

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION DECISION SUMMARY

A. 510(k) Number:

K083171

B. Purpose for Submission:

Addition of 679 base pairs of wild type CFTR sequence to previously cleared Introl™ CF Panel I Control (k060070)

C. Measurand:

Controls for assays detecting Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene mutations and variants

D. Type of Test:

Assayed quality control material

E. Applicant:

Maine Molecular Quality Controls, Inc. (MMQCI)

F. Proprietary and Established Names:

Introl™ CF Panel I Control

G. Regulatory Information:

1. Regulation section:
21 CFR 866.5910 DNA quality control material for genetic testing
2. Classification:
Class II
3. Product code:
NZB, Quality Control material, genetics, DNA
4. Panel:
Immunology (82)

H. Intended Use:

1. Intended use(s):
The intended use is the same as the previous cleared Introl™ CF Panel I Control (k060070) which states:

The Introl™ CF Panel I Control is intended for in vitro diagnostic use as a quality control to monitor analytical performance of the extraction, amplification and detection steps of diagnostic assays used in the detection of the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene mutations and variants. This product is intended to be extracted and analyzed routinely with each CFTR assay run.

The INTROL™ CF Panel I Control is designed to monitor the detection of 38 CFTR mutations associated with cystic fibrosis, including the 23 mutations recommended for testing by American College of Medical Genetics (ACMG) and the American College of Obstetricians and Gynecologists (ACOG). The INTROL™ CF Panel I Control also monitors 3 polymorphisms (I506V, I507V, F508C) and the 5/7/9T variants.

2. Indication(s) for use:
Same as the intended use
3. Special conditions for use statement(s):
For prescription use only

4. Special instrument requirements:

Not applicable

I. Device Description:

The formulation of the modified and cleared INTROL™ CF Panel I Control is the same: INTROL™ CF Panel I Control consists of synthetic CFTR DNA suspended in a matrix of synthetic DNA targets, carrier DNA of a non-human species, preservatives, dye, and stabilizers. CFTR DNA is stabilized in the matrix and released when processed through common extraction methods as if it were a whole blood specimen.

INTROL™ CF Panel I Control modifications from the cleared panel:

CFTR DNA has been modified as follows:

1. Exon 3: additional 106 nucleotides 3'
2. Exon 5: additional 184 nucleotides 3'
3. Exon 14b: additional 100 nucleotides 5' and additional 289 nucleotides 3'

Table I: Number of Intronic Bases Flanking Each Exon of INTROL™ CF Panel I Control

Cleared INTROL™ CF Panel I Control			Modified INTROL™ CF Panel I Control		
EXON	5'	3'	EXON	5'	3'
1	312	91	1	312	91
2	97	273	2	97	273
3	144	125	<u>3</u>	144	<u>231*</u>
4	222	150	4	222	150
5	307	86	<u>5</u>	307	<u>270*</u>
6A	205	109	6A	205	109
6B	255	100	6B	255	100
7	126	99	7	126	99
8	198	134	8	198	134
9	495	402	9	495	402
10	339	246	10	339	246
11	146	235	11	146	235
12	160	289	12	160	289
13	92	128	13	92	128
14A	385	250	14A	385	250
14B	265	259	<u>14B</u>	<u>365*</u>	<u>548*</u>
15	142	133	15	142	133
16	312	259	16	312	259
17A	235	315	17A	235	315
17B	191	154	17B	191	154
18	244	211	18	244	211
19	150	89	19	150	89
20	186	251	20	186	251
21	443	313	21	443	313
22	585	235	22	585	235
23	178	181	23	178	181
24	178	222	24	178	222

*modification

J. Substantial Equivalence Information:

1. Predicate device name(s):
INTROL™ CF Panel I Control
2. Predicate 510(k) number(s):
k060070
3. Comparison with predicate:

Similarities		
Item	PREDICATE	MODIFIED
Intended Use	Monitor analytical performance of extraction, amplification, and detection steps of CFTR mutation detection assays.	Same
Formulation	Synthetic (recombinant) DNA with non-human carrier DNA, preservatives, dye and stabilizers	Same
Physical Format	Ready-to-use liquid	Same
Packaging	Polypropylene bottles	Same
Assay Steps Monitored	Extraction, Amplification and Detection	Same
Recommended Storage	2-8°C	Same
Directions for Use	Handle control in the same manner as the patient sample	Same
Method to Validate CFTR Sequence	Bi-directional sequencing	Same
Method to Verify each Lot	FDA-cleared CFTR detection assay, Bi-directional sequencing	Same

Differences		
Item	Predicate	Modified
Gene Segment SNPs	CFTR (38 mutations; 4 variants)	Additional 679 base pairs of wild type CFTR sequence to the existing SNPs

K. Standard/Guidance Document Referenced (if applicable):

Class II Special Controls Guidance Document: Quality Control Material for Cystic Fibrosis Nucleic Acid Assays

L. Test Principle:

Not applicable

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
 - a. Precision/Reproducibility:
Lot-to-lot reproducibility
Three builds of CF Panel I were manufactured using the same SOPs as for FDA-cleared

CF panel I with calculations adjusted for the new size plasmids. The first two builds are comprised of five bottles each. Each bottle contained specific clones, independently manufactured. The third build is comprised of three bottles, each containing different clones independently manufactured. All lots were tested using the xTAG™ Cystic Fibrosis Kit, eSensor and other amplification methods and found to give the correct calls.

Table 3: Modified INTROL™ CF Panel 1, Build 1

Lot Number /bottle	Method (s)	Results
K08JUN06/ a	Other Amplification Methods	All calls correct
	xTAG™ Cystic Fibrosis Kit	All calls correct
L08JUN06/ b	Other Amplification Methods	All calls correct
	xTAG™ Cystic Fibrosis Kit	All calls correct
	eSensor	All correct except 2 transcription errors
A09JUN06/ c	Other Amplification Methods	All calls correct
	xTAG™ Cystic Fibrosis Kit	All calls correct
	eSensor	All calls correct
B09JUN06/ d	Other Amplification Methods	All calls correct
	xTAG™ Cystic Fibrosis Kit	All calls correct
C09JUN06/ e	Other Amplification Methods	All calls correct
	xTAG™ Cystic Fibrosis Kit	All calls correct

Table 4: Modified INTROL™ CF Panel 1, Build 2 and 3

Lot Number /bottle	Method (s)	Results
B16JAN07/ a	All Amplification Methods	All calls correct
C16JAN07/ b	All Amplification Methods	All calls correct
D16JAN07/ c*	All Amplification Methods	All calls correct
E16JAN07/ d	All Amplification Methods	All calls correct
F16JAN07/ e	All Amplification Methods	All calls correct
A05OCT07/ a	All Amplification methods	All calls correct
B05OCT07/ b	All Amplification methods	All calls correct
C05OCT07/ c*	All Amplification methods	All calls correct

*Bottle c contains same set of plasmids as found separately in bottles d and e

- b. *Linearity/assay reportable range: Reference:*
Not applicable
- c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
Same as k060070
- d. *Detection limit:*
Not applicable
- e. *Analytical specificity:*
Not applicable
- f. *Assay cut-off:*
Not applicable

2. Comparison studies:

The three batches of modified INTROL CF Panel I Control were tested in the following CFTR detection assays: xTAG® (Luminex/ TmBioscience), eSensor® CFCD (Osmetech), and InPlex® (Third Wave) which require the additional CFTR sequence of the modified INTROL CF Panel I Control in order to detect Control alleles 711+1G>T and 2789+5 G>A. All genotype calls were the same as for the predicate INTROL CF Panel I Control with the exception that 711+1G>T and 2789+5 G>A were detected by all assays.

Risk analysis

A risk analysis using Failure Modes and Effects Analysis (FMEA) was performed to assess the impact of the modifications. Results showed that the design outputs of modified INTROL CF Panel I meet design inputs in conformance with design control requirements as specified in 21 CFR 820.30.

3. Clinical studies:

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Not applicable

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.