March 21, 2025

Cytovale, Inc.
Sarah Esterquest
Director, Regulatory Affairs
2 Tower Place, 18th Floor
South San Francisco, California 94404

Re: K250513
Trade/Device Name: IntelliSep Test (CV-ICG-048)
Regulation Number: 21 CFR 866.3215
Regulation Name: Device To Detect And Measure Non-Microbial Analyte(S) In Human Clinical Specimens To Aid In Assessment Of Patients With Suspected Sepsis
Regulatory Class: Class II
Product Code: QUT
Dated: January 29, 2025
Received: February 21, 2025

Dear Sarah Esterquest:

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

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

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

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

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

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

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

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-

assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Noel J. Gerald -S

Noel J. Gerald, Ph. D.
Deputy Division Director
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

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

510(k) Number *(if known)*
K250513

Device Name
IntelliSep Test

Indications for Use *(Describe)*
The Cytovale IntelliSep test is a semi-quantitative test that assesses cellular host response via deformability cytometry of leukocyte biophysical properties and is intended for use in conjunction with clinical assessments and laboratory findings to aid in the early detection of sepsis with organ dysfunction manifesting within the first 3 days after testing. It is indicated for use in adult patients with signs and symptoms of infection who present to the Emergency Department. The test is performed on an EDTA anticoagulated whole blood sample.

The IntelliSep test generates an IntelliSep Index value that falls within one of three discrete interpretation bands based on the probability of sepsis with organ dysfunction manifesting within the first three days after testing. The IntelliSep test represents the probability of the clinical syndrome of sepsis and is intended to be used alongside other clinical information and clinical judgement. It does not identify the causative agent of infection and should not be used as the sole basis to determine the presence of sepsis. The IntelliSep test is intended for in vitro diagnostic use.

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

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

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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

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1. 510(k) Owner/Submitter Information

Name: Cytovale, Inc.
Address: 2 Tower Place, 18th Floor, South San Francisco, CA 94080
Telephone: 1-415-417-2188
Contact Person: Sarah Esterquest
Email Address: sarah.esterquest@cytovale.com

2. Date Summary Was Prepared

March 19, 2025

3. Device Name and Classification

Trade Name: IntelliSep test
Instrument Name: Cytovale System
Classification: Class II (Special Controls)
Classification Name: Device to detect and measure non-microbial analyte(s) in human clinical specimens to aid in assessment of patients with suspected sepsis (21 CFR 866.3215)
Product Code: QUT
Panel: DMD – Division of Microbiology Devices
Submission Type: Special

4. Predicate Device Information

Predicate Product	510(k) Number	Date of Clearance	Classification	Regulation	Classification Product Code
IntelliSep test	K220991	December 20, 2022	Class II (Special Controls)	866.3215	QUT

Table 1: Predicate device information

This Special 510(k) (K250513) describes modifications made to the IntelliSep test software and Cytovale System hardware. These modifications are described in Section 8.

5. Device Description

The Cytovale IntelliSep test is a short turn-around time (STAT) test, producing results in 10 minutes or less, to aid in the early detection of sepsis with organ dysfunction manifesting within the first 3 days after testing. It assesses the state of immune activation in patients with signs and symptoms of infection who present in the Emergency Department (ED).

The IntelliSep test is run on the Cytovale System, a laboratory benchtop analyzer depicted in Figure 1 and Figure 2.

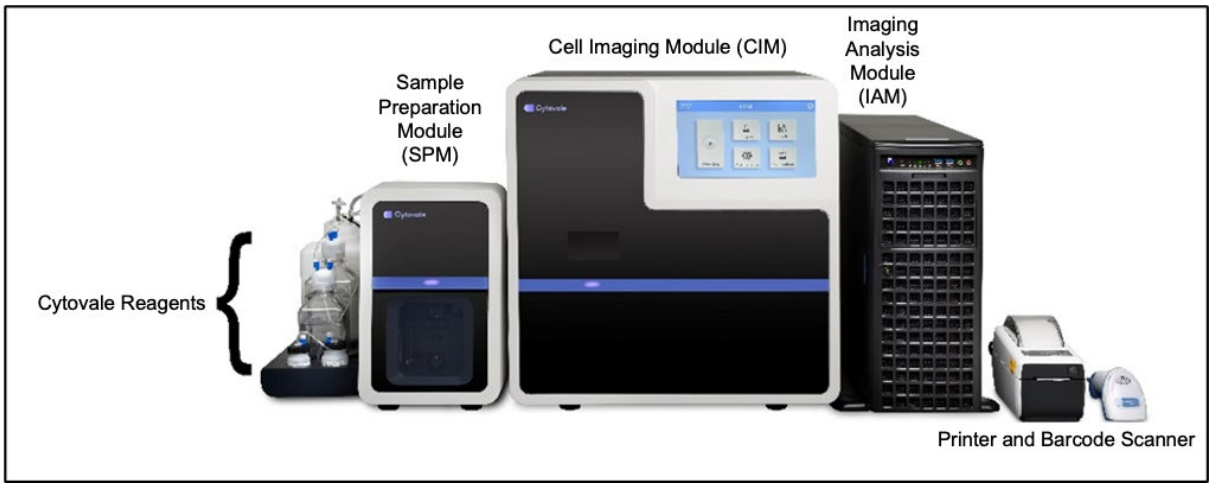

Figure 1: The Cytovale System is a closed system benchtop analyzer, comprised of three modules: Sample Preparation Module, Cell Imaging Module, and Imaging Analysis Module. The original K220991 Imaging Analysis Module is shown in this figure. Also included are the Cytovale System Reagents (Cytovale Reagent Kit, Cytovale Diluent, Cytovale Cleanse), Barcode Scanner and Printer (not shown: IntelliSep Quality Controls, IntelliSep Cartridge, Sample Preparation Tube).

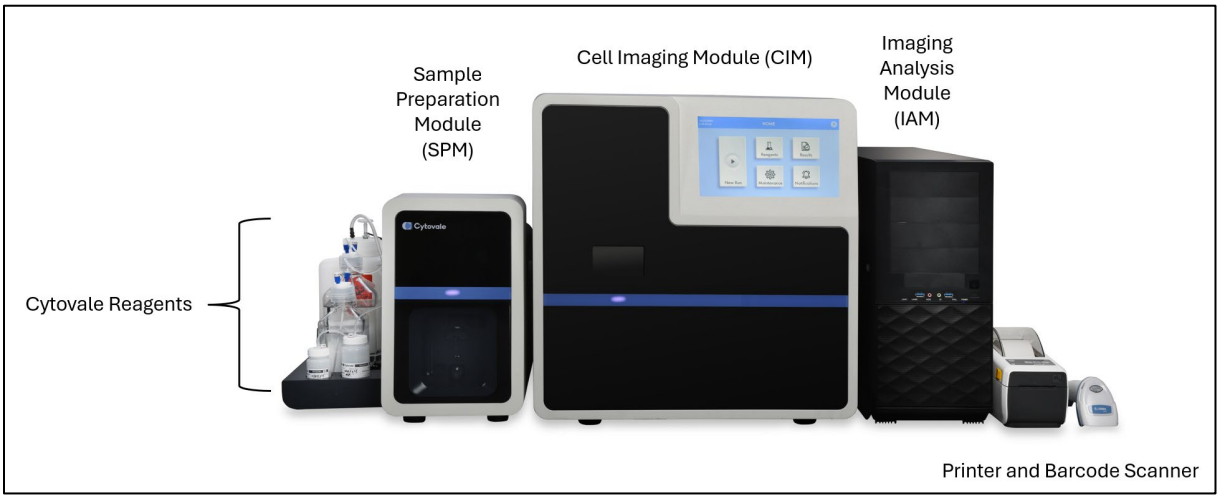

Figure 2: The modified Cytovale System, including an additional Imaging Analysis Module hardware configuration (K250513, described in Section 8). All other Cytovale System materials remain identical to those described in Figure 1 and Table 2.

The IntelliSep test requires use of the materials described in Table 2.

IntelliSep Test Materials & Equipment	Description
Cytovale System: (Required and supplied) • Sample Preparation Module (SPM) • Cell Imaging Module (CIM) • Imaging Analysis Module (IAM)	A closed system benchtop analyzer as shown in Figure 1 and Figure 2. It is comprised of three modules: Sample Preparation Module, Cell Imaging Module, and Imaging Analysis Module.
Barcode scanner (Optional and supplied)	Scanner used to automatically enter sample and material identifiers.

IntelliSep Test Materials & Equipment	Description
Printer (Optional and supplied)	Printer used to print a hard copy of results.
Sample Preparation Tube (Required and supplied)	A single-use, commercial off-the-shelf test tube used for sample preparation.
IntelliSep Cartridge (Required and supplied)	Closed system test cartridge which presents the sample for testing in the Cell Imaging Module.
Cytovale Reagent Kit (Required and supplied)	Nonbiological salt solutions (Reagent A Lysis and Reagent B Quench), for use with the Sample Preparation Module to lyse red blood cells and quench the lysis reaction.
Cytovale Diluent and Cleanse Reagents (Required and supplied)	The Diluent solution is used in the Sample Preparation Module to suspend white blood cells for analysis. The Cleanse is a rinsing solution for the SPM.
IntelliSep Quality Control Kit (Quality controls are required but not supplied)	A two-level Quality Control set, derived from stabilized whole blood. *Note: Per 42 CFR 493.1256, quality controls are required for the IntelliSep test; however, at their discretion, laboratory directors may develop their own quality control materials or order the IntelliSep Quality Control Kit.*

Table 2: Materials and equipment required for the IntelliSep test

To run a test, the laboratory operator transfers 100 µL of whole blood into the sample preparation tube which is then placed into the Cytovale System. The system automatically lyses red blood cells, and washes the purified leukocytes in a diluent, producing a total volume of approximately 1mL of prepared sample, which the operator then transfers to the IntelliSep cartridge for analysis on the Cytovale System. A microfluidic deformability cytometry technique is used to measure the biophysical properties of thousands of individual leukocytes in rapid succession. These properties have been shown to differ in quiescent white blood cell populations when compared to those in septic patients, enabling rapid assessment of the host response and the likelihood of having sepsis with organ dysfunction manifesting within the first 3 days after testing.

Based on these measurements, the test provides a single score, the IntelliSep Index (ISI), ranging from 0.1-10.0, stratified into three discrete interpretation bands (Band 1, Band 2, Band 3) of increasing sepsis likelihood.

6. Intended Use

The Cytovale IntelliSep test is a semi-quantitative test that assesses cellular host response via deformability cytometry of leukocyte biophysical properties and is intended for use in conjunction with clinical assessments and laboratory findings to aid in the early detection of sepsis with organ dysfunction manifesting within the first 3 days after testing. It is indicated for use in adult patients with signs and

symptoms of infection who present to the Emergency Department. The test is performed on an EDTA anticoagulated whole blood sample.

The IntelliSep test generates an IntelliSep Index value that falls within one of three discrete interpretation bands based on the probability of sepsis with organ dysfunction manifesting within the first three days after testing. The IntelliSep test represents the probability of the clinical syndrome of sepsis and is intended to be used alongside other clinical information and clinical judgement. It does not identify the causative agent of infection and should not be used as the sole basis to determine the presence of sepsis. The IntelliSep test is intended for in vitro diagnostic use.

7. Indications for Use

See "Intended Use".

8. Overall Comparison Between Subject Device and Predicate

This Special 510(k) (K250513) describes modifications made to the IntelliSep test software and Cytovale System hardware. There were no changes to the intended use or indications for use for the IntelliSep test, nor were there any changes to the underlying technological characteristics or principles of operation of the Cytovale System.

The modifications are described below.

8.1. Implementation of Optional Remote Log Export Function

The original Cytovale System (K220991) did not include an external network connection, i.e., an internet connection. The modified Cytovale System (K250513) includes an external network connection utilized to export System logs for purposes of remote troubleshooting. This remote log export is unidirectional; the Cytovale System does not accept any incoming data. There is no patient protected health information (PHI) included in the exported System logs.

This external network connection is optional and can be enabled following appropriate assessment by a customer laboratory's Information Technology (IT) department.

8.2. Refinement of Internal Quality Control Metrics

The original IntelliSep test software (K220991) included internal quality control metrics to ensure the validity of IntelliSep test results. The Cytovale System will only report a test result if these internal quality control metrics are met. Otherwise, a test error is reported.

The modified IntelliSep test software (K250513) incorporates modifications to certain internal quality control metrics to refine clog detection within the IntelliSep Cartridge's microfluidic junction and to further discern any assay failures. The modifications also establish new metrics to achieve this same goal.

The modifications are limited to the System's evaluation of the in-process assay results and determination of assay validity. The cell deformability cytometry technique and IntelliSep result calculation process remain unchanged from K220991.

8.3. Additional Imaging Analysis Module Hardware Variant

The additional Imaging Analysis Module (IAM) configuration presented in K250513 was based on the original K220991 IAM configuration, with the same functional and performance requirements applied to both IAM variants.

The original hardware from the K220991 configuration was planned to be obsolesced by the workstation manufacturer, necessitating replacement of the central and graphics processing units with units of equivalent processing capabilities. Due to incidental improvements in component energy efficiency, the number of power supplies was also reduced from two (K220991) to one (K250513).

The IAM is responsible for receiving and processing data from the Cell Imaging Module (CIM) and providing assay results back to the CIM for display; no changes were made to either data interface.

9. Non-Clinical and/or Clinical Tests Summary & Conclusions

Verification and validation testing was successfully performed following risk assessment of the device modifications. This testing included the components listed below. No changes to assay performance or device function were observed, and no new risks were identified.

9.1. Cytovale System Software Verification and Validation

9.1.1.Holistic Assessment of All Modifications

Software supporting all three Cytovale System modules successfully completed software verification and validation. This included both verification and validation of the device modifications, and confirmation of continued System function and assay performance in alignment with final guidance *Content of Premarket Submissions for Device Software Functions* (June 2023).

9.1.2.Specific Activities for Remote Log Export Function

Specific verifications and validations were performed in acknowledgement of the new external network connection. These activities included confirmation of data integrity between the Cytovale System and the external network location, and performance of independent penetration testing to demonstrate controls against physical (kinetic) and digital cyberattacks. All activities were performed in alignment with final guidance *Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions* (September 2023).

9.2. *Internal Quality Control Metrics:* Comparison of Clinical and Analytical Performance Results

In accordance with the applicable special controls listed in 21 CFR 866.3215, Cytovale confirmed that the modified device maintained identical analytical and clinical performance to the cleared K220991 device. This comparison was of special concern due to the modifications to the internal quality control metrics used to determine result validity.

Raw assay videos from the following performance studies were processed on both the modified device (K250513) and the baseline device (K220991). The results were then directly compared to each other and to the original design requirements.

- IntelliSep Clinical Validation Study (CV-CLN-007)

- Within Laboratory Precision (CLSI EP05-A3)
- Reproducibility (CLSI EP05-A3)
- Healthy Reference Range (CLSI EP28-A3C)

No performance differences were observed for these data sets; there are no changes to labeled performance claims or limitations when compared to K220991. All performance claims and limitations may be found in the Decision Summary for K220991[1].

9.3. *Internal Quality Control Metrics:* Comparison of Sequestered Data Set

A comparison of results from a sequestered data set was also evaluated in conformance with *Good Machine Learning Practice for Medical Device Development* (October 2021) as established by the US FDA, Health Canada, and MHRA, specifically "Training Data Sets Are Independent of Test Sets". Raw assay videos from the sequestered data set were processed on both the modified device (K250513) and the baseline device (K220991). The results were then directly compared to each other

No performance differences were observed for the sequestered data set, indicating that the device modifications will not impact future, new assay results or overall assay performance.

9.4. *Additional Imaging Analysis Module Hardware Variant:* Electrical Safety/EMI/EMC Testing

The additional IAM hardware configuration underwent electrical safety, electromagnetic compatibility (EMC), and electromagnetic interference (EMI) testing per IEC 60601-1-2:2014/AMD1:2020, and applicable portions of IEC 61010-1:2010, AMD1:2016 at an ASCA-certified test site (Intertek in Menlo Park, CA, USA). Continued ETL certification and authorization to mark was obtained through this testing.

In alignment with final guidance *Electromagnetic Compatibility (EMC) of Medical Devices* (June 2022), IEC TS 60601-4-2 was successfully employed to assess the immunity of the performance associated with the device's intended use.

10. Proposed Labeling

The labeling is sufficient and meets the requirements of 21 CFR Parts 801 and 809, as applicable, and meets the special controls for this device under 21 CFR 866.3215.

11. Conclusions

The submitted information in this Special 510(k) notification is complete and supports a substantial equivalence determination.

[1] Available at < https://www.accessdata.fda.gov/cdrh_docs/reviews/K220991.pdf>