide a CL value correctly representing the studied electrical activity.
- The algorithm should robustly decide whether provide a value or not.
- As the mapping catheter moves a lot, the output should reduce as much as possible during non-contact / movement / noise perturbations.
- As the mapping catheter CL vary depending on time and space position even with a stable contact during AF, the output could vary but little.

**Results:**

The tests performed showed that the results of the VX1+ LCL algorithm are closer to expert annotations and at least as good as those of the previous VX1 GCL algorithm. The test results are available in RPTSUN-03-003 (provided in **Appendix 18.27**).

Results for VX1:

**Total errors**

| | 0 |
|---|---|
| mean_absolute_error | 31.50 |
| root_mean_square_error | 128.30 |
| root_mean_square_relative_error_ptg | 4.59 |

Results for VX1+:

**Total errors**

| | 0 |
|---|---|
| mean_absolute_error | 9.84 |
| root_mean_square_error | 39.48 |
| root_mean_square_relative_error_ptg | 1.76 |

### 4. Autotagging Algorithm Unit

The Autotagging algorithm unit described in SPECDA-03-004 (provided in **Appendix 18.4**) was tested according to test plan TSPLUN-03-004 (provided in **Appendix 18.28**).

**Method:**

*Dataset insights*

The dataset used to evaluate the module and optimize its parameters consisted of six different atrium mappings (five left, one right) spanning five case studies for which both the location and dispersion data were available for at least 15 consecutive minutes. The studies were recorded in two different hospitals. All studies correspond to primo ablation of persistent AF.

*Annotation process*

In the EP lab, the monitors display raw signals from GE's EP recording system, CardioLab; dispersion live detection from Volta's VX1 software; catheters (including CS, ECG and mapping) positions in the anatomy from Abbott's 3D mapping platform, EnSite X; and X-ray fluoroscopic imaging.

Four cardiologists were provided with the Operating Room (OR) monitors video of five mapping segments and asked to label at which timestamp and bipole they would have tagged a Region of Interest (ROI). Along with the physicians' offline evaluation of some of the studies (Ground Truth - GT), the annotations included the manual tags retrieved from the OR for all six mappings.

This process yielded a total of twenty-four independent annotations, each in the form of a point cloud of tags.

*Metrics*

The main metric used to assess the module's performance was the mean of the pairwise distances between the autotagging's output and each available annotation, across all mappings.

The distance between two 3D mapping tags for a given mapping is assessed by computing the geodesic distance (i.e. the length of shortest path along the surface of the atrium) between the closest respective vertices lying on the anatomical mesh available for the given study. This allows for more physically reliable measures than simply using the 3-dimensional Euclidean distance.

Comparing two point clouds is then achieved through the aggregation of pairwise nearest geodesic distances, with a metric known as DCD. This metric is an extension of the Chamfer Distance, yielding values in the [0, 1] range; it was chosen both for its stronger emphasis on point density and its better robustness to outliers.

*Acceptance criteria*

The main acceptance criteria is to have a higher similarity between automatic tags and the GT than between manual tags from live procedure. Maximizing the similarity is equivalent to minimizing the

distance proposed in the previous section (called DCD). The difference in terms of similarity is only acceptable if it is statistically significant.

*Statistical analysis*

To quantify the difference between the manual and the automatic method, a paired difference test was performed. Observations are the DCD between one method output and the GT for each mapping segment and each annotator. If the observations differences are normally distributed a paired Student's t-test is performed, if not a Wilcoxon signed-rank test is performed.

*Qualitative evaluation*

A qualitative validation was also performed. The dataset used includes the one used for the quantitative evaluation plus 10 studies without annotations (only manual OR tags).

**Results:**

Both proximity tests (between experts' annotations, OR and automatic tags) passed:

Proximity to annotators test: pvalue = 0.04 (threshold: 0.05)

Proximity to OR tags: pvalue = 0.6 (threshold: 0.625)

This test checks that the Autotagging module's output performs better than the original OR tags (Operating Room) when compared to the expert annotated Ground Truth for the available test data.

In addition, it was visually assessed that the density of automatic tags was comparable to the density of tags in the operating room. Particular attention was paid not to overtag.

The test results are available in RPTSUN-03-004 (provided in **Appendix 18.29**).

### C. Usability Engineering Tests

The VX1+ Usability Engineering File APTIU-03-001 provided in **Appendix 20.3** describes the usability engineering process performed for VX1+ in accordance with Standard IEC 62366-1.

**Method:**

The usability validation plan presents the method used to validate the usability of the Primary Operating Functions, and the criteria used to determine the success of the usability validation of the Primary Operating Functions, according to the application specification. Based on these tests and on design iteration, User Interface has been improved during the development.

The usability validation methods can be qualitative and/or quantitative. The usability validation can be made in a simulated use environment or in the real use environment.

*Formative assessment*

During formative assessment, the tests have been made in a simulated environment, by volunteers, non-members of the design team, non-trained to the procedure on VX1+ with no access to user manual. These tests allow observations of the interactions between the user and the device, under conditions similar to the intended ones. During these tests, actions performed by volunteers, as well as the potential errors made, and the impressions of the volunteers have been registered by observers. Furthermore, user interface has been improved during design iterations. User interface improvements have been summarized in sprint reviews.

VX1+ training strategy will remain the same as VX1 one. Users will be trained by Volta Medical representative thanks to a training support and will be supported on various procedures (several training cases to perform in presence with a Volta Medical 's Field Technical Engineer). A certificate will be delivered to trained users. The VX1+ User Manual is provided with each device installed. No new risk and no new use error emerged from formative evaluation.

*Summative assessment*

During summative assessment, several test cases have been performed to ensure usability in the verification and validation test plans. In these test plans, use scenario and acceptance criterion are defined. For UI tests, in order to be in a worst-case scenario, untrained testers (operator and service profile) could perform the tests. They shall follow a predefined scenario to simulate a VX1+ procedure. Those worst-case volunteers validate the usability of all profiles.

The aim of usability validation is to demonstrate that:

- the device can be installed and used safely and according to its intended use
- the user interface is ergonomic and prevent the user from safety related errors
- the user manual is understandable and includes all required information
- risk control measures have been implemented and are adequate and effective

Following tests cases have been performed in a simulated environment at Volta Medical headquarters:

- Onsite installation
- Boston EP recording system configuration
- Onsite maintenance
- Analog procedure
- User Manual
- Cybersecurity
- User Management

Following tests cases have been performed in clinical environment in the scope of VX1+ Clinical Investigation at Saint Joseph hospital in Marseille:

- GE CardioLab EP recording system configuration
- Digital procedure

A usability questionnaire provided in **Appendix 20.16** was provided to investigators during the clinical investigation to evaluate UI ergonomics, and confirm use related risks assessment

*Acceptance criteria*

Acceptance criteria will depend on the type and the severity of related risks. When risks are safety related, the tests shall have a success rate of 100%.

According to annex K of Standard IEC 62366-2, number of testers is defined according to related risk probability. The lower the probability, the more testing will be required to ensure risk control measures are effective.

The following table presents for each item the different scenarios of possible use as well as the acceptance criteria and the number of tests of each scenario.

| Use Scenario | Risk probability average | Number of experts testers | Number of profanes testers | Usability Test Plan / Usability Test Report | Safety related risk | Acceptance criterion |
|---|---|---|---|---|---|---|
| 1 - VX1+ on site installation | 2.4 | 4 | 4 | APTTP-03-002 / APTTR-03-002 | Yes | 100% |
| 2 – EP Recording system configuration (GE CardioLab) | 2.4 | 4 | No profane | APTTP-03-002 / APTTR-03-003 | Yes | 100% |
| 3 – EP Recording system configuration (Boston) | 2.4 | 4 | 4 | APTTP-03-002 / APTTR-03-004 | Yes | 100% |
| 4 – VX1+ system Maintenance | 2.66 | 4 | 4 | APTTP-03-002 / APTTR-03-005 | No | 80% |
| 5 – Analog Procedure | 2 | 3 | 2 | APTTP-03-002 / APTTR-03-006 | Yes | 100% |
| 6 – Digital Procedure | 2 | 4 | No profane | APTTP-03-002/ APTTR-03-007 | Yes | 100% |
| 7 – User Manual | 2 | 4 | 4 | APTTP-03-002 / APTTR-03-008 | No | 80% |

| | | | | | | |
|---|---|---|---|---|---|---|
| 8 – Cybersecurity | 2 | 4 | 4 | APTTP-03-002 / APTTR-03-009 | No | 80% |
| 9 – User Management | 2 | 4 | 4 | APTTP-03-002/ APTTR-03-010 | No | 80% |

**Results:**

The average score for each section of the usability questionnaire provided to 4 investigators involved in the clinical study (who had performed one or more ablation procedures using VX1+) is above average (>3 – neutral) as targeted (complete results available in APTTR-03-011 provided in **Appendix 20.17**).

With the results of the various usability tests all passed (all test plans and test results are provided in **Appendices 20.4** to **20.15**). the VX1+ development team has been able to determine that the measures taken to reduce the risks associated with the use of VX1+ are compliant.

VX1+ usability is validated as no unidentified use error and no risk emerged from formative and summative assessment.

Tests conducted during summative evaluation and thanks to clinical investigation the device safety is confirmed.

Usability risks related to use scenario have been identified and risk reduction measures have been implemented to reduce those risks. Risk reduction measures effectiveness have been verified during summative evaluation.

Once VX1+ will be released on the market, usability will be monitored through post-market surveillance activities and this usability engineering file will be updated when relevant as well as the risk management file.

## XXI. PERFORMANCE TESTING - ANIMAL

No animal data is being provided in support of this submission.

## XXII. PERFORMANCE TESTING - CLINICAL

The VX1+ assists operators in the real-time manual or automatic annotation of 3D anatomical and electrical maps of human atria for the presence of multipolar intra-cardiac atrial electrograms exhibiting spatiotemporal dispersion during Atrial Fibrillation (AF) or Atrial Tachycardia (AT). Because the VX1 is not indicated for use, and the Company is making no claims regarding the use of the device, in directing treatment for or affecting the outcome of any particular heart arrhythmia, clinical data is not required to demonstrate substantial equivalence.

Nevertheless, VX1 has been clinically tested in a prospective, multicentric, nonrandomized study conducted in 85 de novo persistent AF patients, including 8 centers and 17 operators. VX1 allowed for robust center-to-center standardization of acute and long-term ablation outcomes after electrogram-based ablation (Seitz, Mohr Durdez et al. 2022, Deisenhofer 2022). Outcomes were compared to a comparable control group from the original paper from Seitz, Bars et al. 2017, in which dispersion-guided ablation was performed visually by trained operators, resulting in no statistical difference and confirming the relevance of the dispersion provided by VX1.

Further, the automatic tagging feature has been fully verified and validated via bench testing with complete quantitative and qualitative assessments based on real-life data from the Operating Room (see **Section XX.B.4**).

However ,for completeness, the Company herein describes a clinical study of the device which was conducted in France to evaluate the reliability of VX1+ detection of dispersed electrograms and automatic tagging function. Notably, the practice of cardiology is relatively similar between the U.S. and France. Both countries require at least 10 years of training, including a 3-year residency, before beginning to practice. Additionally, each country requires cardiologists to be certified; in the U.S. they are certified by the American Board of Internal Medicine and in France, by the College National des Enseignants de Cardiologie (see “Cardiology Training in Brazil and Developed Countries: Some Ideas for Improvement”, Arq. Bras. Cardiol. vol.113 no.4 São Paulo Oct. 2019 Epub Nov 04, 2019.) By and large, similar to their American counterparts, French cardiac electrophysiologists interested in the analysis of spatio-temporal dispersion of multipolar electrograms during AF have read the Seitz et al. 2017 JACC publication. Additionally, the same mapping and ablation equipment are used in both France and the U.S. More generally, most of the major clinical studies which have shaped the practice of electrophysiology worldwide, including in the U.S., have been conducted in part in clinical centers located in France. Moreover, ablation approaches which are commonly implemented in the U.S were pioneered in centers in France, Germany and Italy (Kuck, Brugada et al. 2016, Kuck, Merkely et al. 2019). Thus, the practice of cardiac electrophysiology, specifically as it pertains to atrial fibrillation ablation, is very similar, if not identical, between Europe and the U.S.

### A. Study Overview

The study evaluates the perioperative performance of VX1+ in a bidirectional configuration with the EnSite 3D mapping system in the real-time detection and automatic annotation of AF drivers; evaluates the estimation of arrhythmia cycle length; evaluates the ergonomics of VX1+ in the operating room; and collects preliminary safety data on VX1+ intraoperatively until the patient’s hospital discharge.

### B. Study Design

This study has the following characteristics:

- Interventional: Enrolled patients underwent an AF ablation including the mapping phase with VX1+.
- Prospective: Patients were enrolled prior to undergoing an AF ablation.
- Single Center: This study took place in one French Investigational site (Saint-Joseph Hospital) with 4 participating investigators.
- Non-Controlled: single arm (AT/AF mapping for all patients was assisted by VX1+ in bidirectional configuration).
- Non-Randomized: Not Applicable.
- Non-Blinded: Not Applicable.

As described in the Study Clinical Investigation Report RAPIC-03-001 provided in **Appendix 22.1**, the study population consisted of 22 adult patients with an indication of AF or AT ablation. Among the 22 patients included, all 22 patients underwent an AF/AT ablation procedure with the use of VX1+ in bidirectional mode (automatic tagging), and 13 were analyzed for algorithm dispersion performance with the last version of the VX1+ software (v1.0.6) as part of the product validation phase. All the 22 patients were analyzed for safety endpoints. The study is still ongoing with a total of 40 patients to be included.

### C. Compliance with Good Clinical Practice

The study was conducted in accordance with Good Clinical Practice (GCP). Pursuant to FDA's 2018 guidance, "Acceptance of Clinical Data to Support Medical Device Applications and Submissions" the Company provides the following information (consistent with 21 CFR 812.28) to demonstrate its GCP compliance:

1. The names of the investigators and names and addresses of the research facilities and sites where records related to the investigation are maintained are available in **Appendix 22.1**.
2. Investigator qualifications are included in **Appendix 22.2.**.
3. A description of the research facility involved in the study is included in **Appendix 22.1**.
4. A detailed summary of the protocol and results of the investigation are included in **Appendix 22.1**.
5. The device used in the clinical investigation is identical to the device that is the subject of this submission.
6. The information provided in this study is valid scientific evidence as detailed in **Appendix 22.1**.
7. As discussed in **Appendix 22.1**, the study was submitted to French Public Health Agency (ANSM) for application completeness validation; and to French Central Ethics Committee (CPP) for favorable opinion. The study was started after receiving a favorable opinion from the CPP Est-IV on 28/JAN/2022. The CPP Est-IV meets the required definition found in 21 CFR 812.3(t); it is an independent review panel that is responsible for ensuring the protection of the rights, safety, and well-being of subjects involved in the study and is comprised of 25 members who have the qualifications and experience to review and evaluate the science, medical aspects and ethics of the study.
8. A summary the CPP Est-IV decision to approve the study is provided in **Appendix 22.1**.

9. A description of how informed consent was obtained is provided in **Appendix 22.1**.
10. No incentives were provided to subjects to participate in the study.
11. A description of the methods the Company used to oversee the conduct of the study and the reporting of study data is provided in **Appendix 22.1**.
12. A description of how the investigation was conducted in accordance with GCP and the protocol is found in **Appendix 22.1**.

### D. Study Analyses

#### 1. VX1+ Reliability in Dispersion Detection (VX1+ vs Operator's Visual Interpretation of EGM)

The VX1+ reliability was assessed through primary endpoint by analyzing discordance between the operator's visual interpretation of intracardiac signal and VX1+ dispersion detection/autotagging.

Only patients who underwent ablation procedures with VX1+ software version v1.0.6 could be taken into consideration for the dispersion algorithm performance analysis of this part as it corresponds to the most stable version for validation phase.

Among the 13 patients enrolled after v1.0.6 was released, 2 patients (AT ablation) were excluded from the performance analysis as there was no dispersion which can be detected through visual nor VX1+ intracardiac signal analysis (only macro-reentries identifiable thanks to standard tools: activation maps and pacing maneuvers).

In terms of dispersed dots detection (individual tag), VX1+ sensitivity was 94% (some dispersion tags were added manually), and VX1+ Positive Predictive Value was 99% (very few VX1+ dispersion tags were removed by the operator).

The results are as follows when considering a bi-atrial segmentation in 26 regions:

VX1+ sensitivity in terms of dispersed region detection is 99% in average (between 86% -100%) which indicates that when the area is dispersed according to an expert eye, there is on average 99% chance that VX1+ will automatically detect and tagged the dispersion on 3D maps.

VX1+ specificity in terms of dispersed region detection is 98% in average (between 80% - 100%), which indicates that when the area is not dispersed according to an expert eye, there is on average 98% chance that VX1+ will not detect any dispersion (no autotag on the 3D maps).

VX1+ Positive Predictive Value in terms of dispersed region detection is 97% in average (between 79% and 100%) which indicates there is on average 97% chance that the electrograms are indeed dispersed when VX1+ lights up (=detection of dispersion/area tagged).

VX1+ Negative Predictive Value in terms of dispersed region detection is 99% in average (between 86%-100%) which indicates that there is on average 99% chance that the electrograms are not dispersed when VX1+ does not light up (=no detection of dispersion/area not tagged).

VX1+ Accuracy (Diagnostic Effectiveness) is the proportion of correct results in the overall results. A mean Diagnostic effectiveness of 0,98 indicate there is on average 98% of the results obtained during the use of VX1+ that are correct.

In terms of crucial dots detection (i.e. AF/AT termination dots by ablation or dots where the cycle length increases by at least 20 ms), the VX1+ have highlighted good performance and, on average, 92% of all AT/AF crucial dots, 100% of all AF crucial dots and 100% of crucial regions have been detected by VX1+ on the validation cohort.

### 2. Cycle Length Estimation by VX1+

As there was no change in the algorithm for measuring the cycle length across the different VX1+ software versions (from v1.0.0 to v1.0.6), all 22 patients enrolled in the study have been considered for the evaluation of Cycle Length measurement by VX1+.

A comparative evaluation was performed between VX1+ cycle length (CL) measurement algorithm and manual cycle length measurements by the operator (average of 10 consecutive cycles via the signals displayed in the EP recording system interface).

A low mean absolute error of 4 ± 6 ms, 8 ± 21 ms and 5 ± 9 ms was obtained, for reference cycle length (measured at the coronary sinus), mapping cycle length (measured in the right atrium) and mapping cycle length (measured in the left atrium), respectively. Taking the errors obtained during preclinical testing as an acceptable limit (16.85ms for Reference Cycle Length and 31.50ms for Mapping Cycle Length), more than 94% of the individual measurements are within the range.

In summary, these results confirm the performance analysis performed during pre-clinical tests (see **Sections XX.B.2** and **B.3**) and the equivalence between VX1 and VX1+. In conclusion,VX1+ display of AFCL accurately mimic the human, visually-guided measurement of physiological-range AFCL values.

### 3. Procedural Characteristics & Acute Outcomes

Importantly, there was no clinical complication related to the use of VX1+. Only one SAE was reported (cardiac tamponade due to perforation) related to the ablation procedure (well-documented and anticipated in routine practice during standard ablation procedures) but not to the use of the VX1+ device.

Overall, 9 minor device deficiencies were observed, among which 5 were corrected between v1.0.0 and v1.0.6. The remaining 4 device deficiencies all concern a loss of signal most probably related to a communication problem with EnSite (See **Section XVIII.J**. for a detailed description). All the device deficiencies have been considered for the VX1+ risk analysis and IFU updates (“Troubleshooting” section) during the validation phase.

The average total procedure time of procedures implementing VX1+ was not significantly different from the one of procedures during which dispersion detection was done by VX1 device predecessor (Mapping time with VX1+ =36±16 min vs Mapping time with VX1=29±11 min ; AF procedure

time=143±36 min with VX1+ vs AF procedure time= 165±48 min for VX1; AT procedure time =126±66 min vs AT procedure time= 127±45 min for VX1).

The average rate of AF termination by ablation is about 70% and SR conversion by ablation is about 60% for validation group (including only patients who underwent the ablation procedure following the VX1+ dispersion maps obtained by VX1+ v1.0.6) which demonstrates acute success outcomes in line with previous studies based on visual dispersion (Seitz, Bar et al. 2017) and VX1-guided dispersion (Seitz, Mohr Durdez et al. 2022).

### 4. User's Feedback

VX1+ usability questionnaires were administered to 4 investigators who performed ablation procedures in the scope of the study. The global average score for each section is above average (>3 – neutral), as targeted. The overall satisfaction of investigators is positive regarding the VX1+ application. Indeed, this survey highlights that VX1+ allows to perform ablation procedures with more specificity than using the VX1 device and/or a standard ablation procedure (auto-tagging, smaller regions). However, this survey also highlights that sounds emitted from VX1+ shall be improved in terms of interpretation and identification. As sounds indications (cosmetic feature for information purposes, not considered as a risk reduction measure in VX1+ risk analysis) have no influence on safety, this feedback will be handled in a future minor software version in the scope of User Interface Improvement, as well as other users feedback gathered during PMS activities.

These results are detailed in the Usability Test Report APTTR-03-011 in **Appendix 20.17** and are part of the summative phase in the VX1+ Usability Engineering File APTIU-03-001 in **Appendix 20.3**.

### 5. Conclusions

This single center clinical investigation has been launched in Marseille (France) where 22 patients were enrolled, and 4 investigators involved. This study aimed at evaluating the usability and efficacy of VX1+ at detecting and auto-tagging dispersion during AF/AT ablation procedures. The results indicate that the implementation of VX1+ in the cardiac electrophysiology analysis during atria mapping is reliable with no associated additional risks or procedure time. This study also highlights that VX1+ dispersion map (regions/dots locations) are comparable to the ones detected by the operator's visual analysis of EGMs. Finally, VX1+ allowed good acute ablation outcomes after electrogram-based ablation, comparable to previous studies based on visual or VX1-guided dispersion. This study did not raise any safety or performance issues when comparing VX1 and VX1+.

Please refer to **Appendix 22.1** for the full report of this testing.

## XXIII. REFERENCES

Reprints of reference documents are available in **Appendix 23.1**. The collection of literature referenced herein serves to provide both scientific context for the reviewer (expert consensus, guidelines, clinical trials, literature on similar device CARTO with CFAE module) and to support the discussion of substantial equivalence between the subject and predicate devices (Seitz et al, JACC 2017, Seitz et al, JCE 2022, Deisenhofer JCE 2022).

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