K033415

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510(k) SUMMARY

IDI-MRSA™ assay
Infectio Diagnostic Inc.

March 17, 2004

Submitted by:

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Contact:

Christian Choquet, PhD.

Name of Device:

Trade Name:	IDI-MRSA™ Assay
Common Name:	Test kit for the detection of methicillin-resistant *Staphylococcus aureus*
Product Code:	NQX
Classification Name	System, Nucleic Acid Amplification Test, DNA, Methicillin Resistant *Staphylococcus aureus*, Direct Specimen

Predicate Device:

PBP2' Latex Agglutination Test (Oxoid)
Mueller Hinton Agar with 4% NaCl and 6 µg/ml oxacillin (Remel)

Device Description:

Intended Use:

IDI-MRSA™ assay is a qualitative *in vitro* diagnostic test for the direct detection of nasal colonization by methicillin-resistant *Staphylococcus aureus* (MRSA) to aid in the prevention and control of MRSA infections in healthcare settings. The test performed on the Smart Cycler® instrument with a nasal swab specimen from patients at risk for colonization, utilizes polymerase chain reaction (PCR) for the amplification of MRSA DNA and fluorogenic target-specific hybridization probes for the detection of the amplified DNA.

IDI-MRSA is not intended to diagnose MRSA infections nor to guide or monitor treatment for MRSA infections. Concomitant cultures are necessary only to recover organisms for epidemiological typing or for further susceptibility testing.

Test Description:

A nasal specimen is collected and transported to the laboratory using the Copan Venturi Transystem®. For testing, the swab is placed in sample preparation buffer. The specimen is concentrated and lysed. An aliquot of the lysate is added to PCR reagents which contain the MRSA-specific primers used to amplify the genetic target [a sequence near the insertion site of Staphylococcal Cassette Chromosome *mec* (SCC*mec*)], if present. The assay also includes

an internal control (IC) used to detect PCR inhibitory specimens and to confirm the integrity of assay reagents in negative specimens. The IC is a DNA fragment of 335-bp including a 277-bp sequence not found in MRSA. Amplified targets are detected with hybridization probes labeled with quenched fluorophores (rnolecular beacons). For the detection of MRSA amplicons, the molecular beacon contains the fluorophore 5'-carboxyfluorescein (amine reactive ester of carboxy-fluorescein commonly called FAM) at the 5' end and the non-fluorescent quencher moiety dabcyl chloride (DABCYL) at the opposite end of the oligonucleotide. For the detection of the IC amplicons, the molecular beacon contains the fluorophore tetrachloro 6-carboxy-fluorescein (TET) at the 5' end and the non-fluorescent quencher moiety DABCYL at the 3' end.

For the recovery of MRSA for epidemiological typing or for further antibiotic susceptibility testing, appropriate culture media can be inoculated during specimen preparation or up to 24 hours after its preparation.

The amount of fluorescence at any given cycle, or following cycling, depends on the amount of specific amplicon present at that time. The Smart Cycler® instrument monitors simultaneously the fluorescence emitted by each beacon, interprets all data and at the end of the cycling program provides a final result. The operation of the Smart Cycler® instrument is based on the proprietary microprocessor-controlled I-CORE® (Intelligent Cooling/Heating Optical Reaction) module. Each Smart Cycler® processing block contains 16 independently controlled, programmable I-Core® modules, each with one reaction site. Thermally optimized proprietary reaction tubes combined with the design of the I-CORE® modules allow very rapid temperature cycling and rapid amplification. Up to 6 Smart Cycler® processing blocks can be daisy-chained together, allowing simultaneous analysis of 96 discrete samples.

Substantial Equivalence:

The Infectio Diagnostic Inc. IDI-MRSA™ assay has been found to be substantially equivalent to the Oxoid PBP2' Latex Agglutination Test (K011710) and to the culture technique consisting of primary isolation on mannitol salt agar followed by the oxacillin screen agar [Mueller Hinton Agar supplemented with 4% NaCl and 6 µg/ml oxacillin (Remel, K850291)] for confirmed isolates of *S. aureus*.

The IDI-MRSA™ assay is conducted directly on nasal swab specimens; determination of methicillin resistance with the PBP2' Latex Agglutination Test and with the oxacillin screen agar test are performed on isolates identified as *Staphylococcus aureus*. All assays detect MRSA.

The IDI-MRSA™ assay determines the presence of MRSA through PCR amplification of a sequence located at the insertion site of the Staphylococcal Cassette Chromosome *mec* (SCC*mec*) and detection of amplified products with fluorogenic target-specific hybridization; PBP2' Test uses latex agglutination for the detection of the PBP2' protein, one of the gene product of the *mecA* gene; the culture technique uses phenotypic characteristics of colonies.

With IDI-MRSA™ assay, interpretation of results is done automatically by the Smart Cycler® Instrument; with the PBP2' Latex Agglutination Test and the culture technique, results are interpreted visually by the user.

The reported performance of the Oxoid PBP2' Latex Agglutination Test In comparison (% agreement) with the oxacillin screen agar test on presumptive *S. aureus* isolates is 100% (232/232) for MRSA and 100% (87/87) for MSSA. Clinical performances of the IDI-MRSA™ assay and of the culture technique in a multi-center study are described below.

Clinical performance

A multi-center study was conducted on 786 nasal swab specimens collected with the Copan Venturi Transystem. The reference method consisted of an initial analysis with the oxacillin screen agar test after selective growth on mannitol salt agar. Specimens negative for MRSA were subjected to an additional analysis consisting of an enrichment step in trypticase soy broth (TSB) containing 6.5% NaCl followed by the oxacillin screen agar test. An MRSA culture-positive specimen was defined as a specimen positive for MRSA by either culture technique. An MRSA culture-negative specimen was defined as a specimen negative for MRSA by both culture techniques.

Compared to the culture method of reference, the IDI-MRSA™ identified 92.5% of the specimens positive for MRSA by either culture techniques and 96.4% of the specimens negative by both culture techniques (Tables 1 and 2). For the population tested, this results in a negative predictive value of 98.2% and a positive predictive value of 85.4%.

Table 1. Results obtained with IDI-MRSA™ assay in comparison to the reference method[1].

		IDI-MRSA™		
		Positive	Negative	Total
Culture techniques	Positive	135	11	146
	Negative	23	609	632
	Total	158	620	778

[1] Eight (8) specimens that gave initially unresolved results remained unresolved upon retesting with IDI-MRSA™ assay and are not included in the table. All 8 were culture negative.

Fourteen (14) of the 23 culture-negative specimens but IDI-MRSA positive were found to be MRSA culture-positive upon further investigation, resulting in a total of 149 culture-positive and IDI-MRSA positive specimens out of a total of 160 culture positive specimens. For 2 of the culture-positive specimens but IDI-MRSA negative, none of the isolates that exhibited methicillin resistance on oxacillin agar plates could be shown to carry the *mecA* gene when tested with the *mecA*-specific PCR assay described by Martineau *et al.*[7]

Table 2. Performance of IDI-MRSA™ assay obtained by the investigational sites when compared to the reference method

	Sensitivity (95% CI)[1]	Specificity (95% CI)[1]	No. of unresolved specimens[2]	Invalid/ total no. of runs
Site 1	86.8% (n=38) (71.9-95.6%)	99.6% (n=261) (97.9-100%)	6	0/26
Site 2	100% (n=30) (88.4-100%)	98.0% (n=102) (93.1-99.8%)	16	0/21
Site 3	89.3% (n=28) (71.8-97.7%)	90.8% (n=119) (84.1-95.3%)	11	1/15
Site 4	94.0% (n=50) (83.5-98.7%)	94.0% (n=150) (88.9-97.2%)	2	2/27
Total	92.5% (n=146) (86.9-96.2%)	96.4% (n=632) (94.6-97.27%)	35	3/89

[1] Binomial 95% confidence intervals.
[2] All specimens were unresolved due to failed internal controls indicative of inhibition or reagent failure. Twenty-seven (27) of the 35 were resolved upon re-testing.

SCC*mec* typing of MRSA culture-positive specimens according to Oliviera and de Lencastre[8] revealed specimens of types I, II and IV. There were no SCC*mec* type III specimens isolated

from the study. However, in a separate study, reference strains and other clinical isolates of all SCC*mec* types were tested and detected with IDI-MRSA™ assay.

Performances obtained by the investigational sites for IDI-MRSA, and the individual culture techniques as compared to the culture reference method (both culture techniques) are presented in Tables 3 and 4.

Table 3. Results obtained for IDI-MRSA™ assay and each culture screening technique with specimens positive for MRSA by the culture reference method.

Site	MRSA prevalence[1]	Sensitivity (95% CI)[2]		
		IDI-MRSA™	OxaMSA[3]	OxaTSB[4]
Site 1	12.7% (38/300)	86.8% (71.9-95.6%)	81.6% (65.7-92.3%)	ND
Site 2	21.7% (30/138)	100% (88.4-100%)	93.3% (77.9-99.2%)	ND
Site 3	18.9% (28/148)	89.3% (71.8-97.7%)	64.3% (44.1-81.4%)	ND
Site 4	25.0% (50/200)	94.0% (83.5-98.7%)	80.0% (66.3-90.0%)	78.0% (64.0-88.5%)
Total	18.6% (146/786)	92.5% (86.9-96.2%)	80.1% (72.7-86.3%)	ND

[1] Determined from results obtained with the culture reference method (combination of OxaMSA and OxaTSB)
[2] Binomial 95% confidence intervals.
[3] Oxacillin screen agar test after selective growth on MSA.
[4] Oxacillin screen agar test after enrichment in TSB with 6.5% NaCl. Site 4 tested all specimens with both culture techniques while the remaining sites tested only specimens negative with the OxaMSA culture method.

Table 4. Results obtained for IDI-MRSA™ assay and each culture screening technique with specimens negative for MRSA by the culture reference method.

Site	MSSA[1]	Specificity (95% CI)[2]		
		IDI-MRSA™	OxaMSA[3]	OxaTSB[4]
Site 1	73/262	99.6% (97.9-100%)	100% (98.6-100%)	ND
Site 2	25/108	98.0% (93.2-99.8%)	100% (96.4-100%)	ND
Site 3	24/120	90.8% (84.1-95.3%)	100% (96.9-100%)	ND
Site 4	16/150	94.0% (88.9-97.2%)	100% (97.6-100%)	100% (97.6-100%)
Total	138/640	96.4% (94.6-97.7%)	100% (99.4-100%)	ND

[1] Number of MSSA in total MRSA culture-negative population
[2] Binomial 95% confidence intervals.
[3] Oxacillin screen agar test after selective growth on MSA
[4] Oxacillin screen agar test after enrichment in TSB with 6.5% NaCl. Site 4 tested all specimens with both culture techniques while the remaining sites tested only specimens negative with the OxaMSA culture method.

As indicated in Table 4, 138 specimens analyzed with culture techniques were deemed by investigational sites to contain methicillin-sensitive *S. aureus* . Seven (7) yielded positive results with IDI-MRSA™ assay. Upon further investigation with more enhanced culture techniques, 4 were shown to actually contain MRSA

DEPARTMENT OF HEALTH & HUMAN SERVICES

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Re: k033415
Trade/Device Name: IDI-MRSA™ Assay
Regulation Number: 21 CFR 866.1640
Regulation Name: Antimicrobial susceptibility test powder
Regulatory Class: Class II
Product Code: NQX
Dated: February 16, 2004
Received: February 18, 2004

Dear Dr. Choquet:

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 (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. 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.

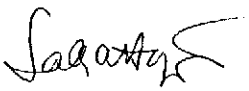
If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

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 Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 594-3084. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/dsma/dsmamain.html.

Sincerely yours,



Sally A. Hojvat, M.Sc., Ph.D.
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Enclosure

Indications for Use

510(k) Number (if known): K033415

Device Name: IDI-MRSA™

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IDI-MRSA™ assay is a qualitative *in vitro* diagnostic test for the direct detection of nasal colonization by methicillin-resistant *Staphylococcus aureus* (MRSA) to aid in the prevention and control of MRSA infections in healthcare settings. The test performed on the Smart Cycler® instrument with a nasal swab specimen from patients at risk for colonization, utilizes polymerase chain reaction (PCR) for the amplification of MRSA DNA and fluorogenic target-specific hybridization probes for the detection of the amplified DNA.

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Prescription Use _X_____ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K033415