SPECIAL 510(K): DEVICE MODIFICATION
OIR DECISION SUMMARY

510(k) Number: K183023

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):**

   This change was for a modification of the thresholds for Probe-1 of the *Salmonella* analyte in the xTAG GPP device, cleared under K140647. The purpose of the threshold change is to address customers concerns regarding an increase in the MFI (median fluorescent intensity) of *Salmonella* Probe-1 in their xTAG GPP runs. The threshold change increases the stringency for *Salmonella* positive calls as a means to reduce potential false positives and as a preventative measure to mitigate against variability at customers' sites. The xTAG GPP package insert has been revised with branding updates, formatting changes, revision of the End-User License Agreement (EULA) for the Luminex Software section, and a notation that accounts for the threshold change.

   The unmodified and modified devices are identical in assay formulation and there has been no change in the test procedure. The only changes are to the software as 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	xTAG Gastrointestinal Pathogen Panel (GPP) (K183023)	xTAG Gastrointestinal Pathogen Panel (GPP) (K140647)
Intended Use	Same as predicate device	The xTAG Gastrointestinal Pathogen Panel

		(GPP) is a multiplexed nucleic acid test intended for the simultaneous qualitative detection and identification of multiple viral, bacterial, and parasitic nucleic acids in human stool specimens or human stool in Cary Blair media from individuals with signs and symptoms of infectious colitis or gastroenteritis. The following pathogen types, subtypes and toxin genes are identified using the xTAG GPP: <u>Viruses</u> • Adenovirus 40/41 • Norovirus GI/GII • Rotavirus A <u>Bacteria</u> • *Campylobacter* (*C. jejuni*, *C. coli* and *C. lari* only) • *Clostridium difficile* (*C. difficile*) toxin A/B • *Escherichia coli* (*E. coli*) O157 • Enterotoxigenic *Escherichia coli* (ETEC) LT/ST • *Salmonella* • Shiga-like Toxin producing *E. coli* (STEC) stx 1/stx 2 • *Shigella* (*S. boydii*, *S. sonnei*, *S. flexneri* and *S. dysenteriae*) • *Vibrio cholerae* (*V. cholerae*) <u>Parasites</u> • *Cryptosporidium* (*C. parvum* and *C. hominis* only) • *Entamoeba histolytica* (*E. histolytica*) • *Giardia* (*G. lamblia* only - also known as *G. intestinalis* and *G. duodenalis*) The detection and identification of specific gastrointestinal microbial nucleic acid from individuals exhibiting signs and symptoms of gastrointestinal infection aids in the diagnosis of gastrointestinal infection when used in conjunction with clinical evaluation, laboratory findings and

		epidemiological information. A gastrointestinal microorganism multiplex nucleic acid-based assay also aids in the detection and identification of acute gastroenteritis in the context of outbreaks. xTAG GPP positive results are presumptive and must be confirmed by FDA-cleared tests or other acceptable reference methods. The results of this test should not be used as the sole basis for diagnosis, treatment, or other patient management decisions. Confirmed positive results do not rule out co-infection with other organisms that are not detected by this test, and may not be the sole or definitive cause of patient illness. Negative xTAG Gastrointestinal Pathogen Panel results in the setting of clinical illness compatible with gastroenteritis may be due to infection by pathogens that are not detected by this test or non-infectious causes such as ulcerative colitis, irritable bowel syndrome, or Crohn's disease. **xTAG GPP is not intended to monitor or guide treatment for *C. difficile* infections.** The xTAG GPP is indicated for use with the Luminex 100/200 and MAGPIX instruments with xPONENT software.
Sample Type	Same as predicate device	Human stool specimens and human stool in Cary-Blair media
Extraction Method	Same as predicate device	Biomérieux NucliSENS EasyMag
Test Principle and Amplification	Same as predicate device	Multiplex end point RT-PCR
Kit Reagents	Same as predicate device	xTAG® GPP Primer Mix, xTAG® OneStep Enzyme Mix, xTAG® OneStep Buffer, xTAG® RNase-Free Water, xTAG® BSA, xTAG® MS2, xTAG® GPP Bead Mix, xTAG® Reporter Buffer, xTAG® 0.22 SAPE
Test Format	Same as predicate device	Multiplex MAGPLEX bead-based universal array
Detection Method	Same as predicate device	Fluorescence based
Quality Control	Same as predicate device	Internal Control (MS2), rotating analyte

		controls and negative control (RNAse-free water)
Assay Result	Same as predicate device	Qualitative
Instrument	Same as predicate device	Luminex MAGPIX
Software	Same as predicate device	xPONENT Software

Differences

The TDAS GPP threshold for *Salmonella* was modified as compared with the predicate device (K140647). The TDAP GPP software also had some minor updates including updating some help images, default splash screen, and EULA.

Comments:

	Modified Device	**Predicate Device**
Features	xTAG Gastrointestinal Pathogen Panel (GPP) (K183023)	xTAG Gastrointestinal Pathogen Panel (GPP) (K140647)
TDAS GPP threshold for *Salmonella*	• If Probe-1 < **300**, call is NEG (Probe-2 is ignored) • If Probe-1 ≥ **100,000**, call is POS (Probe-2 is ignored) • If **300** ≤ Probe-1 < 100,000, reflex to Probe-2: - If Probe-2 < 200, call is NEG - If Probe-2 ≥ 200, call is POS	• If Probe-1 < 200, call is NEG (Probe-2 is ignored) • If Probe-1 ≥ 1400, call is POS (Probe-2 is ignored) • If 200 ≤ Probe-1 < 1400, reflex to Probe-2: - If Probe-2 < 200, call is NEG - If Probe-2 ≥ 200, call is POS

6. **Design Control Activities Summary**:

A risk assessment of the modified device was conducted and documented according to the firm's Quality System requirements. This assessment included Failure Mode and Effects Analysis (FMEA), and hazard and risk analysis with the *Salmonella* threshold change and the corresponding product updates. It was demonstrated that the modification made to the assay does not affect the assay procedure and the change was not expected to impact the performance of the test or its safety and effectiveness. No new hazards or failure modes were identified with the *Salmonella* threshold changes in the assay-specific Assay Protocol File used with the xTAG Data Analysis Software (TDAS) for the xTAG Gastrointestinal Pathogen Panel (GPP). To confirm that the assay performance was not negatively impacted, Luminex Molecular Diagnostics, Inc. performed the following validation studies:

- Limit of Detection
    - No new test runs (i.e., wet testing) was performed. Data acquired for *Salmonella enterica* serotype Typhimurium on the MAGPIX instrument during the original LoD study were retrieved and reanalyzed using the revised TDAS software and updated threshold for that analyte.
    - Testing showed that the original LoD of the *Salmonella* target was unchanged.
- Analytical Reactivity (Inclusivity)

- No new test runs (i.e., wet testing) was performed. Data acquired on the MAGPIX instrument during the original Analytical Reactivity study was subjected to analysis using the revised versions of the TDAS GPP software that had the new thresholds for the *Salmonella* target.
- The *Salmonella* Positive and Negative calls generated by the new software was compared to the calls generated in the original study. Data on the other targets was not analyzed.
- The acceptance criteria for this validation testing is defined as detection of all (100%) *Salmonella* strains tested in the intial study corresponded what was observed with the new *Salmonella* thresholds.
- Testing showed that all the *Salmonella* strains tested in the original study were detected with the revised TDAS software.

- Clinical Specimen Testing
  - The accuracy for the *Salmonella* threshold change was evaluated using pre-selected *Salmonella* positive and negative, de-identified archived clinical specimens.
  - Each clinical sample went through the sample pre-processing step and extraction according to the assay PI.
  - The assay performance accuracy was determined by the *Salmonella* call agreement between the result generated by the revised TDAS and new thresholds as compared to the calls based on supplier information. Further, the overall performance accuracy was compared to that generated by the existing version of the TDAS in terms of the *Salmonella* analyte.
  - The acceptance criteria for the testing is for the performance accuracy of the revised TDAS GPP to be at least equal to the performance of the current software version.

The firm's validation studies showed that the *Salmonella* calls generated by the current (TDAS v1.20) were the same as from the revised (TDAS v1.21) program. This is indicated by the table below—

Table 1. Comparison of Results generated by TDAS GPP (US) v. 1.20 and TDAS GPP (US) v. 1.21

		TDAS GPP (US) v. 1.20			
		Positive	**Negative**	**Invalid**	Total
TDAS GPP (US) v. 1.21	**Positive**	58	0	0	58*
	Negative	0	152	0	152
	Invalid	0	0	14	14
	Total	58*	152	14	

*Four of the samples generated *Salmonella* Positive calls by both TDAS GPP (US) v. 1.20 and v. 1.21. These samples were reported by the Supplier as *Salmonella* Negative and confirmed by BDS to be *Salmonella* Negative. Re-testing (investigational purposes only) of these false-positive samples by GPP generated *Salmonella* Negative calls or were indeterminate (due to the absence of the internal control signal in the initial run of the undiluted extract; internal control was present upon re-run with diluted extract), suggesting that human errors had occurred in the initial runs.

In addition, the following aspects of the system and software were analyzed:

- The new signal thresholds were verified and acceptance criteria was met indicating the assay performance was not negatively impacted.

- The validation of the updated software was through the analysis of clinical study data.
- Regression testing was performed to verify that the changes did not negatively impact the logic calls to generate analysis results.
- Code review was performed on the updated code of TDAS GPP (a change from the original IVD release version, v1.20 to v1.21).
- Verified proper installation of the update TDAS GPP version.
- Executed test cases to verify the code changes.

The firm provided a summary of the results from these verification and validation studies. The results demonstrated that requirements were met and there was no negative impact to assay performance.

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 (or their preamendment) device.