Bruker Daltonik GmbH
Markus Kostrzewa
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Fahrenheitstrasse 4
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June 22, 2018

Re: DEN170081
Trade/Device Name: MALDI Biotyper CA System
Regulation Number: 21 CFR 866.3378
Regulation Name: Clinical Mass Spectrometry Microorganism Identification and Differentiation System
Regulatory Class: Class II
Product Code: QBN
Dated: September 26, 2017
Received: September 29, 2017

Dear Markus Kostrzewa:

This letter corrects our letter dated April 20, 2018. The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your De Novo request for classification of the MALDI Biotyper CA System, a prescription device with the following indications for use:

The MALDI Biotyper CA System is a mass spectrometer system using matrix-assisted laser desorption/ionization - time of flight (MALDI-TOF) for the identification and differentiation of microorganisms cultured from human specimens.

The MALDI Biotyper CA System is a qualitative in vitro diagnostic device indicated for use in conjunction with other clinical and laboratory findings to aid in the diagnosis of bacterial and fungal infections.

Bacteria:	
Abiotrophia defectiva	*Achromobacter xylosoxidans*
Acinetobacter baumannii / *nosocomialis* group	*Acinetobacter calcoaceticus*
Acinetobacter haemolyticus	*Acinetobacter johnsonii*
Acinetobacter junii	*Acinetobacter lwoffii*

Bacteria:	
Acinetobacter pittii	*Acinetobacter radioresistens*
Acinetobacter ursingii	*Actinomyces europaeus*
Actinomyces funkei	*Actinomyces graevenitzii*
Actinomyces hyovaginalis	*Actinomyces meyeri*
Actinomyces neuii	*Actinomyces odontolyticus*
Actinomyces oris	*Actinomyces radingae*
Actinomyces turicensis	*Actinomyces urogenitalis*
Actinotignum schaalii group	*Aerococcus sanguinicola*
Aerococcus urinae	*Aerococcus viridans*
Aeromonas salmonicida	*Aeromonas hydrophila* / *caviae* group
Aggregatibacter actinomycetemcomitans	*Aggregatibacter aphrophilus*
Aggregatibacter segnis	*Alcaligenes faecalis*
Alloiococcus otitis	*Alloscardovia omnicolens*
Anaerococcus murdochii	*Anaerococcus vaginalis*
Arthrobacter cumminsii	*Bacteroides caccae*
Bacteroides fragilis	*Bacteroides nordii*
Bacteroides ovatus group	*Bacteroides pyogenes*
Bacteroides salyersiae	*Bacteroides stercoris* group
Bacteroides thetaiotaomicron group	*Bacteroides uniformis*
Bacteroides vulgatus group	*Bifidobacterium breve*
Bordetella pertussis / *bronchiseptica* / *parapertussis*	*Bordetella hinzii*
Brevibacterium casei	*Brevundimonas diminuta* group
Burkholderia cepacia complex	*Burkholderia gladioli*
Burkholderia multivorans	*Campylobacter coli*
Campylobacter jejuni	*Campylobacter ureolyticus*
Capnocytophaga ochracea	*Capnocytophaga sputigena*
Chryseobacterium gleum	*Chryseobacterium indologenes*

Bacteria:	
Citrobacter amalonaticus complex	*Citrobacter freundii* complex
Citrobacter koseri	*Clostridium beijerinckii*
Clostridium bifermentans	*Clostridium butyricum*
Clostridium clostridioforme group	*Clostridium difficile*
Clostridium innocuum	*Clostridium paraputrificum*
Clostridium perfringens	*Clostridium ramosum*
Clostridium septicum	*Clostridium sordellii*
Clostridium sporogenes / *Clostridium botulinum* (group I)	*Clostridium tertium*
Corynebacterium accolens	*Corynebacterium afermentans* group
Corynebacterium amycolatum	*Corynebacterium aurimucosum* group
Corynebacterium bovis	*Corynebacterium coyleae*
Corynebacterium diphtheriae	*Corynebacterium freneyi*
Corynebacterium glucuronolyticum	*Corynebacterium glutamicum*
Corynebacterium jeikeium	*Corynebacterium kroppenstedtii*
Corynebacterium macginleyi	*Corynebacterium minutissimum*
Corynebacterium mucifaciens / *ureicelerivorans* group	*Corynebacterium propinquum*
Corynebacterium pseudodiphtheriticum	*Corynebacterium pseudotuberculosis*
Corynebacterium resistens	*Corynebacterium riegelii*
Corynebacterium striatum group	*Corynebacterium tuberculostearicum*
Corynebacterium ulcerans	*Corynebacterium urealyticum*
Corynebacterium xerosis	*Cronobacter sakazakii* group
Cupriavidus pauculus group	*Delftia acidovorans* group
Dermabacter hominis	*Dermacoccus nishinomiyaensis*
Edwardsiella tarda	*Eikenella corrodens*
Elizabethkingia meningoseptica group	*Enterobacter aerogenes*
Enterobacter amnigenus	*Enterobacter cloacae* complex

Bacteria:	
Enterococcus avium	*Enterococcus casseliflavus*
Enterococcus durans	*Enterococcus faecalis*
Enterococcus faecium	*Enterococcus gallinarum*
Enterococcus hirae	*Enterococcus mundtii*
Enterococcus raffinosus	*Escherichia coli*
Escherichia hermannii	*Escherichia vulneris*
Ewingella americana	*Facklamia hominis*
Finegoldia magna	*Fluoribacter bozemanae*
Fusobacterium canifelinum	*Fusobacterium necrophorum*
Fusobacterium nucleatum	*Gardnerella vaginalis*
Gemella haemolysans	*Gemella morbillorum*
Gemella sanguinis	*Granulicatella adiacens*
Haemophilus haemolyticus	*Haemophilus influenzae*
Haemophilus parahaemolyticus group	*Haemophilus parainfluenzae*
Hafnia alvei	*Helcococcus kunzii*
Kingella denitrificans	*Kingella kingae*
Klebsiella oxytoca / *Raoultella ornithinolytica*	*Klebsiella pneumoniae*
Klebsiella variicola	*Kocuria kristinae*
Kytococcus sedentarius	*Lactobacillus gasseri*
Lactobacillus jensenii	*Lactobacillus rhamnosus*
Lactococcus garvieae	*Lactococcus lactis*
Leclercia adecarboxylata	*Legionella longbeachae*
Legionella pneumophila	*Leuconostoc citreum*
Leuconostoc mesenteroides	*Leuconostoc pseudomesenteroides*
Listeria monocytogenes	*Macrococcus caseolyticus*
Mannheimia haemolytica group	*Micrococcus luteus*
Micrococcus lylae	*Mobiluncus curtisii*

Bacteria:	
*Moraxella sg Branhamella catarrhalis**	*Moraxella sg Moraxella nonliquefaciens**
*Moraxella sg Moraxella osloensis**	*Morganella morganii*
Myroides odoratimimus	*Myroides odoratus*
Neisseria bacilliformis	*Neisseria cinerea*
Neisseria elongata	*Neisseria flavescens / subflava* group
Neisseria gonorrhoeae	*Neisseria lactamica*
Neisseria meningitidis	*Neisseria sicca* group
Neisseria weaveri	*Nocardia brasiliensis*
Nocardia cyriacigeorgica	*Nocardia farcinica* group
Nocardia nova	*Nocardia otitidiscaviarum*
Ochrobactrum anthropi	*Oligella ureolytica*
Oligella urethralis	*Pantoea agglomerans*
Parabacteroides distasonis	*Parabacteroides goldsteinii*
Parabacteroides johnsonii / merdae group	*Parvimonas micra*
Pasteurella multocida	*Pediococcus acidilactici*
Pediococcus pentosaceus	*Peptoniphilus harei* group
Peptostreptococcus anaerobius	*Plesiomonas shigelloides*
Pluralibacter gergoviae	*Porphyromonas gingivalis*
Porphyromonas somerae	*Prevotella bivia*
Prevotella buccae	*Prevotella denticola*
Prevotella intermedia	*Prevotella melaninogenica*
Propionibacterium acnes	*Proteus mirabilis*
Proteus vulgaris group	*Providencia rettgeri*
Providencia stuartii	*Pseudomonas aeruginosa*
Pseudomonas fluorescens group	*Pseudomonas oryzihabitans*
Pseudomonas putida group	*Pseudomonas stutzeri*
Ralstonia pickettii	*Rhizobium radiobacter*
Rothia aeria	*Rothia dentocariosa*

Bacteria:	
Rothia mucilaginosa	*Salmonella* sp**
Serratia fonticola	*Serratia liquefaciens*
Serratia marcescens	*Serratia odorifera*
Serratia plymuthica	*Serratia rubidaea*
Sphingobacterium multivorum	*Sphingobacterium spiritivorum*
Sphingomonas paucimobilis group	*Staphylococcus aureus*
Staphylococcus auricularis	*Staphylococcus capitis*
Staphylococcus caprae	*Staphylococcus carnosus*
Staphylococcus cohnii	*Staphylococcus delphini*
Staphylococcus epidermidis	*Staphylococcus equorum*
Staphylococcus felis	*Staphylococcus haemolyticus*
Staphylococcus hominis	*Staphylococcus intermedius*
Staphylococcus lentus	*Staphylococcus lugdunensis*
Staphylococcus pasteuri	*Staphylococcus pettenkoferi*
Staphylococcus pseudintermedius	*Staphylococcus saccharolyticus*
Staphylococcus saprophyticus	*Staphylococcus schleiferi*
Staphylococcus sciuri	*Staphylococcus simulans*
Staphylococcus vitulinus	*Staphylococcus warneri*
Staphylococcus xylosus	*Stenotrophomonas maltophilia*
Streptococcus agalactiae	*Streptococcus anginosus*
Streptococcus canis	*Streptococcus constellatus*
Streptococcus dysgalactiae	*Streptococcus equi*
Streptococcus gallolyticus	*Streptococcus gordonii*
Streptococcus intermedius	*Streptococcus lutetiensis*
Streptococcus mitis / *oralis* group	*Streptococcus mutans*
Streptococcus parasanguinis	*Streptococcus pneumoniae*
Streptococcus pyogenes	*Streptococcus salivarius* / *vestibularis* group
Streptococcus sanguinis	*Streptococcus sobrinus*

Bacteria:	
Streptococcus thermophilus	*Sutterella wadsworthensis*
Trueperella bernardiae	*Turicella otitidis*
Vagococcus fluvialis	*Veillonella parvula* group
Vibrio parahaemolyticus	*Vibrio vulnificus*
Weeksella virosa	*Yersinia enterocolitica*
Yersinia frederiksenii	*Yersinia intermedia*
Yersinia kristensenii	*Yersinia pseudotuberculosis*
* = *subgenus* sp** = *species*	

Yeasts:	
Candida albicans	*Candida auris*
Candida boidinii	*Candida dubliniensis*
Candida duobushaemulonii	*Candida famata*
Candida glabrata	*Candida guilliermondii*
Candida haemulonis	*Candida inconspicua*
Candida intermedia	*Candida kefyr*
Candida krusei	*Candida lambica*
Candida lipolytica	*Candida lusitaniae*
Candida metapsilosis	*Candida norvegensis*
Candida orthopsilosis	*Candida parapsilosis*
Candida pararugosa	*Candida pelliculosa*
Candida tropicalis	*Candida valida*
Candida zeylanoides	*Cryptococcus gattii*
*Cryptococcus neoformans var grubii**	*Cryptococcus neoformans var neoformans**
Cyberlindnera jadinii	*Geotrichum candidum*
Geotrichum capitatum	*Kloeckera apiculata*
Malassezia furfur	*Malassezia pachydermatis*

Yeasts:	
Pichia ohmeri	*Rhodotorula mucilaginosa*
Saccharomyces cerevisiae	*Trichosporon asahii*
Trichosporon inkin	*Trichosporon mucoides group*
* = variety	

FDA concludes that this device should be classified into Class II. This order, therefore, classifies the MALDI Biotyper CA System, and substantially equivalent devices of this generic type, into Class II under the generic name clinical mass spectrometry microorganism identification and differentiation system.

FDA identifies this generic type of device as: **Clinical mass spectrometry microorganism identification and differentiation system**.

> A clinical mass spectrometry microorganism identification and differentiation system is a qualitative in vitro diagnostic device intended for the identification and differentiation of microorganisms from processed human specimens. The system acquires, processes, and analyzes spectra to generate data specific to a microorganism(s). The device is indicated for use in conjunction with other clinical and laboratory findings to aid in the diagnosis of bacterial and fungal infection.

Section 513(f)(2) of the Food, Drug and Cosmetic Act (the FD&C Act) was amended by section 607 of the Food and Drug Administration Safety and Innovation Act (FDASIA) on July 9, 2012. This new law provides two options for De Novo classification. First, any person who receives a "not substantially equivalent" (NSE) determination in response to a 510(k) for a device that has not been previously classified under the Act may, within 30 days of receiving notice of the NSE determination, request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act. Alternatively, any person who determines that there is no legally marketed device upon which to base a determination of substantial equivalence may request FDA to make a risk-based classification of the device under section 513(a)(1) of the Act without first submitting a 510(k). FDA shall, within 120 days of receiving such a request, classify the device. This classification shall be the initial classification of the device. Within 30 days after the issuance of an order classifying the device, FDA must publish a notice in the Federal Register classifying the device type.

On September 29, 2017, FDA received your De Novo requesting classification of the MALDI Biotyper CA System. The request was submitted under section 513(f)(2) of the FD&C Act. In order to classify the MALDI Biotyper CA System into class I or II, it is necessary that the proposed class have sufficient regulatory controls to provide reasonable assurance of the safety and effectiveness of the device for its intended use. After review of the information submitted in the De Novo request, FDA has determined that, for the previously stated indications for use, the MALDI Biotyper CA System can be classified in class II with the establishment of special controls for class II. FDA believes that class II (special) controls provide reasonable assurance of the safety and effectiveness of the device type. The identified risks and mitigation measures associated with the device type are summarized in the following table:

Identified Risks to Health and Mitigation Measures

Identified Risks to Health	Mitigation Measures
Incorrect identification or lack of identification of a pathogenic microorganism	General controls and special controls 1, 2, 3, 4, and 5
Failure to correctly interpret test results	General controls and special control (3)
Failure to correctly operate the instrument	General controls and special controls (3)(i), (5)(iv)(H)

In combination with the general controls of the FD&C Act, the clinical mass spectrometry microorganism identification and differentiation system is subject to the following special controls:

(1) The intended use for the 21 CFR 809.10 labeling must include a detailed description of what the device detects, the type of results provided to the user, the clinical indications appropriate for test use, and the specific population(s) for which the device is intended, when applicable.

(2) Any sample collection device used must be FDA-cleared, -approved, or -classified as 510(k) exempt with an indication for in vitro diagnostic use.

(3) The 21 CFR 809.10(b) labeling must include:

(i) A detailed device description, including all device components, control elements incorporated into the test procedure, instrument requirements, ancillary reagents required but not provided, and a detailed explanation of the methodology and all pre-analytical methods for processing of specimens, and algorithm used to generate a final result. This must include a description of validated inactivation procedure(s) that are confirmed through a viability testing protocol, as applicable.

(ii) Performance characteristics for all claimed sample types from clinical studies with clinical specimens that include prospective samples and/or, if appropriate, characterized samples.

(iii) Performance characteristics of the device for all claimed sample types based on analytical studies, including, but not limited to, limit of detection, inclusivity, reproducibility, interference, cross reactivity, interfering substances, carryover/cross contamination, sample stability, and additional studies regarding processed specimen type and intended use claims, as applicable.

(iv) A detailed explanation of the interpretation of test results for clinical specimens and acceptance criteria for any quality control testing.

(4) The device's labeling must include a prominent hyperlink to the manufacturer's website where the manufacturer shall make available their most recent version of the device's 21 CFR 809.10(b) labeling, which must reflect any changes in the performance characteristics of the device. FDA must have unrestricted access to this website or manufacturers must provide this information to FDA

through an alternative method that is considered and determined by FDA to be acceptable and appropriate.

(5) Design verification and validation must include:

(i) Any clinical studies must be performed with samples representative of the intended use population and compare the device performance to results obtained from an FDA accepted reference method and/or FDA accepted comparator method, as appropriate. Documentation from the clinical studies must include the clinical study protocol (including predefined statistical analysis plan, if applicable), clinical study report, and results of all statistical analyses.

(ii) Performance characteristics for analytical and clinical studies for specific identification processes for the following, as appropriate:

(A) Bacteria
(B) Yeasts
(C) Molds
(D) Mycobacteria
(E) Nocardia
(F) Direct sample testing (e.g., Blood culture)
(G) Antibiotic resistance markers
(H) Select Agents (e.g., pathogens of high consequence)

(iii) Documentation that the manufacturer's risk mitigation strategy ensures that their device does not prevent any device(s) with which it is indicated for use, including incorporated device(s), from achieving their intended use (e.g., safety and effectiveness of the functions of the indicated device(s) remain unaffected).

(iv) A detailed device description including the following:

(A) Overall device design, including all device components and all control elements incorporated into the testing procedure.

(B) Algorithm used to generate a final result from raw data (e.g., how raw signals are converted into a reported result).

(C) A detailed description of device software, including, but not limited to, validation activities and outcomes.

(D) Acquisition parameters (e.g., mass range, laser power, laser profile and number of laser shots per profile, raster scan, signal-to-noise threshold) used to generate data specific to a microorganism.

(E) Implementation methodology, construction parameters, and quality assurance protocols, including the standard operating protocol for generation of reference entries for the device.

(F) For each claimed microorganism characteristic, each organism must have a minimum of five reference entries (including the type strain for microorganism identification) or, if there are fewer reference entries, a clinical and/or technical justification, determined by FDA to be acceptable and appropriate, for why five reference entries are not needed.

(G) All type strains and at least 20 % of the non-type strains of a species detected by the device must be characterized by DNA sequence analysis or, if there are fewer strain sequences, then a clinical and/or technical justification, determined by FDA to be acceptable and appropriate, for the reduced number of strains sequenced must be provided.

(H) As part of the risk management activities, an appropriate end user device training program must be offered as an effort to mitigate the risk of failure from user error.

Section 510(m) of the FD&C Act provides that FDA may exempt a class II device from the premarket notification requirements under section 510(k) of the FD&C Act, if FDA determines that premarket notification is not necessary to provide reasonable assurance of the safety and effectiveness of the device type. FDA has determined that premarket notification is necessary to provide reasonable assurance of the safety and effectiveness of the device type and, therefore, the device is not exempt from the premarket notification requirements of the FD&C Act. Thus, persons who intend to market this device type must submit a premarket notification containing information on the clinical mass spectrometry microorganism identification and differentiation system they intend to market prior to marketing the device.

Please be advised that FDA's decision to grant this De Novo request does not mean that FDA has made a determination that your device complies with other requirements of the FD&C Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the FD & C Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the FD & C Act); 21 CFR 1000-1050.

A notice announcing this classification order will be published in the Federal Register. A copy of this order and supporting documentation are on file in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852 and are available for inspection between 9 a.m. and 4 p.m., Monday through Friday.

As a result of this order, you may immediately market your device as described in the De Novo request, subject to the general control provisions of the FD&C Act and the special controls identified in this order.

For comprehensive regulatory information about medical devices and radiation-emitting products, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). 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

(http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

If you have any questions concerning the contents of the letter, please contact Yvonne Shea at 301-796-0576.

Sincerely,

Tamara V. Feldblyum -S for

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