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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
BEFORE THE TRADEMARK TRIAL AND APPEAL BOARD

Proceeding	91194218
Party	Defendant Meridian Bioscience, Inc.
Correspondence Address	J MICHAEL HURST KEATING MUETHING & KLEKAMP 1 E 4TH ST, STE 1400 CINCINNATI, OH 45202 3752 UNITED STATES mhurst@kmklaw.com, trademarks@kmklaw.com
Submission	Testimony For Defendant
Filer's Name	J. Michael Hurst
Filer's e-mail	mhurst@kmklaw.com
Signature	/J. Michael Hurst/
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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
BEFORE THE TRADEMARK TRIAL APPEAL BOARD**

ILLUMINA, INC.,	)	
	)	Opposition No. 91194218 (parent)
	)	Ser. No. 77/768176
Opposer/Petitioner,	)	
	)	Opposition No. 91194219
-v-	)	Ser. No. 77/775316
	)	
MERIDIAN BIOSCIENCE, INC.,	)	Cancellation No. 92053479
	)	Reg. No. 3887164
Applicant/Registrant.	)	
	)	Cancellation No. 92053482
	)	Reg. No. 3868081
	)	

**DECLARATION OF KENNETH J. KOZAK**

I, Kenneth J. Kozak, hereby state and declare as follows:

1. My name is Kenneth J. Kozak, I am over eighteen (18) years of age, and I have personal knowledge of the facts stated in this Declaration.

2. I graduated from Miami University in 1976 with a bachelors degree in Microbiology.

3. I am employed by Meridian Bioscience, Inc. ("Meridian") as its Chief Technical Officer. I have been with Meridian since 1987, starting as a Senior Research Associate in Product Development and working my way up to my current position. Among other positions, I was Meridian's Vice President, Research and Product Development, from May 1999 to May 2007. I have held my current position as Chief Technical Officer since May 2007.

4. In connection with my duties and responsibilities for Meridian, I supervise and direct Meridian's Clinical, Verification, and Product Support teams. In performing my duties at Meridian, I work closely with clinical laboratories that typify Meridian's customers for diagnostic kits (including ILLUMIGENE kits) and diagnostic machines (including ILLUMIPRO and ILLUMIPRO-10). I have personally managed clinical trials for Meridian's new products in such

clinical laboratories, and I have considerable experience meeting with the personnel in those laboratories who purchase and use ILLUMIGENE kits. I have gained substantial personal knowledge, through my work, of our customers' organizational structures and needs. I have also been involved in planning product launches and am made aware of Meridian's marketing strategies, branding and product literature in the course of my job duties. I am also personally aware of Meridian's competitors in the diagnostic field and the products that they offer.

### **The Differing Consumers of Meridian's Products versus Illumina's**

5. Meridian has been in the clinical diagnostics field since its founding in 1977. Meridian has been a leader in the field of clinical diagnostics long before it pioneered its first *C. Difficile* enzyme immunoassay in 1992.

6. Within the broader category of infectious disease, Meridian's clinical diagnostic products are focused in the microbiology space. Meridian's "molecular diagnostic" products test for and identify the microbial invader; Meridian's products do not focus on or have any relationship with the genetics of the *human* patient.

7. There are typically several specializations within a Clinical Diagnostics Laboratory, including for example Microbiology, Chemistry, Hematology, Special Chemistry, and/or others. Each department has a manager or supervisor.

8. The manager/supervisor of each department identifies products needed for the department's work. The manager/supervisor gives the product description, or often a catalog number and supplier name, to a purchasing agent or the laboratory's purchasing department. The purchasing agent or purchasing department identifies a supplier for the product (if none was specified) and places an order under a pre-negotiated contract with the supplier that includes set pricing. Put differently, a supplier like Meridian will have already marketed its products and product capabilities to both the purchasing department and the manager/supervisor, and a contract will have already been entered into between Meridian and

the relevant purchaser, before the purchasing department goes to place an order. As a result, laboratory managers/supervisors and purchasing departments or agents are often aware of vendors and their available product lines from being contacted personally by sales representatives from the vendors. In this context, Meridian and Illumina are the “vendors” or “suppliers.”

9. Purchasing departments typically support the selection of manufacturers and vendors and negotiate contracts with them under which the individual orders for products are placed. The managers/supervisors of the laboratory departments request the products that are needed, but the purchasing personnel of the laboratory typically help select the vendor to supply the products and set up the contracts if more than one vendor provides the same product.

10. When there is more than one vendor of the type of product that a purchasing agent needs to procure, he or she will usually solicit bids from the multiple vendors that might offer that product and select the best overall option based on a number of different criteria including performance characteristics of the product and price.

11. The actual consumers, then, of clinical diagnostic products in the microbiology space – the space that Meridian targets as its primary market for its ILLUMIGENE and ILLUMIPRO products – are typically the Clinical Directors of clinical diagnostic laboratories, who acquire such products often at the request of personnel in the laboratories’ “Infectious Disease” or “Microbiology” departments or with the purpose to supply them to such departments. Since 1977, Meridian has sold diagnostic products to clinical diagnostic laboratories to assist them in diagnosing infectious diseases – specifically, microbiological infectious diseases.

12. The people within the clinical diagnostic laboratories who use Meridian’s clinical diagnostic products are typically situated in a “Microbiology” or “Infectious Disease” group or department. The products sold into this environment must be FDA-cleared for “*in vitro*” use, often referred to as “IVD” products. The ultimate decision-maker for buying Meridian’s clinical

diagnostic products – including Meridian’s ILLUMIGENE products – is typically the head of a clinical diagnostic laboratory, i.e. the Clinical Director (sometimes with input or required consent or “sign-off” from financial personnel such as a Purchasing Department, Materials Management department, or CFO or Director of Finance for the laboratory)

13. The Clinical Director is typically one of two (2) “director-type” positions within the larger laboratory setting of a hospital or reference lab environment. The other director at this level is the “Research Director.” Meridian does not market or sell to, and rarely if ever has any interaction with, the Research Director in a hospital or reference lab setting. As a result, to say that Meridian markets and sells its products to “hospital labs” or “reference labs” is an oversimplification of how the relevant consumer market is structured. In reality, there are two separate and distinct “touch-points” within any “hospital lab” or “reference lab;” the research lab and the clinical diagnostic lab. Meridian’s marketing and sales focus is only to one of those two distinct touch-points – the clinical diagnostic lab.

14. While hospitals and reference labs generally do purchase microbiological clinical diagnostic products, those products are purchased specifically for and by the microbiology departments within the clinical diagnostic labs of such hospitals and reference labs. Put another way, the consumers within a hospital or laboratory who interact with the relevant products in this case – who select products and drive the purchase of products – within each of those markets can be and, in actuality, are very different and very specific.

15. The relevant consumers in the clinical diagnostic laboratories of hospital labs and reference labs have been familiar with Meridian’s infectious disease clinical diagnostic products for more than twenty-five (25) years, and certainly well prior to 2008. Meridian has spent a great deal of money advertising and selling its clinical diagnostic products specifically to such consumers. In 2009, Meridian spent almost \$350,000 in marketing diagnostic products in the United States, with approximately \$250,000 of that expenditure dedicated to promoting

ILLUMIGENE products. The marketing and promotion for ILLUMIGENE's initial launch cost approximately \$100,000, which included both advertising and promotional funds. In 2012, Meridian spent about \$15,000 per month in advertising ILLUMIGENE products in the United States, and Meridian spends an additional \$75,000 annually in trade show promotion of Meridian. Attached as Exhibit A is a copy of Meridian's P&L for the ILLUMIGENE product for FY 2010 and FY 2011 which summarizes its sales revenue and marketing spend for the ILLUMIGENE product during those years. Given Meridian's marketing and sales strategy and the strict separation of the clinical and research disciplines within any given hospital lab or reference lab, the relevant consumers on the research side of such labs – i.e. the consumers of Illumina's products - probably have very little if any familiarity with Meridian. Conversely, Meridian's relevant consumers on the clinical diagnostics side of such labs probably have very little if any familiarity with Illumina.

**Meridian's Competitors in the Clinical Diagnostic Space**

16. Illumina is not and has not been a competitor of Meridian in the diagnostics field and does not offer diagnostic goods to the same consumers as Meridian. Because of the line of business Illumina is in, Illumina's consumers, where they otherwise overlap in the larger hospital lab and reference lab channel of trade, are those on the research side of such labs. Outside of this channel, Illumina also markets to and serves dedicated research institutions where human genomes are sequenced on a massive scale for, among other things, drug development purposes. Meridian has no involvement in that space whatsoever.

17. In working at Meridian for approximately 27 years, I have encountered many competitors and other companies who offer clinical diagnostic products and services, but I have never once heard of Illumina operating in the clinical diagnostic space, never once heard a customer refer to Illumina or its products, and never once encountered Illumina as a competitor. Specifically, Meridian's main competitors currently in the clinical diagnostic space are

BD/GeneOhm, Prodesse, Alere, Quidel, and Cepheid. Attached as Exhibit B are representative documents summarizing how the ILLUMIGENE product compares to the offerings from Meridian's competitors across various, relevant performance metrics. These competitors were identified by Meridian during the very early stages of the development of the ILLUMIGENE product, and competitor branding was considered when developing the ILLUMIGENE branding as shown in the attached Exhibit C.

18. I am personally familiar with Meridian's competitors in the diagnostic field because my work leads me to encounter competitors in a few different ways. For decades, I have had responsibilities related to the development of new diagnostic products, and the prioritization and funding of the research and development of such products is always pursued in the context of market research about the clinical need, and the other products that are currently fulfilling that need, if any. Moreover, in managing clinical trials and supervising the management of clinical trials, Meridian compares its products to the existing standard(s) of care within the clinical laboratories – testing to see if Meridian's products are as effective (or better) than the other available clinical solutions, and whether they are as safe (or safer). This, also, leads me to be keenly aware of the other companies that operate in the clinical diagnostics market.

19. In 2008, Illumina did not offer any FDA-cleared clinical diagnostic products whatsoever and did not offer any products or services related to infectious diseases or microbiology. Rather, Illumina was a company that offered human genetic sequencing services and supplied equipment and components for companies and laboratories to construct their own "assays" (scientific tests). Those products and services are directed toward and used by an entirely different category of consumers from consumers of FDA-cleared clinical diagnostic products.

20. The consumers of Illumina's products have been distinct from the consumers of Meridian's products since Illumina's inception, and were certainly distinct in 2008 and 2009. Today, the relevant consumers of Meridian's and Illumina's products remain distinct notwithstanding Illumina's recent addition of new products.

21. Since its inception, and certainly in the 2008-2009 time frame, Illumina's market for its human genetic services, components, and equipment for assays included research laboratories, *not* infectious disease clinical diagnostic laboratories. These research laboratories would purchase Illumina's human genetics services by sending away samples to be analyzed, and/or would buy components and equipment from Illumina to construct in-house assays ("Lab Developed Tests" or "LDTs"). None of Illumina's products at the time was FDA-cleared, IVD products. Rather, all of Illumina's products were approved for "Research Use Only," often referred to as "RUO" products. RUO products may not be used in clinical diagnostic laboratories to diagnose patients unless the lab itself performs its own validation studies – studies which Illumina by its own admission takes no part in. Illumina's market also includes academic laboratories, government research entities, and large pharmaceutical companies who do substantial research; none of these entities has a clinical laboratory component or uses clinical diagnostic products of the type that Meridian markets.

22. It is inaccurate for Illumina to broadly assert that its consumers were or are part of the "diagnostics" market. The only connection to "diagnostics" that would be possible in this context exists in very few laboratories, and does not involve any overlap between the *consumers* of clinical diagnostic products and the *consumers* of Illumina's products. In a few research laboratories, researchers create their *own, in-house* LDTs. They may use Illumina's products, along with components from many other suppliers, to *build* these assays. But those researchers and the people working with them are not buying "ready-made" clinical diagnostic products such as Meridian's – they are buying components and then *building* in-house

diagnostic assays themselves. Asserting that Illumina's components and equipment compete with Meridian's clinical diagnostic test kits based on this logic would be much like saying a bolt manufacturer competes with an automobile manufacturer because bolts are used to build cars.

23. And just as a consumer would not expect a bolt manufacturer to begin making cars, the personnel working in research laboratories who used Illumina's services and products since Illumina's inception, and certainly in 2008 and 2009, would not have expected Illumina to begin selling "ready-made" IVD diagnostic products. Personnel within clinical diagnostic laboratories in 2008 and 2009 would probably never have even heard of Illumina at all because *Illumina made no products for such personnel to use or purchase.*

24. I have reviewed the deposition testimony of Naomi O'Grady, an employee of Illumina and who gave a statement in this case on behalf of Illumina. Ms. O'Grady, at her deposition, testified that when laboratories use Illumina's products to make diagnostic LDTs, the output is a "test report" sent by the laboratory to the ordering physician, and that Illumina would not review the report, would have no control over the report's content, and would have no control over the report's branding. (O'Grady Deposition, at 92-94) I agree with this part of Ms. O'Grady's testimony, and it means that Illumina's RUO components or equipment used in LDTs would not have given Illumina any market presence or reputation whatsoever in the clinical diagnostics field. The entity providing and branding the diagnostic answer, to the extent this answer is "branded" at all, would always be the laboratory or the institution who has built the LDT – not Illumina – and the recipient of that diagnostic answer would not be aware of the source of any of the equipment used in arriving at the answer.

25. Put differently, and by way of example, if a clinician were to request Johns Hopkins to run a test on a patient sample in its clinical diagnostic laboratory, Johns Hopkins would communicate the results of the test to the clinician in the form of a report. This "deliverable" would carry Johns Hopkins branding, if it carried any branding at all, and nowhere

on this report would Johns Hopkins refer to or indicate the source or the name of the components it used to build its LDT that derived the information appearing in the report. As an analogy, the LDT phenomenon is not unlike the situation where one hires a contractor to build a bathroom in one's home. The consumer in this analogy is not aware of whether the contractor used Black & Decker or Stanley tools to build the bathroom; he is only aware that at the end of the job, he now has a bathroom. As a result, it simply would not make sense to say that the sale of RUO products to laboratories that were making LDTs, in and of itself, somehow puts Illumina in "the diagnostics market." It does not.

26. Illumina's purchase of Epicentre Technologies Corporation, the maker of "DisplaceAce" is only a further example of this dynamic, i.e., the difference between the consumers of Meridian's products and the consumers of Illumina's products. DisplaceAce is a component – a bolt for the car – not a test or kit that can be used to determine whether a particular patient is afflicted with a particular infectious disease. Someone trying to diagnose the presence of an infectious disease in a clinical diagnostic laboratory cannot use DisplaceAce by itself for this purpose, nor would such person be aware whether DisplaceAce was being used as a component within a kit.

27. In November 2008, Meridian applied to register its ILLUMIGENE mark for diagnostic *kits* – FDA-cleared "ready-made" IVD assays to diagnose infectious diseases in Clinical Diagnostic Laboratories. In April 2009, Meridian applied to register its ILLUMIGENE MOLECULAR SIMPLIFIED & design mark for the same products directed to the same market. At the time of Meridian's filings, consumers in the clinical diagnostic laboratory would not have had any awareness of Illumina or its products because Illumina did not offer any products they could use; Illumina had no IVD products in its product portfolio, but rather only RUO products for use by consumers working in research laboratories.

28. Even today, the consumers of Meridian's clinical diagnostic products and the consumers of Illumina's products are not the same. From its website, Illumina's product line still appears to consist of human genetic services and components and equipment for assays. As discussed above, consumers of such services and products are research laboratories, not clinical diagnostic laboratories. It is true that Illumina received FDA approval on April 28, 2010 for the "Illumina VeraCode Genotyping Test for Factor V and Factor II" ("VeraCode Genotyping Test"), but Illumina's website does not appear to market that product, and I have not encountered it in my interactions with consumers in clinical diagnostic laboratories or through my or my staff's attendance at tradeshow in the industry. My understanding is that Illumina has discontinued that product and that it is no longer available.

29. It is also true that Illumina has two current IVD products called the MiSeqDx Cystic Fibrosis 139-Variant Assay and the MiSeqDx Cystic Fibrosis Clinical Sequencing Assay (the "MiSeqDx Cystic Fibrosis Assays"). But the FDA clearance for the MiSeqDx Cystic Fibrosis Assays did not issue until late 2013, years after the 2008-2009 time period.

30. Even if Illumina were given the benefit of the doubt about having an IVD product in the marketplace with its VeraCode Genotyping Test or MiSeqDx Cystic Fibrosis Assays, the fact remains that the consumers of those assays are very different from the consumers of Meridian's infectious disease diagnostic products. The VeraCode Genotyping Test and MiSeqDx Cystic Fibrosis Assays test *human genes* in an effort to identify genetic markers/mutations. Meridian's molecular diagnostic products attempt to identify microbial pathogens, not particular sequences of human DNA.

31. The personnel who would perform tests using Illumina's VeraCode Genotyping Test or MiSeqDx Cystic Fibrosis Assays are found in the clinical diagnostic laboratories' "Hematology," "Oncology," or "Pathology" groups or departments. Such groups or departments are usually separate from the "Infectious Disease" or "Microbiology" departments or groups who

are the consumers of Meridian's clinical diagnostic products. Purely by the nature of the answers each department is seeking in the analysis of a particular sample, the work and tools of the two kinds of clinicians will not typically overlap.

**The High Level Of Sophistication And Attention Of Meridian's and Illumina's Consumers**

32. Although they are distinct groups of people, everyone involved in purchasing and using either Meridian's clinical diagnostic products or Illumina's services and products has an extremely high level of education and sophistication.

33. The user of a Meridian clinical diagnostic product is an educated and highly trained person within an "Infectious Disease" or "Microbiology" department or group in a Clinical Diagnostic Laboratory. He or she would usually have a bachelor's degree in a scientific field and training as a Medical Technologist.

34. The user of Illumina's VeraCode Genotyping Test or MiSeqDx Cystic Fibrosis Assays, to the extent that those products were/are on the market, would also be educated and highly trained. He or she would usually have a bachelor's degree in a scientific field and training in molecular research. The needs of the users of these products would drive the clinical diagnostic laboratory's decision to purchase them. Both of these types of users pay close attention to the product they are selecting and using. The users' ability to use the products at issue are restricted by FDA regulations pertaining to the intended uses of the products, and the users also must take great care because they are diagnosing medical conditions of patients.

35. The decision-maker in setting up a pricing contract with Meridian for purchasing Meridian's clinical diagnostic products, including ILLUMIGENE products, and in this case the relevant consumer of Meridian's products, is typically a Clinical Director, the head of a clinical laboratory. The people in that position typically have even more education and credentials, usually including a Masters degree or Ph.D. They typically have a great deal of experience in clinical laboratories and sophisticated knowledge of the industry. Clinical Directors pay close

attention to the pricing contracts entered into by their laboratories and the products they make available to their personnel through those contracts.

36. The Clinical Director, and the purchasing agents that work with him, are both very familiar with what diagnostic tests are available for various infectious diseases and what companies provide or offer those tests. It is their job to know, and although some of the product names are complex or somewhat similar to one another, they are repeated with enough frequency that they are thoroughly learned.

37. For Clinical Directors, it is a requirement of their job to be well informed about the products that are available, the names of those products, and the companies that offer them.

38. Both the Clinical Director and the purchasing agents working with him pay close attention to the products they buy, the sources of those products, and the price per test. In all circumstances, these individuals are highly knowledgeable of which company (by name) can source a particular product.

39. Further, it typically requires multiple meetings and/or calls between Meridian and its customers to enter into a contract for Meridian's clinical diagnostic products. Meridian and the relevant consumer will engage in significant negotiation over products, volumes, and prices. At all times, Meridian's customers are fully aware of what types of products Meridian can offer and what types it does not offer, as well as the names of those products.

40. I cannot over-emphasize the fact that during these meetings and/or calls, the relevant consumer understands that he is interacting *with Meridian Bioscience* to determine which of Meridian's products, including without limitation the ILLUMIGENE product, are suitable for the consumer's needs. Similarly, the relevant consumer understands that he is interacting *with Illumina* to determine which of Illumina's products, including without limitation its MiSeq, MiSeq, and TruSeq products, might be suitable for the consumer's needs. In this context, it is

the *company's* brand that is foremost in the consumer's mind – not the names of the products that the company offers to meet a particular need.

41. The purchasers of Meridian's diagnostic products are not only very sophisticated, but they seek to answer a very detailed set of questions prior to purchasing. Lab Directors who make purchasing decisions examine in detail, among other things:

- the product's diagnostic target
- the product's intended use
- the product's sensitivity
- the product's specificity
- the product's price
- whether the instrument to read the product costs money to purchase and/or run, and how much
- the sample type the product uses (e.g., throat swabs vs. nasal swabs)
- the type of media used for transfer of the sample or other component
- the available insurance reimbursement
- turnaround time of a result
- required education and training of the technical staff who will run the test
- whether the product will fit with the lab's current work flow.

In conducting this detailed analysis, it would be absurd to even suggest that the Lab Director would look no further than the name(s) appearing on the product and conclude, on that basis, that one product is similar to, related to, compatible with, or a substitute for, another.

42. The consumers of Illumina's human genetics services, and Illumina's components and equipment for assays, are *researchers* in research laboratories, hospital research labs, academic laboratories, government research entities, or large pharmaceutical companies. Such personnel usually have a bachelor's degree in a scientific field and training in

molecular and genetic research, and often have doctorate-level scientific degrees. They are highly trained scientists and laboratory technologists who pay close attention to the equipment, components and services that they use, in part because their results must be precise, verifiable and reproducible. They typically disclose the equipment and components that they use when they write scientific papers that include their methodologies.

#### **The Substantial Price Differences Between Meridian's Products And Illumina's Products**

43. Even if the same consumer encountered both Meridian's clinical diagnostic products (such as the ILLUMIGENE molecular diagnostic kits and the ILLUMIPRO instruments that read/interpret the test results) and Illumina's products (such as Illumina's VeraCode Tests and the BeadXPress equipment that reads them, or MiSeqDx Cystic Fibrosis Assays and the MiSeq platform that reads them), they would not be likely to confuse the source of the products, in part because of the extreme price difference between them.

44. Meridian's ILLUMIGENE molecular diagnostic products are marketed for between \$1,250 and \$3,000 per kit of 50 tests (\$25 to \$60 per test). Meridian's ILLUMIPRO instruments ***are included at no additional charge with the purchase of the initial kit.*** The pricing strategy for Meridian's ILLUMIGENE and ILLUMIPRO products was carefully thought out from the beginning of the product's development. Attached as Exhibit D is the output of a study Meridian commissioned during development to determine the best possible price point for its ILLUMIGENE and ILLUMIPRO products. Documents summarizing Meridian's resulting and current pricing strategy for its ILLUMIGENE and ILLUMIPRO products are attached as Exhibit E.

45. I understand from Illumina's website and the deposition testimony of Illumina's employees Karen Possemato and Naomi O'Grady: (a) that Illumina's BeadXPress readers, used to interpret the VeraCode test results at the time those tests were on the market, were priced at about \$95,000; (O'Grady Deposition, at 104, and Possemato Deposition, at 54); and

(b) that Illumina's MiSeqDx platform, used to interpret the MiSeqDx Cystic Fibrosis Assays, is priced at about \$125,000. (O'Grady Deposition, at 22-25). This price does not include the cost of the components used in the actual test itself. Clearly a purchaser would be very likely to note the dramatically different order of expense between the two companies' products, even apart from the major, obvious differences in what the products are and what they do, as discussed above.

#### **Prefixes In Product Names In the Medical Products Field**

46. I understand Illumina argues that the prefix "ILLUMI" is somehow more noticeable or more entitled to weight than the suffix that follows it in ILLUMIGENE, ILLUMIPRO, and ILLUMIPRO-10. Based on my extensive experience in the field of medical products and knowledge of competitive diagnostic products, I disagree with Illumina's position.

47. In the medical field, the prefixes of product names are often the same or very similar across different companies who compete with each other. For example, "Immuno" is an extremely common prefix used in the product names of many different companies, such as the Quest Immunocap, the Allere ImmunoComb, and the Meridian ImmunoCard. Because of this pattern of concentrations on the same prefixes, consumers of medical products do not merely focus on the prefixes of words more so than, or at the expense of, the suffixes and/or the entirety of the word, or give the prefixes special weight or attention. If anything, given the consequences of using the wrong product by casually focusing on only part of a product name, consumers of medical products are attuned to the need to take in and consider the entirety of the product names.

48. The individuals responsible for purchasing decisions in the relevant channels of trade have a keen awareness of the company names used by the suppliers of the products they purchase. When they request or order products, they focus on and use the name of the supplier of the product as well as the full name of the product itself. They appreciate that

mistakes in medical supply orders are potentially very costly, and they proceed carefully and according to the purchasing process; not impulsively or in a great hurry.

49. An especially clear example of the dynamic described above can actually be found in another product name prefix that *Illumina itself* began using years after Meridian began using it. Meridian has registered the marks TRU RSV, TRU FLU, TRU EBV-M, and TRU EBV-G, TRU BLOCK, TRU LEGIONELLA, and TRU HSV 1 AND 2 IGG. The earliest uses of these marks were in 2006 and 2007 and the earliest registrations of them were in 2008. All of these registrations are in International Class 5, and recite “diagnostic tests” or “diagnostic test kits.”

50. Subsequently, Illumina has registered the mark TRUSEQ, with a claimed first use date of November 22, 2010, and TRUSIGHT, with a claimed first use date of September 1, 2012, and now owns an allowed application for TRUGENOME, a mark which it is currently using. Illumina’s TRUSEQ registration covers “reagents and reagent kits” for use in “diagnostic and clinical research”; “product development” within the “fields of scientific, diagnostic and clinical research”; and “scientific instruments” within the “fields of scientific, diagnostic and clinical research,” and its TRUSIGHT registration covers “reagents, enzymes, and nucleotides for nucleic acid sequencing for medical purposes.” Similarly, its TRUGENOME application (and its use of the mark) covers “nucleic acid sequencing and analysis services for medical purposes.”

51. It is not surprising to me that Illumina did not view the “TRU-” prefix shared by its and Meridian’s marks as particularly problematic for both entities to be using or think that its TRU- mark was too close to Meridian’s TRU- marks based on Meridian’s prior registration and use of several marks with this same prefix. Not only were the products different, but Illumina’s mark had a different suffix, rendering its TRUSEQ, TRUSIGHT, and TRUGENOME marks sufficiently different from Meridian’s TRU RSV, TRU FLU, TRU EBV-M, and TRU EBV-G, TRU BLOCK, TRU LEGIONELLA, and TRU HSV 1 AND 2 IGG.

52. Illumina's apparent position in using and registering its TRU-formative marks, notwithstanding Meridian's prior use and registration of its own TRU-formative marks, makes sense. Its apparent reversal of its position in the current dispute does not make sense. The parties' respective TRU-formative marks cover *the same types of goods and services that are at issue in this proceeding*. Illumina's own efforts in selecting, applying for, using, and registering its TRU-formative marks directly contradict the position it is trying to assert in this proceeding. Consumers of medical and medical research products are careful and sophisticated, and they do not give undue weight to just the beginnings of product names, or ignore the endings.

53. I am not aware of any instances of actual confusion between Illumina's TRU-formative marks and any of Meridian's TRU-formative marks, nor would I expect there to be any confusion, despite the fact that both parties' TRU-formative marks are product marks; not house marks.

**There Is No Actual Confusion Between Meridian's Trademarks And Illumina.**

54. To my knowledge, after extensive marketing of Meridian's ILLUMIGENE clinical diagnostic products and the ILLUMIPRO readers over the course of 6+ years, there have been *no* reported incidents of confusion between these products and Illumina or its products, and had there been instances of actual confusion, I would be aware of them.

55. Meridian first used the ILLUMIGENE name in connection with clinical trials in December 2008. Meridian has promoted ILLUMIGENE under that name since then, at all times, including at trade shows, individual meetings and customer presentations. Representative examples of Meridian's use of its ILLUMIGENE and ILLUMIPRO brands are attached as Exhibit F. Trade shows where Meridian introduced its ILLUMIGENE products to prospective purchasers included: (a) the 2009 Clinical Virology Symposium ("CVS") conference held 19-22 April 2009 in Daytona Beach, Florida; (b) the 2009 American Society for Microbiology ("ASM") conference held 16-18 May 2009 in Philadelphia, Pennsylvania; (c) the 2009 American

Association for Clinical Chemistry (AACC) conference held 19-23 July 2009 in Chicago, Illinois; and (d) the 2009 Association for Molecular Pathology (AMP) conference held 19-22 November 2009 in Orlando, Florida. Internal summaries of Meridian's participation at these trade shows are attached as Exhibit G. Photographs representative of Meridian's presentation of the ILLUMIGENE brand at these trade shows are attached as Exhibit H.

56. I understand that Meridian's public marketing of its ILLUMIGENE and ILLUMIPRO products at these trade shows, in particular the 2009 CVS and 2009 ASM conferences, predates Illumina's filing of its ILLUMINADX application – the first trademark application filed by Illumina which made reference to "clinical diagnostic" products or services.

57. Since obtaining FDA clearance and launching ILLUMIGENE products in July of 2010, Meridian has promoted them through trade shows, advertisements in trade magazines, promotion on Meridian's website, individual meetings, brochures, and customer presentations. Meridian has sold ILLUMIGENE products to more than 700 different accounts in the United States. Beyond those who have actually purchased ILLUMIGENE products, over 4000 potential consumers have been exposed to the ILLUMIGENE and ILLUMIPRO products through our marketing efforts. I estimate that Meridian's ILLUMIGENE advertising and promotion has reached almost 100% of the possible accounts in the marketplace, particularly since ILLUMIGENE is advertised in trade publications that reach virtually every clinical laboratory. With all of this marketing and sales activity, there have still been absolutely no accounts of purchasers or others confusing the source of ILLUMIGENE as being Illumina, nor confusing Meridian as being the source of any Illumina products.

58. In my position, I would expect to hear about any reported confusion from a consumer related to our trade shows or sales in clinical laboratories.

**Attendance At Broad-Based Trade Shows In This Industry Does Not Mean There Is Any Overlap In Consumers.**

59. I understand Illumina argues that simply because it has attended some of the same trade shows as Meridian, the consumers for both Illumina's and Meridian's products are somehow the same. However, in the medical industry, attendance at broad-based trade shows does not mean, in and of itself, that all the companies at the shows are competitors or even sell products to the same consumers.

60. For example, the American Association for Clinical Chemistry Annual Meeting is a broadly-focused trade show where the vast majority of products and services on display, including such things as blood analyzers and gas analyzers, have nothing to do with the clinical diagnostics field. Further, many products on display are designated for Research Use Only ("RUO" products).

61. Similarly, the Association for Molecular Pathology trade show, although it is in the molecular pathology field generally, includes many companies who offer human genetic and polymorphism products and services which are not similar to Meridian's clinical diagnostic products and which do not have the same users. The same is true of the Clinical Lab Expo and the Deutsche Bank Annual Health Care conferences: a wide array of products and services are presented at those conferences to a wide variety of professionals and potential consumers, and simply attending or having a marketing presence at them does not mean that companies are marketing to the same consumers or are competitive with one another.

62. In short, Meridian's clinical diagnostic products are marketed and sold to different consumers than Illumina's products and services, and mere attendance at some of the same trade shows does not change that.

63. What is more, the fact that Illumina and Meridian have attended the same trade shows *and that the companies have experienced absolutely no confusion from the attendees of*

*those trade shows* only goes to show that the customers and potential customers are *not* confused and are by no means *likely* to be confused between the trademarks discussed above.

**If A Company Planned To Market Products In The Diagnostic Market, It Would Design And Manufacture Those Products Under Strict, FDA-Regulated "Design Control" Standards From The Outset.**

64. I understand that Illumina may argue in this proceeding that it always intended to progress seamlessly from RUO products to IVD products and that such progression was natural and expected. I have reviewed the deposition testimony of Illumina's employee Naomi O'Grady, and portions of that testimony lead me to conclude, based on my experience in the diagnostics industry, that Illumina's attempt to move into the diagnostic market was by no means natural or expected, and instead was an unexpected pivot.

65. To explain, I need to discuss the term "design control," which is a way of designing products to meet the rigorous regulations of the FDA for IVD products.

66. To obtain FDA clearance, IVD products must be designed, manufactured and verified according to very strict requirements, sometimes referred to as being made "under design control." The FDA requirements include, but are not limited to:

- Design and Development Planning: This defines the activities required for the new product design. This must be updated throughout the design development process.
- Design Inputs/Design Outputs: We need to establish and maintain documents which adequately evaluate that a design output meets the requirements for the design input.
- Design Verification/Design Validation: We are required to maintain procedures which verify or validate the products design.
- Design Transfer: We need to develop procedures which insure that device design is correctly translated into product specification
- Design History File ("DHF"): All documentation must be contained or referenced in this file, including any design changes.
- qualifying vendors/suppliers to be certified to ensure that their products and quality systems are suitable for our design and conform to regulations

- testing and validation of various kinds, including the stability of the product as a whole as well as the stability of the individual components
- developing and maintain manufacturing specifications for every component of an assay
- end user interface validation to ensure that the product can be run correctly and generate appropriate results
- mitigation of potential problems in risk assessment (FEMA)
- ensure that all software is compliant
- conducting clinical trials on the products and submitting that information to the FDA to obtain clearance to sell in the United States
- keeping detailed records of all of the above activities in the DHF and being prepared for an FDA audit

These requirements are set forth in 21 CFR §8.20.1 et seq. Examples of some of the many, detailed, internal design control documents Meridian produced during the development of its ILLUMIGENE and ILLUMIPRO products are attached as Exhibit I.

67. At pages 169 to 174 of Ms. O’Grady’s deposition, she discusses a product that Illumina had designed and built named iScan. Ms. O’Grady testified that in July 2009, iScan was being sold and labeled as an RUO product. She then testified that in making a plan to build an IVD iScan system that could be submitted to the FDA in a 510(k) submission, Illumina would have to do something called “document remediation,” or alternatively a new scanner would need to be designed under “design control.” (O’Grady Deposition, at 168-174)

68. “Document remediation” in this context means a process of taking an existing, designed product, and then going back through all of its parts, suppliers and processes to validate them to the same extent as if they had been originally designed under FDA-mandated “design control.” It is not a simple process, and carries with it a great amount of risk and cost. Even assuming that every part, vendor, and process coincidentally meets the regulatory requirements, the process would carry a large cost, as each aspect must be re-validated and re-

qualified. On top of that, there is a very significant risk that the parts, vendors, and processes, when tested, will not meet the regulatory requirements. If that is the case, not only would the non-qualifying aspect need to be replaced with one that can be sufficiently validated, but also the parts and processes that interact with the non-qualifying would need to be re-designed and re-validated to accommodate the change.

69. For these reasons, designing a product for RUO purposes originally, and then doing “document remediation” to make the design records suitable for submission to the FDA for potential clearance as an IVD product, would likely cost 1.5x to 2x what it would cost to design a product under “design control” from the beginning (and perhaps much more). And there is a risk that a complex problem with a vendor, process, or part would arise that would make it many times more expensive.

70. Because of the costs and risks involved with “document remediation,” a reasonable company that planned *from the beginning* to make an IVD product would not design it outside of “design control” principles. If a reasonable company is considering “document remediation” for a product, it is because they never intended to make it an IVD product at the outset, and only thought about the IVD field later, after the RUO product had already been designed.

71. At pages 215-216 of Ms. O’Grady’s deposition, she testified about potential “delays in QSR compliance” as a risk to the achievement of some revenues that were being forecasted. “QSR compliance” is another aspect of “design control” principles, in this case specific to manufacturing techniques. The FDA requires QSR (Quality System Regulation) compliance in the manufacturing of devices that it clears. Again, if a reasonable company is “backing up” in a sense and changing its existing manufacturing techniques to be QSR compliant, it is unlikely that it intended from the beginning to operate in the IVD, FDA-regulated market. Otherwise, the manufacturing would be designed to be QSR compliant from the outset,

at much less cost than setting up the manufacturing in some other way and then going back to fix it.

Pursuant to 37 C.F.R. § 2.20, the undersigned being warned that willful false statements and the like are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001, and that such willful false statements and the like may jeopardize the validity of the application or document or any registration resulting therefrom, declares that all statements made of my own knowledge are true; and all statements made on information and belief are believed to be true.

Executed on February 6, 2015.



Kenneth J. Kozak

**KOZAK EXHIBIT A  
(CONFIDENTIAL)**

**KOZAK EXHIBIT B  
(CONFIDENTIAL)**

**KOZAK EXHIBIT C  
(CONFIDENTIAL)**

**KOZAK EXHIBIT D  
(CONFIDENTIAL)**

**KOZAK EXHIBIT E  
(CONFIDENTIAL)**

# **KOZAK EXHIBIT F**



 **illumigene**<sup>™</sup>  
*Molecular Simplified*



 **Meridian**  
**Bioscience, Inc.**  
Inspired Science. Trusted Solutions.®

# **illumigene™** Molecular Diagnostic System

## Introducing *illumigene*— the smart evolution in molecular testing

Meridian Bioscience has combined Loop Mediated Isothermal Amplification (LAMP) technology with a unique set of features to create *illumigene*™.

*illumigene*™ reduces the complexity of molecular testing making it simple, fast, and flexible. With its small footprint and elegant design, it eliminates the need for costly capital equipment. And it fits easily into any lab and budget.

*illumigene*™—molecular simplified for your lab.



# illumigene™ Assay Procedure



1. Collect Stool with Sample Brush.



2. Place Brush in Diluent . Vortex 10 seconds.



3. Squeeze 5 Drops into Extraction Tube.

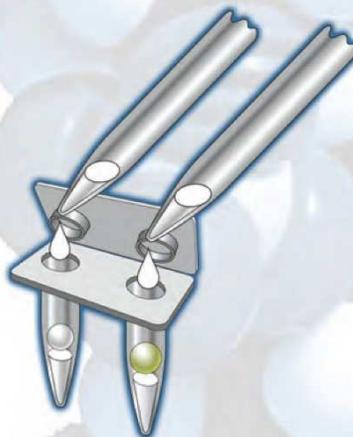


4. Heat at 95°C for 10 minutes. Vortex 10 seconds.

## SAMPLE EXTRACTION



5. Add 50µl of Extracted Sample to Reaction Buffer Tube. Vortex 10 seconds.



6. Transfer 50µl of Sample to BOTH Test and Control Ports of Illumigene Device. Close Device Lid.



7. Place Device in Illumipro-10™. Create Run and Press "START."

## DILUTION & PREPARATION

## AUTOMATED AMPLIFICATION & DETECTION

## Simple:

*illumigene*<sup>™</sup> delivers the power of molecular technology in a simplified format.

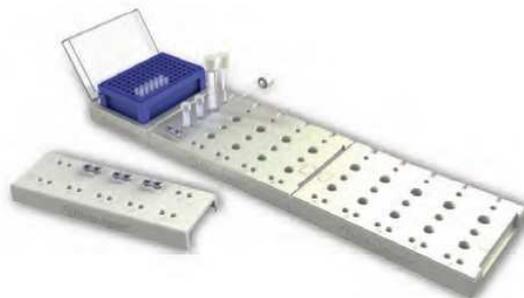
- Easy 7-step procedure
- Molecular results in under an hour
- No extensive sample purification required
- Walk-away automation with user-friendly *illumipro-10*<sup>™</sup> instrument
- No auxiliary computer required to operate system



## Flexible:

*illumigene*<sup>™</sup> integrates easily into any facility regardless of volume or expertise.

- Flexibility to stop and restart assay procedure
- Optional workstation adapts to any user or workflow
- Adapts to large or small batch sizes
- Small footprint allows for placement in any lab space



# **illumigene™** Molecular Diagnostic System

## FEATURES

## BENEFITS

### Simple 7-step procedure

Assay able to be performed by any technologist regardless of experience  
 No off-site training required  
 Fast implementation into laboratory workflow  
 Minimizes hands-on time (<2 minutes/sample)

### Highly accurate results

No algorithms needed to achieve high performance  
 Peace of mind/confidence in results

### Rapid turnaround time—results in under an hour

Adapts to any laboratory's workflow  
 Provides quicker results to physicians—for better patient care

### Small system footprint

Fits into any lab space  
 No remodeling of lab required to add system/assays

### No capital equipment burden

Very cost-effective solution for any facility  
 No additional charge for service agreement  
 24-hour unit replacement

### Room temperature storage of kits

No refrigeration space required  
 No equilibration steps required—ready to run at all times

### Optional system accessories

Flexible printing options in minimal bench space  
 QWERTY keyboard and built-in barcode reader allows for flexible sample ID entry  
 Workstation allows for organization of procedural workflow



#### WORLD HEADQUARTERS

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#### Italy

Via dell'Industria, 7  
 20020 Villa Cortese, Milano  
 Italy  
 Telephone..... + 39 0331 43 36 36  
 Fax..... + 39 0331 43 36 16  
 E-mail: info@mdeur.com



For more information, contact an **illumigene™** specialist at 1-888-763-6769 or visit us on the web at [www.meridianbioscience.com](http://www.meridianbioscience.com).

#### Belgium

Rue de l'Industrie 7  
 1400 Nivelles  
 Belgium  
 Telephone..... + 32 67 89 59 59  
 Fax..... + 32 67 89 59 58  
 E-mail: info@mdeur.be

#### France

Le Quadra  
 455, Promenade des Anglais  
 06299 Nice Cedex 3  
 France  
 Telephone..... + 33 4 93 18 72 10  
 Fax..... + 33 4 93 18 72 11  
 E-mail: info@meridianbioscience.fr

#### The Netherlands

Halderheiweg 6  
 5282 SN Boxtel  
 The Netherlands  
 Telephone..... + 31 411 62 11 66  
 Fax..... + 31 411 62 48 41  
 E-mail: meridian.info@planet.nl

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ILLUMI\_FOLDER  
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ME-00040535

# **illumigene**™ *C. difficile* Assay

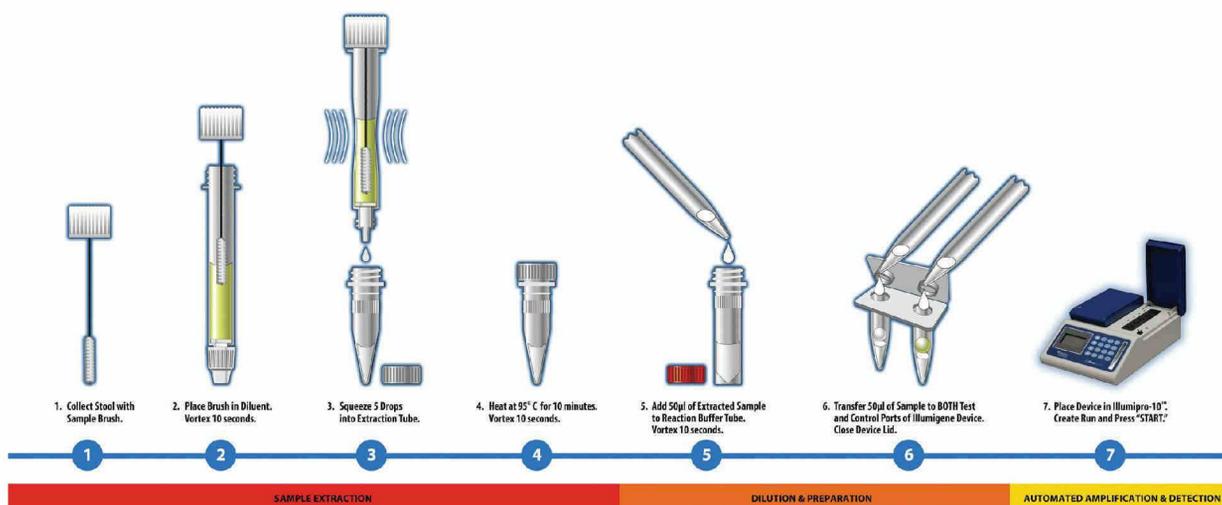
Highly accurate *C. difficile* results in less than an hour.

- 50 test kit
- Room temperature storage
- No sample purification
- No centrifugation
- Mercury-free



The **illumigene**™ *C. difficile* assay allows any laboratory to produce cost-effective, rapid molecular results. Utilizing a flexible 7-step process, and requiring less than two minutes of hands on time per sample, this user-designed assay provides the simple effective solution that you requested with the high quality results you deserve.

## **illumigene**™ *C. difficile* Assay Process



**illumigene**™ Molecular Diagnostic System

**Meridian**  
Bioscience, Inc.  
Inspired Science. Trusted Solutions.™

**illumigene™** Molecular Diagnostic System

*illumigene™ C. difficile* assay specifications

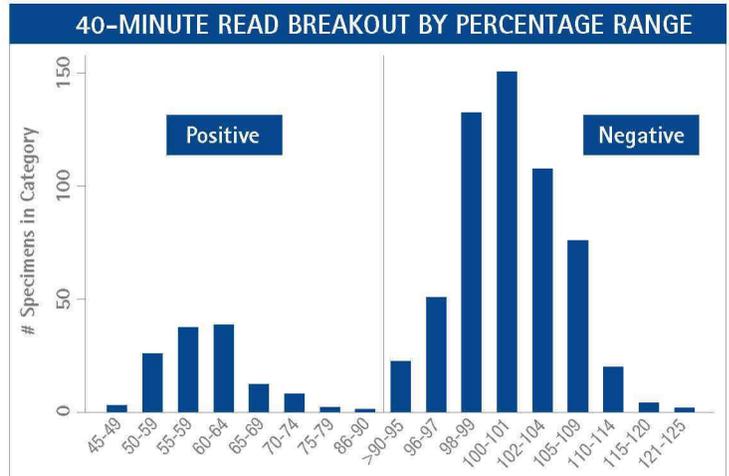
OVERALL PERFORMANCE DATA			
Cytotoxic bacteria culture	<i>illumigene™ C. difficile</i>		
	Positive	Negative	Total
Positive	99	5**	104
Negative	27*	546	573
Total	126	551	677
95% CI			
Sensitivity	99/104	95.2%	89.2 – 97.9%
Specificity	546/573	95.3%	93.2 – 96.7%
Correlation	645/677	95.3%	93.4 – 96.6%
Invalid Rate	11/697	1.6%	0.9 – 2.8%

\* 15/27 false positive results were positive by another FDA cleared molecular assay. Of the remaining 12 false positive results, 8 were positive by an FDA cleared assay for the detection of GDH.  
 \*\* 2/5 false negative results were negative by another FDA cleared molecular assay.

**Conclusions**

- Sensitivity and specificity are 95.2% and 95.3% respectively when compared directly to cytotoxic bacterial culture.
- Discrepant analysis by an FDA-cleared molecular assay confirmed 15 *illumigene™ C. difficile*-positive, culture-negative specimens.
- 8 additional *illumigene™ C. difficile*-positive samples were positive for common antigen suggesting the presence of *C. difficile*.

The *illumigene™* assay is part of the Meridian Bioscience high-quality portfolio of *C. difficile* diagnostic products. More high performing solutions from the unparalleled global leader in *C. difficile* testing.



***illumipro-10™* Results Distribution**

The *illumipro-10™* final read (40 minutes) values for the 697 clinical trial samples were analyzed and shown in the graph chart. A ratio of signal final to signal initial is expressed as a percentage where by a percentage greater than or equal to 90% represents a negative result. A percentage less than 90% represents a positive result. The graph demonstrates there is a clear separation between positive and negative results in this study.



**Ordering information**

<i>illumigene™ C. difficile</i> .....	280050
<i>illumigene™ C. difficile</i> External Control Kit.....	279920



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**Italy**  
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 Italy  
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For more information, contact an *illumigene™* specialist at 1-888-763-6769 or visit us on the web at [www.meridianbioscience.com](http://www.meridianbioscience.com).

**Belgium**  
 Rue de l'Industrie 7  
 1400 Nivelles  
 Belgium  
 Telephone... +32 67 89 59 59  
 Fax... +32 67 89 59 58  
 E-mail: info@mdeur.be

**France**  
 Le Quadra  
 455, Promenade des Anglais  
 06299 Nice Cedex 3  
 France  
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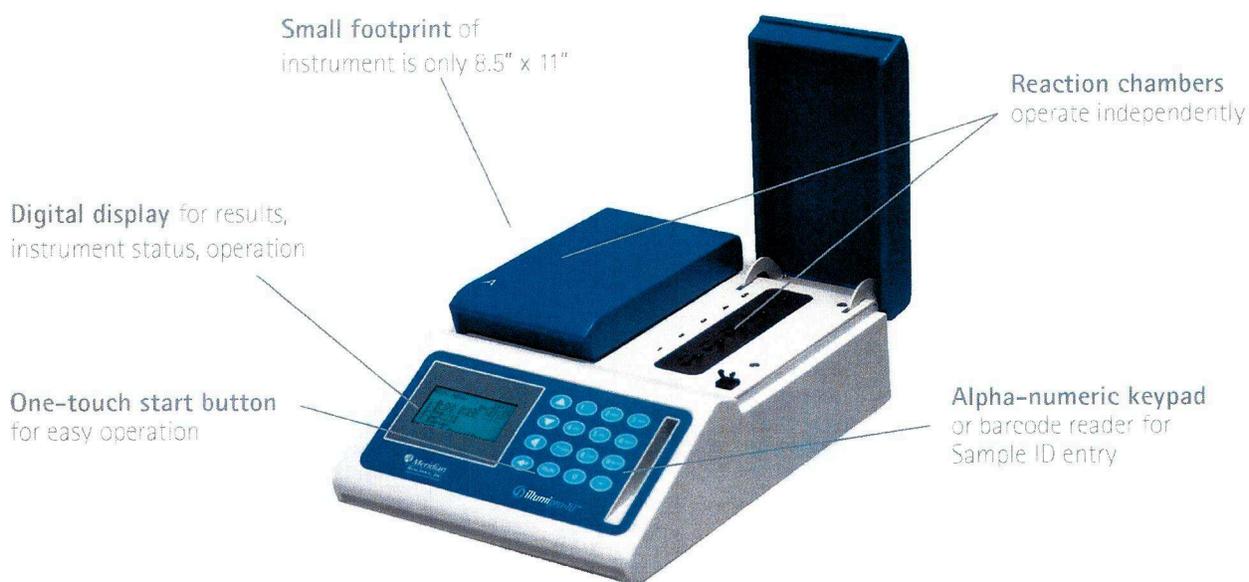
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 5282 SN Boxtel  
 The Netherlands  
 Telephone... +31 411 62 11 66  
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ILLUMI\_C.DIFF\_ASSAY\_INSRT  
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# illumipro-10™

Automated isothermal amplification and detection system that provides fast accurate results in a flexible package that fits into any lab.



- Optimal flexibility for stat or batch runs
- True walk away capability for optimized workflow
- Very low maintenance requirements enhances efficiency
- Rapid analysis with results in ~40 minutes



Internal barcode reader for fast and flexible sample ID entry



Independently operating wells allows optimized workflow for runs of 1-10 samples

**i illumipro-10™**



1. Load samples



2. Press "RUN"



3. Enter patient ID

**illumipro-10™ instrument specifications:**

- Electrical
  - Voltage Range: 120 V AC
  - Operating Range, Supply: 100 – 240 V AC, 50/60 Hz
  - Voltage and Current Rating: 12 V CD, 4.5 Amp
- Physical
  - Dimensions: 21 cm x 29.2 cm x 9.5 cm
  - Weight: 2.95 ± 0.05 kg
- Environmental
  - Operating Temperature: 15 – 30 C
  - Storage Temperature: 10 – 40 C
  - Relative Humidity, Operating: 10 – 90%, non-condensing
  - Relative Humidity, Storage: 10 – 95%

**illumipro-10™ instrument accessories:**

- Printer
- Keyboard

**Printer Specifications**

- Electrical
  - Supply Voltage : Input voltage [S, P] 12 V DC
- Environmental
  - Operating Temperature: 0 – 40 C
  - Storage Temperature: -10 – 50 C
  - Relative Humidity, Operating: 30 – 80%
  - Relative Humidity, Storage: 10 – 90%

**Ordering information**

<b>illumipro-10™ Incubator Reader.....</b>	<b>610172</b>
<b>illumipro-10™ Printer.....</b>	<b>610173</b>
<b>illumipro-10™ Keyboard.....</b>	<b>610174</b>
<b>illumipro-10™ Operations Manual.....</b>	<b>11007</b>



**WORLD HEADQUARTERS**

4770 River Hills Drive  
 Plymouth, MI 48178-3014  
 USA  
 Tel: +1 734 761 2000  
 Fax: +1 734 761 2001  
 Email: [illumipro@meridianbioscience.com](mailto:illumipro@meridianbioscience.com)

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**Italy**

viale Feltrina, 20  
 31043 Biadene dell'Istria  
 (TV) - Italy  
 Tel: +39 0422 860000  
 Fax: +39 0422 860001  
 Email: [illumipro@meridianbioscience.com](mailto:illumipro@meridianbioscience.com)



For more information, contact an **illumigene™** specialist at 1 888 763 6769 or visit us on the web at [www.meridianbioscience.com](http://www.meridianbioscience.com).

**Belgium**

nummer 10, straat  
 1000 Brussel  
 Belgium  
 Tel: +32 2 734 6000  
 Fax: +32 2 734 6001  
 Email: [illumipro@meridianbioscience.com](mailto:illumipro@meridianbioscience.com)

**France**

10, rue de  
 la République, 92000  
 Nanterre Cedex  
 France  
 Tel: +33 1 47 37 10 00  
 Fax: +33 1 47 37 10 01  
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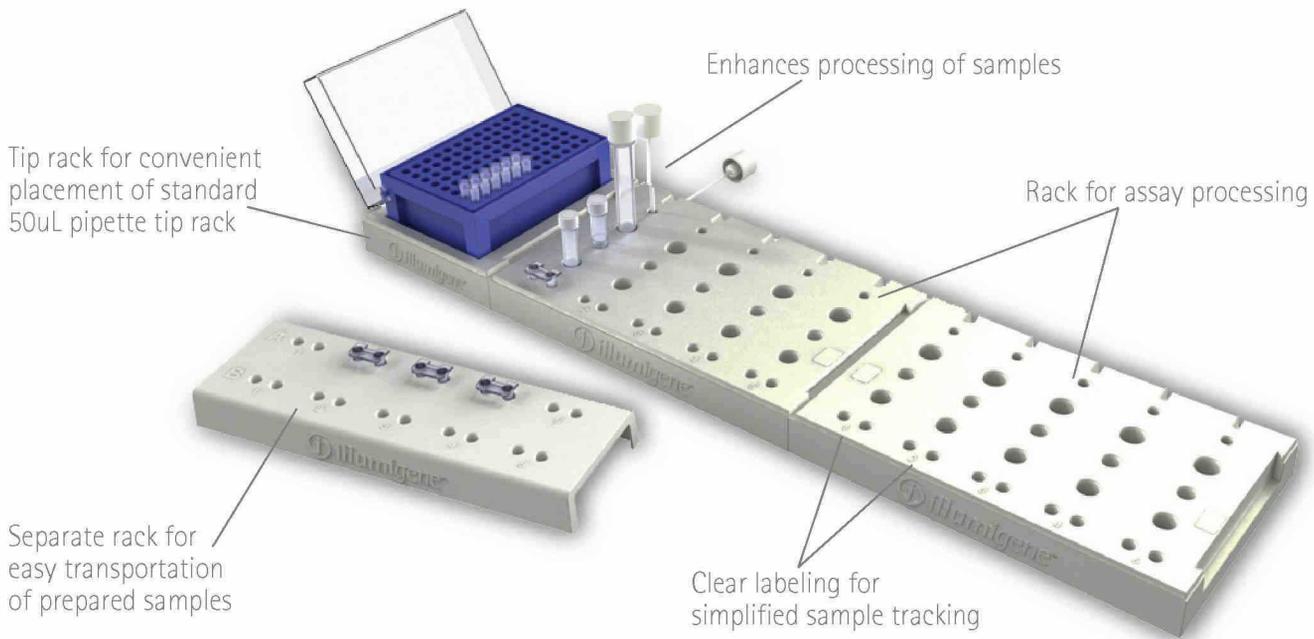
**The Netherlands**

10, rue de  
 la République  
 92000 Nanterre  
 France  
 Tel: +33 1 47 37 10 00  
 Fax: +33 1 47 37 10 01  
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ILLUMIPRO\_INSERT  
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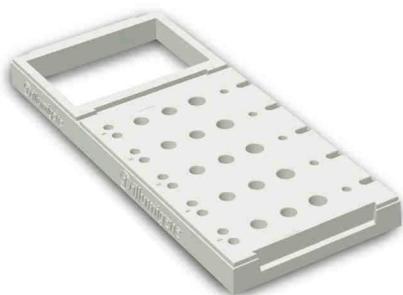
# **illumigene™** *C. difficile* Assay Workstation

Optimizing flexibility and efficiency for your molecular assay processing.

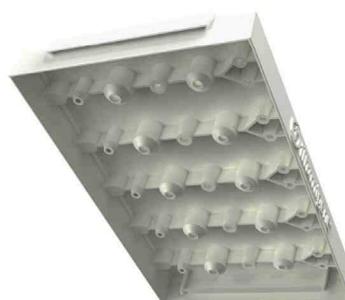


- Optimized flexibility
  - Configurable to small or large batch sizes
  - Adjustable to left- or right-handed operators
- Enhanced efficiency
  - Simple tracking of samples throughout workflow
  - **illumigene™** device transport rack matches **illumipro-10™** configuration
- Incredible ease of use
  - Clean/decontaminate through simple bleach submersion
  - Quick assembly/disassembly/reconfiguration of all parts

**illumigene™** Molecular Diagnostic System



Flexible interlocking design allows for adaptation to run sizes as well as left- or right-handed operation.



Flow through wells for ease of cleaning and draining for optimized contamination control.



Interlocking stackable design to facilitate storage and maintain low footprint of **illumigene™** system.



Separate sample transport block matched with **illumipro-10™** design to enhance ease of use and tracking of patient samples .



The **illumigene™** workstation is designed to enhance the simplicity, efficiency, and workflow of the **illumigene™** *C. difficile* assay system. Another innovation from the unparalleled global leader in *C. difficile* testing.

Ordering information

**illumigene™** *C. difficile* Assay Workstation.....610169



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**Italy**  
Via dell' Industria, 7  
20020 Villa Cortese, Milano  
Italy  
Telephone..... + 39 0331 43 36 36  
Fax..... + 39 0331 43 36 16  
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**Belgium**  
Rue de l'Industrie 7  
1400 Nivelles  
Belgium  
Telephone... + 32 67 89 59 59  
Fax..... + 32 67 89 59 58  
E-mail: info@mdeur.be

**France**  
Le Quadra  
455, Promenade des Anglais  
06299 Nice Cedex 3  
France  
Telephone..... + 33 4 93 18 72 10  
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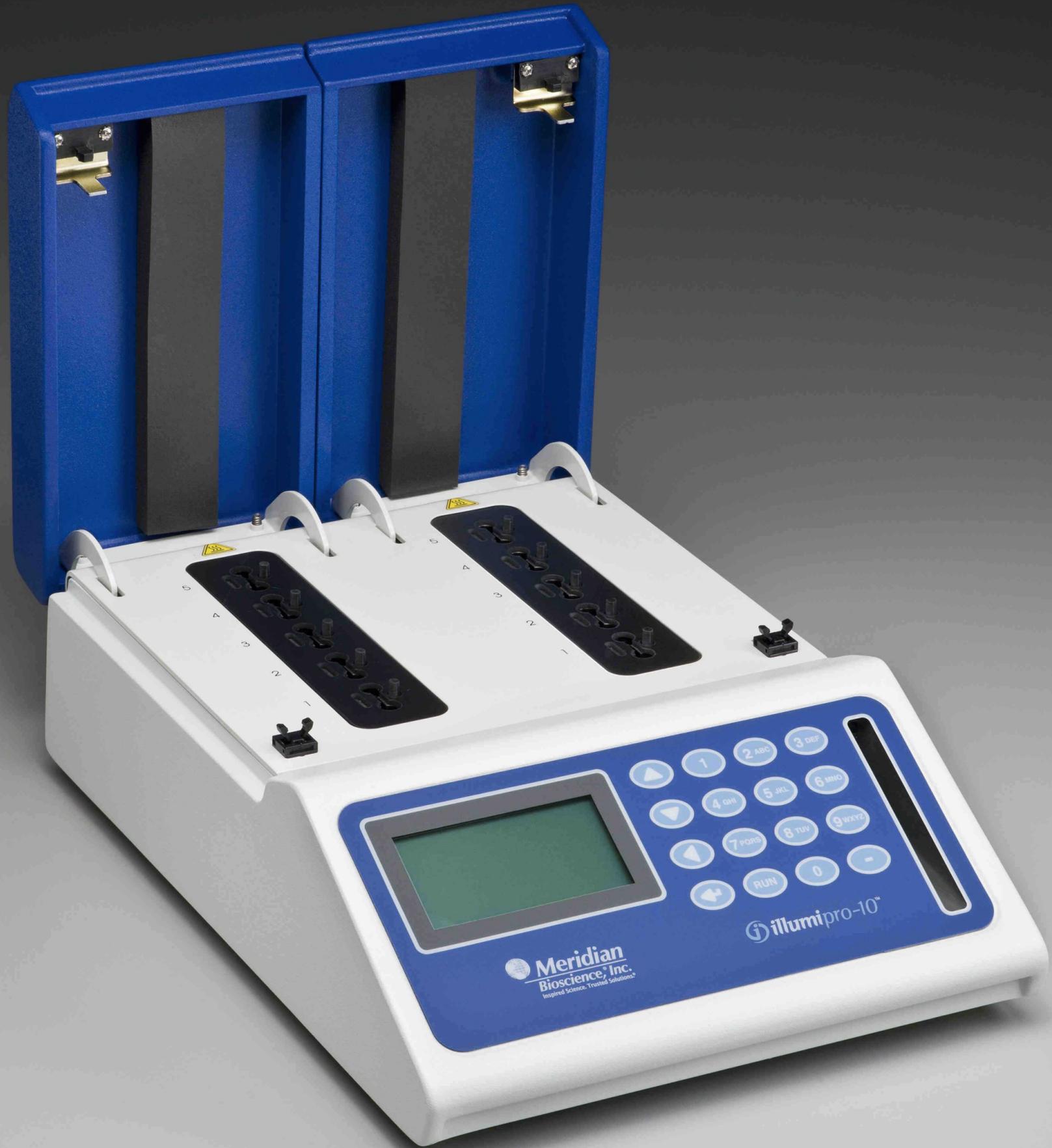
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ILLUMI\_WRKSTN\_INSRT  
REV. 07/10







**illumigene™** For the rapid detection of  
*C. difficile* in human specimens  
*C. difficile*

**External Control Kit**

Σ 18 TESTS

0.9 mL CONTROL +

LOT 2802.005 EXP 2011-09-16

0.9 mL CONTROL -

2803.006 2011-09-16

To Place An Order: 1-800-543-1980  
For Technical Support: 1-800-343-3858 (US only)

REF 279920

IVD

Manufactured by: Meridian Bioscience, Inc., 3471 River Hills Drive, Cincinnati, OH 45244  
Authorized representative: MBE-Via dell'Industria, 7, 20020 Villa Cortese, (Milano) Italy

LOT 279920.005

EXP 2011-09-16

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3-Results  
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5-System  
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**Bioscience, Inc.**  
Inspired Science. Trusted Solutions.

illumipro-10™

illumigene™

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# FOR INVESTIGATIONAL USE ONLY



DNA Amplification Assay for the Detection of Cytotoxicigenic *C. difficile* in Stool Specimens

REF 280050

For Investigational Use Only

## INTENDED USE

The *illumigene C. difficile* assay utilizes loop-mediated isothermal amplification (LAMP)<sup>1,2</sup> technology to detect the pathogenicity locus (PaLoc)<sup>3</sup> of toxigenic *Clostridium difficile*. The *Clostridium difficile* PaLoc is a gene segment present in all known toxigenic *C. difficile* strains. The *C. difficile* PaLoc codes for both the Toxin A gene (*tcdA*) and the Toxin B gene (*tcdB*), has conserved border regions, and is found at the same site on the *C. difficile* genome for all toxigenic strains.<sup>3</sup> The *illumigene C. difficile* assay detects the PaLoc by targeting a partial DNA fragment on the Toxin A gene. The *tcdA* target region was selected as an intact region remaining in all known A+B+ and A-B+ toxinotypes.

The *illumigene C. difficile* assay is intended for Investigational Use Only.

## SUMMARY AND EXPLANATION OF THE TEST

The *illumigene C. difficile* DNA molecular assay is based on loop-mediated amplification technology, which uses specifically designed primers to the PaLoc pathogenicity locus to provide for specific and continuous isothermal DNA amplification. A by-product of this amplification is the formation of magnesium pyrophosphate, which forms a white precipitate leading to a turbid reaction solution. This presence of turbidity signifies a positive reaction while the absence of turbidity represents a negative reaction. The *illumigene C. difficile* assay contains primers that specifically amplify a 204 bp region of the conserved 5' sequence of the *tcdA* gene within the PaLoc of toxigenic *C. difficile* in diarrheal stool samples from patients suspected of having *C. difficile* associated disease (CDAD). The results of the assay are determined using the Meridian *illumipro-10* Incubator / Reader.

## BIOLOGICAL PRINCIPLES

Toxigenic *Clostridium difficile* is a major cause of antibiotic associated diarrhea and colitis and is the causative agent for virtually all cases of pseudomembranous colitis. Although about 2% of normal healthy adults are colonized with *C. difficile*, many patients acquire this organism through nosocomial infection. Exposure to most antibiotics is thought to allow proliferation of toxigenic *C. difficile* by disrupting the normal intestinal flora. Two large toxin proteins (TcdA [or toxin A] and TcdB [toxin B]) are thought to be the primary virulence factors of *C. difficile*. These toxins are encoded by two separate genes, named *tcdA* and *tcdB*, respectively. Together, with three additional genes, they form a 19.6 kb pathogenicity locus called PaLoc.

## REAGENTS/MATERIALS PROVIDED

The maximum number of tests obtained from this test kit is listed on the outer box.

- illumigene C. difficile* Sample Preparation Apparatus:** Sampling unit consisting of sample preparation chamber, dropper tip, cap and Sample Dilution Buffer (Phosphate Buffered Saline and formalin treated *Staphylococcus aureus*, with sodium azide (0.09%) as a preservative)
- illumigene* Reaction Buffer:** Tris-buffered solution containing sodium azide (0.09%) as a preservative
- illumigene C. difficile* Test Device:** Two separate chambers containing dry reagent lysospheres comprised of DNA polymerase, Deoxyribonucleoside Triphosphate (dNTPs), and either *C. difficile* specific primers (TEST Chamber) or *S. aureus* primers (CONTROL Chamber)
- Sample Collection Brushes**
- illumigene* Extraction Tubes**

## MATERIALS PROVIDED SEPARATELY

*illumigene* External Control Kit, Catalog Number: 279920

## MATERIALS NOT PROVIDED

- Disposable latex gloves, powder free
- DNase/RNase free, aerosol resistant pipette tips
- Extraction Control (known positive clinical sample or a negative sample spiked with toxigenic *C. difficile*)

## EQUIPMENT NOT PROVIDED

- Dry-bath with 12 mm heat block capable of 95 C
- Vortex mixer
- Interval timer
- Micropipette capable of dispensing 50 µL
- Micropipette capable of dispensing 200 µL
- illumipro-10*

## PRECAUTIONS

- All reagents are for in vitro diagnostic use only.
- Follow Biosafety Level 2 and Good Laboratory practices during testing.<sup>4</sup> Treat all specimens and used Test Devices as capable of transmitting infectious agents. Do not eat, drink or smoke in areas where specimens or kit reagents are handled.

- Wear disposable gloves while handling specimens and thoroughly wash hands afterwards.
- Quality Control Programs for Molecular Testing Laboratories should be employed.<sup>5</sup>
- illumigene* Sample Dilution Buffer contains formalin inactivated-organisms and should be treated as potentially infectious.
- The *illumigene C. difficile* Test Device contains lyophilized reagents. The protective pouch should not be open until ready to perform the assay.
- The *illumigene C. difficile* Test Device includes a latch feature that is designed to prevent contamination of the test area with amplification product. Do NOT use Test Devices with broken latches.
- Dispose of used *illumigene* Test Devices immediately after processing, leaving the device latch securely in place. Opening the device after amplification may result in contamination of the test area with amplification product.

## SHELF LIFE AND STORAGE

The expiration date is indicated on the kit label. Store the kit at 2-27 C.

## SPECIMEN COLLECTION AND PREPARATION

**Sample type:** Unformed samples indicative of CDAD.

**Human stool samples, unpreserved:** Samples should be transported and stored at 2-8 C prior to testing. Samples should be tested as soon as possible, but may be held up to 24 hours at 21-27 C or 5 days at 2-8 C. Samples that will not be tested within these times should be frozen immediately upon receipt and stored at ≤ -20 C until tested. Specimens may be frozen and thawed once.

**Human stool samples, preserved in Cary-Blair-based media:** Samples should be transported and stored at 2-8 C prior to testing. Samples should be tested as soon as possible, but may be held up to 5 days at 2-8 C. Samples that will not be tested within this time should be frozen immediately upon receipt and stored at ≤ -20 C until tested. Specimens may be frozen and thawed once.

## REAGENT PREPARATION

Ensure kit reagents are at room temperature (21-27 C) before use.

## SPECIMEN PREPARATION

**NOTE:** Ensure that the *illumipro-10* instrument is powered on and required performance verifications have been completed prior to initiation of SPECIMEN PREPARATION. Refer to the *illumipro-10* Operator's Manual for further information regarding instrument set-up and operation.

- Mix stool sample thoroughly.
- Collect mixed sample specimen using Sample Collection Brush.
  - Liquid Stool: Immerse Sample Collection Brush completely into specimen.
  - Semi-solid Stool: Rotate Sample Collection Brush over specimen surface, lightly coating the surfaces of the brush bristles. Approximately one-half of the brush should be coated; over-collection of stool may lead to clogging of the sample collection device.
- Add the Sample Collection Brush to the *illumigene C. difficile* Sample Preparation Apparatus containing Sample Diluent and secure the cap. For stool in Cary-Blair-based media, transfer 200 µL of specimen to the *illumigene C. difficile* Sample Preparation Apparatus and secure the cap. Vortex the Sample Preparation Apparatus for a minimum of 10 seconds. Specimen in *illumigene C. difficile* Sample Preparation Apparatus prior to extraction may be held at 2-27 C for up to 24 hours prior to testing.
- Remove the tip cap from the Sample Preparation Apparatus and squeeze five to ten drops of sample into a clean *illumigene* Extraction Tube.
- Repeat Sample Preparation Steps for all samples to be processed.
- Heat the *illumigene* Extraction Tubes containing mixed sample in a dry-bath/heat block at 95 C for 10 +/- 2 minutes.
- Remove the tubes from the dry-bath/heat block and vortex for approximately 10 seconds. Extracted Samples may be held at 2-8 C for 4 hours OR may be frozen and stored at ≤ -20 C for 1 day prior to addition to Reaction Buffer. Extracted Samples may be frozen and thawed once.

## TEST PROCEDURE

**This test should be performed per applicable local, state, or federal regulations or accrediting agencies.**

**NOTE:** A maximum of 10 samples can be processed in a single *illumipro-10* run.

- Transfer 50 µL of extracted sample to an appropriately labeled *illumigene* Reaction Buffer tube.
- Vortex the Reaction Buffer Tube containing extracted sample for approximately 10 seconds.
- Repeat steps 1 and 2 for all the samples to be analyzed before proceeding.
- Remove 1 *illumigene C. difficile* Test Device from its protective pouch per sample. Carefully open the device, holding the tubes such that the lyophilized reagent will not fall out upon opening. Place device on a flat surface or in a rack that can accommodate the device.
- Using a new pipette tip, transfer 50 µL from the Reaction Buffer tube containing extracted sample to the TEST chamber (White Bead) of the *illumigene* Test Device. Do not insert air bubbles. Using a new pipette tip, transfer 50 µL from the Reaction Buffer tube containing extracted sample to the CONTROL chamber (Yellow Bead) of the *illumigene* Test Device. Do not insert air bubbles. Close the *illumigene* Test Device and fasten the latch securely.
- Tap device on the bench top to mix and to remove air bubbles. Carefully examine the reaction tubes to ensure that there are no air bubbles left in the tube.
- Insert the *illumigene* Test Device into the *illumipro-10* and initiate amplification reaction and detection. Results will be displayed at the conclusion of the run.

## INTERPRETATION OF RESULTS

Sample ID	Reported Result	Interpretation
Patient Specimen	POSITIVE	Sample contains toxigenic <i>C. difficile</i> strain with the pathogen locus (PaLoc).
	NEGATIVE	No toxigenic <i>C. difficile</i> detected.
	INVALID	<b>No reportable result. Repeat the test using the original stool sample.</b> Inhibitory patient specimen, improper sample preparation, reagent failure, instrument failure or internal control failure.
Extraction Control	POSITIVE	Valid Extraction Control. Extractions performed correctly.
	NEGATIVE	<b>Extraction Failure. Do not report test result. Repeat the extraction process for all stool samples.</b>
	INVALID	<b>No reportable result. Do not report test result. Repeat the extraction process for all stool samples.</b> Inhibitory patient specimen, improper sample preparation, reagent failure, instrument failure or internal control failure.
Positive Control	POSITIVE	Valid positive control result. Reagents active at time of use, <i>illumipro-10</i> performing correctly.
	NEGATIVE	<b>Incorrect control result. Repeat control testing as the first step in determining the root cause of the failure.</b> If control failures are repeated please contact Meridian's Technical Services at 1-800-343-3858 (US) or your local distributor.
	INVALID	<b>No reportable result. Repeat entire assay run using original stool samples.</b> Improper sample preparation, reagent failure, instrument failure or internal control failure.
Negative Control	POSITIVE	<b>Incorrect control result. Repeat control testing as the first step in determining the root cause of the failure.</b> If control failures are repeated please contact Meridian's Technical Services at 1-800-343-3858 (US) or your local distributor.
	NEGATIVE	Valid negative control result. Reagents active at time of use, <i>illumipro-10</i> performing correctly.
	INVALID	<b>No reportable result. Repeat entire assay run using original stool samples.</b> Improper sample preparation, reagent failure, instrument failure or internal control failure.
EMPTY WELL	NONE	No <i>illumigene</i> Test Device in the <i>illumipro-10</i> Well. <b>OR</b> The <i>illumigene</i> Test Device present is compromised due to sample preparation failure, dirty device or improperly seated device. <b>Repeat the test using original sample.</b>

## QUALITY CONTROL

- Each device contains an internal control well that controls for amplification inhibition, assay reagents and sample processing effectiveness.
- Good laboratory practice recommends the use of control materials. Users should follow the appropriate federal, state and local guidelines concerning the running of external quality controls.
- illumigene C. difficile* External Control Reagents are supplied separately (Catalog 279920). It is recommended that the reactivity of each new lot and each new shipment of *illumigene C. difficile* be verified on receipt and before use. External control tests should be performed thereafter in accordance with appropriate federal, state and local guidelines. The *illumigene C. difficile* test kit should not be used in patient testing if the external controls do not produce the correct results.
- A separate device must be used for each external control reagent.
- DO NOT extract the Positive or Negative Control samples.
- An Extraction Control (a known positive or clinical sample or negative sample spiked with toxigenic *C. difficile*) should be included in each extraction run. The Extraction Control should be treated as a sample.

## LIMITATIONS OF THE PROCEDURE

- illumigene C. difficile* Assay is intended for Investigational Use Only.
- This test is for use with unformed stool samples, preserved or unpreserved, only.

- This assay does not identify antimicrobial susceptibility.
- This test detects but does not differentiate the NAP1 (Ribotype 027) strain from other toxigenic strains of *C. difficile*.
- The detection of bacterial nucleic acid is dependent on proper specimen collection, handling (including transportation and storage) and preparation (dilution and extraction). Failure to follow instructions for collection, handling and preparation may cause incorrect results.

## ASSAY REACTIVITY

The following *C. difficile* stock cultures from different sources were tested and produced positive reactions at 64 CFU/test with *illumigene C. difficile*:  
 Type O: Strains 10463, 2004111, 2004205, 2005070, 2005257, 2008029, 2008162, 2008341, 2008351, 2009066, 2009099, B1, G1, J7, K12, Y1; Type III: 2004052, 2004118, 2007431, B117, B18; Type V: 2005325, 2006240, 2008188, 2009018, 2009065, BK6; Type VIII: 43598, 2008016, CF1; Type X 8864; Type XII 2007435; Type IX/XXIII 2007858; Unknown Type 2009132, 2009155, 2009277.

## CROSSREACTIVITY STUDIES

Crossreactivity studies were performed with positive and negative stool specimens inoculated with bacterial or fungal organisms to a final concentration of  $1.2 \times 10^6$  or virus at a minimum of  $1 \times 10^{5.06}$  TCID<sub>50</sub>/mL. None of the following organisms in stool reacted with *illumigene C. difficile*:

*Aeromonas hydrophila*, *Bacteroides fragilis*, *Campylobacter coli*, *Campylobacter fetus*, *Campylobacter jejuni*, *Candida albicans*, *Citrobacter freundii*, *Clostridium sordellii*, *Clostridium perfringens*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Escherichia coli*, *Escherichia coli O157:H7*, *Escherichia fergusonii*, *Escherichia hermannii*, *Helicobacter pylori*, *Klebsiella pneumoniae*, *Lactococcus lactis*, *Listeria monocytogenes*, *Peptostreptococcus anaerobius*, *Plesiomonas shigelloides*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas fluorescens*, *Salmonella* Groups B-E, *Serratia liquefaciens*, *Serratia marcescens*, *Shigella boydii*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Vibrio parahaemolyticus*, *Yersinia enterocolitica*, Adenovirus Types 40 and 41, Coxsackievirus, Echovirus, Rotavirus.

## TESTS FOR INTERFERING SUBSTANCES

The following substances, at the specified saturated solvent/diluents concentrations, do not interfere with test results in the final concentrations listed: Barium sulfate (5 mg/mL), fecal fat (equivalent to 2.65 mg stearic plus 1.3 mg palmitic acids per mL), hemoglobin (as methemoglobin) (3.2 mg/mL), IgA (5 mg/mL), Imodium AD® (0.00667 mg/mL), Kaopectate® (0.87 mg/mL), Metronidazole (12.5 mg/mL), mucin (3.33 mg/mL) Mylanta® (4.2 mg/mL), Pepto-Bismol® (0.87 mg/mL), Prilosec® (0.5 mg/mL), Tagamet® (0.5 mg/mL), TUMS® (0.5 mg/mL), Vancomycin (12.5 mg/mL), white blood cells (5% V/V), whole blood (5% V/V).

## REFERENCES

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	Meridian Bioscience, Inc. USA/Corporate Office 3471 River Hills Drive Cincinnati, Ohio 45244 Telephone: (513) 271-3700 Orders/Customer Service: (800) 543-1980 Technical Support Center: (800) 343-3858 Information Fax:(513) 272-5432 Ordering Fax:(513) 271-0124
	Meridian Bioscience Europe Via dell'Industria, 7 20020 Villa Cortese (MI) Italy Tel.: +39 0331 433636 Fax: +39 0331 433616 e-mail: info@mdeur.com

Meridian Bioscience Europe France  
 Le Quadra  
 455, Promenade des Anglais  
 06299 Nica Cedex-3  
 France  
 Tel.: +33 (4) 93 18 72 10  
 Fax: +33 (4) 93 18 72 11  
 e-mail: info@meridianbioscience.fr

Meridian Bioscience Europe s.a. / n.v.  
 Rue de l'Industrie 7  
 1400 Nivelles  
 Belgium  
 Tel.: +32 (0) 67 89 59 59  
 Fax: +32 (0) 67 89 59 58  
 e-mail: info@mdeur.be

Meridian Bioscience Europe b.v.  
 Halderhelweg 6  
 5282 SN Boxtel  
 The Netherlands  
 Tel.: +31 (411) 621166  
 Fax: +31 (411) 624841  
 e-mail: meridian.info@planet.nl

**INTERNATIONAL SYMBOL USAGE**

You may see one or more of these symbols on the labeling/packaging of this product:  
**Key guide to symbols (Guida ai simboli, Guide des symbols, Guia de simbolos, Erläuterung der graphischen symbole)**

	Use by / Utilizzare entro / Utiliser jusqu' / Fecha de caducidad / Verwendbar bis	<b>CONTROL +</b>	Positive control / Controllo positivo / Contrôle positif / Control positivo / Positive Kontrolle
<b>LOT</b>	Batch Code / Codice del lotto / Code du lot / Código de lote / Chargenbezeichnung	<b>CONTROL -</b>	Negative control / Controllo negativo / Contrôle négatif / Control negativo / Negative Kontrolle
<b>IVD</b>	In vitro diagnostic medical device / Dispositivo médico-diagnóstico in vitro / Dispositif médical de diagnostic in vitro / Dispositivo médico para diagnóstico in vitro / In-Vitro-Diagnostikum	<b>SMP PREP OIL SPE</b>	Sample Preparation Apparatus containing Sample Diluent / Appareto per la preparazione del campione contenente il diluente del campione / Système pour la préparation de l'échantillon, diluant inclus / Aparato para Preparación de Muestra con Diluyente de Muestra / System zur Probenbearbeitung, in dem sich Probenverdünnungspuffer befindet
<b>CE</b>	This product fulfills the requirements of Directive 98/79/EC on in vitro diagnostic medical devices / Questo prodotto soddisfa i requisiti della Direttiva 98/79/CE relative aux dispositifs médicaux de diagnostic in vitro / Este producto cumple con los requisitos de la Directiva 98/79/CE sobre los productos sanitarios para diagnóstico in vitro / Dieses Produkt entspricht den Anforderungen der Richtlinie über In Vitro Diagnostika 98/79/EG.	<b>EC REP</b>	Authorized Representative in the European Community / Rappresentante Autorizzato nella Comunità Europea / Mandataire dans la Communauté européenne / Representante autorizado en la Comunidad Europea / Bevollmächtigter in der Europäischen Gemeinschaft
<b>REF</b>	Catalogue number / Numero di catalogo / Référence du catalogue / Número de catálogo / Bestellnummer		Do not freeze / Non congelare / Ne pas congeler / No congelar / Nicht Einfrieren
	Consult instructions for Use / Consultare le istruzioni per l'uso / Consulter les instructions d'utilisation / Consulte las instrucciones de uso / Gebrauchsanweisung beachten	<b>RoHS</b>	Restriction of Hazardous Substances / Restrizione all'uso di sostanze pericolose / Limitation de substances dangereuses / Restricción de Substancias Nocivas / Beschränkung der Verwendung bestimmter gefährlicher Stoffe
	Manufacturer / Fabricante / Fabricant / Fabricator / Hersteller		Caution, consult accompanying documents / Attention, vedere le istruzioni per l'uso / Attention voir notice d'instructions / Atención, ver instrucciones de uso / Achtung, Siehe Dokumente beachten
	Contains sufficient for <=> tests / Contiene sufficiente per "n" test / Contenu suffisant pour "n" tests / Contiene suficiente para <=> ensayos / Inhalt ausreichend für <=> Prüfungen	<b>BUF RXN</b>	Reaction Buffer / Tampone di reazione / Solution de réaction tamponnée / Tempòs de Reacció / Reaktionspuffer
	Temperature limitation / Limiti di temperatura / Limites de température / Límite de temperatura / Temperaturbegrenzung		ETL Registered Mark / Certified / Marchio di certificazione registrato a livello nazionale / Certifié Conforme ETL / Marca de Certificación Registrada Nacional / ETL Konform beglaubigt
<b>SN</b>	Serial number / Numero di serie / Numéro de série / Número de serie / Seriennummer		Recycle - do not dispose of as general waste / Riciclare - non smaltire come rifiuto generico / Recycle - ne pas jeter dans une poubelle / Recycle - no desecha como basura general / Recycling - dieses Produkt nicht über den Hausmüll entsorgen
<b>TEST</b>	Test Device / Dispositivo test / Dispositif de test / Dispositivo de Prueba / Testgerät	<b>EX TUBE</b>	Extraction tube / Provette per l'estrazione / Tubes d'Extraction / Tube de Extracción / Röhre zur Probextraktion
	Date of manufacture / Data di fabbricazione / Date de fabrication / Fecha de fabricación / Herstellungsdatum		For IVD Performance Evaluation Only / Scatolo per valutazione delle prestazioni / Riservato IVD riservato à l'évaluation des performances / Sólo para evaluación del funcionamiento / Nur zur IVD Leistungsbewertung
	LASER RADIATION: Avoid Exposure to Beam / RADIAZIONE LASER: Evitare l'esposizione al raggio / RAYONNEMENT LASER: Eviter toute exposition au faisceau / Radiación Laser: Evite la exposición a los Rayos / LASERSTRAHLUNG: Direkten Kontakt mit dem Strahl vermeiden		HOT SURFACE: Keep hands away from Hot Surfaces / Superficie calda: tenere le mani lontane dalle superfici calde / SURFACES CHAUDES: Ne pas toucher les surfaces chaudes / Superficie Caliente: Mantenga las manos alejadas de la superficie caliente / Heiße Oberfläche: Kontakt mit heißen Oberflächen vermeiden
	CAUTION: Laser Radiation / ATTENZIONE: Radiazione Laser / AVERTISSEMENT: Rayonnement laser / Precaución: Radiación Laser / WARNUNG: Laserstrahlung	<b>IPX-0</b>	CAUTION: Protect from water / ATTENZIONE: Proteggere dall'acqua / AVERTISSEMENT: Protéger de l'eau / WARNING: Vor Feuchtigkeit schützen
	CAUTION: Risk of DANGER / ATTENZIONE: Pericolo / AVERTISSEMENT: Risques de danger / Precaución: Peligro / WARNUNG: Risikogefahr		

For technical assistance, call Technical Support Services at 800-343-3858 between the hours of 8AM and 6PM, USA Eastern Standard Time. To place an order, call Customer Service Department at 800-543-1980.

# illumigene™ *C. difficile* External Controls

## External Control Materials for use with *illumigene C. difficile* DNA Amplification Assay

REF 279920

IVD In vitro diagnostic medical device

### INTENDED USE

The *illumigene C. difficile* External Control Kit contains Positive and Negative Control Reagents for use with the *illumigene C. difficile* test kit. External controls are used as part of a routine quality control program.

### SUMMARY AND EXPLANATION OF THE TEST

Quality control testing is performed to detect factors such as reagent deterioration, adverse environmental or test conditions, or variance in operator performance that can cause test errors. External control reagents, such as *illumigene C. difficile* External Positive Control and Negative Control, are reagents that are not built into the test system, but are tested in the same manner as patient specimens.

### BIOLOGICAL PRINCIPLES

To verify that *illumigene C. difficile* DNA Amplification test kits are performing correctly; they should be tested with known positive and negative external control reagents on a periodic basis. The frequency with which a laboratory performs external controls will be affected by:

1. The proficiency level of the laboratory,
2. The laboratory's own internal requirements,
3. The requirements of the laboratory's accrediting agencies,
4. The number of new and different operators performing the test,
5. Whether a new kit lot is being added to testing,
6. Whether the kit lot is from a different shipment, and
7. Whether deviations from the manufacturer's stated storage or handling conditions have occurred.

When unacceptable quality control test results are obtained, all test results should be considered invalid. QC test failures are an indication that either reagents, test environment or operator performance have changed.

### REAGENTS/MATERIALS PROVIDED

**The maximum number of tests obtained from this test kit is listed on the outer box.**

1. ***illumigene* Positive Control:** Tris-buffered solution containing non-infectious Plasmid DNA (*S. aureus* and *C. difficile* inserts) with azide (0.09%) as a preservative.
2. ***illumigene* Negative Control:** Tris-buffered solution containing non-infectious Plasmid DNA (*S. aureus* insert) with azide (0.09%) as a preservative.

### MATERIALS NOT PROVIDED

1. *illumigene C. difficile* DNA Amplification Test Kit (Product Code 280050)
2. Disposable latex gloves, powder free
3. DNase/RNase free, aerosol resistant pipette tips

### EQUIPMENT NOT PROVIDED

1. Vortex Mixer
2. Interval Timer
3. Micropipette capable of dispensing 50 µL
4. *illumipro-10*

### PRECAUTIONS

1. All reagents are for in vitro diagnostic use only.
2. This is a quality control reagent and is used to evaluate the performance of the *illumigene C. difficile* DNA Amplification Assay. It is not directly used to test patient samples.
3. Transport and store these reagents at 2-8 C when not in use. Do not freeze.
4. DO NOT extract the Positive or Negative External Control samples.
5. Do not eat, drink or smoke in areas where specimens or kit reagents are handled.
6. Wear disposable gloves while handling specimens and thoroughly wash hands afterwards.
7. CDC/NIH manual "Biosafety in Microbiology and Biomedical Laboratories", 2007
8. Quality Control Programs for Molecular Testing Laboratories should be employed.
9. The *illumigene C. difficile* Test Device contains lyophilized reagents. The protective pouch should not be open until ready to perform the assay.
10. The *illumigene C. difficile* Test Device includes a latch feature that is designed to prevent contamination of the test area with amplification product. Do NOT use Test Devices with broken latches.
11. Dispose of used *illumigene* Test Devices immediately after processing, leaving the device latch securely in place. Opening the device after amplification may result in contamination of the test area with amplification product.

### SHELF LIFE AND STORAGE

The expiration date is indicated on the kit label. Store the kit at 2-8 C.

### QUALITY CONTROL TEST PROCEDURE

**This test should be performed per applicable local, state, or federal regulations or accrediting agencies.**

1. Bring *illumigene* External Controls and all kit components to room temperature (21-27 C) before testing. Incorrect results may be obtained if Control Materials are not brought to room temperature prior to use.

2. Use one *illumigene C. difficile* Test Device for each Positive Control and Negative Control reagent to be tested.

3. Transfer 50 µL of Negative Control to an appropriately labeled *illumigene* Reaction Buffer tube.
4. Vortex the Reaction Buffer Tube containing Negative Control for approximately 10 seconds.
5. Transfer 50 µL of Positive Control to an appropriately labeled *illumigene* Reaction Buffer tube.
6. Vortex the Reaction Buffer Tube containing Positive Control for approximately 10 seconds.
7. Remove one *illumigene C. difficile* Test Device from its protective pouch for the Negative Control. Carefully open the device, holding the tubes such that the lyophilized reagent will not fall out upon opening. Place device on a flat surface or in a rack that can accommodate the device.
8. Using a new pipette tip, transfer 50 µL from the Reaction Buffer tube containing Negative Control to the TEST chamber (White Bead) of an appropriately labeled *illumigene* Test Device. Do not insert air bubbles. Using a new pipette tip, transfer 50 µL from the reaction buffer tube containing Negative Control to the CONTROL chamber (Yellow Bead) of the *illumigene* device. Do not insert air bubbles. Close the *illumigene* Test Device and fasten the latch securely.
9. Remove one *illumigene C. difficile* Test Device from its protective pouch for the Positive Control. Carefully open the device, holding the tubes such that the lyophilized reagent will not fall out upon opening. Place device on a flat surface or in a rack that can accommodate the device.
10. Using a new pipette tip, transfer 50 µL from the Reaction Buffer tube containing Positive Control to the TEST chamber (White Bead) of an appropriately labeled *illumigene* Test Device. Do not insert air bubbles. Using a new pipette tip, transfer 50 µL from the reaction buffer tube containing Positive Control to the CONTROL chamber (Yellow Bead) of the *illumigene* device. Do not insert air bubbles. Close the *illumigene* Test Device and fasten the latch securely.
11. Tap each device on the bench top to mix and remove bubbles.
12. Insert each *illumigene* Test Device into the *illumipro-10* and initiate amplification reaction and detection. Results will be displayed at the conclusion of the run.

6. Il lotto del kit proviene da una differente spedizione e

#### INTERPRETATION OF RESULTS

The *illumipro-10* measures the change in absorbance of the reaction mixture at  $650 \pm 20$  nm. Assay results are reported as Invalid, Positive, or Negative.

- External Positive Control reagents should give a Positive Result.
- External Negative Control reagents should give a Negative Result.
- Invalid test results indicate improper sample preparation or improper CONTROL Chamber reaction and must be repeated.

If the expected control reactions are not observed, repeat the control tests as the first step in determining the root cause of the failure. If control failures are repeated please contact Meridian's Technical Services Department at 1-800-343-3858 (US) or your local distributor.

#### LIMITATIONS OF THE PROCEDURE

The Positive Control is manufactured in an aqueous solution matrix. Although specimen matrix interference has not been observed with this assay, the aqueous matrix of the controls may not adequately control for specimen matrix effects. If the user wishes to supply controls in the sample matrix, the user is referred to the Clinical and Laboratory Standards Institute guideline EP14-A2, Evaluation of Matrix Effects: Approved Guideline – second edition, January 2005.

## ITALIANO

 *C. difficile* External Controls

**Reagenti di controllo esterno da usare insieme al Test di Amplificazione di DNA *illumigene C. difficile***

REF 279920

IVD Dispositivo medico-diagnostico in vitro

#### FINALITA' D'USO

Il Kit di controllo esterno *illumigene C. difficile* contiene reagenti per il controllo positivo e negativo da usare insieme al kit di analisi *illumigene C. difficile*. I reagenti di controllo esterno sono usati all'interno di un normale programma di controllo qualità.

#### SOMMARIO E SPIEGAZIONE DEL TEST

Il controllo di qualità serve a rilevare fattori che possono essere causa di errori, quali il deterioramento del reagente, condizioni ambientali o di analisi avverse, oppure variazioni nelle prestazioni degli operatori. I reagenti di controllo esterno, quali i reagenti esterni per il controllo positivo e negativo *illumigene C. difficile*, non sono inclusi all'interno del sistema di analisi, tuttavia vengono analizzati con le stesse modalità previste per i campioni dei pazienti.

#### PRINCIPI BIOLOGICI

Al fine di verificare il corretto funzionamento dei kit per il Test di Amplificazione di DNA *illumigene C. difficile*, è necessario analizzarli periodicamente con reagenti noti di controllo positivo e negativo esterni. La frequenza con cui un laboratorio esegua l'analisi dei controlli esterni dipenderà dai seguenti fattori:

1. Il livello di esperienza del laboratorio,
2. I requisiti di controllo interni al laboratorio,
3. I requisiti degli enti di accreditamento cui il laboratorio fa riferimento,
4. Il numero dei vari operatori incaricati di eseguire le analisi,
5. Un nuovo lotto del kit è stato aggiunto per le analisi,

- Se si sono verificate deviazioni dalle istruzioni di conservazione e manipolazione fornite dal produttore.

Qualora il controllo di qualità produca risultati inaccettabili, tutti i risultati delle analisi non devono essere considerati validi. Fallimenti nelle analisi del controllo di qualità indicano variazioni nei reagenti, nell'ambiente di analisi o nell'esecuzione delle analisi da parte degli operatori.

#### REAGENTI/MATERIALI FORNITI

Il numero massimo di analisi eseguibili con questo kit è indicato sulla confezione esterna.

- Controllo positivo *illumigene*:** soluzione tampone Tris contenente DNA plasmidico non infettivo (con un inserto di *S. aureus* e di *C. difficile*) con sodio azide (0.09%) come conservante.
- Controllo negativo *illumigene*:** soluzione tampone Tris contenente DNA plasmidico non infettivo (con un inserto di *S. aureus*) con sodio azide (0.09%) come conservante.

#### MATERIALI NON FORNITI

- Kit per Test di Amplificazione di DNA *illumigene C. difficile* (Numero di catalogo 280050)
- Guanti di lattice monouso senza talco
- Puntali per pipette privi di DNase/RNase e resistenti alla contaminazione da aerosol

#### DISPOSITIVI NON FORNITI

- Vortex
- Timer
- Micropipetta per in grado di dispensare 50 µL
- illumipro-10*

#### PRECAUZIONI

- Tutti i reagenti sono esclusivamente per uso diagnostico in vitro.
- Questo prodotto è un reagente per controllo di qualità inteso per la valutazione delle prestazioni del Test di Amplificazione di DNA *illumigene C. difficile*. Il prodotto non va usato direttamente per analizzare i campioni dei pazienti.
- Quando non vengono usati, trasportare e conservare i reagenti a una temperatura compresa fra 2 e 8 C. Non congelare.
- NON estrarre i campioni del Controllo Esterno Positivo o Negativo.
- Non mangiare, bere o fumare nelle aree dove si maneggiano i campioni o i reagenti del kit.
- Indossare guanti monouso quando si maneggiano i campioni e in seguito lavarsi le mani con cura.
- Manuale CDC/NIH "Biosafety in Microbiology and Biomedical Laboratories" (2007)
- Applicare i requisiti indicati nei Programmi di controllo di qualità per i laboratori di diagnostica molecolare.
- Il dispositivo di analisi *illumigene C. difficile* contiene reagenti liofilizzati. Non aprire la busta di protezione finché non si è pronti ad eseguire l'analisi.
- Il dispositivo di analisi *illumigene C. difficile* include una linguetta di chiusura per evitare che l'area di analisi venga contaminata con il prodotto di amplificazione. NON usare dispositivi di analisi con linguette danneggiate.
- Eliminare i dispositivi di analisi *illumigene* subito dopo l'uso, lasciando chiuse le linguette. L'apertura del dispositivo dopo l'amplificazione può causare la contaminazione dell'area di analisi con il prodotto di amplificazione.

#### STABILITÀ E CONSERVAZIONE

La data di scadenza è indicata sull'etichetta del kit. Conservare il kit a una temperatura compresa fra 2 e 8 C.

#### PROCEDURA DE TEST DEL CONTROLLO QUALITÀ

Il test va eseguito conformemente ai requisiti stabiliti dai competenti enti locali, statali, nazionali o dagli enti di accreditamento.

- Prima di dare inizio alle analisi, portare i controlli esterni e tutti i componenti del kit *illumigene* a temperatura ambiente (21-27 C). Possono verificarsi risultati incorretti se i reagenti di controllo non sono stati portati a temperatura ambiente prima dell'uso.
- Usare un dispositivo di analisi *illumigene C. difficile* per ciascun reagente di controllo positivo e negativo da analizzare.
- Trasferire 50 µL di controllo negativo in una provetta con il tampone di reazione *illumigene* adeguatamente etichettata.
- Agitare con il vortex la provetta con il tampone di reazione contenente il controllo negativo per circa 10 secondi.
- Trasferire 50 µL di controllo positivo in una provetta con il tampone di reazione *illumigene* adeguatamente etichettata.
- Agitare con il vortex la provetta con il tampone di reazione contenente il controllo positivo per circa 10 secondi.
- Estrarre dalla busta di protezione un dispositivo di analisi *illumigene C. difficile* per il controllo negativo. Aprire il dispositivo con attenzione, maneggiando le provette in modo da evitare la dispersione del reagente liofilizzato dopo l'apertura. Porre il dispositivo su una superficie piana o inserirlo in un portaprovette di misura adeguata.
- Utilizzando un nuovo puntale per pipette, trasferire 50 µL dalla provetta con il tampone di reazione contenente il controllo negativo ed erogarlo nella provetta TEST (sfera bianca) di un dispositivo di analisi *illumigene* adeguatamente etichettato. Evitare di inserire bolle d'aria. Utilizzando un nuovo puntale per pipette, trasferire 50 µL dalla provetta con il tampone di reazione contenente il controllo negativo ed erogarlo nella provetta CONTROLLO (sfera gialla) del dispositivo *illumigene*. Evitare di inserire bolle d'aria. Chiudere il dispositivo di analisi *illumigene* fissando bene la linguetta di chiusura.

- Estrarre dalla busta di protezione un dispositivo di analisi *illumigene C. difficile* per il controllo positivo. Aprire il dispositivo con attenzione, maneggiando le provette in modo da evitare la dispersione del reagente liofilizzato dopo l'apertura. Porre il dispositivo su una superficie piana o inserirlo in un portaprovette di misura adeguata.
- Utilizzando un nuovo puntale per pipette, trasferire 50 µL dalla provetta con il tampone di reazione contenente il controllo positivo ed erogarlo nella provetta TEST (sfera bianca) di un dispositivo di analisi *illumigene* adeguatamente etichettato. Evitare di inserire bolle d'aria. Utilizzando un nuovo puntale per pipette, trasferire 50 µL dalla provetta con il tampone di reazione contenente il controllo positivo ed erogarlo nella provetta CONTROLLO (sfera gialla) del dispositivo *illumigene*. Evitare di inserire bolle d'aria. Chiudere il dispositivo di analisi *illumigene* fissando bene la linguetta di chiusura.
- Picchiettare ciascun dispositivo sulla superficie di lavoro per miscelare il contenuto e rimuovere eventuali bolle d'aria.
- Inserire ciascun dispositivo di analisi *illumigene* nell'apparecchio *illumipro-10* e dare inizio alla reazione di amplificazione e rilevamento. I risultati saranno visualizzati alla fine del ciclo.

#### INTERPRETAZIONE DEI RISULTATI

L'incubatore/lettore *illumipro-10* misura la variazione di assorbanza della miscela di reazione a 650 = 20 nm. I risultati di analisi vengono riportati con le diciture: Non valido, Positivo o Negativo.

- I reagenti di controllo positivo esterno devono produrre un risultato positivo.
- I reagenti di controllo negativo esterno devono produrre un risultato negativo.
- I risultati non validi indicano una errata preparazione del campione errata o una reazione inadeguata all'interno della provetta CONTROLLO, pertanto le analisi dovranno essere ripetute.

Se non si ottengono i risultati attesi con i Controlli, come prima opzione per identificare la causa del fallimento ripetere i test di controllo. Se il fallimento dei test di controllo dovesse ripetersi, contattare il Servizio di Assistenza tecnica Meridian (negli USA 001-800-343-3858) o il Distributore Locale.

#### LIMITAZIONI DELLA PROCEDURA

Il controllo positivo è preparato in una matrice acquosa. Sebbene in questo dosaggio non sia stata osservata alcuna interferenza della matrice dei campioni, la matrice acquosa dei controlli può non essere in grado di controllare adeguatamente gli effetti matrice dei campioni. Qualora l'utente desideri eseguire controlli sulla matrice dei campioni, si prega di consultare le linee guida EP14-A2 del Clinical and Laboratory Standards Institute, "Evaluation of Matrix Effects: Approved Guideline", seconda edizione, gennaio 2005.

#### FRANCAIS

 *C. difficile* External Controls

Réactifs de contrôle externe à utiliser avec le test d'amplification de l'ADN *illumigene C. difficile*

REF 279920

IVD Dispositif médical de diagnostic in vitro

#### BUT DE LA METHODE

La trousse de contrôle externe *illumigene C. difficile* contient des réactifs de contrôle positif et négatif à utiliser avec la trousse de test *illumigene C. difficile*. Les contrôles externes sont utilisés dans le cadre du programme de routine de contrôle de la qualité.

#### RESUME ET EXPLICATION DU TEST

Les tests de contrôle de la qualité sont effectués pour détecter des facteurs tels qu'une détérioration des réactifs, des conditions adverses de l'environnement ou du test, ou des variations de la performance de l'opérateur qui peuvent occasionner des erreurs du test. Les réactifs de contrôle externes, tels que le contrôle externe positif et le contrôle externe négatif *illumigene C. difficile*, sont des réactifs qui ne font pas partie du système de test mais qui sont testés de la même manière que les échantillons de patients.

#### PRINCIPE DU TEST

Pour vérifier que les trousse de test d'amplification de l'ADN *illumigene C. difficile* fonctionnent normalement, elles doivent être testées avec des réactifs de contrôle externe positif et négatif de façon périodique. La fréquence à laquelle un laboratoire effectue les contrôles externes dépend de plusieurs facteurs:

- Le niveau de compétence du laboratoire,
- Les exigences internes propres au laboratoire,
- Les exigences des organismes d'accréditation du laboratoire,
- Le nombre de nouveaux opérateurs ou d'opérateurs différents qui effectuent le test
- Le test d'un nouveau lot de trousse,
- L'utilisation d'un lot de trousse envoyé séparément,
- La présence de déviations des conditions de conservation ou de manipulation par rapport aux instructions du fabricant,

Lorsque les résultats d'un test de contrôle de la qualité ne sont pas admissibles, tous les résultats du test doivent être considérés comme non valides. Les échecs des tests de CQ indiquent que les réactifs, l'environnement du test ou la performance de l'opérateur ont changé.

## MATERIEL FOURNI

Le nombre maximal de tests pouvant être réalisés à partir de ce coffret est indiqué sur la boîte.

1. Contrôle positif *illumigene*: tampon Tris contenant de l'ADN plasmidique non infectieux (inserts de *S. aureus* et *C. difficile*) avec azoture de sodium (0.09%) comme conservateur.
2. Contrôle négatif *illumigene*: tampon Tris contenant de l'ADN plasmidique non infectieux (insert de *S. aureus*) avec azoture de sodium (0.09%) comme conservateur.

## MATERIEL NON FOURNI

1. Trousse de test d'amplification de l'ADN *illumigene C. difficile* (référence 280050)
2. Gants en latex jetables, non poudrés
3. Embouts de pipettes sans désoxyribonucléase/ribonucléase, résistant aux aérosols

## EQUIPEMENT NON FOURNI

1. Mélangeur vortex
2. Minuterie
3. Micropipette pouvant distribuer 50 µL
4. *illumipro-10*

## PRECAUTIONS D'EMPLOI

1. Tous les réactifs sont pour usage in vitro uniquement.
2. Il s'agit de réactifs de contrôle de la qualité utilisés pour évaluer la performance du test d'amplification de l'ADN *illumigene C. difficile*. Ces réactifs ne sont pas utilisés pour traiter directement les échantillons de patients.
3. Transporter et conserver ces réactifs entre 2 et 8 C lorsqu'ils ne sont pas utilisés. Ne pas congeler.
4. NE PAS extraire les réactifs de contrôle externe positif et négatif.
5. Ne pas manger, boire ou fumer dans les zones de manipulation des échantillons ou trousse.
6. Porter des gants jetables lors de la manipulation des échantillons et se laver les mains soigneusement après la procédure.
7. Manuel « Biosafety in Microbiology and Biomedical Laboratories » (Biosécurité dans les laboratoires biomédicaux et de microbiologie) des Centres de contrôle et de prévention des maladies et des Instituts nationaux de la santé des Etats-Unis (CDC/NIH), 2007
8. Des programmes de contrôle de la qualité à l'usage des laboratoires de diagnostic moléculaire doivent être utilisés.
9. Le dispositif de test *illumigene C. difficile* contient des réactifs lyophilisés. La pochette de protection ne doit être ouverte que juste avant d'effectuer le test.
10. Le dispositif de test *illumigene C. difficile* comprend un mécanisme de verrouillage conçu pour empêcher la contamination de la zone de test avec le produit de l'amplification. NE PAS utiliser un dispositif si son mécanisme de verrouillage est endommagé.
11. Eliminer les dispositifs de test *illumigene* immédiatement après leur utilisation, en s'assurant de bien laisser le verrou en place. Si le dispositif était ouvert après la procédure, la zone de test pourrait être contaminée avec le produit de l'amplification.

## DUREE DE CONSERVATION ET STOCKAGE

La date de péremption de la trousse est indiquée sur l'étiquette de celle-ci. Conserver la trousse entre 2 et 8 C.

## PROCEDURE DU TEST DE CONTROLE DE QUALITE

Ce test doit être réalisé en fonction des exigences des réglementations locales et / ou nationales ou des directives des organismes d'accréditation.

1. Laisser les contrôles externes et tous les composants de la trousse *illumigene* se réchauffer à température ambiante (21 à 27 C) avant d'effectuer le test. En cas de non respect, un résultat incorrect peut être observé.
2. Utiliser un dispositif de test *illumigene C. difficile* pour chaque réactif de contrôle positif et négatif à analyser.
3. Transférer 50 µL du contrôle négatif dans un tube de tampon de réaction *illumigene* marqué de façon appropriée.
4. Mélanger le tube de tampon de réaction contenant le contrôle négatif au vortex pendant 10 secondes environ.
5. Transférer 50 µL du contrôle positif dans un tube de tampon de réaction *illumigene* marqué de façon appropriée.
6. Mélanger le tube de tampon de réaction contenant le contrôle positif au vortex pendant 10 secondes environ.
7. Retirer un dispositif de test *illumigene C. difficile* de sa pochette de protection pour le contrôle négatif. Ouvrir le dispositif avec précaution, en tenant les tubes de manière à ne pas laisser tomber les réactifs lyophilisés au moment de l'ouverture. Placer le dispositif sur une surface plane ou un portoir approprié.
8. En utilisant un nouvel embout de pipette, transférer 50 µL de contrôle négatif du tube de tampon de réaction vers le compartiment de TEST (bille blanche) d'un dispositif de test *illumigene* marqué de façon appropriée. Faire attention à ne pas introduire de bulles d'air. En utilisant un nouvel embout de pipette, transférer 50 µL de contrôle négatif du tube de tampon de réaction vers le compartiment de CONTROLE (bille jaune) du dispositif de test *illumigene*. Faire attention à ne pas introduire de bulles d'air. Fermer le dispositif de test *illumigene* et bien engager le mécanisme de verrouillage.
9. Retirer un dispositif de test *illumigene C. difficile* de sa pochette de protection pour le contrôle positif. Ouvrir le dispositif avec précaution, en tenant les tubes de manière à ne pas laisser tomber les réactifs lyophilisés au moment de l'ouverture. Placer le dispositif sur une surface plane ou un portoir approprié.

10. En utilisant un nouvel embout de pipette, transférer 50 µL de contrôle positif du tube de tampon de réaction vers le compartiment de TEST (bille blanche) d'un dispositif de test *illumigene* marqué de façon appropriée. Faire attention à ne pas introduire de bulles d'air. En utilisant un nouvel embout de pipette, transférer 50 µL de contrôle positif du tube de tampon de réaction vers le compartiment de CONTROLE (bille jaune) du dispositif de test *illumigene*. Faire attention à ne pas introduire de bulles d'air. Fermer le dispositif de test *illumigene* et bien engager le mécanisme de verrouillage.
11. Tapoter chaque dispositif sur la paillasse pour mélanger et éliminer les bulles.
12. Insérer chaque dispositif de test *illumigene* dans l'*illumipro-10* et commencer la réaction d'amplification et de détection. Les résultats s'afficheront à la fin du test.

## INTERPRETATION DES RESULTATS

L' *illumipro-10* mesure le changement d'absorbance du mélange de réaction à 650 ± 20 nm. Les résultats du test sont donnés comme non valide, positif, ou négatif.

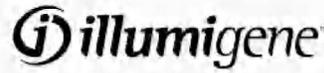
- Les réactifs de contrôle externe positif devraient donner un résultat positif.
- Les réactifs de contrôle externe négatif devraient donner un résultat négatif.
- Un test non valide indique une préparation incorrecte de l'échantillon ou une réaction incorrecte du compartiment de CONTROLE, et doit être répété.

Si les réactions attendues ne sont pas observées, la première étape pour déterminer la cause de l'échec est de répéter les tests de contrôle. Contacter le Service Technique de Meridian Bioscience ou votre distributeur local pour assistance si les résultats de contrôle escomptés ne sont pas observés de façon répétée.

## LIMITES DU TEST

Le contrôle positif est fabriqué dans une matrice de solution aqueuse. Bien qu'aucune interférence de la matrice du spécimen n'ait été observée avec ce test, la matrice aqueuse des contrôles pourrait ne pas contrôler de façon adéquate les effets de la matrice du spécimen. Si l'utilisateur désire ajouter des contrôles dans la matrice de l'échantillon, il doit se reporter aux directives de l'Institut des normes cliniques et de laboratoire (Clinical and Laboratory Standards Institute), EP14-A2, Evaluation des effets de matrice: directives approuvées – deuxième édition, janvier 2005.

## ESPAÑOL

 *C. difficile* External Controls

Sustancias de Control Externo para utilizar con la Prueba de amplificación de DNA *illumigene C. difficile*

REF 279920

IVD Dispositivo médico para diagnóstico in vitro

## USO INDICADO

El equipo de Control Externo *illumigene C. difficile* contiene reactivos de Control Positivo y Control Negativo para usar con el equipo de pruebas *illumigene C. difficile*. Los controles externos se usan como parte de un programa establecido de control de calidad.

## RESUMEN Y EXPLICACIÓN DE LA PRUEBA

Las pruebas de control de calidad se hacen para detectar factores tales como el deterioro de los reactivos, condiciones adversas ambientales o de la prueba, o variación en el desempeño del operador que puede causar errores en la prueba. Los reactivos de control externo, como el Control Positivo Externo y el Control Negativo Externo de *illumigene C. difficile*, no forman parte del sistema de pruebas, pero se analizan del mismo modo que las muestras de los pacientes.

## PRINCIPIOS BIOLÓGICOS

Para verificar que los equipos de Prueba de Amplificación de DNA *illumigene C. difficile* estén funcionando correctamente, deben probarse con reactivos de control positivo y control negativo externo de manera periódica. La frecuencia con la cual un laboratorio realiza pruebas de control externo se verá afectada por:

1. El nivel de competencia del laboratorio,
2. Los requisitos internos del mismo laboratorio,
3. Los requisitos de las agencias acreditadoras del laboratorio,
4. El número de operadores nuevos y distintos que realizan la prueba,
5. Si se ha añadido un lote nuevo de equipo a las pruebas,
6. Si el lote del equipo es de un envío diferente, y
7. Si se produjeron desviaciones en las recomendaciones del fabricante con respecto a las condiciones de almacenamiento o manejo.

Cuando se obtienen resultados inaceptables en las pruebas de control de calidad, todos los resultados de la prueba deben considerarse inválidos. Las fallas en las pruebas de Control de Calidad (CC) son una indicación de que hubo cambios ya sea en los reactivos, en las condiciones en que se realizó la prueba, o en el desempeño del operador.

## REACTIVOS/MATERIALES PROPORCIONADOS

El número máximo de pruebas que se puede obtener con este equipo está indicado en el exterior de la caja.

1. Control Positivo de *illumigene*: Solución tamponada con Tris que contiene DNA plasmidico no infeccioso (con insertos de *S. aureus* y *C. difficile*) con azida de sodio (0,09%) como conservante.
2. Control Negativo de *illumigene*: Solución tamponada con Tris que contiene DNA plasmidico no infeccioso (con inserto de *S. aureus*) con azida de sodio (0,09%) como conservante.

## MATERIALES NO PROPORCIONADOS

1. Prueba de amplificación de DNA *illumigene C. difficile* (número de catálogo 280050)
2. Guantes de látex desechables sin talco
3. Puntas para micropipetas con protección contra aerosoles libres de DNAasa y RNAasa

## EQUIPO NO PROPORCIONADOS

1. Agitador vorticial (Vórtex)
2. Cronómetro de intervalos.
3. Micropipeta con capacidad para dispensar 50 µL
4. *illumipro-10*

## PRECAUCIONES

1. Todos los reactivos son para uso diagnóstico in vitro solamente.
2. Este es un reactivo de control de calidad y se usa para evaluar el funcionamiento de la Prueba de amplificación de DNA *illumigene C. difficile*. No se debe utilizar directamente para analizar muestras de pacientes.
3. Transporte y almacene estos reactivos entre 2 y 8 C cuando no se estén usando. No los congele.
4. NO extraiga las muestras de Control Externo Positivo o Negativo.
5. No coma ni beba ni fume en las áreas en las que se estén manejando muestras o reactivos del equipo.
6. Use guantes desechables mientras maneje las muestras y lávese las manos cuidadosamente al terminar.
7. Manual de seguridad biológica en laboratorios microbiológicos y biomédicos de los Centros para el control y prevención de enfermedades de los EE. UU. y de los Institutos Nacionales de Salud de los EE. UU., 2007 (CDC/NIH manual "Biosafety in Microbiology and Biomedical Laboratories", 2007).
8. Deben emplearse los Programas de Control de Calidad para laboratorios que hacen pruebas moleculares.
9. El Dispositivo para la prueba *illumigene C. difficile* contiene reactivos liofilizados. La bolsa protectora no debe abrirse hasta que no esté todo listo para realizar la prueba.
10. El Dispositivo para la Prueba *illumigene C. difficile* contiene un sistema de cierre diseñado para prevenir la contaminación del área de la prueba con el producto de amplificación. NO use Dispositivos para la Prueba con cierres dañados.
11. Inmediatamente después del procedimiento, deseche los Dispositivos para la Prueba *illumigene*, y asegúrese de que la pestaña de cierre del dispositivo está en su sitio. La apertura del dispositivo después de la amplificación puede causar contaminación del área de prueba con producto de amplificación.

## VIDA UTIL Y ALMACENAMIENTO

La fecha de caducidad está indicada en la etiqueta del equipo. Almacene el kit entre 2-8 C.

## PROCEDIMIENTO DE LA PRUEBA DEL CONTROL DE CALIDAD

**Esta ensayo debe ser realizado siguiendo las regulaciones de acreditación locales, estatales o federales.**

1. Permita que los Controles Externos *illumigene* y todos los componentes del equipo alcancen la temperatura ambiente (21-27 C) antes de realizar la prueba. Resultados incorrectos pueden ser obtenidos si el Material de Control no alcanza temperatura ambiente (21-27 C) antes de realizar la prueba.
2. Utilice un Dispositivo para la Prueba *illumigene C. difficile* por cada reactivo de Control Positivo y Control Negativo que vaya a analizarse.
3. Transfiera 50 µL de Control Negativo a un tubo con Tampón de Reacción de *illumigene* adecuadamente marcado.
4. Mezcle en un agitador vorticial durante unos 10 segundos el tubo con Tampón de Reacción que contiene el Control Negativo.
5. Transfiera 50 µL de Control Positivo a un tubo adecuadamente marcado con Tampón de Reacción de *illumigene*.
6. Mezcle en un agitador vorticial durante unos 10 segundos el tubo con Tampón de Reacción que contiene el Control Positivo.
7. Saque un Dispositivo para la Prueba *illumigene C. difficile* de la bolsa protectora en que viene para el Control Negativo. Abra cuidadosamente el dispositivo de tal manera que el reactivo liofilizado no se caiga al abrirlo. Coloque el dispositivo en una superficie plana o en una gradilla que pueda acomodarlo.
8. Usando una punta de pipeta nueva, transfiera 50 µL del tubo de Tampón de Reacción que contiene el Control Negativo a la cámara de TEST (perla blanca) de un Dispositivo de Prueba *illumigene* adecuadamente marcado. No introduzca burbujas. Usando una punta de pipeta nueva, transfiera 50 µL del tubo de tampón de reacción que contiene el Control Negativo a la cámara de CONTROL (perla amarilla) del dispositivo para la Prueba *illumigene*. No introduzca burbujas. Cierre el Dispositivo para la Prueba *illumigene* y ajuste el cierre de modo que quede seguro.
9. Saque un Dispositivo para la Prueba *illumigene C. difficile* de la bolsa protectora en que viene para el Control Positivo. Abra cuidadosamente el dispositivo de tal manera que el reactivo liofilizado no se caiga al abrirlo. Coloque el dispositivo en una superficie plana o en una gradilla que pueda acomodarlo.
10. Usando una punta de pipeta nueva, transfiera 50 µL del Tampón de Reacción que contiene el Control Positivo a la cámara de TEST (perla blanca) de un Dispositivo de Prueba *illumigene* adecuadamente marcado. No introduzca burbujas. Usando una punta de pipeta nueva, transfiera 50 µL del tubo de tampón de reacción que contiene el Control Positivo a la cámara de CONTROL (perla amarilla) del dispositivo para la Prueba *illumigene*. No introduzca burbujas. Cierre el Dispositivo para la Prueba *illumigene* y ajuste el cierre de modo que quede seguro.
11. Dé golpecitos ligeros sobre el mesón con cada dispositivo con el objeto de mezclar y eliminar las burbujas.

12. Introduzca cada Dispositivo para la Prueba *illumigene* dentro del *illumipro-10* e inicie la reacción de amplificación y detección. Los resultados se mostrarán al concluir la prueba.

## INTERPRETACIÓN DE RESULTADOS

El *illumipro-10* mide el cambio de absorbancia a 650 ± 20 nm en la mezcla de reacción. Los resultados de la prueba se califican como Inválido, Positivo o Negativo.

- Los reactivos de Control Positivo Externo deben dar un resultado positivo.
- Los reactivos de Control Negativo Externo deben dar un resultado negativo.
- Los resultados inválidos de la prueba indican una preparación inadecuada de la muestra o una reacción inadecuada en la cámara de CONTROL y deben repetirse.

Si los resultados esperados para el control no son observados, repita la prueba de control como primer paso para determinar la causa de la falla. Si se repite la falla luego de repetir el control contacte el Departamento de Servicios Técnicos de Meridian al 1-800-343-3858 (USA) o su distribuidor local.

## LIMITACIONES DEL PROCEDIMIENTO

El Control Positivo se fabrica en una matriz de solución acuosa. A pesar de que con esta prueba no se ha demostrado interferencia entre la muestra y la matriz, la matriz acuosa de los controles puede no controlar adecuadamente los efectos de la matriz de la muestra. Si el usuario desea proporcionar controles en la matriz de la muestra, debe consultar la Clinical and Laboratory Standards Institute guideline EP14-A2, Evaluation of Matrix Effects: Approved Guideline – second edition, January 2005 (Directriz EP14-A2 de Estándares clínicos y de laboratorio, Evaluación de los efectos de matriz: directriz aprobada, segunda edición, enero de 2005)

## DEUTSCH

 *C. difficile* External Controls

Externe Kontrollmaterialien zur Verwendung mit dem  
*illumigene C. difficile*-DNA-Amplifikationsassay

REF 279920

IVD In-vitro-Diagnostikum

## VERWENDUNGSZWECK

Der Externkontroll-*illumigene C. difficile*-Testkit enthält positive und negative Kontrollreagenzien zur Verwendung mit dem *illumigene C. difficile*-Testkit. Externe Kontrollen sind Teil eines routinemäßigen Qualitätssicherungsprogramms.

## ZUSAMMENFASSUNG UND ERLÄUTERUNG DES TESTS

Qualitätskontrolltests werden durchgeführt, um potenziell zu Testfehlern führende Faktoren, wie Reagenzienzerfall, abträgliche Umgebungs- oder Testbedingungen oder auch wechselnde Benutzerleistung zu identifizieren. Externe Kontrollreagenzien, wie die externe positive und die negative *illumigene C. difficile*-Kontrolle, sind Reagenzien, die nicht im Testsystem integriert sind, sondern in der gleichen Weise wie Patientenproben analysiert werden.

## TESTPRINZIP

Um zu bestätigen, dass die *illumigene C. difficile*-DNA-Amplifikations-Testkits einwandfrei funktionieren, sind diese regelmäßig mit bekannten positiven und negativen externen Kontrollreagenzien zu testen. Die Häufigkeit der Analyse externer Kontrollen im Labor ist abhängig von folgenden Faktoren:

1. Dem professionellen Leistungsniveau des Labors.
2. Den laborinternen Auflagen,
3. Den Auflagen der betreffenden Laborzulassungsbehörden,
4. Der Anzahl der neuen und verschiedenen Benutzer, die den Test durchführen,
5. Ob der Testanordnung eine neue Kit-Charge hinzugefügt wird,
6. Ob die Kit-Charge aus einer anderen Lieferung stammt,
7. Ob die Herstellerangaben bezüglich Lagerungs- oder Handhabungsbedingungen eingehalten wurden.

Bei inakzeptablen Qualitätskontrolltestergebnissen sind sämtliche Testergebnisse als ungültig zu erachten. Fehlgeschlagene QK-Tests sind ein Anzeichen für veränderte Reagenzien, Testumgebungsbedingungen oder Benutzerleistung.

## REAGENZIEN/ENTHALTENE MATERIALIEN

Die Höchstzahl der mit diesem Testkit durchführbaren Tests ist auf der Aussenseite der Packung angegeben.

1. Positive *illumigene*-Kontrolle: Tris-gepufferte Lösung, die nicht infektiöse Plasmid-DNA (*S. aureus*- und *C. difficile*-Inserts) mit Azid als Konservierungsmittel enthält (0,09%).
2. Negative *illumigene*-Kontrolle: Tris-gepufferte Lösung, die nicht infektiöse Plasmid-DNA (*S. aureus*-Insert) mit Azid als Konservierungsmittel enthält (0,09%).

## BENÖTIGTE, ABER NICHT ENTHALTENE MATERIALIEN

1. *illumigene C. difficile*-DNA-Amplifikations-Testkit (Bestell-Nr. 280050)
2. Einmal-Handschuhe aus Latex, puderfrei
3. DNAse/RNAse-freie, aerosolresistente Pipettenspitzen

## NICHT IM LIEFERUMFANG ENTHALTENE GERÄTSCHAFTEN

1. Vortexmischer
2. Intervallzeitgeber
3. Mikropipette mit Abgabekapazität von 50 µL



## VORSICHTSMASSNAHMEN

- Sämtliche Reagenzien sind ausschließlich für die In-vitro-Diagnostik bestimmt.
- Dies ist ein Qualitätskontrollreagenz, das zur Beurteilung der Leistung des *illumigene C. difficile*-DNA-Amplifikations-Assay dient. Es dient nicht unmittelbar für das Testen von Patientenproben.
- Diese Reagenzien bis zum Gebrauch bei 2–8 C transportieren und lagern. Nicht einfrieren.
- Die externen positiven und negativen Kontrollen NICHT extrahieren.
- In Bereichen, in denen Proben oder Kit-Reagenzien gehandhabt werden, darf nicht gegessen, getrunken oder geraucht werden.
- Bei der Handhabung von Proben stets Einmal-Handschuhe tragen und danach die Hände gründlich waschen.
- CDC/NIH-Handbuch „Biosafety in Microbiology and Biomedical Laboratories“, 2007
- Es sollten Qualitätssicherungsprogramme für Labors eingesetzt werden, die die Molekulartests durchführen.
- Das *illumigene C. difficile*-Testgerät enthält lyophilisierte Reagenzien. Der Schutzbeutel sollte erst unmittelbar vor der Durchführung des Assays geöffnet werden.
- Das *illumigene C. difficile*-Testgerät besitzt eine Verschlusslasche, die vor Kontaminierung des Testbereichs durch das Amplifikationsprodukt schützen soll. KEINE Testgeräte mit defekten Verschlusslaschen verwenden.
- Gebrauchte *illumigene*-Testgeräte unmittelbar nach der Verarbeitung entsorgen und die Verschlusslaschen dabei fest geschlossen belassen. Falls das Gerät nach der Amplifikation geöffnet wird, könnte der Testbereich mit Amplifikationsprodukt kontaminiert werden.

## HALTBARKEIT UND LAGERUNG

Das Verfallsdatum ist auf dem Kit-Etikett angegeben. Den Test bei 2–8 C lagern.

## QUALITÄTSKONTROLL-TESTDURCHFÜHRUNG

Den Test gemäß der einschlägigen lokalen, bundesstaatlichen oder nationalen bzw. zulassungsbehördlichen Auflagen durchführen.

- Die externen *illumigene*-Kontrollen sowie alle Kit-Komponenten vor dem Testen auf Zimmertemperatur bringen (21–27 C). Werden die Kontrollmaterialien vor dem Einsatz nicht auf Zimmertemperatur gebracht, kann dies zu inkorrekten Ergebnissen führen.
- Für jedes zu testende positive und negative Kontrollreagenz ein *illumigene C. difficile*-Testgerät verwenden.
- 50 µL der negativen Kontrolle in ein entsprechend gekennzeichnetes *illumigene*-Reaktionspufferröhrchen transferieren.
- Das Reaktionspufferröhrchen mit der negativen Kontrolle etwa 10 Sekunden lang mit dem Vortexmischer mischen.
- 50 µL der positiven Kontrolle in ein entsprechend gekennzeichnetes *illumigene*-Reaktionspufferröhrchen transferieren.
- Das Reaktionspufferröhrchen mit der positiven Kontrolle etwa 10 Sekunden lang mit dem Vortexmischer mischen.
- Für die negative Kontrolle ein *illumigene C. difficile*-Testgerät aus dem Schutzbeutel nehmen. Das Gerät sorgfältig öffnen und die Röhrchen so halten, dass das lyophilisierte Reagenz nach dem Öffnen nicht herausfällt. Das Gerät auf einer ebenen Fläche oder in einem geeigneten Gestell platzieren.
- Mit Hilfe einer neuen Pipettenspitze 50 µL des Reaktionspufferröhrchens mit der negativen Kontrolle in die KONTROLL-Kammer (weiße Kugel) eines entsprechend gekennzeichneten *illumigene*-Testgeräts transferieren. Keine Luftblasen einbringen. Mit Hilfe einer neuen Pipettenspitze 50 µL des Reaktionspufferröhrchens mit der negativen Kontrolle in die KONTROLL-Kammer (gelbe Kugel) des *illumigene*-Geräts transferieren. Keine Luftblasen einbringen. Das *illumigene*-Testgerät schließen und die Verschlusslasche gut fixieren.
- Für die positive Kontrolle ein *illumigene C. difficile*-Testgerät aus dem Schutzbeutel nehmen. Das Gerät sorgfältig öffnen und die Röhrchen so halten, dass das lyophilisierte Reagenz nach dem Öffnen nicht herausfällt. Das Gerät auf einer ebenen Fläche oder in einem geeigneten Gestell platzieren.
- Mit Hilfe einer neuen Pipettenspitze 50 µL des Reaktionspufferröhrchens mit der positiven Kontrolle in die TEST-Kammer (weiße Kugel) eines entsprechend gekennzeichneten *illumigene*-Testgeräts transferieren. Keine Luftblasen einbringen. Mit Hilfe einer neuen Pipettenspitze 50 µL des Reaktionspufferröhrchens mit der positiven Kontrolle in die KONTROLL-Kammer (gelbe Kugel) des *illumigene*-Geräts transferieren. Keine Luftblasen einbringen. Das *illumigene*-Testgerät schließen und die Verschlusslasche gut fixieren.
- Jedes Gerät auf die Arbeitsfläche klopfen, um den Inhalt zu mischen und Luftblasen zu entfernen.
- Jedes *illumigene*-Testgerät in den *illumipro-10* geben und die Amplifikationsreaktion und den Nachweis einleiten. Die Ergebnisse werden nach dem Abschluss des Laufs angezeigt.

## AUSWERTUNG DER ERGEBNISSE

Der *illumipro-10* misst die Extinktionsänderung der Reaktionsmischung bei 650 ± 20 nm. Die Assay-Ergebnisse werden als „Invalid“ (ungültig), „Positive“ (positiv) oder „Negative“ (negativ) ausgegeben.

- Externe positive Kontrollreagenzien sollten ein positives Ergebnis erbringen.
- Externe negative Kontrollreagenzien sollten ein negatives Ergebnis erbringen.
- Ungültige Testergebnisse weisen auf eine fehlerhafte Probenvorbereitung oder eine fehlerhafte KONTROLL-Kammer-Reaktion hin und müssen wiederholt werden.

Wenn die erwarteten Reaktionen für die Kontrollen nicht beobachtet werden, zur Ermittlung der Ursache des Versagens als Erstes die Kontrolltests wiederholen. Lassen sich auch bei wiederholten Tests die erwarteten Reaktionen nicht erzielen, bitten Sie den Technischen Support von Meridian Bioscience an (USA): (001) 800-343-3858 oder wenden Sie sich an Ihren zuständigen Auslieferer.

## EINSCHRÄNKUNGEN

Die positive Kontrolle wird in einer wässrigen Lösungsmatrix hergestellt. Obwohl bei diesem Assay keine Störung durch die Probenmatrix beobachtet wurde, kann es sein, dass die wässrige Matrix der Kontrollen Probenmatrixeffekte nicht adäquat kompensiert. Falls der Benutzer der Probenmatrix Kontrollen hinzufügen möchte, wird er auf die folgende Richtlinie des US-amerikanischen Normenausschusses Clinical and Laboratory Standards Institute hingewiesen: EP14-A2, Evaluation of Matrix Effects: Approved Guideline – 2. Ausgabe, Januar 2005.



SN11273

REV. 07/10

Manufactured By

Meridian Bioscience, Inc.  
USA/Corporate Office  
3471 River Hills Drive  
Cincinnati, Ohio 45244  
Telephone: (513) 271-3700  
Orders/Customer Service:  
(800) 543-1980  
Technical Support Center:  
(800) 343-3858  
Information Fax: (513) 272-5432  
Ordering Fax: (513) 271-0124

---

Meridian Bioscience Europe  
Via dell'Industria, 7  
20020 Villa Cortese (MI)  
Italy  
Authorized Representative Tel: +39 0331 433635  
Fax: +39 0331 433618  
e-mail: info@mdeur.com

Meridian Bioscience Europe France  
Le Quadra  
455, Promenade des Anglais  
06295 Nice Cedex-3  
France  
Tel: +33 (4) 93 18 72 10  
Fax: +33 (4) 93 18 72 11  
e-mail: info@meridianbioscience.fr

Meridian Bioscience Europe s.a. / n.v.  
Rue de l'Industrie 7  
1400 Nivelles  
Belgium  
Tel: +32 (0) 67 89 59 59  
Fax: +32 (0) 67 89 59 58  
e-mail: info@mdeur.be

Meridian Bioscience Europe b.v.  
Haldorheiweg 6  
5282 SN Boxtel  
The Netherlands  
Tel: +31 (411) 621166  
Fax: +31 (411) 624841  
e-mail: meridian.info@planet.nl

## INTERNATIONAL SYMBOL USAGE

You may see one or more of these symbols on the labeling/packaging of this product:  
Key guide to symbols (Guida ai simboli, Guide des symboles, Guía de símbolos, Erläuterung der graphischen symbole)

	Use By / Utilizzare entro / Utiliser jusque / Fecha de caducidad / Verwendbar bis	<b>CONTROL +</b>	Positive control / Controllo positivo / Contrôle positif / Control positivo / Positive Kontrolle
<b>LOT</b>	Batch Code / Codice del lotto / Codo do lot / Código de lote / Chargenbezeichnung	<b>CONTROL -</b>	Negative control / Controllo negativo / Contrôle négatif / Control negativo / Negative Kontrolle
<b>IVD</b>	In vitro diagnostic medical device / Dispositivo médico-diagnóstico in vitro / Dispositif médical de diagnostic in vitro / Dispositivo médico para diagnóstico in vitro / In-Vitro-Diagnostikum	<b>SMP PREP DIL SPE</b>	Sample Preparation Apparatus containing Sample Diluent / Appareat per la preparazione del campione contenente il diluente del campione / Système pour la préparation de l'échantillon, objet inclus / Appareat para Preparación de Muestra con Diluyente de Muestra / System zur Probenzubereitung, in dem sich Probenverdünnungspuffer befindet
<b>CE</b>	This product fulfils the requirements of Directive 98/79/EC on in vitro diagnostic medical devices / Questo prodotto soddisfa i requisiti della Direttiva 98/79/CE sui dispositivi medico-diagnostici in vitro / Ce produit répond aux exigences de la Directive 98/79/CE relative aux dispositifs médicaux de diagnostic in vitro / Este producto cumple con las exigencias de la Directiva 98/79/CE sobre los productos sanitarios para diagnóstico in vitro / Dieses Produkt entspricht den Anforderungen der Richtlinie über die In-Vitro-Diagnostika 98/79/EG	<b>EC REP</b>	Authorized Representative in the European Community / Rappresentante Autorizzato nella Comunità Europea / Mandatario dans la Communauté européenne / Bewillmächtigter in der Europäischen Gemeinschaft
<b>REF</b>	Catalogue number / Numéro de catalogue / Referência do catálogo / Número de catálogo / Bestellnummer		Do not heat / Non riscaldare / Ne pas chauffer / No congeal / Nicht Erhitzen
	Consult instructions for Use / Consultare le istruzioni per l'uso / Consulter les instructions d'utilisation / Consulta las instrucciones de uso / Gebrauchsanweisung beachten	<b>RoHS</b>	Restriction of Hazardous Substances / Restrizione all'uso di sostanze pericolose / Limitation de substances dangereuses / Restricción de sustancias peligrosas / Beschränkung gefährlicher Stoffe
	Manufacturer / Fabricante / Fabricant / Fabricante / Hersteller		Caution consult accompanying documents / Attention, vedere e attenersi per l'uso / Attention voir notice d'instructions / Atención, ver instrucciones de uso / Achtung, Begleitdokumente beachten
	Contains sufficient for <n> tests / Contiene sufficiente per <n> test / Contient suffisant pour <n> tests / Contiene suficiente para <n> ensayos / Inhalt ausreichend für <n> Prüfungen	<b>BUF RXN</b>	Reaction Buffer / Tampon de reazione / Solution de réaction tamponée / Tampon de Réaction / Reaktionspuffer
	Temperature limitation / Limiti di temperatura / Limites de température / Límite de temperatura / Temperaturbegrenzung	<b>ETL</b>	ETL Registered Mark Certified / Marchio di certificazione registrato a livello nazionale / Certifié Conformité ETL / Marca de Certificación Registrada Nacional / ETL Konform bestätigt
<b>SN</b>	Serial number / Numero di serie / Número de serie / Numéro de série / Seriennummer		Recycle – do not dispose of as general waste / Riciclare – non smaltire come rifiuto generico / Recycler – ne pas jeter dans une poubelle / Reciclar – no desheche como basura general / Recycling dieses Produkt nicht über den normalen Entsorgung
<b>TEST</b>	Test Device / Dispositivo test / Dispositif de test / Dispositivo de Prueba / Testgerät	<b>EX TUBE</b>	Extraction tube / Provette per festrazione / Tubes d'Extraction / Tubo de Extracción / Röhrchen zur Probenextraktion
	Date of manufacture / Data di fabbricazione / Date de fabrication / Fecha de fabricación / Herstellungsdatum		For IVD Performance Evaluation Only / Solamente per valutazione delle prestazioni / Masclle IVD reserved a l'évaluation des performances / Solo para evaluación del funcionamiento / Nur zur IVD Leistungsbewertung
	LASER RADIATION: Avoid Exposure to Beam / RADIATION LASER: Evitare l'esposizione al raggio / RAYONNEMENT LASER: Éviter toute exposition au faisceau / Radiación Laser: Evite l'exposición a los Rayos / LASERSTRALUNG: Direktion Kontakt mit dem Strahl vermeiden		HOT SURFACE: Keep hands away from Hot Surfaces / Surface chaude: Tenir les mains éloignées des surfaces chaudes / SURFACES CHAUDES: Ne pas toucher les surfaces chaudes / Superficies Calientes: Mantenga las manos alejadas de la superficie caliente / Heiß Oberfläche: Kontakt mit heißen Oberflächen vermeiden
<b>CAUTION</b>	CAUTION: Laser Radiation / ATTENZIONE: Radiazione Laser / AVERTISSEMENT: Rayonnement laser / Precaución: Radiación Laser / WARNUNG: Laserstrahlung	<b>IPX-0</b>	CAUTION: Protect from water / ATTENZIONE: Proteggere dall'acqua / AVERTISSEMENT: Prévenir de l'humidité / Precaución: Proteja de agua / WARNUNG: Vor Feuchtigkeit schützen
	CAUTION: Risk of Danger / ATTENZIONE: Pericolo / AVERTISSEMENT: Risque de danger / Precaución: Peligro / WARNUNG: Risikogefahr		

For technical assistance, call Technical Support Services at 800-343-3858 between the hours of 8AM and 6PM, USA Eastern Standard Time. To place an order, call Customer Service Department at 800-543-1980.





# illumipro-10

## User Manual



*Investigational Use Only: Performance Characteristics for this Device Have Not Been Established.*

## Instrument Intended Use and Function

The *illumipro-10* is an automated isothermal amplification and detection system for use with Meridian Bioscience, Inc. *illumigene* Loop-Mediated Amplification products.

The *illumipro-10* is intended to be used by trained laboratory professional users in moderately complex laboratory settings.

## Installation Procedures and Requirements

The *illumipro-10* and its accessories are securely packaged to prevent damage during shipment to the end user. The *illumipro-10 shipping* container and packaging should be inspected for damage prior to installation. Damaged instrumentation should not be installed as this could create a hazard to the end user. Report any damage to Meridian's Technical Support staff at 1-800-343-3859.

### *illumipro-10* Package Contents

- ① *illumipro-10* Automated Isothermal Amplification and Detection System
- ② *illumipro-10* Power Supply and Power Cord
- ③ *illumipro-10* Verification Standards
- ④ *illumipro-10* User Manual Binder

### External Thermal Printer Package Contents

*(Not included with IUO Device; shipped separately):*

- ⑤ Printer
- ⑥ Printer Cable
- ⑦ Printer Power Supply (12VDC Linear Adaptor)
- ⑧ Thermal Roll Paper (1 Roll)

### *illumipro-10* Optional Accessories

*(Not available with IUO Device)*

- ⑨ External Keyboard

### *illumipro-10* User Manual

*(Not included with IUO Device; shipped separately)*

## *illumipro-10* Installation

Installation of the *illumipro-10* and its accessories can be performed after contents have been inspected and the requirements described in this User Manual have been reviewed.

The *illumipro-10* should be placed on a sturdy, level surface. Set-up the instrument for use as follows:

- **Printer:** Connect the external printer to the *illumipro-10* using the supplied cabling. The printer connection is located at the back of the instrument. The connection port for the printer is identified with the following symbol: . Secure the printer connection and connect the power supply cable provided with the printer packaging to the printer.



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- **External Keyboard (optional):** Connect the optional, external keyboard to the unit using the supplied cabling. The External Keyboard connection is located at the back of the instrument. The connection port for the Keyboard is identified by the following symbol: . The Keyboard must be installed with the *illumipro-10* is powered off.
- **Power Supply:** Connect the power supply cable provided with the *illumipro-10* packaging to the unit. The power supply connection is located at the back of the instrument. The connection port for the power supply is identified with the following symbol: 12V ---- @4.5A. Connect the power supply cable to the power supply box.
- Plug the pronged ends of the *illumipro-10* and printer power cords to an appropriate power receptacle.

### ***illumipro-10* Set-up**

Instrument set-up is completed under the SYSTEM Menu. The user will be able to set the time format, date format and preferred language.

### ***illumipro-10* Performance Verification**

Performance verification must be performed after installation and prior to use. Optical verification is completed according to the instructions provided under the SERVICE Menu.

## Principles of Operation

The *illumipro*-10 is an automated isothermal amplification and detection system for target nucleic acid sequences found in human specimens. The instrument is used in conjunction with Meridian Bioscience, Inc's *illumigene* LOOP-Mediated Amplification in vitro diagnostic products.

The *illumipro*-10 is a menu driven laboratory instrument with two independent sample processing blocks, identified as Block A and Block B. Sample heating and optical detection is carried out for up to five two-chambered *illumigene* devices per Block. Each two-chambered *illumigene* device contains a Sample Chamber and a Control Chamber. Amplification of target DNA occurs during the heat cycle and results in the formation of precipitate detected by the *illumipro*-10 optics system. The precipitate generated by the presence of amplified target DNA leads to a turbid Sample/Control reaction solution which is then measured by absorbance. The *illumipro*-10 uses the change in turbidity of each Sample/Control reaction solution to report assay results as INVALID, POSITIVE, or NEGATIVE.

The *illumipro*-10 operates in four basic modes: ASSAY, RESULTS, SERVICE, and SYSTEM. Assay Selection and Sample Amplification occurs in the ASSAY mode; Test Results are managed in the 'RESULTS mode; basic instrument set-up is performed in the SYSTEM mode; and optical performance verification is completed in the SERVICE mode.

# Performance Characteristics and Specifications

## Performance Characteristics

*Performance characteristics have not yet been established for this device.*

## *illumipro-10* Specifications

- **Electrical**

Voltage Range:	120V AC
Operating Range, Supply:	100 – 240 VAC, 50/60 Hz
Voltage and Current Rating:	12 V DC, 4.5 Amp

- **Physical**

Dimensions:	21 cm x 29.2 cm x 9.5 cm
Weight:	2.95 ± 0.05 kg

- **Environmental**

Operating Temperature:	15 – 30C
Storage Temperature:	10 – 40C
Relative Humidity, Operating:	10 – 90%, non-condensing
Relative Humidity, Storage:	10 – 95%

## Printer Specifications

- **Electrical**

Supply Voltage (SMPS):	Input voltage (S, P) 12 V DC
------------------------	------------------------------

- **Environmental**

Operating Temperature:	0 – 40 C
Storage Temperature:	-10 – 50C
Relative Humidity, Operating:	30 – 80%
Relative Humidity, Storage:	10 – 90%

## Operating Instructions

The *illumipro-10* operates in four basic modes: ASSAY, RESULTS, SERVICE, and SYSTEM. Assay Selection and Sample amplification occurs in the ASSAY mode; Test Results are managed in the 'RESULTS mode; and basic instrument set-up is performed in the SYSTEM mode. The SERVICE mode is reserved for trained service professionals and is not accessible by the Laboratory User. General information regarding each mode of operation is provided in this chapter.

### Keypad

The functions of the *illumipro-10* are navigated through the keypad. The Keypad provides a simple user interface and allows for basic menu navigation, input of alphanumeric characters for sample identification, and Assay RUN initiation. Keypad functions will be referred to throughout this manual; keypad layout and symbols used are defined below.

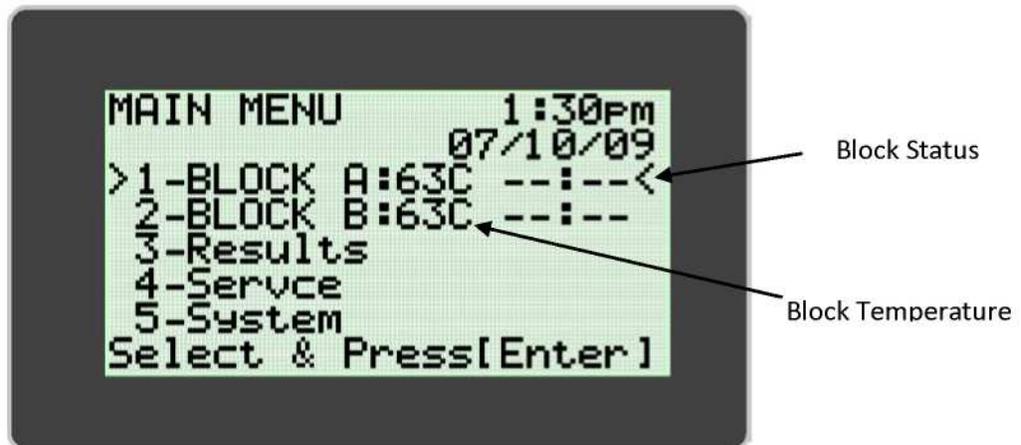


**NOTE:** For keypad buttons with multiple characters, scroll by pressing the keypad button multiple times.

Keypad Button	Character / Function
1	<SPACE>, 1
2	A, B, C, 2
3	D, E, F, 3
4	G, H, I, 4
5	J, K, L, 5
6	M, N, O, 6
7	P, Q, R, S, 7
8	T, U, V, 8
9	W, X, Y, Z, 9
0	0
-	-
▲	Scroll Up
▼	Scroll Down
◀	Scroll Back, Backspace
↵	Enter
<b>RUN</b>	Run Selected Assay Protocol

## Main Menu

The Main Menu screen allows the user to view Time Date, Assay Status and Block Temperature. The Main Menu is used to access the Results, Service and System Modes.



## Conventions Used:

Graphic	Description
***	BLOCK STATUS: Warming up; Block not at temperature
--:--	BLOCK STATUS: Idle; Block at Temperature
!!!	Warning, Instrument Requires Attention
...	Assay Menu Expansion Indicator
	Printer: Connect Printer to unit at this port. <i>(Back of instrument)</i>
	USB Port: Connect unit to external computer at this port. <i>(Back of instrument)</i>
PS/2 	External Keyboard: Connect unit to external keyboard (optional) at this port. <i>(Back of instrument)</i>
12V ---- @4.5A	<i>illumipro-10</i> Power Supply: Connect Power Supply to unit at this port. <i>(Back of instrument)</i>

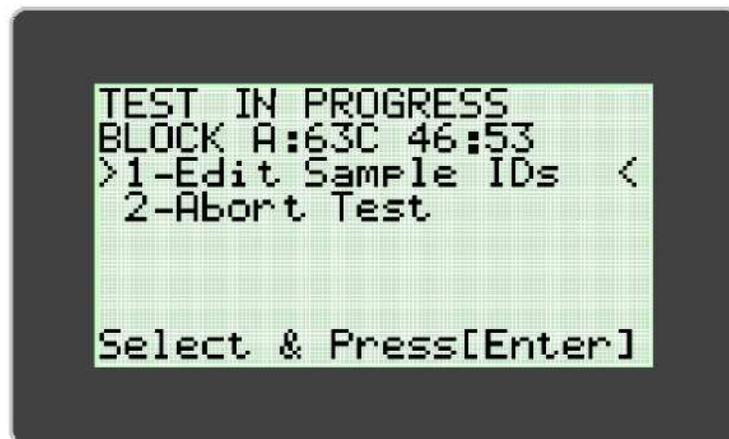
## ASSAY MODE

The ASSAY MODE allows the user to access and run programs on the *illumipro-10*. The user selects the Block to be used from the Main Menu and then selects the Assay to be run. Each Block can be selected and run independently. Upon selection of the Block to be used, the Assay Mode Menu appears. The User selects the assay to be run and follows the instructions displayed on the *illumipro-10* display.



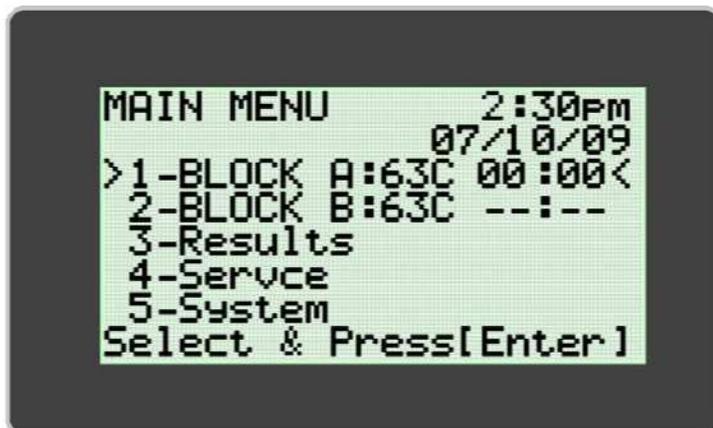
The *illumipro-10* display indicates that a Test is in process and prompts the user to enter Sample Identification information. Sample Identification information can be entered directly using the Keypad or may be scanned using the *illumipro-10* barcode scanner. Additional information regarding the Barcode Scanner is located in Appendix C of this manual.

The User enters Sample Identification Information by following the instructions shown on the *illumipro-10* display and initiates the Assay Run.



*NOTE: Block temperature will appear in the 'TEMP' field. The 'Block Status' field will display a timer indicated time until assay completion.*

The *illumipro-10* will complete the selected assay program and the Block Status on the MAIN MENU will be shown as '00:00'. Results for the selected assay can be viewed by selecting the Block displaying completed status and following the instructions shown on the *illumipro-10* display. Results can be printed manually by selecting the print option at the end of the results display or by enabling the Auto-Print feature during System Set-up.



Upon completion of the assay run, the user must remove the *illumigene* devices from the unit and discard appropriately.

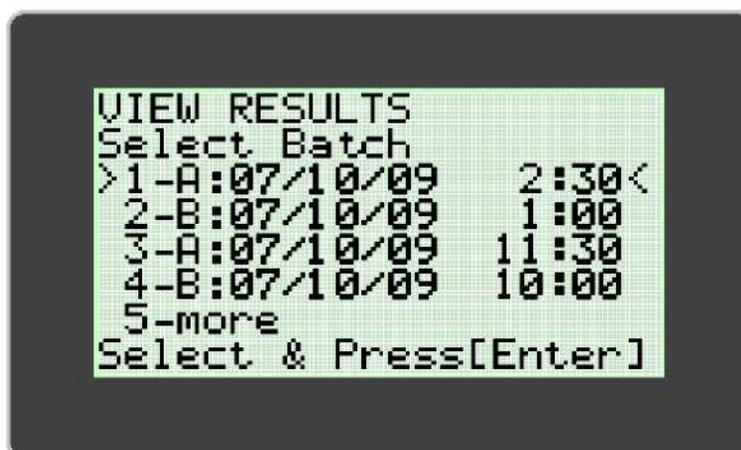
**NOTE: Care must be taken to avoid contamination of the equipment and workspace by target and/or amplified nucleic acids. DO NOT open illumigene devices after assay completion.**

## RESULTS MODE

The RESULTS MODE allows the user to view stored results, delete stored results and enable the auto-printer. The *illumipro-10* will store up to 1000 individual test results or 200 Batches. The instrument displays a warning to the user when result storage is approaching maximum capacity. RESULTS MODE is accessed by following the instructions shown on the *illumipro-10* display.

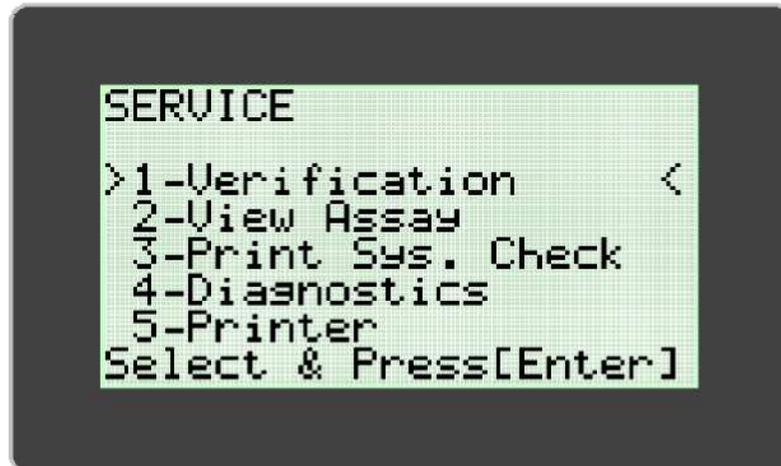


The User can view stored results by selecting the 'View Results' option. The 'View Results' menu allows the user to access stored data by Date and Block. Selected Batch Data is displayed and can be printed manually by selecting the print option at the end of the results display.



## SERVICE MODE

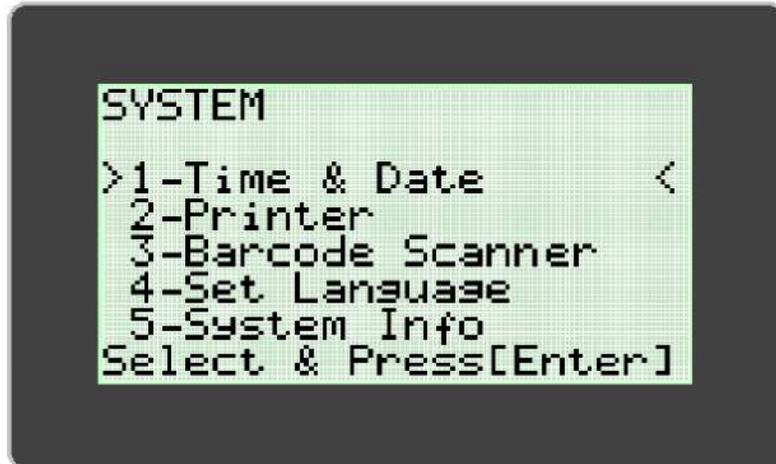
The SERVICE MODE allows the user to perform optics system verification, view assay parameters, print system check information, and configure the printer. **NOTE:** *The SERVICE MODE menu includes a 'Diagnostics' Option which can be accessed only by trained service personnel.*



**OPTICS SYSTEM VERIFICATION** is required to ensure proper function of the *illumipro-10*. Instructions for completion of the Optics System Verification are provided within the **CALIBRATION PROCEDURE** Section of this manual.

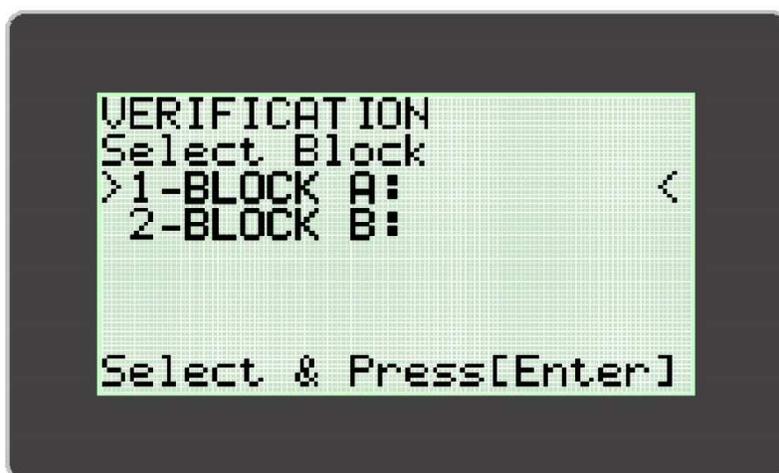
## SYSTEM MODE

The SYSTEM MODE allows the user to set and format time and date, configure the printer and barcode scanner, set user language, and view system information. The user may set time, date, or language (English, Italian, French, Spanish and German) based on local requirements and/or preference. The SYSTEM MODE allows the user to enable or disable automatic printing and the barcode scanner. System configuration is completed by following the instructions shown on the *illumipro-10* display.



## Calibration Procedures:

Calibration of the *illumipro-10* is not required. Verification of the OPTICS SYSTEM for each Block must be performed monthly to ensure proper function. Verification is completed using the Red Verification Standard included with the *illumipro-10*. Stepwise instructions for Optics System Verification are provided on the *illumipro-10* display, utilizing the SERVICE MODE menu.



Optic System Verification includes two stages. The first stage ensures that the optical path is clear and free of obstruction. The second stage confirms that the optics system is transmitting and detecting emitted light particles properly. Transmission and detection verification requires the use of the *illumipro-10* Red Verification Standard. The *illumipro-10* steps through the Verification protocol and prompts the user for action as necessary.

The Red Verification Standard must be seated firmly in the Heat Block wells. The Verification Standard should be should oriented with the asset number tag at the Well 1 position.

Upon completion of the Verification Protocol, the *illumipro-10* will display verification test results as either 'Pass' or 'Fail'. In the event that Verification testing does not give acceptable results, the user should verify the optical path is free of obstructions, the standard is free of visible defects, and repeat the verification testing. If repeat testing does not give passing verification results, contact Meridian's Technical Support Staff for further assistance.

**NOTE:** Each Block of the *illumipro-10* functions independently. For example, a failed verification test for Block A will not prevent use of Block B when Block B verification testing passes.

**WARNING:** *Do NOT leave verification standards in the illumipro-10. Verification Standards will get hot and could burn the user. Exposure to temperature may impact the*

## Operational Precautions and Limitations

The *illumipro-10* is intended for investigational use only. Performance characteristics for this device have not yet been established.

### WARNINGS:

	<p><b>CAUTION: Risk of Danger.</b> The <i>illumipro-10</i> is an electromechanical device that can cause physical shock or injury to the operator in not used in accordance with the procedures described in this manual.</p>
	<p><b>LASER RADIATION: Avoid Exposure to Beam.</b> The <i>illumipro-10</i> contains a class 3R laser product. The laser will not function when the lid is in the open position, however, care should be taken in the handling and use of this instrument.</p>
	<p><b>HOT SURFACE: Keep hands Away from Hot Surfaces.</b> The <i>illumipro-10</i> contains a heat block producing temperatures between 55 – 65 C during operation. Care should be taken to avoid direct contact with the heat block.</p>
	<p><b>CAUTION: Laser Radiation.</b> The <i>illumipro-10</i> contains a laser product. Service of the unit should be performed only by qualified personnel as optical exposure to the laser beam may cause injury.</p>
<p><b>IPX-0</b></p>	<p><b>CAUTION: Protect from water.</b> The <i>illumipro-10</i> does not protect from the egress of water. Do not expose to water or submerge the instrument.</p>

### PRECAUTIONS:

- The *illumipro-10* is an automated instrument that utilizes isothermal Loop-Mediated Amplification Technology. Care must be taken to avoid contamination of the equipment and workspace by target and/or amplified nucleic acids. Only qualified personnel should perform molecular testing.
- The *illumipro-10* is used in conjunction with Meridian Bioscience, Inc's *illumigene* LOOP-Mediated Amplification in vitro diagnostic products. Samples processed in the *illumipro-10* should be handled in accordance with the instructions provided in specific *illumigene* product instructions for use.
- Selected Language cannot be changed while a run is in process.
- Optical System Verifiers must be stored in the case provided. The optical verifiers must be protected from light and damage. Optical system verifiers should not be stored in the *illumipro-10*.
- Do not hot swab the optional *illumipro-10* keyboard. CAPS Lock will come on at power-up to indicate keyboard is online.
- The optional Keyboard must be plugged in while the *illumipro-10* is powered-off.
- When not in use, the *illumipro-10* should be stored with the lid closed.

## Service and Maintenance

Servicing of the *illumipro-10* should be performed by qualified professionals only. Contact Meridian Bioscience Technical Support at (800) 343-3858 for technical support or to make arrangements for service. **DO NOT ATTEMPT TO SERVICE THE *illumipro-10*.**

### Surface Cleaning

Cleaning of the exterior surfaces of the *illumipro-10* and the immediate work area should be performed as necessary, no less than daily when in use. Allow instrument to cool and wipe surfaces with a lint-free cloth moistened with DNase/RNase cleaning solution.

**WARNING:** Surface cleaning should be performed only when the instrument is powered-off AND disconnected from the power source. **DO NOT** use saturated clothes for cleaning.

### Heat Block Cleaning

Cleaning of the instrument heat block should be performed by qualified personnel only. Cleaning of the heat block should be performed only when contamination of the heat block is suspected. Contamination of the heat block may be DNA Sourced, or non-DNA Sourced. The cleaning protocol followed should be based on the source of the contamination as shown below:

- **DNA Contamination Cleaning Protocol**

1. Gently wipe heat block chamber with a dry Foam Swab.
2. Gently wipe heat block chamber with a foam swab moistened with xx% Bleach Solution.
3. Gently wipe heat block chamber with a dry Foam Swab.
4. Gently wipe heat block chamber with a foam swab moistened with xx% Alcohol.
5. Gently wipe heat block chamber with a dry Foam Swab.

**DO NOT** use saturated foam swabs for cleaning.

- **non-DNA Contamination Cleaning Protocol**

1. Gently wipe heat block chamber with a dry Foam Swab.
2. Gently wipe heat block chamber with a dry Foam Swab.
3. Gently wipe heat block chamber with a dry Foam Swab.

**DO NOT** use saturated foam swabs for cleaning.

**WARNING:** Heat block cleaning should be performed only when the instrument is powered-off AND disconnected from the power source. **DO NOT** use saturated swabs for cleaning.

**WARNING:** Do not attempt to clean the *illumipro-10* using compressed air.

**ALWAYS** perform Optical Verification Testing after Heat Block Cleaning.



The *illumipro-10* has been tested and found to be in compliance with the following requirements and Standards:

Standard	Description
IEC 61010-1	Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 1: General requirements
IEC 61010-2-010	Safety requirements for electrical equipment for measurement, control, and laboratory use- Part 2-010: Particular requirements for laboratory equipment for the heating of materials
IEC 61010-2-081	Safety requirements for electrical equipment for measurement, control, and laboratory use- Part 2-081: Particular requirements for automatic and semi-automatic laboratory equipment for analysis and other purposes
IEC 61010-2-101	Safety requirements for electrical equipment for measurement, control and laboratory use - Part 2-101: Particular requirements for in vitro diagnostic (IVD) medical equipment
UL 61010-1	UL standard for Safety Electrical Equipment for Measurement, Control, and Laboratory Use - Part 1: General Requirements
CSA C22.2# 61010-1	UL standard for Safety Electrical Equipment for Measurement, Control, and Laboratory Use - Part 1: General Requirements
CSA C22.2#61010-2-010	Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 2-010: Particular requirements for laboratory equipment for the heating of materials
CSA C22.2#61010-2-081	Safety Requirements for Electrical Equipment for Measurement, Control and Laboratory Use - Part 2-081: Particular Requirements for Automatic and Semi-Automatic Laboratory Equipment for Analysis and Other Purposes
CSA C22.2#61010-2-101	Safety Requirements for Electrical Equipment for Measurement, Control, and Laboratory use - Part 2-101: Particular Requirements for In Vitro Diagnostic (IVD) Medical Equipment

 <b>Manufactured By</b>	<b>Meridian Bioscience, Inc.</b> <b>USA/Corporate Office</b> 3471 River Hills Drive Cincinnati, Ohio 45244 Telephone: (513) 271-3700 Orders/Customer Service: (800) 543-1980 Technical Support Center: (800) 343-3858 Information Fax:(513) 272-5432 Ordering Fax:(513) 271-0124
 <b>Authorized Representative</b>	<b>Meridian Bioscience Europe</b> Via dell' Industria, 7 20020 Villa Cortese (MI) Italy Tel.: +39 0331 433636 Fax: +39 0331 433616 e-mail: info@mdeur.com

**Meridian Bioscience Europe France**  
 Le Quadra  
 455, Promenade des Anglais  
 06299 Nice Cedex-3  
 France  
 Tel.: +33 (0) 49 3187210  
 Fax: +33 (0) 49 3187211  
 e-mail: info@meridianbioscience.fr

**Meridian Bioscience Europe s.a. / n.v.**  
 Rue de l'Industrie 7  
 1400 Nivelles  
 Belgium  
 Tel.: +32 (0) 67 89 59 59  
 Fax: +32 (0) 67 89 59 58  
 e-mail: info@mdeur.be

**Meridian Bioscience Europe b.v.**  
 Halderheiweg 6  
 5282 SN Boxtel  
 The Netherlands  
 Tel.: +31 (411) 621166  
 Fax: +31 (411) 624841  
 e-mail: meridian.info@planet.nl

### INTERNATIONAL SYMBOL USAGE

You may see one or more of these symbols on the labeling/packaging of this product:

	<b>Consult operating instructions</b>		<b>Caution, consult accompanying documents</b>
	<b>Use by</b>		<b>Date of manufacture</b>
	<b>Batch code</b>		<b>Catalogue number</b>
	<b>Serial number</b>		<b>Authorised Representative in the European Community</b>
	<b>Positive Control</b>		<b>Negative Control</b>
	<b>Manufacturer</b>		<b>Sufficient For &lt;n&gt; tests</b>
	<b>For IVD Performance Evaluation Only</b>		<b>In Vitro Diagnostic Medical Device</b>
	<b>Temperature Limitation</b>		<b>This product fulfills the requirements of Directive 98/79/EC on in vitro diagnostic medical devices.</b>

For technical assistance, call Technical Support Services at (800) 343-3858 between the hours of 8AM and 6PM, USA Eastern Standard Time. To place an order, call Customer Service Department at (800) 543-1980.

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MERIDIAN BIOSCIENCE, INC.



Training guide



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**illumigene™ C. difficile**

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## 1.1 Introduction

Toxigenic *Clostridium difficile* is a major cause of antibiotic associated diarrhea and colitis and is the causative agent for virtually all cases of pseudomembranous colitis. Although about 2% of normal healthy adults are colonized with *C. difficile*, many patients acquire this organism through nosocomial infection. Exposure to most antibiotics is thought to allow proliferation of toxigenic *C. difficile* by disrupting the normal intestinal flora. Two large toxin proteins (TcdA [or toxin A] and TcdB [toxin B]) are thought to be the primary virulence factors of *C. difficile*. These toxins are encoded by two separate genes, named *tcdA* and *tcdB*, respectively. Together, with three additional genes, they form a 19.6kb pathogenicity locus called PaLoc.

The *illumigene*™ *C. difficile* assay utilizes loop-mediated isothermal amplification (LAMP) technology to detect the pathogenicity locus (PaLoc) of toxigenic *Clostridium difficile*. The *Clostridium difficile* PaLoc is a gene segment present in all known toxigenic *C. difficile* strains. The *C. difficile* PaLoc codes for both the Toxin A gene (*tcdA*) and the Toxin B gene (*tcdB*), has conserved border regions, and is found at the same site on the *C. difficile* genome for all toxigenic strains. The *illumigene*™ *C. difficile* assay detects the PaLoc by targeting a partial DNA fragment on the Toxin A gene. The *tcdA* target region was selected as *tcdA* is more conserved, while *tcdB* is more variant.

## 2.1 *illumigene*™ Technology

The *illumigene*™ *C. difficile* DNA amplification assay is based on loop-mediated amplification technology, which uses specifically designed primers to the PaLoc pathogenicity locus to provide for specific and continuous isothermal DNA amplification. A by-product of this amplification is the formation of magnesium pyrophosphate, which forms a white precipitate leading to a turbid reaction solution. This presence of turbidity signifies a positive reaction while the absence of turbidity represents a negative reaction. The *illumigene*™ *C. difficile* assay contains primers that specifically amplify a 204 bp region of the conserved 5' sequence of the *tcdA* gene within the PaLoc of toxigenic *C. difficile* in diarrheal stool samples from patients suspected of having CDAD. The results of the assay are determined using the Meridian *illumipro-10*™ Incubator / Reader.

*illumigene*™ *C. difficile* is intended for prescription use in moderately complex laboratory settings. The device is not intended for point-of-care use

## 3.1 *illumipro-10*™ Instrumentation

The *illumipro-10*™ is a menu driven laboratory instrument with two independent sample processing blocks, identified as Block A and Block B. The blocks can be run at the same time or separately. This makes the *illumipro-10* have flexibility when needed. Sample heating and optical detection is carried out for up to five two-chambered *illumigene*™ devices per Block. Each two-chambered *illumigene*™ device contains a Sample Chamber and a Control Chamber. Amplification of target DNA occurs during the heat cycle and results in the formation of precipitate detected by the *illumipro-10*™ optics system. The precipitate generated by the presence of amplified target DNA leads to a turbid Sample/Control reaction solution which is then measured by absorbance. The *illumipro-10*™ uses the change in turbidity of each Sample/Control reaction solution to report assay results as INVALID, POSITIVE, or NEGATIVE.

## 3.2 INSTALLATION AND SET-UP OF *illumipro-10™*

### Placement and Inspection

#### *illumipro-10™* Package Contents:

- a. *illumipro-10™* instrument
- b. Power Supply and Power Cord
- c. Verification Standards
- d. User Manual Binder
- e. USB data cable (optional)
- f. External keyboard (optional)

#### External Thermal Printer Package Contents:

- a. Printer
- b. Printer Cable
- c. Printer Power Adaptor and Cord
- d. Thermal Roll Paper

1. Place the instrument on a flat level surface, away from direct sun or bright lights.
2. Clean the area thoroughly with 0.525% Bleach solution, Bleach-rite, or equivalent.
3. Wipe down with 70% alcohol to clean and remove bleach.
4. Check the condition of the outer/inner packaging. Note any damage to Meridian's Technical Support at 1-800-343-3859.

### Connections

1. Connect the power supply cable provided with the *illumipro-10™* packaging to the unit. The power supply connection is located at the back of the instrument.
2. Connect the power supply cable to the power supply box.
3. Connect the external printer to the *illumipro-10™* using the cabling supplied in the printer packaging. The printer connection is located at the back of the instrument identified by-. 
4. Connect the power supply cable provided with the printer packaging to the printer.
5. Connect the printer power supply cable to the power supply box.
6. Turn on *illumipro-10™* and printer.
7. Optional – External Keyboard - connect the external keyboard to the unit using the supplied cabling. The External Keyboard connection is located at the back of the instrument. The Keyboard must be plugged in while the *illumipro-10™* is powered-off.

### 3.3 INITIAL SET-UP OF *illumipro-10™*

#### ***Setting and Formatting the Date and Time***

1. From the Main Menu Screen **Press#5** for “System”.
2. **Press #1** for “Set Time” on the Time & Date menu screen.
3. The “Set Time” screen will appear, use the keypad to enter the time in 24 hour format.
4. Press Enter  (The instrument will automatically go back to the Time & Date Menu)
5. **Press #2** for “Time Format”.
6. **Press#1** for am/pm or **Press#2** for 24 hour format. (Instrument will automatically go back to the Time & Date Menu).
7. **Press #3** to set the date.
8. Using the keypad, enter the day, month and year.
9. Press Enter  (Instrument will go back to the Time and Date Menu Screen)
10. **Press #4** for “Date Format”.
11. Press the # number of the desired format from the “Date Format” menu.
12. Press Enter 

#### ***Set the Language***

1. From the Main Menu screen **Press #5** for “System”
2. **Press #4** for “Select Language” from the “System” menu screen
  - a) **Press#1** - English
  - b) **Press#2** - Spanish
  - c) **Press#3** - French
  - d) **Press#4** - Italian
  - e) **Press#5** - Deutsch
3. Press Enter 

#### ***Enable/Disable Printer***

When the printer is enabled, the batch record results will print when the batch number is selected from the View Results Screen. The assay parameters print when the assay is selected from the View Assay Screen.

When the printer is disabled, the batch record results print when the “0” button is pressed.

1. From the Main Menu **Press # 5** for “System”
2. **Press #2** for “Printer” From the System menu screen
3. **Press #1** to Enable or **Press#2** to Disable

#### ***Enable/Disable Barcode Scanner***

1. From the Main Menu **Press # 5** for “System”
  2. **Press #3** for “Barcode Scanner” from the System menu screen
- From the Barcode Scanner screen **Press #1** to Enable or **Press#2** to Disable

### 3.4 OPTICAL VERIFICATION FOR *illumipro-10*<sup>™</sup>

- Performance verifications must be performed as part of installation and prior to use. Upon installation, the reader will heat to 63°C and display !!! and read **warning, instrument requires attention**. This indicates the verification standards must be run.
- After initial installation Verification should then be performed on a monthly basis.

**Caution** should be taken in removing the standards for they will be warm to the touch when complete.

#### Verification of the Optics

1. From the Main Menu **Press#4** for “Service”.
  2. From the “Service” screen **Press#1** for “Verification”.
  3. From the “Verification” screen **Press#1** for Block A or **#2** for Block B.
  4. Press Down and Lift Lid.
  5. Remove all Sample Tubes if needed.
  6. Press Enter 
  7. Close Lid.
  8. Empty Well Test Verification is performed (machine will click once complete).
  9. Insert Red Verification Standards with serial number to the front.
  10. Press Enter 
  11. Close Lid.
  12. Red Verification test performed.
  13. Remove Standards (**caution** standards may be warm to the touch).
  14. Press Enter  (Results will printout automatically).
  15. Record results on Verification Log.
- \*If Verification Fails- Remove Standards and proceed to cleaning procedures

#### System Self Check

When the reader is turned on, the *illumipro-10*<sup>™</sup> performs a system self check, displaying the Main Menu Screen until complete. Should the instrument fail to pass the self test a beep will sound, and an error code will display. Customer is able to print these results for record keeping.

1. From the Main Menu Screen **Press#4** “Service”.
2. From the Service Screen **Press#3** for “Print System Check”.
3. System Self Check will print.

### 3.5 Entering Patient ID, Printing and Deleting Results

#### *Editing Patient ID When a Run is in Progress*

When a test run is initiated, Edit Sample ID will be viewed on the screen. Patient results may be entered at that time. Alternately, the user may edit the sample ID several minutes after the run is in progress.

1. **Press#1** for Block A or **Press#2** for Block B.
2. The screen will read TEST IN PROGRESS.
3. **Press #1** to edit sample IDs.
4. At the next screen choose the number of the sample you want to edit.
5. Enter the sample ID using the keypad, keyboard or barcode scanner.
6. Press enter 
7. Repeat steps 3-5 for each specimen ID to be edited.

#### *Reviewing and Printing Results*

1. From the Main menu screen, **Press #3** for “Results”.
2. **Press #1** – for “View results”.
3. Select the number of the run that you want to print or scroll the cursor to the run and press enter.
4. Selected results will automatically print.

#### *Deleting Results*

1. From the Main Menu Screen **Press #3** for “Results”.
2. From the Stored Results Menu **Press #2** for “Delete All”.
3. From the Delete All Menu select Cancel or Delete.

### 3.6 Maintenance & Cleaning of *illumipro-10™*

#### **Materials Needed for Cleaning procedures:**

- Cleaning Material
  - ✓ 10% Bleach
  - ✓ Alcohol
  - ✓ Disposable lint free cloth (kimwipes)
  - ✓ Foam swabs (Decontamination cleaning only)
- Training Manual
  - ✓ Daily QC Log (Appendix A)

#### **Preparation of Bleach Cleaning Solution (Optional)**

1. Using a graduated cylinder, measure 225mL of deionized (DI) water.
2. Add DI water to squirt or spray bottle.
3. Using a graduated cylinder, measure 25mL of Common Household Bleach.
4. Add to the DI water in squirt or spray bottle.
5. Mix well.

#### **General Cleaning Procedure**

1. Allow the instrument to cool.
2. Moistened a lint free cloth with Bleach-Rite Spray, .10% bleach. (prepared above)
3. Wipe outer surfaces with the moistened lint free cloth.
4. Record cleaning information of the *illumipro-10™* cleaning log.

#### **Heat Block and Well DNA Contaminated Cleaning Protocol**

1. Gently wipe heat block chamber with a dry foam swab.
2. Gently wipe heat block chamber with a foam swab moistened with 10% bleach solution.
3. Gently wipe heat block chamber with a dry foam swab.
4. Gently wipe heat block chamber with a foam swab moistened with 70% Alcohol solution.
5. Gently wipe heat block chamber with a dry foam swab.

#### **Instrument Service and Repair**

- Should the site have any problems with the *illumipro-10™*, please contact Meridian's Technical Support Department 800-343-3858 in the US.
  - If troubleshooting cannot fix the issue Technical Services will issue a Return Material Authorization number.
  - Instrument must be decontaminated prior to return.
  - Decontamination certificated located in the *illumipro-10™* manual must accompany the instrument being returned.
- Replacement instrument will be shipped within 24 hours.

## 4.1 illumigene™ - Running the assay

### Assay Preparation Steps

1. Before beginning specimens preparation, turn instrument on by flipping the switch located on the back right of the instrument.
2. Allow instrument to come to correct temperature. The main screen will show an asterisk \* while warming. The display will change to underscore \_ when ready.
3. Upon initial installation !!! will appear when the instruments gets to the correct temperature. This indicates the verification standards need run. See pag 7 for running verification standards.
4. Ensure the Heat Block is turned on and allowed to reach 95°C.
5. Clean the Specimen Preparation area thoroughly with 10% Bleach solution, Bleach-rite, or equivalent.
6. Wipe down with 70% alcohol to clean and remove bleach.

### Specimen Preparation

1. Prior to handling specimens, remove one specimen brush and Sample Preparation Apparatus for each specimen to be tested.  
\*An extraction control needs to be run with each extraction batch. (Use a known positive specimen or may be ordered from Meridian, item #500618)
2. Label the Sample Preparation Apparatus with the patient Identification.
3. Mix stool sample thoroughly.
4. Collect mixed sample specimen using Sample Collection Brush.
  - a. Liquid Stool: Immerse Brush completely into specimen.
  - b. Semi-solid Stool: Rotate Sample Collection Brush to lightly coat half the brush surface.
5. Insert the brush in the Collection device and tighten.
6. Vortex the specimen in the device for a minimum of 10 seconds.
7. Repeat Steps 3-6 for all samples to be processed.

### Extraction

1. Remove one **Clear Capped** Sample extraction tube for each specimen being tested.
2. Label each extraction tube with the patient identification.
3. Unscrew tip cap from the Sample Preparation Apparatus and the extraction tube.
4. Squeeze five to ten drops of sample into a clean *illumigene™* Sample Extraction Tube.
5. Place all Extraction Tubes containing diluted specimens into dry-bath/heat block set at 95°C.
6. Incubate specimens in heat block for 10 +/- 2 minutes.
7. To keep the area Clean and to promote Good Molecular Practice:
  - a. While specimens are in the heat block, put away raw stool specimens.
  - b. Thoroughly clean the area with 10% Bleach solution, Bleach-rite, or equivalent.
  - c. Wipe down with 70% alcohol to remove bleach. Change gloves
- \*Use Caution as extraction tubes may be hot.
8. After 10 minute incubation remove the tubes from the dry-bath/heat block and vortex for approximately 10 seconds.

### External Controls

1. External controls are run as extracted specimens.
2. Remove and Label one **Red Capped** Reaction Buffer Tube for the positive and one for the negative control.
3. Using a precision pipette, transfer 50µL of the positive control to the reaction buffer tube labeled positive control.
4. Using a new pipette tip, transfer 50µL of the negative control to the reaction buffer tube labeled negative control.
5. External controls should be run per lot or shipment or in accordance with federal, state or local requirements.

### Diluting Extracted Specimens

1. Remove one **Red Capped** Reaction Buffer tube for each specimen being tested.
2. Label each Reaction Buffer tube with the patient identification.
3. Transfer 50 µL of each extracted sample to an appropriately labeled *illumigene™* Reaction Buffer tube (Red Cap).
4. Vortex the Reaction Buffer Tube containing extracted sample for approximately 10 seconds.
5. Repeat steps 3 and 4 for all the samples to be tested before proceeding.

### *illumigene™* - Running the assay

#### Adding Specimens to Master Mix

1. Remove one *illumigene™* C. difficile Device per sample or control and place in an appropriate rack.
2. Using an RNase free aerosol barrier pipette tip, transfer 50 µL from the Reaction Buffer tube containing extracted sample or control to the TEST chamber (White Bead).
3. Using a new pipette tip, transfer 50 µL from the reaction buffer tube to the CONTROL chamber (Yellow Bead).
4. Close and lock the *illumigene™* device. **DO NOT** open once device is locked.
5. Perform steps 2-3 for each specimen or control to be tested.
6. Finger flick devices to mix, then tap on the bench top to remove bubbles.
7. Visually inspect each device to ensure all air bubbles are removed. Take specimens to the *illumipro-10™* for amplification and results interpretation.

#### *illumipro-10™* - empty well test

1. To run specimens on the *illumipro-10™*, From Main Menu select Block A or Block B.
  2. Press Enter 
  3. From Select Assay Menu select assay number to be run.
    - a. (#1=C. difficile)
  4. Press Down on lid to release the lock and lift lid.
  5. Remove any sample tubes left in instrument.
  6. Press enter 
  7. Close lid.
  8. Empty Well Test Verification is performed.
- \*Machine will click once complete

### **Amplification**

- 1 After successful empty well test, continue by pressing down on the lid to Release the lock.
- 2 Lift the lid. (User has two minutes to begin the run).
- 3 Insert samples.
- 4 Close lid.
- 5 Press **RUN**.
- 6 The timer will begin counting down.

### **Entering Specimen Identification**

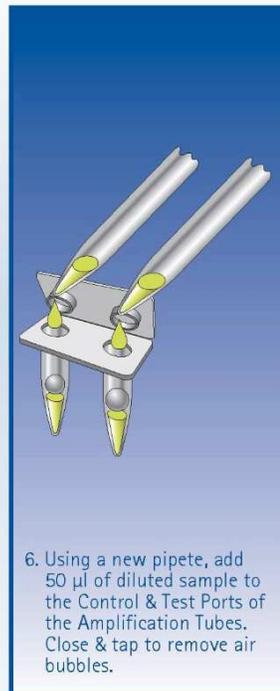
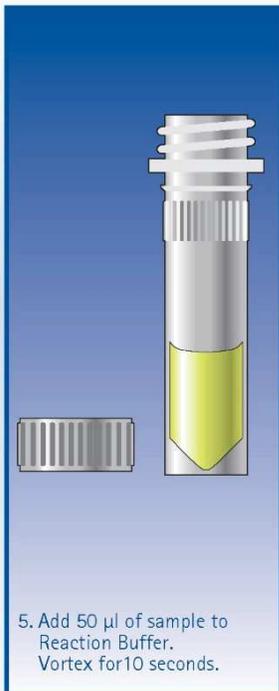
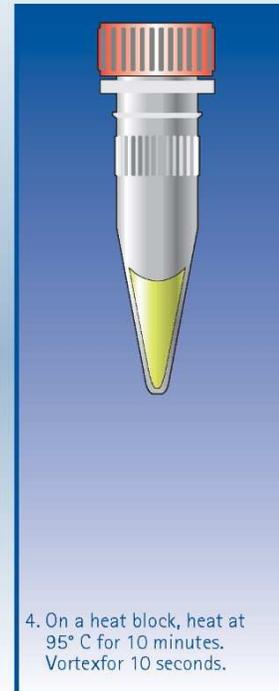
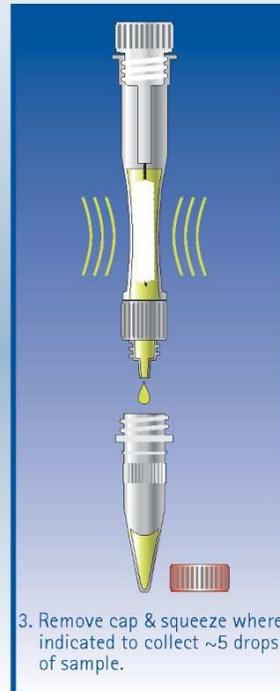
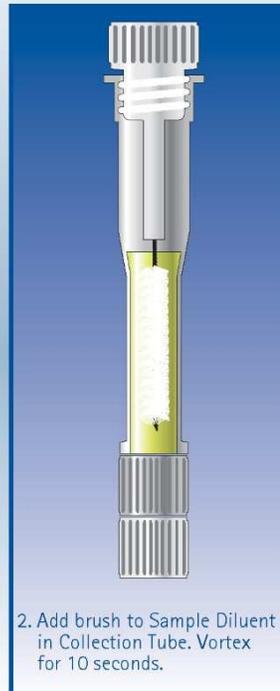
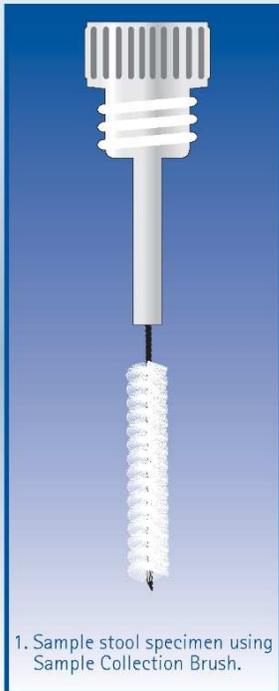
1. After Pressing the RUN button to start an assay, “Edit Sample ID” will appear on the screen of the instrument. (ID can be entered immediately or any time before the run is complete)
2. Select the well of the Specimen identification (ID) to be entered.
3. Enter sample ID by using keypad, barcode scanner, or keyboard.
4. Press Enter.
5. Repeat steps 2-4 for each specimen to be entered.

### **Printing Results**

1. When the Assay is complete the *illumipro-10*<sup>™</sup> screen will display zeros across the screen.
2. Press 1 and the results will then print if the printer is enabled.

Results can also be viewed on the screen by well number. Press the enter key to scroll down to see results in the last few wells.

# **illumigene** TEST PROCEDURE *How to perform the test*



This illustration is representative of the current Package Insert at the time of publication.

Please refer to the most current version of the package insert for complete instructions.

Treating illumigene in text for Word and PowerPoint:

This document attempts to provide guidance on how to use the brand name *illumigene*<sup>™</sup> of in text for Word and PowerPoint. Using Arial as your main font allows for *illumigene* to stand out. It is set in Times Roman italic.

The objective is to treat *illumigene* as closely as possible with the logo mark. This is the logo mark:



*illumigene* is in the Scrapbook. Find wherever *illumigene* is in your document, select it, and using the Scrapbook window, select the *illumigene* treatment and use the paste function found in that window. It will replace your typed *illumigene* with the treated version.

You may notice that the new type treatment is 13 pt. It is set that way to compensate for its smaller profile compared to Arial.

Using Times Roman as main font is not optimal, but usable. *illumigene* doesn't stand out as much.

**KOZAK EXHIBIT G  
(CONFIDENTIAL)**

# **KOZAK EXHIBIT H**



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results in under an hour.*



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