SPECIAL 510(K): DEVICE MODIFICATION
OIR DECISION SUMMARY

510(k) Number: K183176

This 510(k) submission contains information/data on modifications made to the applicant's own class II or class I devices requiring 510(k). The following items are present and acceptable:

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1. The name and 510(k) number of the applicant's previously cleared device. (For a preamendments device, a statement to this effect has been provided.)

2. Applicant's statement that the **INDICATION/INTENDED USE** of the modified device as described in its labeling **HAS NOT CHANGED** along with the proposed labeling which includes instructions for use, package labeling, and, if available, advertisements or promotional materials (labeling changes are permitted as long as they do not affect the intended use).

3. Description of the device **MODIFICATION(S):**

   The following modifications have been made:

   - Blood sample storage has been extended from 90 minutes at room temperature prior to analysis to 180 minutes at room temperature prior to analysis.
   - EAA assay reagent has been changed from a liquid to a solid lyophilized form.
   - EAA kit configuration has been changed from multi- to single use.
   - Storage conditions of the assay test tubes have been changed from unopened at room temperature until expiry date and opened at room temperature for 30 days to 2°C - 25°C for the shelf life duration of 18 months, which remains unchanged.
   - Storage conditions of the assay reagent have been changed from unopened at 2°C - 8°C until expiration and opened at 2°C - 8°C for 30 days to 2°C - 25°C for the shelf life duration of 18 months, which remains unchanged.
   - Smart Line TL Tube luminometer has been validated for use with the assay.
   - Additional data has been obtained for linearity and precision.
   - Instructions for use have been updated to reflect the changes described above.

4. The **FUNDAMENTAL SCIENTIFIC TECHNOLOGY** of the modified device **has not changed**.

5. **Comparison Information** (similarities and differences) to applicant's legally marketed predicate device including labeling, intended use, physical characteristics, and assay information:

SIMILARITIES

	Modified Device	Predicate Device
Features	Endotoxin Activity Assay (EAA) (K183176)	Endotoxin Activity Assay (EAA) (DEN030002)
Intended Use	The EAA™ is a rapid in vitro diagnostic test that utilizes a specific monoclonal antibody to measure the endotoxin activity in EDTA whole blood specimens. The information, when used in conjunction with other clinical information and other relevant diagnostic tests aids in the risk assessment of patients in the ICU for progression to severe sepsis. Patients tested on their first day of admission to the ICU where the endotoxin activity (EA) value is ≥ 0.60, are three times more likely to develop severe sepsis within the next three days than subjects whose EA values are < 0.40 and should be closely monitored for such occurrence.	The EAA™ is a rapid in vitro diagnostic test that utilizes a specific monoclonal antibody to measure the endotoxin activity in EDTA whole blood specimens. The information, when used in conjunction with other clinical information and other relevant diagnostic tests can aid in the risk assessment for progression to severe sepsis. Patients tested on their first day of admission to the ICU where the endotoxin activity (EA) value is ≥ 0.60, are three times more likely to develop severe sepsis within the next three days than subjects whose EA values are < 0.40 and should be closely monitored for such occurrence.
Sample Type	Same as predicate device	EDTA whole blood specimens
Test Principle and Amplification	Same as predicate device	Chemiluminescent assay
Detection Method	Same as predicate device	Endotoxin activity is a chemiluminescent measure of the biological response of the neutrophils in a patient's blood to an immunological complex of endotoxin and exogenous antibody. The measurement of endotoxin activity is specific towards LPS.
Quality Control	Same as predicate device	Low and high QC
Assay Result	Same as predicate device	Quantitative
Software	N/A	N/A

DIFFERENCES

	Modified Device	Predicate Device
Features	Endotoxin Activity Assay (EAA) (K183176)	Endotoxin Activity Assay (EAA) (DEN030002)
Sample Storage	180 minutes at room temperature	90 minutes at room temperature
Kit configuration	Single use	Multi-use
Kit Reagents	Solid lyophilized	Liquid
Reagent Storage (Assay Test Tubes)	Unopened 2°C - 25°C for the shelf life duration of 18 months	Unopened at room temperature until expiry date and opened at room temperature for 30 days
Reagent Storage (Assay Reagents)	2°C - 25°C for the shelf life duration of 18 months	Unopened at 2°C - 8°C until expiration and opened at 2°C - 8°C for 30 days
Instrument	Smart Line TL Tube Luminometer	Berthold AutoLumat LB 953

6. **Design Control Activities Summary**:

Smart Line TL Tube Luminometer

A risk assessment and validation study were performed to assess the performance of the EAA assay for use with the SmartLine TL Tube luminometer compared to the Berthold AutoLumat LB 953. Data from a total of 84 independent whole blood samples was evaluated for inclusion in the method comparison study dataset. The mean difference between methods, as well as the 95% confidence interval for the mean difference, was estimated. In addition, the mean difference and the maximum difference between methods was summarized for the low, intermediate, and high categories. In this analysis, samples were classified as low, intermediate, or high based on the value of the current method (LB 953). The instruments were also compared with respect to a categorical scale derived from the numeric EA value. The categories were low (0.00-0.39), intermediate (0.40-0.59), and high (0.6-1.0). Results are summarized in Table 1 below.

Table 1: SmartLine TL Tube Luminometer Validation Summary

		Limits of 95%		Minimum Value	Maximum Value	Lower and Upper Limits of 95%	
Category	**N**	**Mean**	**SD**	**Value**	**Value**	**Confidence**	**Interval**
0.0-0.39	36	0.0084	0.0513	-0.082	0.110	-0.0089	0.0258
0.4-0.59	29	0.0096	0.0823	-0.210	0.178	-0.0218	0.0409
0.6-1.00	15	0.0231	0.0413	-0.085	0.075	0.0002	0.0459

The results demonstrated that design requirements were met and there was no negative impact to EAA assay performance with use of the SmartLine TL Tube luminometer.

Specimen Stability

A study was performed to evaluate the stability of endotoxin activity (EA) measurement in EDTA anti-coagulated whole blood when left undisturbed at room temperature at 18-25 °C.

To examine the relationship of EA at multiple time points with baseline EA values, least squares regression was performed. The presence of endotoxemia was evaluated with 55 patient blood samples stored at room temperature (18-25 °C) across multiple time points (Baseline – Time 0, 90, 120, and 185 Minutes) in patients admitted to ICU and healthy volunteers. The purpose of the data analysis was to establish stability of blood samples when stored at room temperature (18-25 °C) for 3 hours. Studies demonstrated that ETDA whole blood samples are stable for 180 minutes at room temperature.

7. **Truthful and Accurate Statement**, a **510(k) Summary or Statement** and the **Indications for Use Enclosure**.

   The labeling for this modified subject device has been reviewed to verify that the indication/intended use for the device is unaffected by the modification. In addition, the applicant's description of the particular modification(s) and the comparative information between the modified and unmodified devices demonstrate that the fundamental scientific technology has not changed. The applicant has provided the design control information as specified in The New 510(k) Paradigm and on this basis, I recommend the device be determined substantially equivalent to the previously cleared device.