November 2024

QIAstat-Dx® Gastrointestinal Panel 2 Instructions for Use

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Version 1

IVD For In Vitro Diagnostic Use

For use with QIAstat-Dx Analyzer 1.0, QIAstat-Dx Analyzer 2.0, and QIAstat-Dx Rise

CE 0197

REF 691413

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Sample to Insight

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Intended Use

The QIAstat-Dx Gastrointestinal Panel 2 is a multiplexed nucleic acid test intended for use with the QIAstat-Dx Analyzer 1.0 , QIAstat-Dx Analyzer 2.0, and QIAstat-Dx Rise for the simultaneous qualitative detection and identification of nucleic acids from multiple viruses, bacteria, and parasites directly from stool samples Cary–Blair or modified Cary–Blair transport media obtained from individuals with signs and/or symptoms of gastrointestinal infection. The following viruses, bacteria (including several diarrheagenic *E. coli/Shigella* pathotypes), and parasites are identified with the QIAstat-Dx Gastrointestinal Panel 2:

- Adenovirus F40/F41
- Astrovirus
- Norovirus (GI/GII)
- Rotavirus A
- Sapovirus (GI, GII, GIV, GV)
- *Campylobacter* (*C. jejuni*, *C. coli* and *C. upsaliensis*)
- *Clostridium difficile* (toxin A/B)
- Enteroaggregative *Escherichia coli* (EAEC)
- *Shigella*/Enteroinvasive *Escherichia coli* (EIEC)
- Enteropathogenic *Escherichia coli* (EPEC)
- Enterotoxigenic *Escherichia coli* (ETEC) *lt/st*
- *Plesiomonas shigelloides*
- *Salmonella spp.*
- Shiga-like toxin-producing *Escherichia coli* (STEC) *stx1/stx2** (including specific identification of *E. coli* O157 serogroup within STEC)
- *Vibrio vulnificus*
- *Vibrio parahaemolyticus*
- *Vibrio cholerae*
- *Yersinia enterocolitica*
- *Cryptosporidium*
- *Cyclospora cayetanensis*
- *Entamoeba histolytica*
- *Giardia lamblia*

*Shiga-like toxin-producing *E. coli* (STEC) genes (*stx1* and *stx2*) are differentiated by QIAstat-Dx Gastrointestinal Panel 2.

Concomitant culture is necessary for organism recovery and further typing of bacterial agents.

The QIAstat-Dx Gastrointestinal Panel 2 is indicated as an aid in the diagnosis of specific agents of gastrointestinal illness, in conjunction with other clinical, laboratory, and epidemiological data. Positive results do not rule out co-infection with organisms not detected by the QIAstat-Dx Gastrointestinal Panel 2. The organisms detected may not be the sole or definitive cause of the disease.

QIAstat-Dx Gastrointestinal Panel 2 is not intended to monitor or guide treatment for *C. difficile* infections.

Negative QIAstat-Dx Gastrointestinal Panel 2 results in the setting of clinical illness compatible with gastroenteritis may be due to infection by pathogens that are not detected by this assay test or non-infectious causes such as ulcerative colitis, irritable bowel syndrome, or Crohn's disease.

The QIAstat-Dx Gastrointestinal Panel 2 also aids in the detection and identification of acute gastroenteritis in the context of outbreaks. The QIAstat-Dx Gastrointestinal Panel 2 is intended for professional use only and is not intended for self-testing. The QIAstat-Dx Gastrointestinal Panel 2 is intended for in vitro diagnostic use.

Intended User

This kit is intended for professional use.

The product is to be used only by personnel specifically instructed and trained in molecular biology techniques and familiar with this technology.

Description and Principle

Pathogen information

Acute gastrointestinal infections can be caused by a variety of pathogens, including parasites, bacteria and viruses, and generally present with nearly indistinguishable clinical signs and symptoms (1). The rapid and accurate determination of the presence or absence of potential causative agent(s) help make timely decisions regarding treatment, hospital admission, infection control and return of the patient to work and family (2–4). It may also greatly support improved antimicrobial stewardship and other important public health initiatives (3,5).

The QIAstat-Dx Gastrointestinal Panel 2 Cartridge allows detection and differentiation of 22 parasitic, viral, and bacterial pathogens that cause gastrointestinal symptoms, which includes specific identification of *E. coli* O157 serogroup within STEC, resulting in 23 targets in total. Testing requires a small sample volume and minimal hands-on time, and the results are available in approximately 78 minutes.

Pathogens that can be detected and identified with the QIAstat-Dx Gastrointestinal Panel 2 are listed in Table 1.

Table 1. Pathogens detected by the QIAstat-Dx Gastrointestinal Panel 2

Pathogen	Classification (genome type)
Adenovirus F40/F41	Adenovirus (DNA)
Astrovirus	Astrovirus (RNA)
Norovirus GI/GII	Calicivirus (RNA)
Rotavirus A	Reovirus (RNA)
Sapovirus (GI, GII, GIV, GV)	Calicivirus (RNA)
Campylobacter (C. jejuni, C. upsaliensis, C. coli)	Bacterium (DNA)
Clostridium difficile (toxin A/B)	Bacterium (DNA)
Enteroaggregative *E. coli* (EAEC)	Bacterium (DNA)
Enteroinvasive *E. coli* (EIEC)/*Shigella*	Bacterium (DNA)
Enteropathogenic *E. coli* (EPEC)	Bacterium (DNA)
Enterotoxigenic *E. coli* (ETEC) *lt/st*	Bacterium (DNA)
Plesiomonas shigelloides	Bacterium (DNA)
Salmonella spp.	Bacterium (DNA)
Shiga-like toxin-producing *E. coli* (STEC) *stx1/stx2* (including specific identification of *E. coli* O157 serogroup within STEC)	Bacterium (DNA)
Vibrio vulnificus	Bacterium (DNA)
Vibrio parahaemolyticus	Bacterium (DNA)
Vibrio cholerae	Bacterium (DNA)
Yersinia enterocolitica	Bacterium (DNA)
Cryptosporidium	Parasite (DNA)
Cyclospora cayetanensis	Parasite (DNA)
Entamoeba histolytica	Parasite (DNA)
Giardia lamblia	Parasite (DNA)

Summary of detected organisms

Bacteria

Campylobacter spp. (C. jejuni/C. coli/C. upsaliensis) is a genus of gram-negative bacteria, that includes more than 30 species (6). *Campylobacter jejuni* and *Campylobacter coli* are the most common *Campylobacter* species associated with diarrheal illness, with *C. jejuni* being responsible for 90% of cases (7,10). The consumption of undercooked poultry or raw milk are the most common sources of *Campylobacter* infections (9,10). *Campylobacter* are highly infectious, with an infectious dose as low as 500 bacteria (11); however, person-to-person spread is uncommon (10). Systemic disease, associated with significant morbidity and mortality, may occur in individuals who are immunocompromised (9,11). Infection can result in long-term consequences such as arthritis, irritable bowel syndrome, and Guillain–Barré syndrome (9,11).

Clostridioides difficile **(previously, *Clostridium difficile*)** is a gram-positive, spore-forming, anaerobic bacillus that is found in the intestinal tract of humans and animals (12). The virulence of *C. difficile* is mediated by host-destructive enzymes and toxins A and B (12). Although *C. difficile* infection is responsible for <2% diarrheal deaths globally, it is the leading cause of diarrhea-associated deaths in countries with a high social-democratic index (13). Patients at the highest risk of *Clostridiodes difficile* infections are those who are hospitalized, in long-term care facilities, >65 years old, and/or with recent antibiotic use (14,15). Symptoms of *C. difficile* infection range from mild to moderate diarrhea, to life-threatening pseudomembranous colitis, toxic megacolon, and sepsis (12,13,14,16). *C. difficile* can manifest itself in two different ways: colonization and true infection (14). *C. difficile* spores are highly resistant to disinfectants and can persist in the environment with little loss of viability; as a result, spread and reinfection are common (13). In mild cases of antibiotic-associated *C. difficile* infection, the cessation of antibiotics in order to restore normal gut flora may be sufficient for recovery (17,18).

Plesiomonas shigelloides is a facultatively anaerobic gram-negative bacterium that can cause enteric disease in humans. The prevalence of *P. shigelloides* enteritis varies considerably, with higher rates reported from Southeast Asia and Africa and lower numbers from North America and Europe. It is unknown how many people suffer from disease caused by *P. shigelloides* each year, but mortality is rare. Infection especially occurs following the consumption of raw seafood or contaminated water (19).

Salmonella is a gram-negative bacterium comprising more than 2600 serovars, including the distinct typhoidal serotypes, Typhi and Paratyphi A–C (20,21). Enteric (typhoid) fever is an invasive, life-threatening, systemic infection with predominantly non-gastrointestinal symptoms (20,22). Non-typhoidal salmonellosis is an acute, usually self-limiting gastroenteritis that is characterized by symptoms such as watery diarrhea, fever, abdominal pain, and sometimes vomiting (20,22,23). Less common, non-typhoidal *Salmonella* serovars cause invasive disease due to bloodstream infections that are not usually associated with diarrhea (20,22). There are 100–200 million cases of non-typhoidal salmonellosis each year, resulting in approximately 85,000–155,000 deaths (22,24). The incidence of non-typhoidal *Salmonella* gastroenteritis is highest in the developing world but is also of considerable importance in developed countries (20).

Vibrio cholerae is a water-borne, gram-negative bacterium with more than 200 serogroups (25,26). The serogroups O1 and O139 can cause cholera and gastroenteritis, while non-O1 and non-O139 *V. cholerae* strains are most commonly the causative agents of gastroenteritis (27). Although globally *V. cholerae* is not a common cause of diarrhea, it is the third leading cause of diarrhea mortality (28). Death rates are as high as 70%, mainly due to delays in rehydrating patients (25). Classical cholera is endemic in South Asia, whereas parts of South America and Africa have sporadic epidemics (29), and is usually characterized by substantial volumes of watery diarrhea (25,26,27). Although globally *V. cholerae* is not a common cause of diarrhea, it is the third leading cause of diarrhea mortality (28). Death rates are as high as 70%, mainly due to delays in rehydrating patients (25). Three oral vaccines for *V. cholerae*

are available (not in the United States); however, they do not provide long-term immunity (26,28).

Vibrio parahaemolyticus is a gram-negative bacterium that can be found in free-living marine environments and can cause noncholera vibriosis in humans. *Vibrio parahaemolyticus* is not transmitted person-to-person or via the fecal–oral route; it is spread via the consumption of raw or undercooked seafood, being the leading cause of seafood-associated diarrheal disease worldwide. In severe cases, *V. parahaemolyticus* infection can result in sepsis (30).

Vibrio vulnificus is a gram-negative bacterium that causes noncholera vibriosis in humans (27). One study indicated that, between 2002 and 2007, 92.8% of all *V. vulnificus* cases in the United States were in individuals who had consumed raw oysters (31). It is estimated that 15–30% of *V. vulnificus* infections are fatal (32). For this reason, early treatment with antibiotics is advised in order to avoid complications such as sepsis (33).

Yersinia enterocolitica is a gram-negative bacterium that has more than 70 serotypes (34); serotypes most commonly associated with infection are O:3, O:9, O:8, and O:5,27 (35). *Yersinia enterocolitica* infection have been reported frequently in northern Europe, particularly in Belgium, Norway, and the Netherlands; it is rarely observed in tropical countries (36). *Y. enterocolitica* is usually transmitted through the consumption of raw meats, unpasteurized dairy products, contaminated water, or via the fecal–oral route (37). Symptoms range from self-limiting enteritis with diarrhea, low-grade fever, and abdominal pain to severe disease such as terminal ileitis and mesenteric lymphadenitis, which also mimics appendicitis (38–40).

Diarrheagenic *Escherichia coli/Shigella*

Escherichia *E.coli (EIEC)/Shigella* are gram-negative facultative anaerobic bacteria belonging to the Enterobacteriaceae family. In addition to being part of the normal intestinal microflora of mammals, *E. coli/Shigella* contains several pathotypes that cause a variety of diseases (41,42). There are four major pathotypes of diarrhoeagenic *E. coli/Shigella*, which each

have unique features in their interaction with eukaryotic cells: Enteropathogenic *E. coli* (EPEC), Enterohaemorrhagic *E. coli*/Shiga-like toxin-producing *E. coli* (EHEC/STEC), Enterotoxigenic *E. coli* (ETEC), and Enteroinvasive *E. coli* (EIEC)/*Shigella* (41,42). *E. coli/Shigella* have a conserved core genome and a flexible gene pool containing virulence and fitness genes, which are carried on mobile genetic elements (41,42). Gene gain, via horizontal transfer, and gene loss afford the pathogenic traits to *E. coli/Shigella* that give rise to the different pathotypes (42).

Enteroaggregative *E. coli* (EAEC) is increasingly recognized as a global enteric pathogen and a common cause of traveller's diarrhea, causing both acute and chronic diarrhea, but it has been heavily associated with asymptomatic carriage as well (43,44,45,46,47). EAEC is commonly present in co-infections with other gastrointestinal pathogens (48,49), and high levels of multidrug resistance have been reported among its strains (43). EAEC pathogenesis involves three steps: adherence to the intestinal epithelium via adherence aggregative fimbriae, biofilm formation, and secretion of toxins; mucosal inflammation; and cytotoxic damages (50).

Enteroinvasive *E. coli* (EIEC) and *Shigella*. EIEC is an invasive strain of *E. coli* that is very closely related in virulence and other pathogenic properties to *Shigella* (51,52). Sequencing indicates that EIEC is more related to *Shigella* than to non-invasive *E. coli*; however, they are currently classified as distinct species (41,51,53). The virulence of this pathogen is primarily due to plasmid-encoding virulence factors that allow the adhesion and invasion to the epithelial cells (50). EIEC is under-represented in epidemiological studies because of its less severe manifestation and potential misclassification as *Shigella* (42). EIEC infection often leads only to self-limiting, mild watery diarrhea; in rare situations, it can cause symptoms of shigellosis, but complications are uncommon (42). *Shigella* is the second leading cause of diarrhea mortality, causing approximately 13% diarrhea deaths (54). Numbers of deaths are greatest in young children and the elderly (54). It is recommended that individuals with shigellosis should not take anti-diarrheal medications such as loperamide, as these can make symptoms worse (55).

Enteropathogenic *E. coli* (EPEC) is primarily a disease of infants <2 years (42,56–57), and is commonly present in co-infections with other gastrointestinal pathogens (49). EPEC are classified into typical (tEPEC) and atypical (aEPEC) strains based on the presence of the *E. coli* adherence factor plasmid (pEAF). tEPEC is considered an important cause of infantile diarrhea in developing countries (58). Infections in adults, including travelers to developing countries, are rarely reported (42,57). aEPEC is frequently detected in both developing countries and industrialized countries, and is suggested to be more prevalent that tEPEC (56). aEPEC is an important cause of both endemic diarrhea and outbreaks (56).

Enterotoxigenic *E. coli* (ETEC) is characterized by the production of heat-labile enterotoxins (LT) and heat-stable enterotoxins (ST) (59,60). ETEC is the most common diarrhea-associated *E. coli*, and although infections are usually self-limiting (60), is the eighth leading cause of diarrhea globally and accounts for >50,000 deaths every year (54). It also remains a major cause of diarrhea in travelers to low resource countries (60). ETEC is a frequent antimicrobial resistant (60).

Shiga-like toxin-producing *E. coli* (STEC) *stx1/stx2,* including *E. coli* O157, is defined by the production of Shiga toxin 1 (stx1) or 2 (stx2), which show homology to stx toxins from Shigella dysenteriae (27). There are >400 serotypes of STEC, of which O157:H7 is the most common (27). Symptoms of STEC infection range from mild intestinal disease to hemorrhagic diarrhea and can lead to hemolytic uremic syndrome (HUS), end-stage renal disease, and death (27,40). Approximately 5–10% of individuals diagnosed with STEC infections develop HUS, which can be a life-threatening complication (41). The impacts of STEC are often greater in infants and children, compared to other ages (40). Antibiotics should not be used to treat STEC infections as there is currently no evidence that they aid recovery and have instead been associated with a worsening of symptoms and the development of HUS (41).

Parasites

***Cryptosporidium* spp.** are protozoan parasites that can infect humans and other animals, with *C. hominis* and *C. parvum* being the causative strains of the majority of humans infections (63). *Cryptosporidium* spp. are found globally, but those in developing countries, particularly in sub-Saharan Africa, are at greater risk of infection due to poorer water treatment and food sanitation (54,64). It is also one of the leading causes of diarrheal mortality in children <5 years of age (54,65).

Cyclospora cayetanensis is a single-cell protozoa parasite, and the only known species of the genus *Cyclospora* to infect humans (66,67). It is endemic in tropical/subtropical areas, and in non-endemic regions, cases and outbreaks of cyclosporiasis are usually linked to international travel and consumption of contaminated produce imported from endemic regions (66–68). Direct fecal–oral transmission cannot occur; the unsporulated oocysts sporulate in water and food environments, enabling them to infect another host (66,67,69).

Entamoeba histolytica is an anaerobic, protozoan parasite (70). *Entamoeba histolytica* is common in developing countries, particularly those in the tropics and sub-tropics with poor sanitation (70–72). Only 10–20% of individuals infected with *E. histolytica* are symptomatic (70,73). Through destruction of the intestinal walls, trophozoites can also spread systemically to the liver, lungs, and central nervous system (70–73). The liver is the most common extra-intestinal site of infection (70–72).

Giardia lamblia is a unicellular, protozoan parasite that can cause disease in humans and other mammals (74,75). *G. lamblia* has a global distribution and is common in both children and adults (76,77). Prevalence of infection is higher in developing regions of the world and in children (74,76,77). The majority (50–75%) of *G. lamblia* infections are asymptomatic (78). In immunocompetent individuals, infections are usually self-limiting, although some may become chronic (74).

Viruses

Adenovirus F40/41 is a double-stranded DNA, non-enveloped virus (79,80), with many distinct serotypes described and classified into 7 species (A–G) (79). Serotypes F40/41 are the most common cause of acute gastroenteritis in young children, causing 5–20% cases. More than 80% of diagnosed infections occur in children aged <4 years (80). Adenoviruses have a worldwide distribution, and infections occur throughout the year without significant seasonal variability (79). Infections are usually mild and self-limiting in immunocompetent individuals but can be fatal in individuals who are immunocompromised (79,81,82).

Astroviruses are non-enveloped, positive-sense, single-stranded RNA viruses (83). Human astroviruses are distributed all over the world and are associated with 2–9% of cases of acute, nonbacterial diarrhea in children (83,84). It is estimated that 90% of the global population aged ≥9 years have antibodies against astrovirus type 1 (83). Many infections in healthy children and adults are asymptomatic, although they can cause severe diarrhea in children, older adults and those who are immunocompromised or have comorbidities (83,84).

Noroviruses GI/GII are small, non-enveloped, positive-stranded RNA viruses from the family Caliciviridae (85). They are responsible for >90% of viral gastroenteritis and around 50% of all-cause gastroenteritis outbreaks globally (86), causing approximately 685 million cases every year (87). Approximately 200 million cases are in children aged <5 years, leading to 50,000 child deaths (87). Norovirus is commonly known as the "winter-vomiting bug"; outbreaks are more common during the winter months, but infection can occur at any time of year (87). Norovirus is infectious at very low doses and is transmitted via aerosolized droplets and touching of contaminated surfaces (87). Individuals infected with norovirus usually recover within 1–3 days, but infections in infants, older adults, and immunocompromised individuals can be severe and sometimes fatal (87). In some individuals, viral shedding can occur for many weeks/months after they have stopped experiencing symptoms, and this is a large contributing factor for outbreaks (6).

Rotavirus A is a non-enveloped, double-stranded RNA virus of the Reoviridae family, with 10 species that cause infection in humans (A–J). However, rotavirus A is the most common species and causes >90% of all rotavirus infections (89,90). Rotavirus is a leading cause of diarrhea in children <5 years (89), with a seasonal infection pattern that differs across the world, particularly in middle–high income countries (91). Severe infection is most common in young children and infants; in adults, infections are often associated with milder symptoms (92). Two oral rotavirus vaccines are approved in the United States (93) and have been available in >100 countries since 2006 (93). These vaccines have substantially reduced the burden of rotavirus-associated illness (92).

Sapovirus (Genogroups I, II, IV, and V) are single-stranded, positive-sense RNA, non-enveloped viruses of the Caliciviridae family (94). There are 15 genogroups of sapoviruses, of which 4 (GI, GII, GIV, and GV) infect humans (95). Sapovirus is a major public health problem as people of all ages are susceptible to infection in both outbreaks and sporadic cases worldwide (94). Although, most individuals recover within a few days, in severe cases, it can lead to hospitalization (94). Symptoms are clinically indistinguishable from those of norovirus, making laboratory diagnosis essential for diagnosis and for identifying outbreaks (94).

Summary and explanation

QIAstat-Dx Gastrointestinal Panel 2 Cartridge description

The QIAstat-Dx Gastrointestinal Panel 2 Cartridge (Figure 1) is a disposable plastic device that allows performance of fully automated molecular assays for the detection of gastrointestinal pathogens. Main features of the QIAstat-Dx Gastrointestinal Panel 2 Cartridge include compatibility with a liquid sample type, hermetical containment of the pre-loaded reagents necessary for testing, and true walk-away operation. All sample preparation and assay testing steps are performed within the cartridge.

All reagents required for the complete execution of a test run are pre-loaded and self-contained in the QIAstat-Dx Gastrointestinal Panel 2 Cartridge. The user does not need to come in contact with and/or manipulate any reagents. The QIAstat-Dx Analyzer 1.0, QIAstat-Dx Analyzer 2.0, and QIAstat-Dx Rise houses air filters for both incoming and outgoing air, further safeguarding the environment. After testing, the cartridge stays hermetically closed at all times, greatly enhancing its safe disposal.

Within the cartridge, multiple steps are automatically performed in sequence using pneumatic pressure to transfer samples and fluids via the transfer chamber to their intended destinations.

Description of the process

After sample is manually loaded, the diagnostic tests with the QIAstat-Dx Gastrointestinal Panel 2 are performed on the QIAstat-Dx Analyzer 1.0. All of the sample preparation and analysis steps are performed automatically by the QIAstat-Dx Analyzer 1.0, QIAstat-Dx Analyzer 2.0, and QIAstat-Dx Rise.

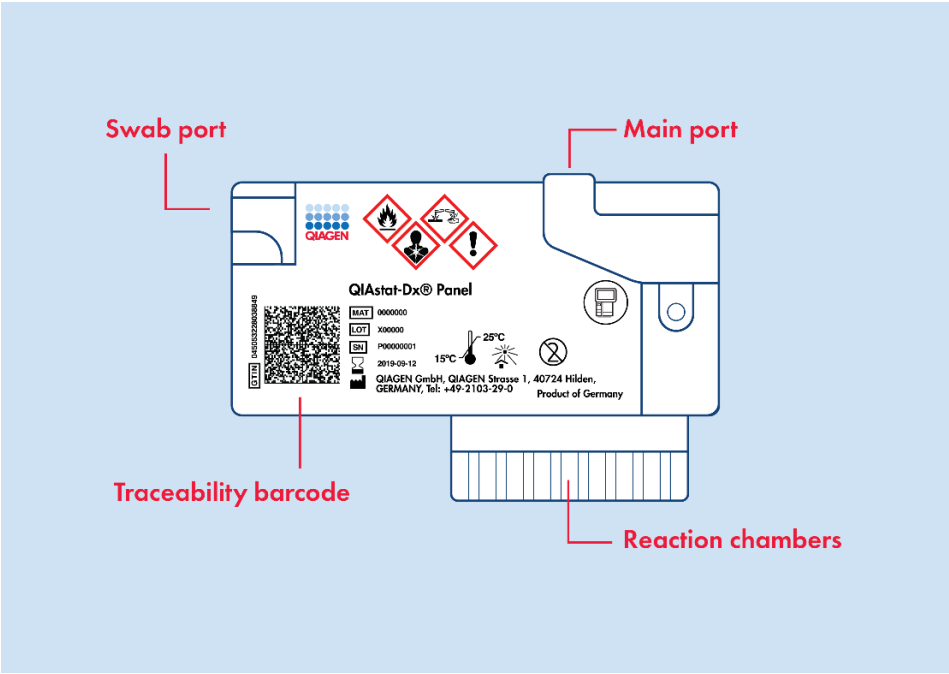


Figure 1. Layout of the QIAstat-Dx Gastrointestinal Panel 2 Cartridge and its features.

Principle of the Procedure

Sample collection and cartridge loading

The collection of samples and their subsequent loading into the QIAstat-Dx Gastrointestinal Panel 2 Cartridge should be performed by personnel trained in safe handling of biological samples.

The following steps are performed:

1. Fresh unpreserved stool specimen is collected and resuspended in Cary–Blair transport medium as soon as possible after collection following the manufacturer's instructions. Attention should be given not to exceed the maximum fill line of the Cary–Blair container.
2. The sample information is manually written on or a sample label is affixed to the top of a QIAstat-Dx Gastrointestinal Panel 2 Cartridge.
3. Liquid sample (stool resuspended in Cary-Blair transport medium) is loaded manually into the QIAstat-Dx Gastrointestinal Panel 2 Cartridge.

   Note: Cary-Blair preserved stool specimens should present a homogenous suspension (easily vortexed).

   Note: The user must perform a visual check of the sample inspection window to confirm that the liquid sample has been loaded.
4. The sample barcode (if available) and the QIAstat-Dx Gastrointestinal Panel 2 Cartridge barcode are scanned by the QIAstat-Dx Analyzer 1.0, QIAstat-Dx Analyzer 2.0, or QIAstat-Dx Rise. If sample barcode is not available, the sample ID is manually written using the virtual keyboard of the touchscreen.

5. The QIAstat-Dx Gastrointestinal Panel 2 Cartridge is introduced into the QIAstat-Dx Analyzer 1.0, QIAstat-Dx Analyzer 2.0, or the QIAstat-Dx Rise.
6. The test is started on the QIAstat-Dx Analyzer 1.0 , QIAstat-Dx Analyzer 2.0, or the QIAstat-Dx Rise.

Sample preparation, nucleic acid amplification, and detection

The extraction, amplification, and detection of nucleic acids in the sample are performed automatically by the QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0.

1. The liquid sample is homogenized, and cells are lysed in the lysis chamber of the QIAstat-Dx Gastrointestinal Panel 2 Cartridge, which includes a rotor that turns at high speed and silica beads that provide effective cell disruption.
2. Nucleic acids are purified from the lysed sample via binding to a silica membrane in the purification chamber of the QIAstat-Dx Gastrointestinal Panel 2 Cartridge in the presence of chaotropic salts and alcohol.
3. The purified nucleic acids are eluted from the membrane in the purification chamber and are mixed with the lyophilized PCR chemistry in the dried-chemistry chamber of the QIAstat-Dx Gastrointestinal Panel 2 Cartridge.
4. The mixture of sample and PCR reagents is dispensed into the QIAstat-Dx Gastrointestinal Panel 2 Cartridge PCR chambers, which contain air-dried assay-specific primers and probes.
5. The QIAstat-Dx Analyzer 1.0, QIAstat-Dx Analyzer 2.0, or QIAstat-Dx Rise creates the optimal temperature profiles to carry out effective multiplex real-time RT-PCR and performs real-time fluorescence measurements to generate amplification curves.
6. The QIAstat-Dx Analyzer 1.0, QIAstat-Dx Analyzer 2.0, or QIAstat-Dx Rise Software interprets the resulting data and process controls and delivers a test report.

Materials Provided

Kit contents

QIAstat-Dx Gastrointestinal Panel 2 Cartridge Catalog number Number of tests	 691413 6
QIAstat-Dx Gastrointestinal Panel 2 Cartridges	6*
Transfer pipettes†	6*

*Individually packaged cartridges containing all reagents needed for sample preparation and multiplex real-time RT-PCR, plus Internal Control.

†Individually packaged transfer pipettes for dispensing liquid sample into the QIAstat-Dx Gastrointestinal Panel 2 Cartridge.

Components of the kit

Table 2. Reagents supplied

Reagent	Critical/Active/Reactive Ingredients	Concentration/Range
QIAstat-Dx Gastrointestinal 2 Cartridge	Internal Control	40,000–60,000 CFU/cartridge
	Proteinase K	≥0.1 – <1%
	Reverse Transcriptase (included in MasterMix as universal component for PCR)	20–100 U/cartridge
	dNTPs (included in master mix as universal component for PCR)	1–5 mM
	DNA Polymerase (included in MasterMix as universal component for PCR)	10–100 U/cartridge
	Target-specific primers	100–1000 µM
	Target-specific fluorophore–labelled detection Probes	100–1000 µM

External control information

All external quality control requirements and testing should be performed in accordance with local, state, and federal regulations or accreditation organizations and should follow the user's laboratory standard quality control procedures.

Materials Required but Not Provided

Platform and software

Important: Prior to use, ensure that the instruments have been checked and calibrated according to the manufacturer's recommendations.

QIAstat-Dx Gastrointestinal Panel 2 is designed for use with the QIAstat-Dx Analyzer 1.0, QIAstat-Dx Analyzer 2.0, and QIAstat-Dx Rise. Before beginning a test, make sure the following are available:

- QIAstat-Dx Analyzer 1.0, QIAstat-Dx Analyzer 2.0, or QIAstat-Dx Rise
    - For QIAstat-Dx Analyzer 1.0: at least one Operational Module and one Analytical Module must be inside the machine to work, with software version 1.4 or 1.5†.
    - For QIAstat-Dx Analyzer 2.0: at least one Operational Module PRO and one Analytical Module must be inside for the machine to work, with software version 1.6 or later.
    - For QIAstat-Dx Rise: at least two Analytical Modules must be inside for the machine to work, with software version 2.2 or later.

  Note: Application software version 1.6 or later cannot be installed on QIAstat-Dx Analyzer 1.0.
- *QIAstat-Dx Analyzer 1.0 User Manual* (for use with software version 1.4 or 1.5); or

  *QIAstat-Dx Analyzer 2.0 User Manual (*for use with software version 1.6 or later; or

  QIAstat-Dx Rise User Manual (for use with software version 2.2 or later).
- QIAstat-Dx latest Assay Definition File software for Gastrointestinal Panel 2 installed on the Operational Module, Operational Module PRO, or QIAstat-Dx Rise.

†DiagCORE® Analyzer instruments running QIAstat-Dx software version 1.4 or 1.5 can be used as an alternative to QIAstat-Dx Analyzer 1.0 instruments.

Warnings and Precautions

- The QIAstat-Dx Gastrointestinal Panel 2 is for in vitro diagnostic use.
- The QIAstat-Dx Gastrointestinal Panel 2 is to be used by laboratory professionals trained in the use of QIAstat-Dx Analyzer 1.0, QIAstat-Dx Analyzer 2.0, and the QIAstat-Dx Rise.
- Please be aware that you may be required to consult your local regulations for reporting serious incidents that have occurred in relation to the device to the manufacturer and the regulatory authority in which the user and/or the patient is established.

Safety information

- When working with chemicals, always wear a suitable lab coat, disposable gloves, and protective goggles. For more information, please consult the appropriate safety data sheets (SDSs). These are available online in convenient and compact PDF format at **www.qiagen.com/safety** where you can find, view, and print the SDS for each QIAGEN kit and kit component.
- Observe standard laboratory procedures for keeping the working area clean and contamination-free. Guidelines are outlined in publications such as the *Biosafety in Microbiological and Biomedical Laboratories* from the Centers for Disease Control and Prevention and the National Institutes of Health (96).
- Specimens and samples are potentially infectious. Discard sample and assay waste according to your local safety procedures.
- Always wear appropriate personal protective equipment and follow your institution's safety procedures for handling biological samples. Handle all samples, cartridges, and transfer pipettes as if they are capable of transmitting infectious agents.

- Always observe safety precautions as outlined in relevant guidelines, such as the Clinical and Laboratory Standards Institute® (CLSI) *Protection of Laboratory Workers from Occupationally Acquired Infections; Approved Guideline* (M29), or other appropriate documents provided by local authorities.
- The QIAstat-Dx Gastrointestinal Panel 2 Cartridge is a closed, single-use device that contains all reagents needed for sample preparation and multiplex real-time RT-PCR within the QIAstat-Dx Analyzer 1.0, QIAstat-Dx Analyzer 2.0, and QIAstat-Dx Rise. Do not use a QIAstat-Dx Gastrointestinal Panel 2 Cartridge that is past its expiration date, appears damaged, or leaks fluid.
- Dispose of used or damaged cartridges in accordance with all national, state and local health and safety regulations and laws.

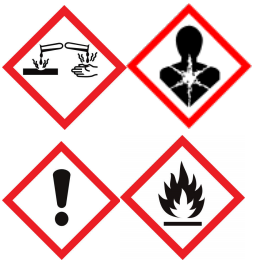
Emergency information

CHEMTREC

Outside USA & Canada +1 703-527-3887

Precautions

The following hazard and precautionary statements apply to components of the QIAstat-Dx Gastrointestinal Panel 2.



Contains: ethanol; guanidine hydrochloride; guanidine thiocyanate; isopropanol; proteinase K; t-Octylphenoxypolyethoxyethanol. Danger! Highly flammable liquid and vapor. Harmful if swallowed or if inhaled. May be harmful in contact with skin. Causes severe skin burns and eye damage. May cause allergy or asthma symptoms or breathing difficulties if inhaled. May cause drowsiness or dizziness. Harmful to aquatic life with long lasting effects. Contact with acids liberates very toxic gas. Corrosive to the respiratory tract. Keep away from heat/sparks/open flames/hot surfaces. No smoking. Avoid breathing dust/fume/gas/mist/vapors/spray. Wear protective gloves/protective clothing/eye protection/face protection. Wear respiratory protection. IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. IF exposed or concerned: Immediately call a POISON CENTER or doctor. Rinse mouth. Do NOT induce vomiting. Remove person to fresh air and keep comfortable for breathing. Wash contaminated clothing before reuse. Store in a well-ventilated place. Keep container tightly closed.

To reduce the risk of contamination when handling stool samples, it is recommended that the below guidelines are applied (96).

- When handling the stool sample, a biosafety cabinet, dead air box, splash shield, or face shield should be used.
- The work area used for cartridge loading should be separate from the work area used for stool pathogen testing (i.e., stool culture, EIA) to prevent cross-contamination.
- Prior to sample handling, the work area should be thoroughly cleaned using 10% bleach or similar disinfectant.
- QIAstat-Dx Gastrointestinal Panel 2 Cartridges and samples should be processed one at a time.
- Change gloves prior to removing cartridges from shipping boxes.
- Change gloves and clean the work area between processing each sample.
- Dispose of used cartridges in a biohazard container immediately after the run is complete and avoid excessive handling.

Precautions related to public health reporting

State and local public health authorities have published guidelines for notification of reportable diseases in their jurisdictions (e.g., following the *Official Journal of the European Union 6.7.2018 L 170/1*, the list includes *Campylobacter enteritis*, Cholera, *Clostridium difficile* nosocomial infection, Cryptosporidiosis, Giardiasis (lambliasis), *Salmonella enteritis*, Shiga toxin/verocytotoxin-producing *E. coli* infection (STEC/VTEC), including Haemolytic-uraemic syndrome (HUS), Shigellosis and enteritis due to *Yersinia enterocolitica*) to determine necessary measures for verification of results to identify and trace outbreaks and for epidemiological investigations. Laboratories are responsible for following their state or local regulations for submission of clinical material or isolates on positive specimens to their state public health laboratories.

Reagent Storage and Handling

Store the QIAstat-Dx Gastrointestinal Panel 2 Cartridges in a dry, clean storage space at room temperature (15–25°C). Do not remove the QIAstat-Dx Gastrointestinal Panel 2 Cartridges or the transfer pipettes from their individual packaging until actual use. Under these conditions, QIAstat-Dx Gastrointestinal Panel 2 Cartridges can be stored until the expiration date printed on the individual packaging. The expiration date is also included in the QIAstat-Dx Gastrointestinal Panel 2 Cartridge barcode and is read by the QIAstat-Dx Analyzer 1.0, QIAstat-Dx Analyzer 2.0, and QIAstat-Dx Rise when the cartridge is inserted into the instrument to run a test. Once the cartridge is removed from the pouch, it should be protected from sunlight.

Attention should be paid to the expiration dates and storage conditions printed on the box and labels of all components. Do not use expired or incorrectly stored components.

In-use stability

When stored under the specified storage conditions, the QIAstat-Dx Gastrointestinal Panel 2 is stable until the stated expiration date on box label.

After the cartridge package is opened, sample should be introduced into the QIAstat-Dx Gastrointestinal Panel 2 Cartridge within 30 minutes. Sample-loaded cartridges should be loaded into the QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0 within 90 minutes and immediately into the QIAstat-Dx Rise instrument tray.

Specimen Storage and Handling

The QIAstat-Dx Gastrointestinal Panel 2 Kit is for use with stool samples re-suspended on Cary-Blair transport medium. All samples should be treated as potentially infectious. Discard sample and assay waste according to your local safety procedures.

Specimen collection

Stool samples should be collected and handled according to the Cary-Blair transport medium manufacturer's recommended procedures.

Recommended storage conditions for stool resuspended in Cary-Blair transport medium (Para-Pak® C&S (Meridian Bioscience) or FecalSwab™ (COPAN)) specimens are listed below:

- Room temperature up to 4 days at 15–25°C
- Refrigerated up to 4 days at 2–8°C

Procedure

Protocol: Processing Raw Stool samples in Cary-Blair transport medium

Important point before starting

- Ensure all materials required but not provided are available.
- The QIAstat-Dx Gastrointestinal Panel 2 Cartridge (cat. no 691413) is identified by a purple-colored (●) bar on the label and an icon indicating gastrointestinal tract ( , see "Symbols" on page 159).

Sample collection, transport, and storage

Collect and resuspend the stool sample in Cary-Blair transport medium according to the manufacturer's recommended procedures.

Loading a sample into the QIAstat-Dx Gastrointestinal Panel 2 Cartridge

1. Open the package of a QIAstat-Dx Gastrointestinal Panel 2 Cartridge using the tear notches on the sides of the packaging (Figure 2).

   Important: After the package is opened, sample should be introduced into the QIAstat-Dx Gastrointestinal Panel 2 Cartridge within 30 minutes. Sample-loaded cartridges should be loaded into the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 within 90 minutes, or immediately into the QIAstat-Dx Rise.

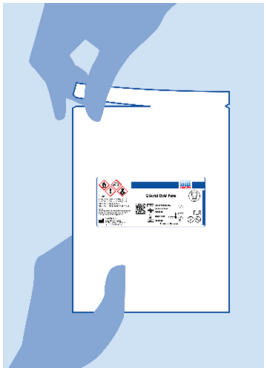


Figure 2. Opening the QIAstat-Dx Gastrointestinal Panel 2 Cartridge.

2. Remove the QIAstat-Dx Gastrointestinal Panel 2 Cartridge from the packaging and position it so that the barcode on the label faces you.
3. Manually write the sample information or place a sample information label on the top of the QIAstat-Dx Gastrointestinal Panel 2 Cartridge. Make sure that the label is properly positioned and does not block the lid opening (Figure 3). See the QIAstat-Dx Rise workflow section for proper cartridge labelling.

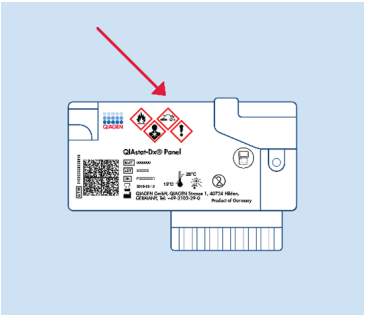


Figure 3. Sample information placement on top of the QIAstat-Dx Gastrointestinal Panel 2 Cartridge.

4. Place the QIAstat-Dx Gastrointestinal Panel 2 Cartridge flat on the clean work surface so that the barcode on the label faces upwards. Open the sample lid of the main port on the front of the QIAstat-Dx Gastrointestinal Panel 2 Cartridge (Figure 4).

   Important: Do not flip the QIAstat-Dx Gastrointestinal Panel 2 Cartridge or agitate it while the main port lid is open. The main port contains silica beads used in the sample disruption. The silica beads could fall out of the QIAstat-Dx Gastrointestinal Panel 2 Cartridge if it is agitated while the lid is open.

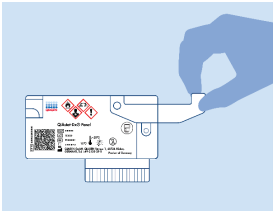


Figure 4. Opening the sample lid of main port.

Note: The swab port is not used for the QIAstat-Dx Gastrointestinal Panel 2 assay.

5. Thoroughly mix the stool in the Cary-Blair transport medium, for example, by vigorously agitating the tube 3 times (Figure 5).

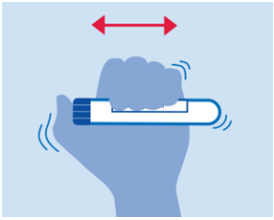


Figure 5. Mixing stool sample in Cary-Blair transport medium.

6. Open the tube with the sample to be tested. Use the supplied transfer pipette to draw up fluid. Draw the sample to the second fill line on the pipette (i.e., 200 µL) (Figure 6).

   Important: Do not draw air, mucus, or particles into the pipette. If air, mucus, or particles are drawn into the pipette, carefully expel the sample fluid in the pipette back into the sample tube and draw up fluid again. In the event that the supplied transfer pipette is lost, please use another one from the package or any other commercially available pipette with a minimum volume of 200 µL.

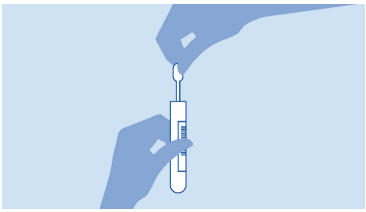


Figure 6. Drawing up sample into the supplied transfer pipette.

   Note: In the case the test should be repeated due to previous cartridge error related to sample concentration too high, draw the sample to the first fill line on the pipette instead (100 µL) (See the Troubleshooting Guide" section for further details on error codes).

7. Carefully transfer the sample into the main port of the QIAstat-Dx Gastrointestinal Panel 2 Cartridge using the supplied single-use transfer pipette (Figure 7).

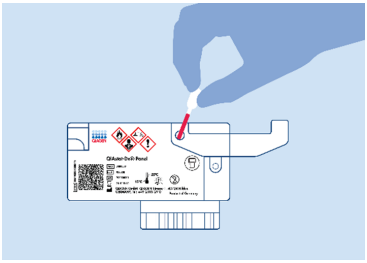


Figure 7. Transferring sample to main port of QIAstat-Dx Gastrointestinal Panel 2 Cartridge.

8. Firmly close the lid of the main port until it clicks (Figure 8).

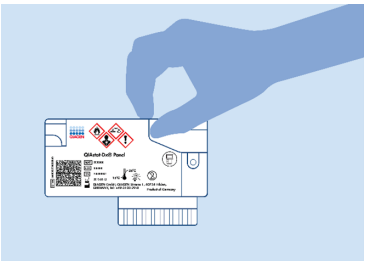


Figure 8. Closing the lid of the main port.

9. Visually confirm that the sample has been loaded by checking the sample inspection window of the QIAstat-Dx Gastrointestinal Panel 2 Cartridge (Figure 9). A mixture of sample and silica beads should be observed.

   Important: After the sample is placed inside the QIAstat-Dx Gastrointestinal Panel 2 Cartridge, the cartridge must be loaded into the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 within 90 minutes, or immediately placed on the QIAstat-Dx Rise tray once all samples are loaded into the cartridges. The maximum waiting time for a cartridge that is already loaded into the QIAstat-Dx Rise (on-board stability) is about 145 minutes. The QIAstat-Dx Rise will automatically detect and warn the user if the cartridge has been placed into the instrument for a longer time than is permitted.

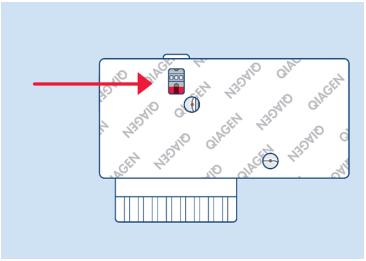


Figure 9. Sample inspection window (red arrow).

Running a test with a QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0

1. Power on the QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0 using the **ON/OFF** button on the front of the instrument.

   Note: The power switch at the back of the Analytical Module must be set in the "I" position. The QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0 status indicators will turn blue.

2. Wait until the Main screen appears and the QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0 status indicators turn green and stop blinking.

3. Enter your username and password for QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0 to log in.

   Note: The Login screen will appear if User Access Control is activated. If the User Access Control is disabled, username/password will not be required and the Main screen will appear.

4. If the Assay Definition File software is not installed on the QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0, follow the installation instructions prior to running the test (see "Appendix A" for additional information).

5. Press **Run Test** in the top right corner of the touchscreen of the QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0.

6. When prompted, scan the sample ID barcode on the Cary-Blair sample or scan the specimen information barcode located on the top of the QIAstat-Dx Gastrointestinal Panel 2 Cartridge (see step 3) using the integrated front barcode reader of the QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0 (Figure 10).

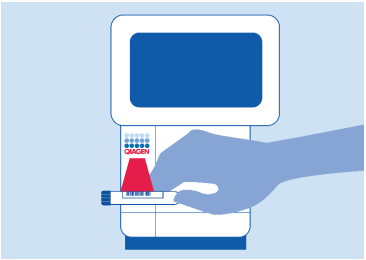


Figure 10. Scanning sample ID barcode.

Note: It is also possible to enter the sample ID using the virtual keyboard of the touchscreen by selecting the Sample ID field.

Note: Depending on the selected system configuration, entering the patient ID may also be required at this point.

Note: Instructions from the QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0 appear in the Instructions Bar at the bottom of the touchscreen.

7. When prompted, scan the barcode of the QIAstat-Dx Gastrointestinal Panel 2 Cartridge to be used (Figure 11). The QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0 will automatically recognize the assay to be run based on the cartridge barcode.

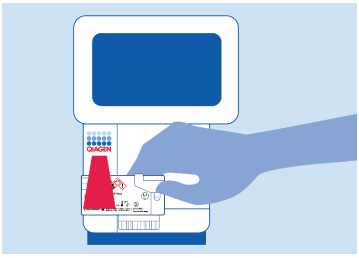


Figure 11. Scanning QIAstat-Dx Gastrointestinal Panel 2 Cartridge barcode.

Note: The QIAstat-Dx Analyzer 1.0 will not accept QIAstat-Dx Gastrointestinal Panel 2 Cartridges with lapsed expiration dates, previously used cartridges, or cartridges for assays that have not been installed on the unit. An error message will be shown in these cases and the QIAstat-Dx Gastrointestinal Panel 2 Cartridge will be rejected. Refer to the *QIAstat-Dx Analyzer 1.0* or *QIAstat-Dx Analyzer 2.0 User Manual* or "Appendix A" for further details on how to install assays.

8. The Confirm screen will appear. Review the entered data and make any necessary changes by selecting the relevant fields on the touchscreen and editing the information.

9. Press **Confirm** when all the displayed data are correct. If needed, select the appropriate field to edit its content, or press **Cancel** to cancel the test (Figure 12).

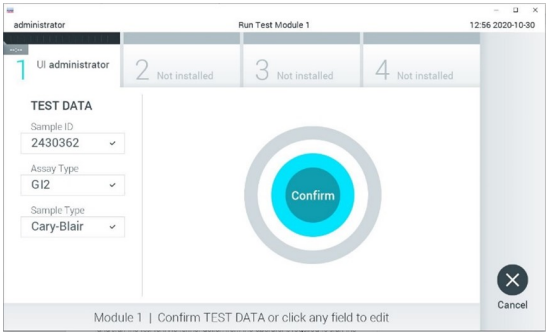


Figure 12. Confirming data entry.

10. Ensure that both the sample lids of the swab port and main port of the QIAstat-Dx Gastrointestinal Panel 2 Cartridge are firmly closed.

11. When the cartridge entrance port on the top of the QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0 automatically opens, insert the QIAstat-Dx Gastrointestinal Panel 2 Cartridge with the barcode facing to the left and the reaction chambers facing down (Figure 13).

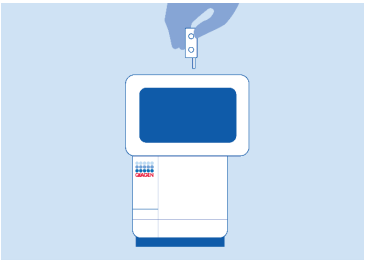


Figure 13. Inserting QIAstat-Dx Gastrointestinal Panel 2 Cartridge into the QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0.

Note: Depending on the system configuration, the operator may be required to re-enter their user password to start the test run.

Note: Up to this point, it is possible to cancel the test run by pressing **Cancel** at the bottom right corner of the touchscreen.

12. Upon detecting the QIAstat-Dx Gastrointestinal Panel 2 Cartridge, the QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0 will automatically close the lid of the cartridge entrance port and start the test run. No further action from the operator is required to start the run.

    Note: There is no need to push the QIAstat-Dx Gastrointestinal Panel 2 Cartridge into the QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0.

    Note: The QIAstat-Dx Analyzer 1.0 and the QIAstat-Dx Analyzer 2.0 will not accept a QIAstat-Dx Gastrointestinal Panel 2 Cartridge other than the one used and scanned during the test setup. If a cartridge other than the one scanned is inserted, an error will be generated, and the cartridge will be automatically ejected.

    Note: The lid of the cartridge entrance port will close automatically after 30 seconds if a QIAstat-Dx Gastrointestinal Panel 2 Cartridge is not positioned in the port. If this occurs, repeat the procedure starting from step 5.

13. While the test is running, the remaining run time is displayed on the touchscreen.

14. After the test run is completed, the Eject screen will appear (Figure 14) and the Module status bar will display the test result as one of the following options:

    - TEST COMPLETED: The test was completed successfully
    - TEST FAILED: An error occurred during the test
    - TEST CANCELED: The user canceled the test

    Important: If the test fails, refer to the "Troubleshooting" section in the *QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0 User Manual* or possible reasons and instructions on how to proceed. For additional information about specific QIAstat-Dx Gastrointestinal Panel 2 error codes and messages, please see the Troubleshooting Guide section of this document.

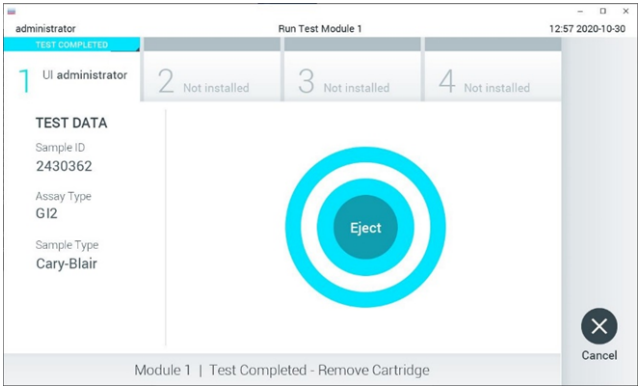


Figure 14. Eject screen display.

15. Press  **Eject** on the touchscreen to remove the QIAstat-Dx Gastrointestinal Panel 2 Cartridge and dispose of it as biohazardous waste in accordance with all national, state, and local health and safety regulations and laws. The QIAstat-Dx Gastrointestinal Panel 2 Cartridge should be removed when the cartridge entrance port opens and ejects the

cartridge. If the cartridge is not removed after 30 seconds, it will automatically move back into the QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0 and the cartridge entrance port lid will close. If this occurs, press **Eject** to open the lid of the cartridge entrance port again and then remove the cartridge.

Important: Used QIAstat-Dx Gastrointestinal Panel 2 Cartridges must be discarded. It is not possible to re-use cartridges for tests for which the execution was started but then subsequently cancelled by the operator, or for which an error was detected.

16. After the QIAstat-Dx Gastrointestinal Panel 2 Cartridge has been ejected, the results Summary screen will appear. Refer to Interpretation of Results on page 63 for further details. To begin the process for running another test, press **Run Test**.

    Note: For further information on the use of the QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0, refer to the *QIAstat-Dx Analyzer 1.0 User Manual* or *QIAstat-Dx Analyzer 2.0 User Manual*, respectively.

Running a test on the QIAstat-Dx Rise

Starting the QIAstat-Dx Rise

1. Press the **ON/OFF** button on the front panel of the QIAstat-Dx Rise to start the unit.

   Note: The power switch at the rear-left connection box must be set to the "I" position.

2. Wait until the Login screen appears, and the LED status indicators turn green.
3. Log in to the system once the login screen appears (Figure 15)

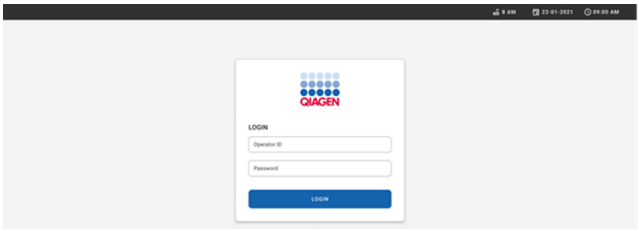


Figure 15. Log in screen

Note: After successful initial installation of the QIAstat-Dx Rise, the system administrator needs to log in for the initial configuration of the software.

Preparing the QIAstat-Dx Gastrointestinal Panel 2 cartridge

Remove the QIAstat-Dx Gastrointestinal Panel 2 cartridge from its packaging. For details about adding the sample to the QIAstat-Dx Gastrointestinal Panel 2 cartridge and for information specific to the assay to be run, refer to "Loading a sample into the QIAstat-Dx Gastrointestinal Panel 2 Cartridge".

Always make sure that both sample lids are firmly closed after adding a sample to the QIAstat-Dx Gastrointestinal Panel 2 cartridge.

Adding a sample barcode to the QIAstat-Dx Gastrointestinal Panel 2 cartridge

Place a barcode on the top-right side of the QIAstat-Dx Gastrointestinal Panel 2 Cartridge (indicated by the arrow) (Figure 16).

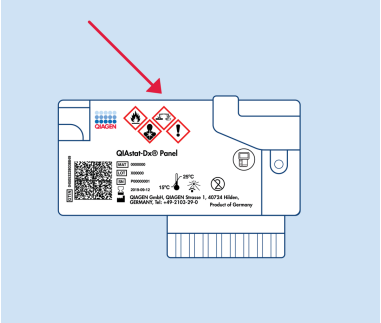


Figure 16. Placing sample ID barcode.

The maximum barcode size is: 22 mm x 35 mm. The barcode must always be on the right side of the cartridge (as it is shown above with red marked area), as the left side of the cartridge is critical for sample autodetection (Figure 17).

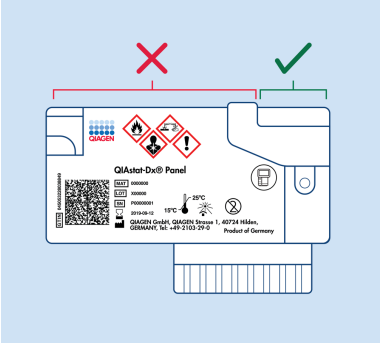


Figure 17. Positioning sample ID barcode.

Note: To process samples on the QIAstat-Dx Rise, it is required to provide a machine-readable sample ID barcode on the QIAstat-Dx Gastrointestinal Panel 2 Cartridge.

1D and 2D barcodes can be used.

Usable 1D barcodes are the following: EAN-13 and EAN 8, UPC-A and UPC-E, Code128, Code39, Code 93, and Codabar.

Usable 2D barcodes are the following: Aztec Code, Data Matrix, and QR code.

Make sure that the barcode quality is sufficient. The system is capable of reading a printing quality of grade C or better, as defined in ISO/IEC 15416 (linear) or ISO/IEC 15415 (2D).

Procedure to run a test

Note: All operators should wear appropriate personal protective equipment, such as gloves, lab coat, and protective glasses when handling the QIAstat-Dx Rise touchscreen and cartridges.

1. Press **OPEN WASTE DRAWER** at the lower-right corner of the main test screen (Figure 18).
2. Open the waste drawer and remove used cartridges from previous runs. Check the waste drawer for spilled liquids. If necessary, clean the waste drawer as described in the "Maintenance" section of the *QIAstat-Dx Rise User Manual*.
3. Close the waste drawer after removal of the cartridges. The system will scan the tray and return to the main screen (Figure 18). If the tray was removed for maintenance purposes, make sure it is correctly inserted before closing the drawer.
4. Press **OPEN INPUT DRAWER** at the lower-right corner of the screen (Figure 18).

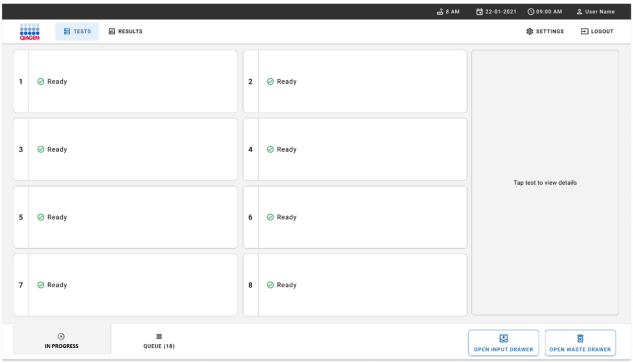


Figure 18. Main test screen.

5. Wait until the input drawer is unlocked (Figure 19).

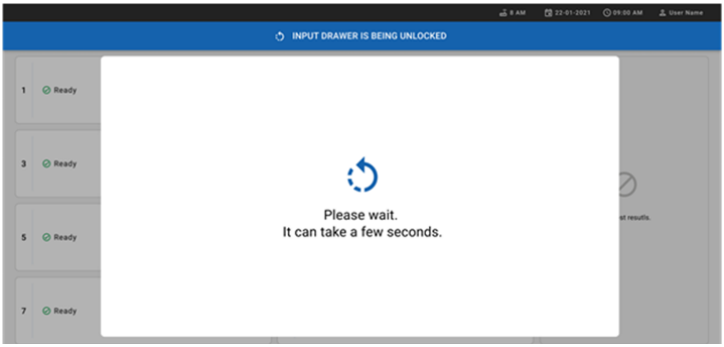


Figure 19. Input drawer waiting dialog box.

6. When prompted, pull the input drawer to open (Figure 20).

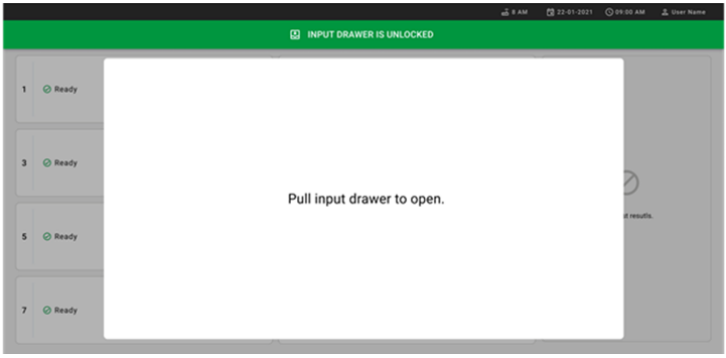


Figure 20. Input drawer open dialog box.

7. The Add Cartridge dialog appears, and the scanner in front of the instrument will be activated. Scan the sample ID barcode on top of the QIAstat-Dx Gastrointestinal 2 cartridge in front of the instrument (position indicated by the arrow [Figure 21]).

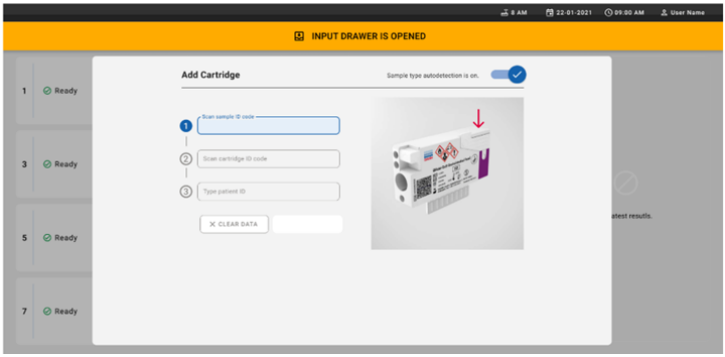


Figure 21. Scan sample ID screen.

8. After entering the sample ID barcode, scan the barcode of the QIAstat-Dx Gastrointestinal Panel 2 cartridge to be used (position indicated by the arrow). The QIAstat-Dx Rise will automatically recognize the assay to be run, based on the QIAstat-Dx Gastrointestinal Panel 2 cartridge barcode (Figure 22).

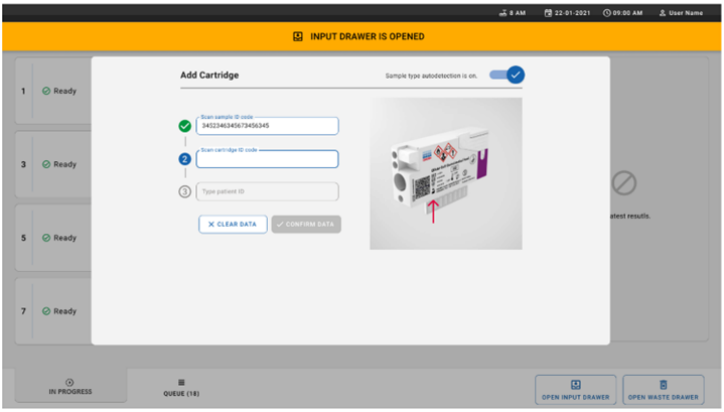


Figure 22. Scanning the QIAstat-Dx Gastrointestinal Panel 2 cartridge ID screen.

Note: Make sure that **Sample type autodetection** is set to **on**. The system will automatically recognize the used sample type (if applicable for the assay used).

If **Sample type autodetection** is set to **off**, you might need select the appropriate sample type manually (if applicable for the assay used).

Note: The QIAstat-Dx Rise will not accept QIAstat-Dx Gastrointestinal Panel 2 cartridges that have lapsed expiration dates, were previously used, or if the QIAstat-Dx Gastrointestinal Panel 2 assay definition file is not installed on the unit. An error message will be shown in this case

9. Enter the patient ID (Patient ID has to be set to on) then confirm the data (Figure 23 and Figure 24).

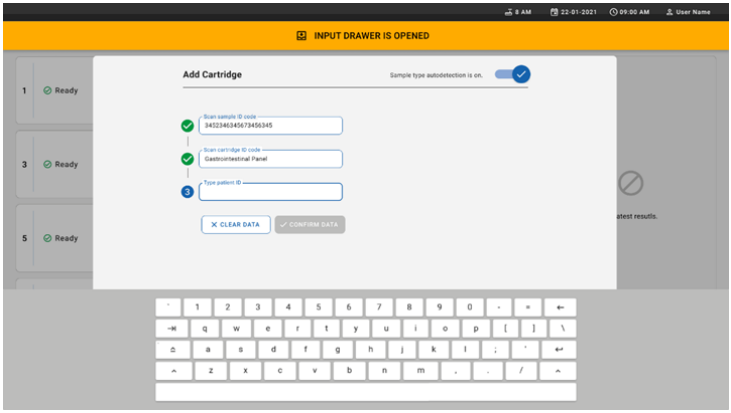


Figure 23. Typing the patient ID.

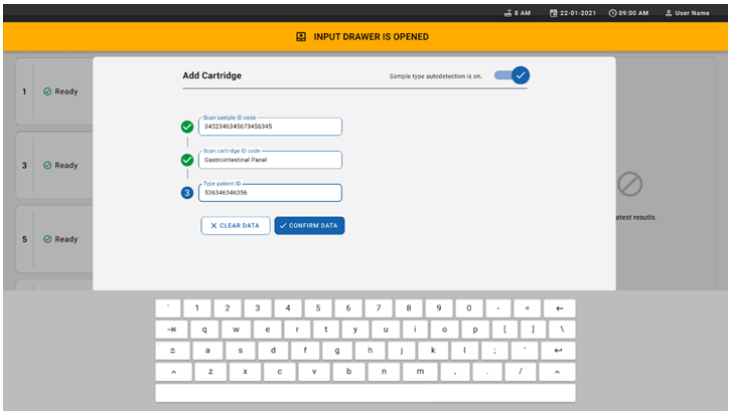


Figure 24. Type patient ID then confirm the data screen.

10. After a successful scan, the following dialog box appears briefly on top of the screen (Figure 25 below).

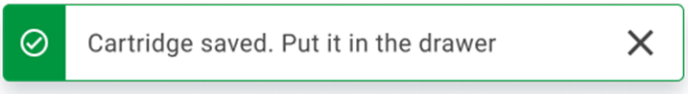


Figure 25. Cartridge saved screen

11. Place the cartridge into the input drawer. Make sure that the cartridge is inserted properly into the tray (Figure 26).

12. Continue scanning and inserting cartridges by following the previous steps.

    Important: Please be aware that QIAstat-Dx Rise can handle up to 16 QIAstat-Dx Gastrointestinal Panel 2 cartridges at the same time, within the input drawer. For further information, refer to the current *QIAstat-Dx Rise User Manual*.

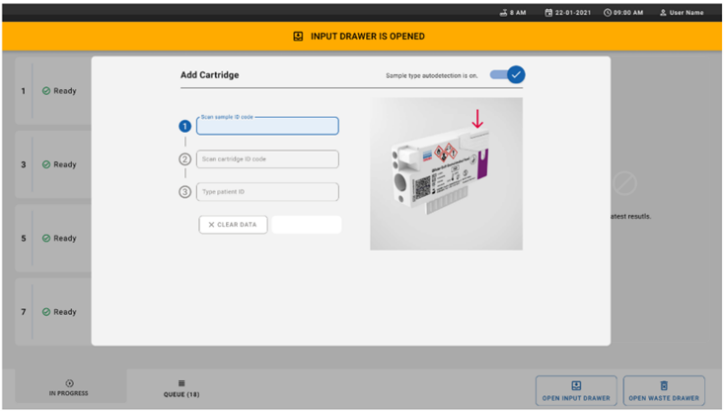


Figure 26. Add cartridge screen.

13. Close the input drawer when all cartridges have been scanned and inserted. The system will scan the cartridges and prepare a queue (Figure 27).

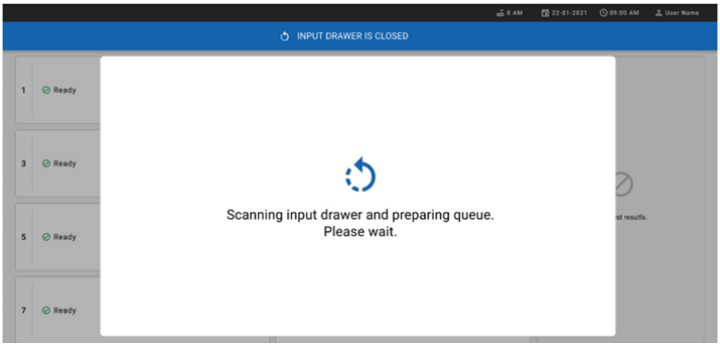


Figure 27. Preparing queue screen.

14. After successful scanning, the queue will be shown (Figure 28). Review the data and in case of an error, press **OPEN INPUT DRAWER** to remove and re-scan the respective cartridge, following steps 10–13.

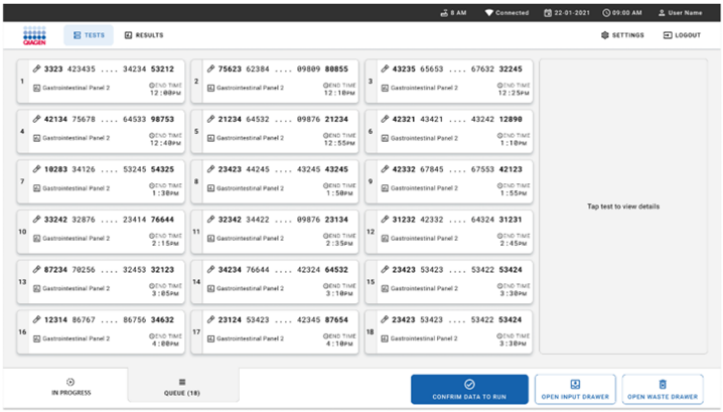


Figure 28. Sample queue screen.

Note: The sample order on the screen may not match the cartridge order in the input drawer (it only matches when all the cartridges are queued together) and cannot be changed without opening the input tray and removing cartridges.

The sample queue/processing order is generated by QIAstat-Dx Rise based on the following rules:

- Stability time. QIAstat-Dx Gastrointestinal Panel 2 cartridges with the shortest on-board stability time will be prioritized irrespective of the position in the loading tray.
- Within the same assay type, the position in the loading tray determines the order in queue.

If you select a test on the touchscreen, additional information is displayed in the TEST DETAILS section of the screen (Figure 29).

Note: The system will reject cartridges that exceed the maximum on-board stability time within the input drawer (about 145 minutes).

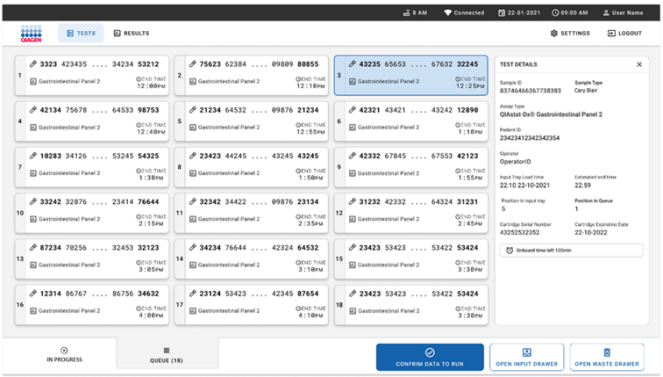


Figure 29. Sample queue screen with selected assay showing additional information.

The following information is shown in the TEST DETAILS section (Figure 30):

- Sample ID
- Sample Type (depending on the assay)
- Assay Type (QIAstat-Dx Gastrointestinal Assay Panel 2)
- Patient ID
- Operator
- Input Tray Load Time
- Estimated end time
- Position in input drawer
- Position in Queue (**Note**: the position may differ based on sample stability time)
- Cartridge Serial Number
- Cartridge Expiration Date
- On-board time left

Note: The on-board time is defined in the respective assay and triggers the order of samples in the queue.

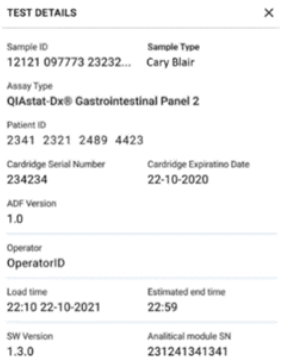


Figure 30. Test details

15. Press **CONFIRM DATA TO RUN** at the bottom of the screen when all the displayed data are correct (Figure 30). Thereafter, a final confirmation is required from the operator to run the tests (Figure 31).

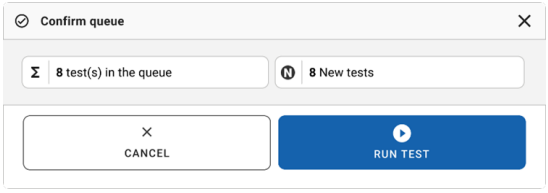


Figure 31. Final confirmation to run rest.

16. While the tests are running, the remaining run time and other information for all queued tests are displayed on the touchscreen (Figure 32).

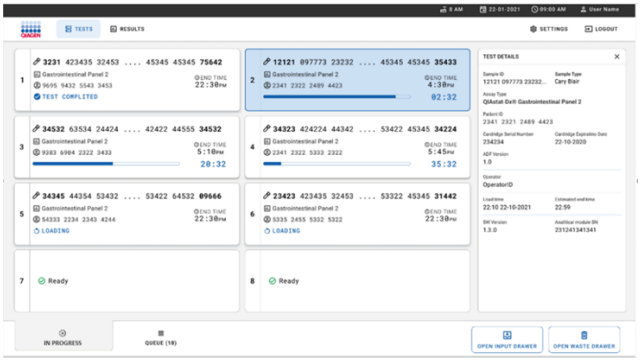


Figure 32. Test execution information on queue screen.

17. If the cartridge is being loaded into an Analytical Module, a "TEST LOADING" message and the estimated end time are displayed (Figure 33).

Figure 33. Test loading message and end time.

18. If the test is running, the elapsed run time and the approximate end time are displayed (Figure 34).

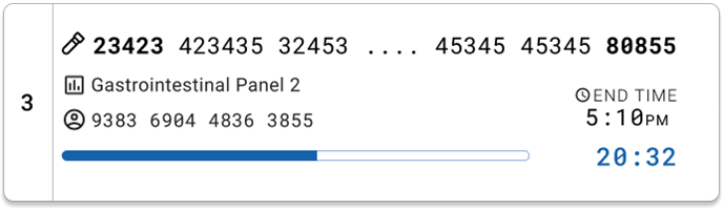


Figure 34. Elapsed run time and approximate end time view.

19. If the test is completed, a "TEST COMPLETED" message and the run end time are displayed (Figure 35).

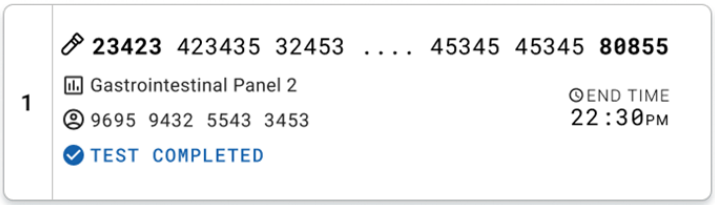


Figure 35. Test completed view.

Prioritizing samples

If a sample needs to be run urgently, it is possible to select this sample on the sample queue screen and run as a first sample (Figure 36). Please note that it is not possible to prioritize a sample after confirmation of the queue.

Prioritizing sample before starting run

The urgent sample is selected on the queue screen and marked "URGENT" from right-hand side of the sample queue screen before confirm data to run (Figure 36 below). Following this, the sample is moved to the first position of the queue (Figure 37).

Note: Only one sample can be prioritized.

Note: It is required to open and close the input drawer; otherwise it is not possible to prioritize a cartridge that has already been confirmed. At this point, if the **Urgent** button is not active. The operator need to switch between **QUEUE** and **IN PROGRESS** tabs on the GUI to see the active **Urgent** button.

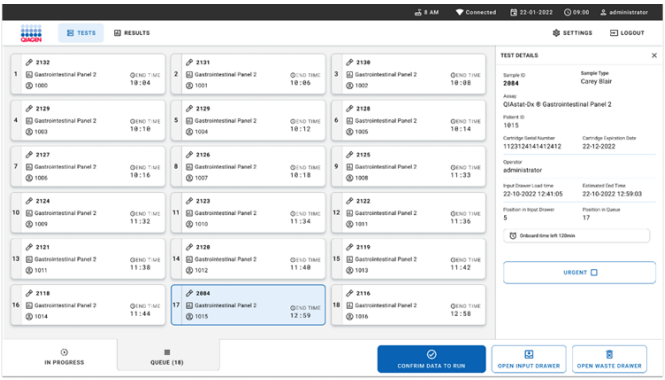


Figure 36. Sample queue screen while selecting sample to be prioritized.

Some other samples may run out of stability time due to prioritization of a sample. This warning can be seen on the right corner of the screen (Figure 37).

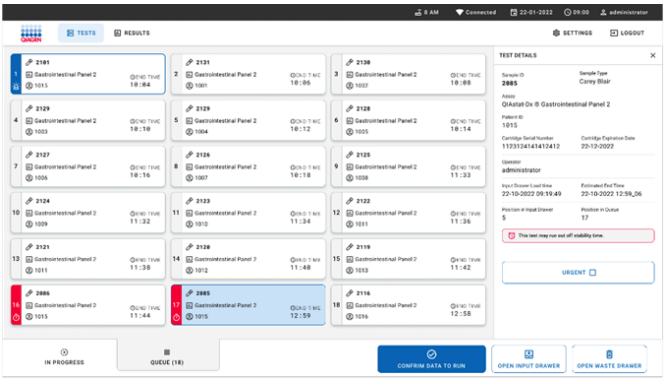


Figure 37. Sample queue screen after a sample is prioritized.

After confirmation of the queue the run can be started (Figure 38 below).

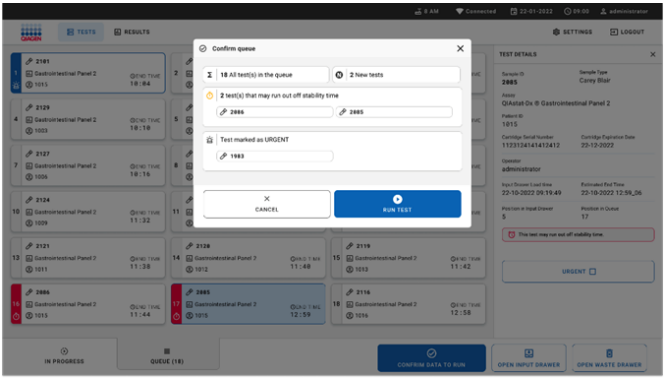


Figure 38. Confirmation of the run screen.

Prioritizing sample during run

A sample can be also prioritized for any reason during the run. In this case, if there is no available AM, any other ongoing sample needs to be aborted to perform prioritization (Figure 39).

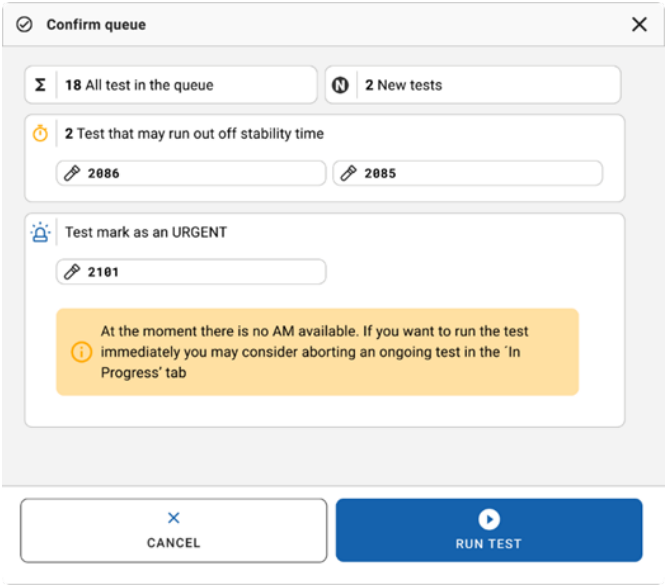


Figure 39. Confirmation dialog during run.

Abortion of running sample

A sample can be aborted during scanning, loading, and running.

Important: The sample cannot be used again once it is aborted. This is also true for the sample that is aborted during scanning and loading.

1. To abort a sample go to **IN PROGRESS** tab of the screen and select the sample and press **Abort** on the right corner of the screen (Figure 40).

   Note: It is not possible to abort a run while a sample is about to load into AM or about to complete to run and the system is retrieving result data or/and technical logs from the respective AM.

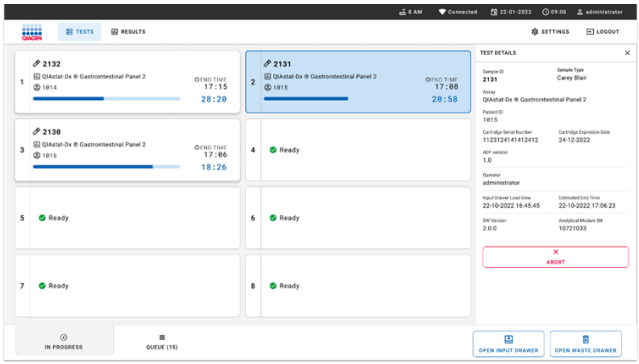


Figure 40. Abortion of a running sample.

2. The system needs a confirmation to abort the sample (Figure 41).

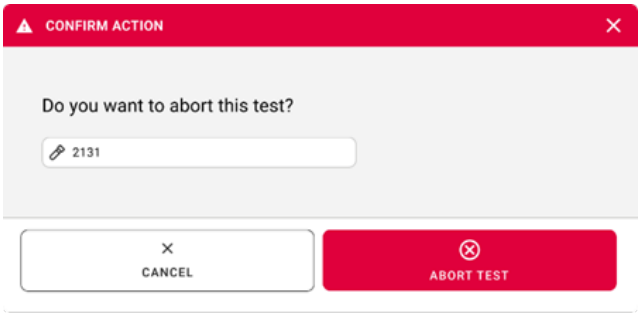


Figure 41. Confirmation dialog to abort running sample.

3. After a while, the sample can be seen as "Aborted" on the screen (Figure 42 and Figure 43).

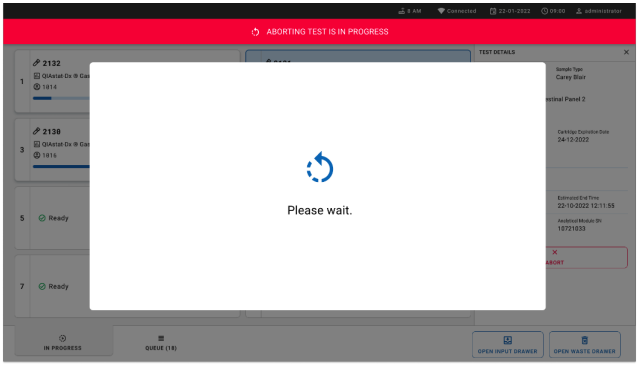


Figure 42. Sample abortion waiting dialog.

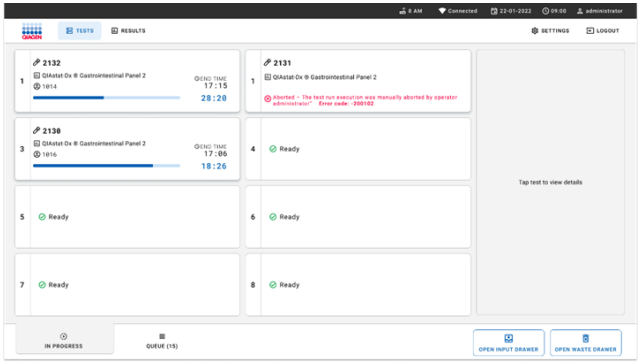


Figure 43. Aborted sample after confirmation of the abortion.

Handling reagents

Transfer pipettes provided in the kit are single use. In case transfer pipettes is dropped or contaminated due to user error, use any other commercially available pipette with a minimum volume of 200 µL.

Interpretation of Results

Internal control interpretation

The QIAstat-Dx Gastrointestinal Panel Cartridge includes a full process Internal Control, which is titered *Schizosaccharomyces pombe*. *Schizosaccharomyces pombe* is a yeast (fungi) that is included in the cartridge in dried form and is rehydrated upon sample loading. This Internal Control material verifies all steps of the analysis process, including sample homogenization, lysis of viral, and cellular structures (by means of chemical and mechanical disruption), nucleic acid purification, reverse transcription, and real-time PCR.

A passed result for the Internal Control indicates that all processing steps performed by the QIAstat-Dx Gastrointestinal Panel Cartridge were successful.

A failed result of the Internal Control does not negate any positive results for detected and identified targets, but it does invalidate all negative results in the analysis. Therefore, the test should be repeated if the Internal Control signal is negative.

Viewing results with the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0

The QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0 automatically interprets and saves test results. After ejecting the QIAstat-Dx Gastrointestinal Panel 2 Cartridge, the results Summary screen is automatically displayed (Figure 44).

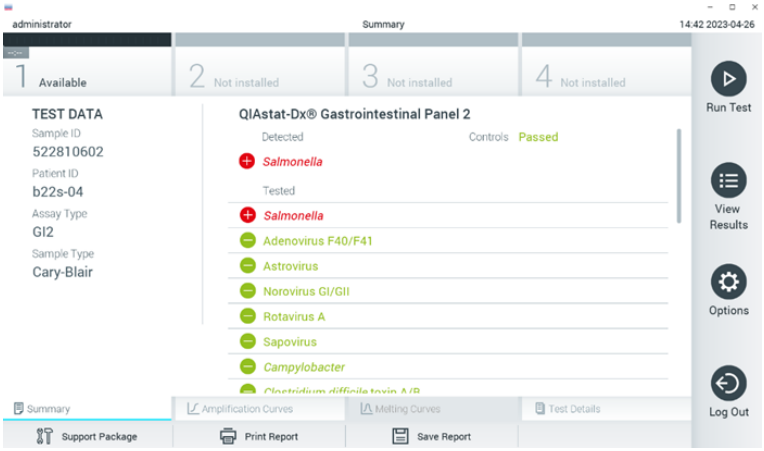


Figure 44. Results Summary screen example showing Test Data on the left panel and Test Summary in the main panel in the QIAstat-Dx Analyzer 1.0.

Figure 45 shows the screen for the QIAstat-Dx Analyzer 2.0.

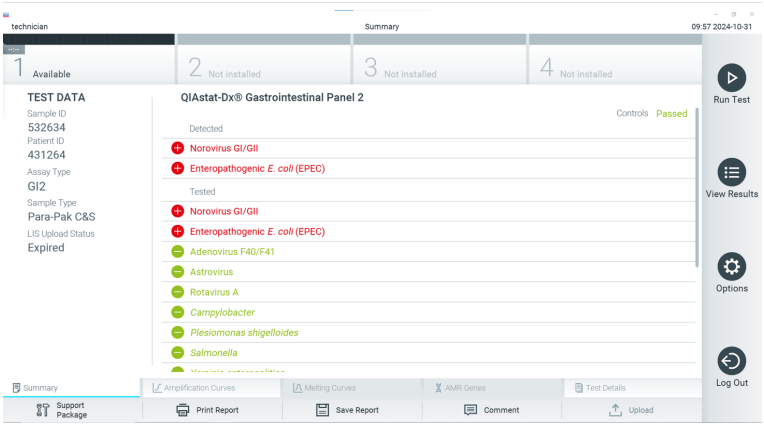


Figure 45. Results Summary screen example showing test Data on the left panel and Test Summary in the main panel in QIAstat-Dx Analyzer 2.0.

QIAstat-Dx Analyzer 2.0 includes an additional tab:

AMR Genes: It is disabled for the QIAstat-Dx Gastrointestinal Panel 2.

Note: From this point forward, example screen shots will be used when referring to the QIAstat-Dx Analyzer 1.0 and/or QIAstat-Dx Analyzer 2.0 where the functions being explained are the same.

The main part of the screen provides the following lists and uses color-coding and symbols to indicate the results:

- The first list, under the heading "Detected", includes all pathogens detected and identified in the sample, which are preceded by a  sign and are colored red.
- The second list, under the heading "Tested" is includes all pathogens tested in the sample. Pathogens detected and identified in the sample are preceded by a  sign and are colored red. Pathogens that were tested but not detected are preceded by a  sign and are colored green. Invalid and not applicable pathogens are also displayed in this list.
- The third, under the heading "Tested", includes all pathogens tested in the sample. Pathogens detected and identified in the sample are preceded by a  sign and are colored green. Invalid pathogens are also displayed in this list.

Note: Pathogens detected and identified in the sample are shown in both the **Detected** and **Tested** lists.

If the test failed to complete successfully, a message will indicate **Failed** followed by the specific Error Code.

The following Test Data is shown on the left side of the screen:

- Sample ID
- Patient ID (if available)
- Assay Type
- Sample Type

Further data about the assay is available, depending on the operator's access rights, through the tabs at the bottom of the screen (e.g., amplification plots and test details).

A report with the assay data can be exported to an external USB storage device. Insert the USB storage device into one of the USB ports of the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 and press **Save Report** in the bottom bar of the screen. This report can be exported later at any time by selecting the test from the "View Result" List.

The report can also be sent to the printer by pressing **Print Report** in the bottom bar of the screen.

Viewing amplification curves

To view test amplification curves of pathogens detected, press the **Amplification Curves** tab (Figure 46).

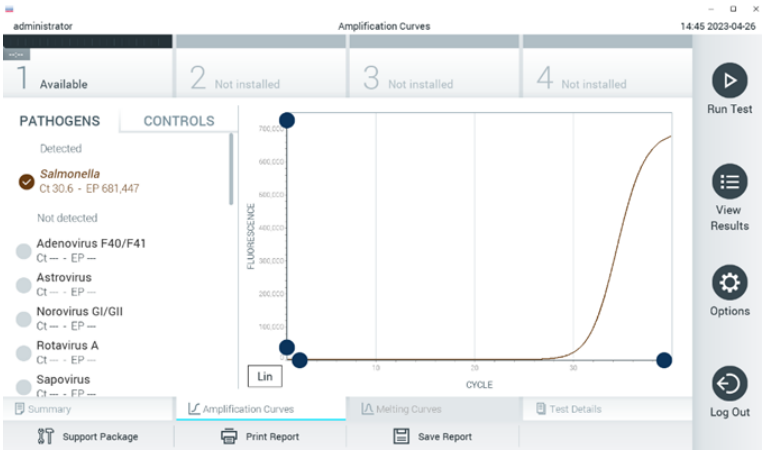


Figure 46. Amplification Curves screen (PATHOGENS tab).

Details about the tested pathogens and controls are shown on the left and the amplification curves are shown in the center.

Note: If User Access Control is enabled on the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0, the **Amplification Curves** screen is only available for operators with access rights.

Press the **PATHOGENS** tab on the left side to display the plots corresponding to the tested pathogens. Press on the pathogen name to select which pathogens are shown in the amplification plot. It is possible to select single, multiple, or no pathogens. Each pathogen in the selected list will be assigned a color corresponding to the amplification curve associated with the pathogen. Unselected pathogens will be shown in gray.

The corresponding C_T and endpoint fluorescence (EP) values are shown below each pathogen name.

Press the **CONTROLS** tab on the left side to view the controls in the amplification plot. Press the circle next to the control name to select or deselect it (Figure 47).

Figure 47. Amplification Curves screen (CONTROLS tab).

The amplification plot displays the data curve for the selected pathogens or controls. To alternate between logarithmic or linear scale for the Y-axis, press the **Lin** or **Log** button at the bottom left corner of the plot.

The scale of the X-axis and Y-axis can be adjusted using the **blue pickers** on each axis. Press and hold a blue picker and then move it to the desired location on the axis. Move a blue picker to the axis origin to return to the default values.

Viewing test details

Press **Test Details** in the Tab Menu bar at the bottom of the touchscreen to review the results in more detail. Scroll down to see the complete report.

The following Test Details are shown in the center of the screen (Figure 48):

- User ID
- Cartridge SN (serial number)
- Cartridge Expiration Date
- Module SN
- Test Status (Completed, Failed or Canceled by operator)
- Error Code (if applicable)
- Test Start Date and Time
- Test Execution Time
- Assay Name
- Test ID
- Test Result
    - **Positive** (if at least one gastrointestinal pathogen is detected/identified)
    - **Positive with warning** (if at least one pathogen is detected, but the Internal Control failed)
    - **Negative** (if no gastrointestinal pathogen is detected)
    - **Failed** (an error occurred or the test was canceled by the user)

- List of analytes tested in the assay, with C_T and endpoint fluorescence in the event of a positive signal
- Internal Control, with C_T and endpoint fluorescence

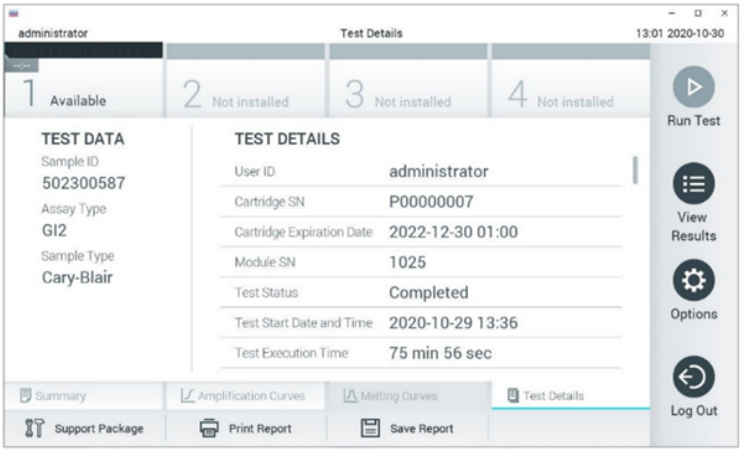


Figure 48. Example screen showing Test Data on the left panel and Test Details in the main panel.

Browsing results from previous tests

To view results from previous tests that are stored in the results repository, press **View Results** on the Main Menu bar (Figure 49).

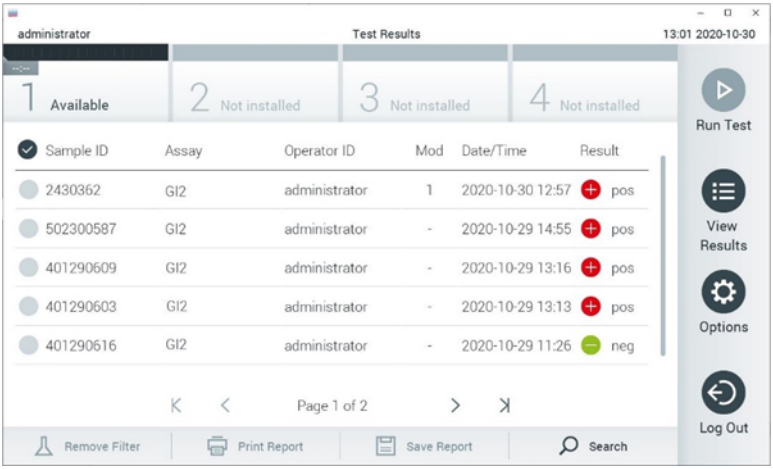


Figure 49. Example View Results screen.

The following information is available for every executed test (Figure 21):

- Sample ID
- Assay (name of test assay which is "GI2" for Gastrointestinal Panel 2)
- Operator ID
- Mod (Analytical Module on which the test was executed)
- Date/Time (date and time when the test was finished)
- Result (outcome of the test: positive [pos], negative [neg], failed [fail], or successful [suc])

Note: If User Access Control is enabled on the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0, the data for which the user has no access rights will be hidden with asterisks.

Select one or more test results by pressing the gray circle to left of the sample ID. A checkmark will appear next to selected results. Unselect test results by pressing this checkmark. The entire list of results can be selected by pressing the **checkmark** in the top row (Figure 50).

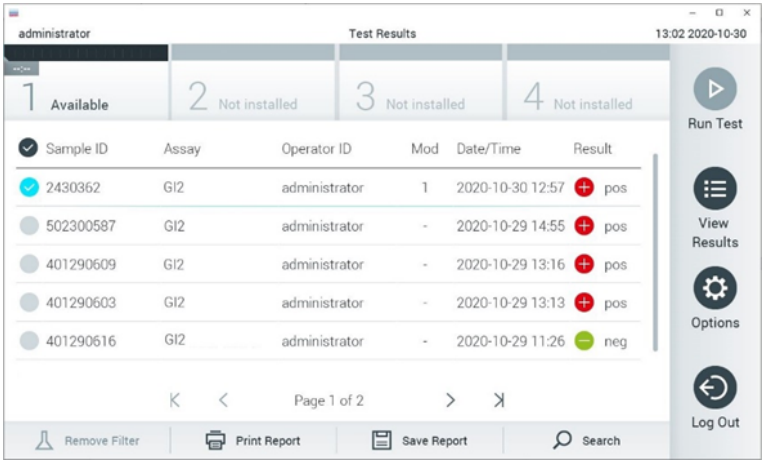


Figure 50. Example of selecting Test Results in the View Results screen.

Press anywhere in the test row to view the result for a particular test.

Press a column headline (e.g., Sample ID) to sort the list in ascending or descending order according to that parameter. The list can be sorted according to only one column at a time.

The Result column shows the outcome of each test (Table 3).

Table 3. Descriptions of the test results in View Results Screen

Outcome	Result	Description	Action
Positive	pos	At least one pathogen is positive	Refer to the Summary Result Screen or Result Printout for pathogen specific results. Description of pathogen results can be found in Table 4.
Positive with warning	pos*	At least one pathogen is positive, but the Internal Control failed	Refer to the Summary Result Screen or Result Printout for pathogen specific results. Description of pathogen results can be found in Table 4.
Negative	neg	No analytes were detected	Refer to the Summary Result Screen or Result Printout for pathogen specific results. Description of pathogen results can be found in Table 4.
Failed	fail	The test failed because either an error occurred, the test was canceled by the user, or no pathogens were detected and the internal control failed.	Repeat the test using a new cartridge. Accept the results of the repeat testing. If the error persists, contact QIAGEN Technical Services for further instructions.
Successful	Suc	The test is either positive or negative, but the user does not have the access rights to view the test results.	Login from a user profile with rights to view the results.

Make sure a printer is connected to the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0, and the proper driver is installed. Press **Print Report** to print the report(s) for the selected result(s).

Press **Save Report** to save the report(s) for the selected result(s) in PDF format to an external USB storage device.

Select the report type: **List of Tests** or **Test Reports**.

Press **Search** to search the test results by Sample ID, Assay, and Operator ID. Enter the search string using the virtual keyboard and press **Enter** to start the search. Only the records containing the search text will be displayed in the search results.

If the results list has been filtered, the search will only apply to the filtered list.

Press and hold a column headline to apply a filter based on that parameter. For some parameters, such as Sample ID, the virtual keyboard will appear so the search string for the filter can be entered.

For other parameters, such as Assay, a dialog will open with a list of assays stored in the repository. Select one or more assays to filter only the tests that were performed with the selected assays.

The  symbol to the left of a column headline indicates that the column's filter is active.

A filter can be removed by pressing Remove Filter in the Submenu bar.

Exporting results to a USB drive

From any tab of the View Results screen, select **Save Report** to export and save a copy of the test results in PDF format to a USB drive. The USB port is located on the front of the QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0.

Printing results

Make sure a printer is connected to the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0, and the proper driver is installed. Press **Print Report** to send a copy of the PDF test results to the printer.

Sample Result Interpretation

A result for a gastrointestinal organism is interpreted as "Positive" when the corresponding PCR assay is positive, except for EPEC, STEC, and *E. coli* O157. The result interpretation for EPEC, STEC, and *E. coli* O157 follows the rationale explained in Table 4, below.

Table 4. Interpretation of EPEC, STEC, and *E.coli* O157 results

EPEC Result	STEC *stx1/stx2* Result*			*E. coli* O157 Result	Description
	stx1	*stx2*	*stx1 + stx2*		
Negative			Negative	N/A	Enteropathogenic *E. coli* (EPEC) was not detected and Shiga-like toxin-producing *E. coli* (STEC) *stx1/stx2* is negative as both *stx1* and *stx2* have not been detected. *E. coli* O157 result is not applicable (N/A) when Shiga-like toxin-producing *E. coli* (STEC) *stx1/stx2* is not detected due to *E. coli* O157 being a specific serotype of STEC.
Positive			Negative	N/A	Enteropathogenic *E. coli* (EPEC) was detected and Shiga-like toxin-producing *E. coli* (STEC) *stx1/stx2* is negative as both *stx1 and stx2* have not been detected. *E. coli* O157 result is not applicable (N/A) when Shiga-like toxin-producing *E. coli* (STEC) *stx1/stx2* is not detected due to *E. coli* O157 being a specific serotype of STEC.
N/A	Positive			Negative	EPEC result is not applicable because EPEC detection cannot be differentiated when STEC *stx1* or *stx2* is detected. *E. coli* O157 was not detected.

Table 4. Interpretation of EPEC, STEC, and E.coli O157 results (continued)

EPEC Result	STEC *stx1*/*stx2* Result*			*E. coli* O157 Result	Description
	stx1	*stx2*	*stx1* + *stx2*		
N/A		Positive		Negative	EPEC result is not applicable because EPEC detection cannot be differentiated when STEC *stx1*or *stx2* is detected.
					E. coli O157 was not detected.
N/A			Positive	Negative	EPEC result is not applicable because EPEC detection cannot be differentiated when both STEC *stx1* and *stx2* are detected. *E. coli* O157 was not detected.
N/A	Positive			Positive	EPEC result is not applicable because EPEC detection cannot be differentiated when STEC *stx1* or *stx2* is detected.
					E. coli O157 was detected.
N/A		Positive		Positive	EPEC result is not applicable because EPEC detection cannot be differentiated when STEC *stx1* or *stx2* is detected. *E. coli* O157 was detected.
N/A			Positive	Positive	EPEC result is not applicable because EPEC detection cannot be differentiated when both STEC *stx1* and *stx2* are detected.
					E. coli O157 was detected.

*Amplification curve, EP, and Ct values, when STEC *stx1 + stx2* is detected, correspond to the STEC *stx2* only.

Internal control results are to be interpreted according to Table 5.

Table 5. Interpretation of Internal Control results

Control Result	Explanation	Action
Passed	The Internal Control amplified successfully.	The run was completed with success. All results are validated and can be reported. Detected pathogens are reported as "positive" and undetected pathogens are reported as "negative".
Failed	The Internal Control failed.	Positively detected pathogen(s) are reported, but all negative results (tested but not detected pathogen[s]) are invalid. Repeat the testing using a new Cartridge. Accept the results of the repeat testing. If the invalid result persists, contact QIAGEN Technical Services for further instruction

The software provides an overall test result (Table 3) as well as a result for individual pathogens. Possible results for each organism include Detected/Positive, Not Detected/Negative, N/A, and Invalid (Table 6). If the internal control has failed and no positive signal was detected or if there is an instrument error, there will be no pathogen results provided.

Table 6. Description of Pathogen results as displayed on Summary Result Screen and the Result Printout

Result	Symbol	Explanation	Action
Positive/ Detected		A positive signal was detected for this pathogen. Result of the Internal Control is passed.	None. Report results.
Positive/ Detected with Warning		A positive signal was detected for this pathogen, but the result of the internal control has failed.	Report positive analyte. Repeat the test using a new cartridge. Accept the results of the repeat testing. If the invalid result persists, contact QIAGEN Technical Services for further instructions.
Negative/ Not Detected		No signal was detected for this pathogen. The Internal Control passed.	None. Report results.
N/A (applies to E. coli O157 and EPEC only)		The run was successfully completed and the Internal Control passed. For E. coli O157 N/A: Shiga-like toxin-producing E. coli (STEC) was not detected. For EPEC N/A: Shiga-like toxin producing E. coli (STEC) was detected.	None. Report results.
Invalid		No signal was detected for this pathogen and the Internal Control failed (but other pathogens have been detected).	Repeat the test using a new cartridge. Accept the results of the repeat testing. If the invalid result persists, contact QIAGEN Technical Services for further instructions.

Interpretation of results with QIAstat-Dx Rise

Viewing results with QIAstat-Dx Rise

The QIAstat-Dx Rise automatically interprets and saves test results. After the run completed, the results can be seen in the Results summary screen (Figure 51).

Note: Visible information will be dependent on the operator's access rights.

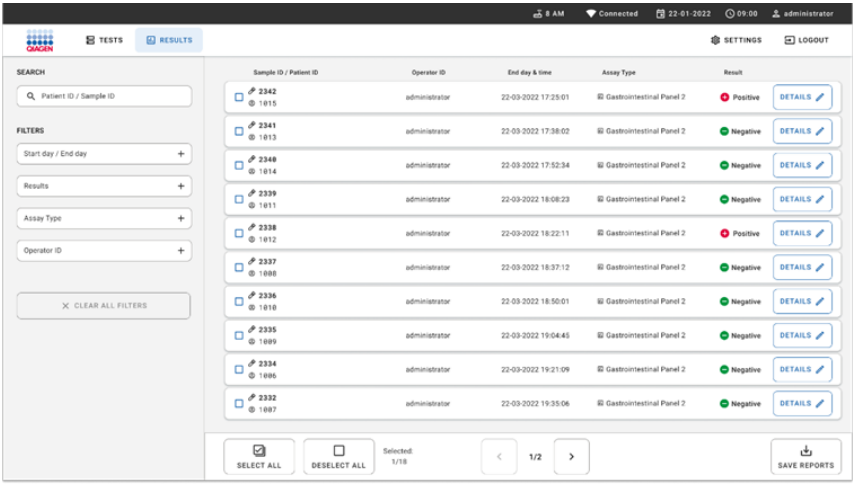


Figure 51. The results summary screen.

The main part of the screen provides an overview of the completed runs and uses color-coding and symbols to indicate the results:

- If at least one pathogen is detected in the sample, the word Positive is shown in the result column, preceded by a ⊕ sign.

- If no pathogen is detected, and the internal control is valid, the word Negative is shown in the result column, preceded by a − sign.
- If at least one pathogen is detected in the sample, and the internal control was invalid, the term Positive with warning is shown in the result column, preceded by a ⊕ ! sign.
- If the test failed to complete successfully, a message will indicate Failed followed by the specific Error Code.

The following Test Data are on the screen (Figure 47):

- Sample ID/Patient ID
- Operator ID
- End day and time
- Assay Type

Viewing test details

Further data about the assay is available, depending on the operator's access rights, through the Details button at the right side of the screen (e.g., amplification plots and test details (Figure 52).

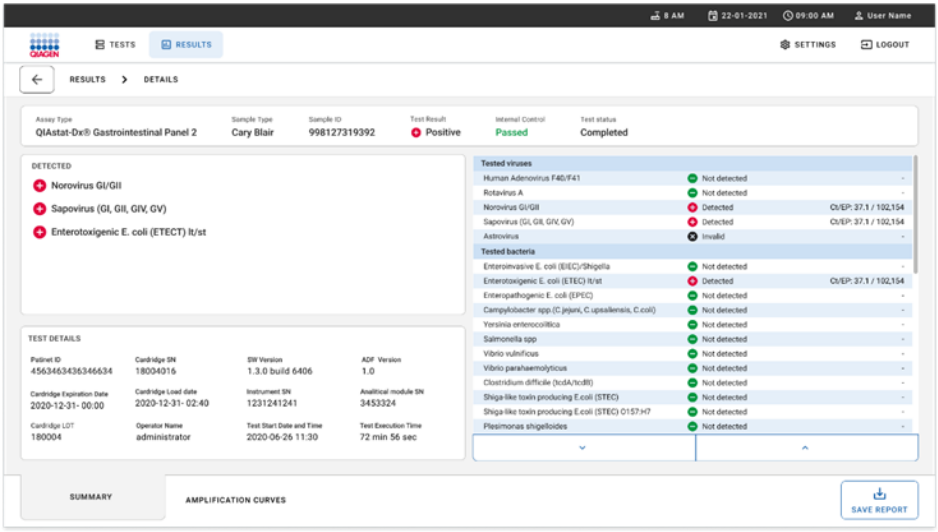


Figure 52. The test details screen.

The upper part of the screen shows general information about the test. It includes assay and sample type, Sample ID, overall test result, status of the internal control, and the test status.

On the left side of the screen, all detected pathogens are shown; the middle part of the screen shows all pathogens that the assay can detect.

Note: Categories and type of pathogens displayed depend on the assay used.

On the right side of the screen, the following test details are shown: Sample ID, operator ID, cartridge lot number, cartridge serial number, cartridge expiration date, cartridge load date and time, test execution date and time, test execution duration, Software and ADF version, and the analytical Module serial number.

Viewing amplification curves

To view the test amplification curves, press the **Amplification Curves** tab at the bottom of the screen (Figure 53 below).

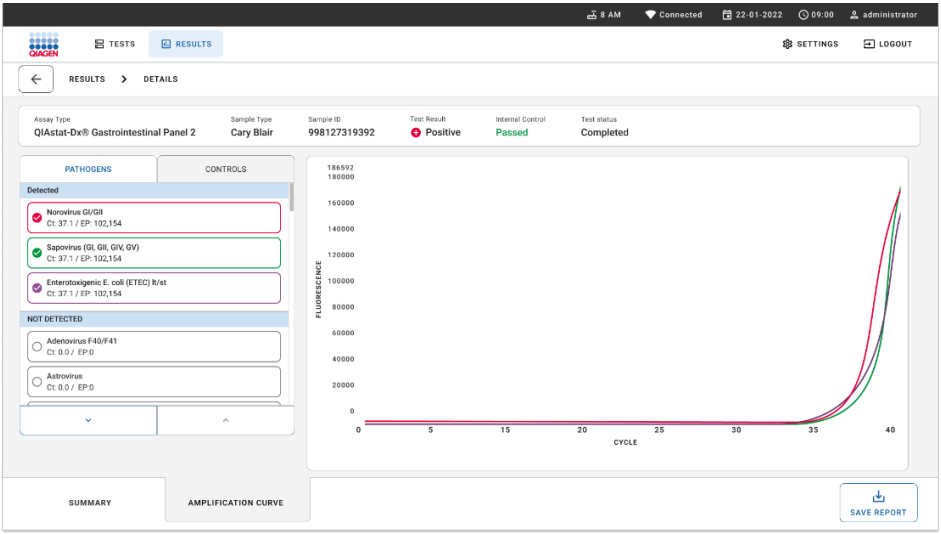


Figure 53. The amplification curves screen.

Press the **PATHOGENS** tab on the left side to display the plots corresponding to the tested pathogens. Press on the pathogen name to select which pathogens are shown in the amplification plot. It is possible to select single, multiple, or no pathogens. Each pathogen in

the selected list will be assigned a color corresponding to the amplification curve associated with the pathogen. Deselected pathogens will not be shown.

The corresponding C_T and endpoint fluorescence values are shown below each pathogen name. Pathogens are grouped into detected, and not detected.

Press the **CONTROLS** tab on the left side to view the controls, and select which controls are shown in the amplification plot.

Browsing results from previous tests

To view results from previous tests that are stored in the results repository, use the search functionality in the main results screen (Figure 54).

Note: The functionality may be restricted or disabled due to user profile settings.

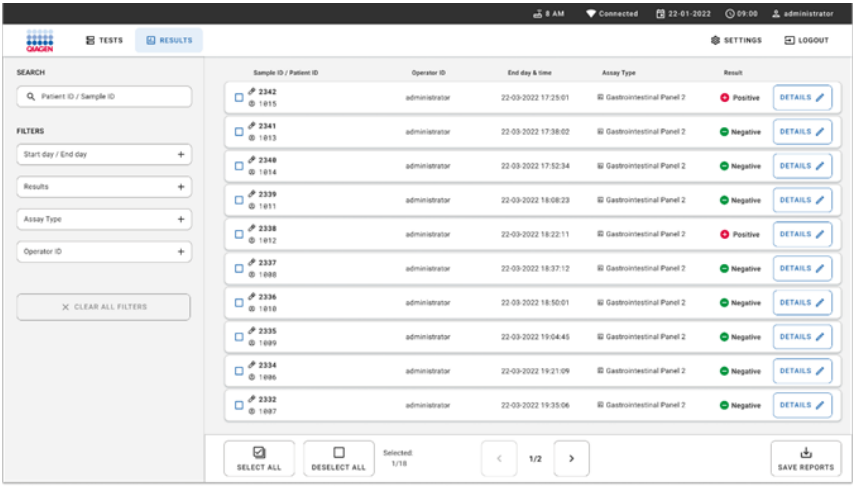


Figure 54. Search functionality in the results screen.

Exporting results to a USB storage device

From the Results screen, select individually or all with the **Select All** button to export and save a copy of the test reports in PDF format to a USB storage device (Figure 54). The USB port is located in front and on the rear of the instrument.

Note: It is recommended to use the USB storage device for short-term data saving and transfer only. The use of a USB storage device is subject to restrictions (e.g., the memory capacity or the risk of overwriting, which should be considered before usage).

Limitations

- Results from the QIAstat-Dx Gastrointestinal Panel 2 are not intended to be used as the sole basis for diagnosis, treatment, or other patient management decisions.
- Due to high rates of asymptomatic carriage of *Clostridium difficile*, especially in very young children and hospitalized patients, the detection of toxigenic *C. difficile* should be interpreted within the context of guidelines developed by the testing facility or other experts (97,98).
- For prescription use only.
- The QIAstat-Dx Gastrointestinal Panel 2 is not intended for testing of samples other than those described in these Instructions for Use. The performance of this test has only been validated with human stool collected in Cary-Blair transport medium, according to the media manufacturers' instructions. It has not been validated for use with other stool transport media, rectal swabs, raw stool, vomitus, or endoscopy stool aspirates. The QIAstat-Dx Gastrointestinal Panel 2 should not be used to test Cary-Blair vials from collection devices that have been overfilled with stool. Only stool resuspended following the collection device manufacturer's instructions should be used.
- The detection of viral, bacterial, or parasitic sequences is dependent upon proper specimen collection, handling, transportation, storage, and preparation (including extraction). Failure to observe proper procedures in any one of these steps can lead to incorrect results. There is a risk of false negative values resulting from improperly collected, transported, or handled specimens.
- Positive results do not rule out co-infection with organisms not included in the QIAstat-Dx Gastrointestinal Panel 2. The agent detected may not be the definitive cause of the disease.
- Not all agents of acute gastrointestinal infection are detected by this assay.

- The QIAstat-Dx Gastrointestinal Panel 2 is intended to be used in conjunction with standard of care culture for organism recovery, serotyping and/or antimicrobial susceptibility testing where applicable.
- The QIAstat-Dx Gastrointestinal Panel 2 can be used only with the QIAstat-Dx Analyzer 1.0, QIAstat-Dx Analyzer 2.0, and QIAstat-Dx Rise.
- The identification of multiple diarrheagenic *E. coli* pathotypes has historically relied upon phenotypic characteristics, such as adherence patterns or toxigenicity in certain tissue culture cell lines (42). The QIAstat-Dx Gastrointestinal Panel 2 targets genetic determinants characteristic of most pathogenic strains of these organisms but may not detect all strains having phenotypic characteristics of a pathotype. In particular, the QIAstat-Dx Gastrointestinal Panel 2 will only detect Enteroaggregative *E. coli* (EAEC) strains carrying the *aggR* and/or *aatA* markers on the pAA (aggregative adherence) plasmid; it will not detect all strains exhibiting an aggregative adherence pattern.
- Genetic virulence markers associated with diarrheagenic *E. coli /Shigella* pathotypes are often carried on mobile genetic elements (MGEs) that can be transferred horizontally between different strains (42); therefore, "Detected" results for multiple diarrheagenic *E. coli/Shigella* may be due to co-infection with multiple pathotypes or, less frequently, may be due to the presence of a single organism containing genes characteristic of multiple pathotypes. An example of the latter is the 2019 *E. coli* hybrid ETEC/STEC strains found in Sweden (99).
- The QIAstat-Dx Gastrointestinal Panel 2 detects Enteropathogenic *E. coli* (EPEC) through targeting of the *eae* gene, which encodes the adhesin intimin. As some Shiga-like toxin-producing *E. coli* (STEC) also carry *eae* (in particular, strains identified as enterohemorrhagic *E. coli*; EHEC) (42), the QIAstat-Dx Gastrointestinal Panel 2 cannot distinguish between STEC containing *eae* and a co-infection of EPEC and STEC. Therefore, the EPEC result is not applicable (N/A) and not reported for specimens in which STEC has also been detected. In rare cases, STEC may be reported as EPEC when a STEC carrying

eae (EHEC) is present in a specimen below the LoD of the STEC oligonucleotide design(s). Rare instances of other organisms carrying *eae* have been documented (e.g., *Escherichia albertii*, and *Shigella boydii* (100)).

- *Shigella dysenteriae* serotype 1 possesses a shiga toxin gene (*stx*) that is identical to the *stx1* gene of STEC (42). Stx genes have been more recently found in other *Shigella* species (e.g., *S. sonnei* and *S. flexneri*) (101,102). The detection of both *Shigella*/Enteroinvasive *E. coli* (EIEC) and STEC *stx1/stx2* analytes in the same specimen may indicate the presence of *Shigella* species such as *S. dysenteriae*. Rare instances of the detection of Shiga-like toxin genes in other genera/species have been reported (e.g., *Acinetobacter haemolyticus*, *Enterobacter cloacae* and *Citrobacter freundii* (103,104,105)).
- *E. coli* O157 result is only reported as specific serogroup identification in association with STEC *stx1/stx2*. While non-STEC O157 strains have been detected in human stool (106), their role in disease has not been established (107). Serotype O157 EPEC has been identified and will be detected by the QIAstat-Dx Gastrointestinal Panel 2 (by the EPEC oligonucleotides design) due to their carriage of the *eae* gene.
- The QIAstat-Dx Gastrointestinal Panel 2 cannot distinguish between infections with a single toxigenic STEC O157 or rare co-infections of STEC (non-O157) with a *stx1/stx2*-negative *E. coli* O157.
- This test only detects *Campylobacter jejuni*, *C. coli* , and *C. upsaliensis*, and does not differentiate between these three species of *Campylobacter*. Additional testing is required to differentiate between these species and to detect other *Campylobacter* species that may be present in stool specimens. In particular, the *Campylobacter upsaliensis* oligonucleotides design may cross-react with the *Campylobacter* species, *C. lari* and *C. helveticus* organisms.
- Negative results do not exclude the possibility of gastrointestinal infection. Negative test results may occur from sequence variants in the region targeted by the assay, the presence of inhibitors, technical errors, sample mix-ups, or an infection caused by an organism not

detected by the panel. Test results may also be affected by use of certain medications (e.g., calcium carbonate), concurrent antimicrobial therapy or levels of organism in the sample that are below the limit of detection for the test. Sensitivity in some clinical settings may differ from that described in the Instructions for Use. Negative results should not be used as the sole basis for diagnosis, treatment, or other management decisions.

- Organism and amplicon contamination may produce erroneous results for this test. Particular attention should be given to the Laboratory Precautions noted under the Laboratory Precautions section.
- There is a risk of false-positive values resulting from cross-contamination by target organisms, their nucleic acids or the amplified product, or from non-specific signals in the assay.
- There is a risk of false negative results due to the presence of strains with sequence variability in the target regions of the oligonucleotides design. Refer to the Inclusivity (analytical reactivity) section of this document for additional information.
- The performance of the QIAstat-Dx Gastrointestinal Panel 2 has not been established in individuals who received Rotavirus A vaccine. Recent oral administration of a Rotavirus A vaccine may cause positive results for Rotavirus A if the virus is passed in the stool.
- The performance of this test has not been evaluated for immunocompromised individuals.
- The performance of this test has not been established for monitoring treatment of infection with any of the targeted microorganisms.
- Analyte targets (virus, bacteria, or parasite nucleic acid sequences) may persist in vivo independent of virus, bacteria, or parasite viability. Detection of analyte target(s) does not guarantee that the corresponding live organism(s) is present, or that the corresponding organism(s) is the causative agent for clinical symptoms.
- Underlying polymorphisms in primer-binding regions can affect the targets being detected and subsequently the test results returned.

- Positive and negative predictive values are highly dependent on prevalence. False negative test results are more likely when prevalence of disease is high. False positive test results are more likely when prevalence is low.
- The effect of interfering substances has only been evaluated for those listed in the labeling at its indicated amount or concentration. Interference by substances other than those described in the “Interfering Substances” section of the Instruction for Use can lead to erroneous results.
- Cross- reactivity with gastrointestinal tract organisms other than those listed in the “Analytical Specificity” section of the package insert may lead to erroneous results.
- This test is a qualitative test and does not provide the quantitative value of detected organism present.
- The assay sensitivity to detect *Cyclospora cayetanensis*, Adenovirus F41, *Entamoeba histolytica* and the Shiga-like toxin- producing *Escherichia coli* (STEC) might be reduced up to 3.16-fold when using half-input sample volume (100 µL) workflow detailed in "Appendix C: Additional instructions for use".

Performance Characteristics

Analytical performance

The analytical performance shown below was demonstrated using QIAstat-Dx Analyzer 1.0.

The QIAstat-Dx Analyzer 2.0 uses the same Analytical Module as QIAstat-Dx Analyzer 1.0; therefore the performance is not impacted by QIAstat-Dx Analyzer 2.0.

With regards to QIAstat-Dx Rise, specific studies to demonstrate the carryover and the repeatability were executed. The rest of analytical performance parameters shown below were demonstrated using QIAstat-Dx Analyzer 1.0. The QIAstat-Dx Rise uses the same Analytical Module as QIAstat-Dx Analyzer 1.0; therefore the performance is not impacted by QIAstat-Dx Rise.

Limit of detection

The Limit of Detection (LoD) is defined as the lowest concentration at which ≥95% of the tested samples generate a positive call.

The LoD for each of the QIAstat-Dx Gastrointestinal Panel 2 target pathogenic organisms was assessed, using in total 48 pathogen strains, by analyzing serial dilutions of analytical samples prepared from culture isolates from commercial suppliers (e.g., ZeptoMetrix® and ATCC®), confirmed clinical isolates, or artificial samples for target analytes commercially unavailable. Each sample tested was prepared in human stool matrix, which consists of a pool of previously tested negative clinical stool specimens resuspended in Cary-Blair transport medium.

Each of the 48 strains was tested in human stool matrix prepared following the manufacturer's instructions for the Para-Pak C&S® collection device. A matrix equivalency study between

Para-Pak C&S and FecalSwab transport media was conducted to support the conclusions in the section.

Individual LoD values for each QIAstat-Dx Gastrointestinal Panel 2 target is shown in Table 7.

Table 7. LoD values obtained for the different gastrointestinal target strains tested with the QIAstat-Dx Gastrointestinal Panel 2

Pathogen	Strain	Source	Concentration (molecular units)* copies/mL	Concentration (microbiological units)	Detection rate
Campylobacter	*Campylobacter coli* 76-GA2 [LMG 21266]	ATCC 43478	5802	1.2 CFU/mL	20/20
	Campylobacter coli CIP 7080	ATCC 33559	8941	0.6 CFU/mL	20/20
	Campylobacter jejuni Z086	ZeptoMetrix 0801650	14491	1660 CFU/mL	20/20
	Campylobacter jejuni subsp. Jejuni RM3193	ATCC BAA-1234	7210	110 CFU/mL	19/20
	Campylobacter upsaliensis NCTC 11541	ZeptoMetrix 0801999	56165	2259.4 CFU/mL	20/20
	Campylobacter upsaliensis RM3195	ATCC BAA-1059	7631	35 CFU/mL	19/20
Clostridium difficile toxin A/B	(NAP1A) Toxinotype III A+ B+	ZeptoMetrix 0801619	11083	515 CFU/mL	19/20
	Toxinotype 0 A+ B+	ATCC 9689	101843	853.2 CFU/mL	20/20
Plesiomonas shigelloides	Z130	ZeptoMetrix 0801899	481	2291 CFU/mL	20/20
	Bader	ATCC 14029	116	2.7 CFU/mL	19/20

Table 7. LoD values obtained for the different gastrointestinal target strains tested with the QIAstat-Dx Gastrointestinal Panel 2 (continued)

Pathogen	Strain	Source	Concentration (molecular units)* copies/mL	Concentration (microbiological units)	Detection rate
Salmonella	*Salmonella enterica* Serovar choleraseus	ATCC 13312	647	91.6 CFU/mL	20/20
	Salmonella enterica Serovar Typhimurium Z005	ZeptoMetrix 0801437	1441	4518.8 CFU/mL	20/20
Vibrio cholerae	Z132; toxigenic	ZeptoMetrix 0801901	28298	13600 CFU/mL	20/20
	Z133; non-toxigenic	ZeptoMetrix 0801902	79749	54668 CFU/mL	20/20
Vibrio parahaemolyticus	EB 101	ATCC 17802	12862	1600 CFU/mL	20/20
	Z134	ZeptoMetrix 0801903	8904	143 CFU/mL	20/20
Vibrio vulnificus	329 [CDC B3547]	ATCC 33817	109131	260 CFU/mL	20/20
	324 [CDC B629]	ATCC 27562	2983	1905.1 CFU/mL	20/20
Yersinia enterocolitica	Z036	ZeptoMetrix 0801734	719	2070 CFU/mL	20/20
	subsp. *enterocolitica* NTCC 11175, Biotype 4, serotype 3	ATCC 700822	2496	120.1 CFU/mL	20/20
Enteroaggregative *E. coli* (EAEC)	*Escherichia coli* 92.0147, O77:HN	ZeptoMetrix 0801919	1075	634 CFU/mL	20/20
	Escherichia coli CDC3250-76, O111a, 111b: K58:H21	ATCC 29552	842	87 CFU/mL	19/20

Table 7. LoD values obtained for the different gastrointestinal target strains tested with the QIAstat-Dx Gastrointestinal Panel 2 (continued)

Pathogen	Strain	Source	Concentration (molecular units)* copies/mL	Concentration (microbiological units)	Detection rate
Enteroinvasive *E. coli* (EIEC)/ *Shigella*	*Shigella sonnei* Z004	ZeptoMetrix 25931	488	0.2 CFU/mL	20/20
	Escherichia coli CDC EDL 1282, O29:NM	ATCC 43892	1431	41.3 CFU/mL	20/20
Enteropathogenic *E. coli* (EPEC)	*Escherichia coli* O111:NM (EPEC)	ZeptoMetrix 0801747	1817	2581.7 CFU/mL	20/20
	Escherichia coli 7.1493; EPEC; O84:H28	Zeptometrix 0801938	29021	1190 CFU/mL	20/20
Enterotoxigenic *E. coli* (ETEC) *lt/st*	*Escherichia coli* H10407, O78:H11	ATCC 35401	367	10.1 CFU/mL	19/20
	Escherichia coli ETEC; ST+, LT+	ZeptoMetrix 0801624	855	567 CFU/mL	20/20
Shiga-like toxin-producing *E. coli* (STEC) *stx1/stx2*	*Escherichia coli* O26:H4	ZeptoMetrix 0801748	2012	726.8 CFU/mL	20/20
Shiga-like toxin-producing *E. coli* (STEC) *E. coli* O157	*Escherichia coli* O157:H7; EDL933	ZeptoMetrix 0801622	1217	2281.5 CFU/mL	STEC stx 1: 19/20 STEC stx2: 19/20 O157: 19/20
Cryptosporidium	*Cryptosporidium hominis*	Public Health Wales UKM 84	357	N/A	20/20
	Cryptosporidium parvum – Iowa isolate	Waterborne® P102C	661	N/A	20/20

Table 7. LoD values obtained for the different gastrointestinal target strains tested with the QIAstat-Dx Gastrointestinal Panel 2 (continued)

Pathogen	Strain	Source	Concentration (molecular units)* copies/mL	Concentration (microbiological units)	Detection rate
Cyclospora cayetanensis	N/A	LACNY-Clinical sample LAC2825	53	N/A	19/20
	N/A	LACNY Clinical sample LAC2827	137	N/A	20/20
Entamoeba histolytica	HM-1:IMSS (Mexico City 1967	ATCC 30459	7	0.2 cells/mL	20/20
	HK-9 (Korea)	ATCC 30015	1	0.13 cells/mL	19/20
Giardia lamblia	WB (Bethesda)	ATCC 30957	11850	790 cells/mL	19/20
	Portland-1	ATCC 30888	14500	635 cells/mL	20/20
Adenovirus F40/F41	Type 40 (Dugan)	ZeptoMetrix 0810084CF	11726	0.1 $TCID_{50}$/mL	20/20
	Type 41 (Tak)	ZeptoMetrix 0810085CF	979	0.05 $TCID_{50}$/mL	19/20
Astrovirus	ERE IID 2371 (type 8)	Zeptometrix 0810277CF	11586371	11.7 $TCID_{50}$/mL	20/20
	ERE IID 2868 (type 4)	Zeptometrix 0810276CF	52184	1.3 $TCID_{50}$/mL	19/20
Norovirus GI/GII	GI.1 (recombinant)	ZeptoMetrix 0810086CF	24629	891.1 $TCID_{50}$/mL	19/20
	GII.4 (recombinant)	ZeptoMetrix 0810087CF	8998	10.5 $TCID_{50}$/mL	20/20

Table 7. LoD values obtained for the different gastrointestinal target strains tested with the QIAstat-Dx Gastrointestinal Panel 2 (continued)

Pathogen	Strain	Source	Concentration (molecular units)* copies/mL	Concentration (microbiological units)	Detection rate
Rotavirus A	69M	ZeptoMetrix 0810280CF	5787	436.1 $TCID_{50}$/mL	19/20
	Wa	ZeptoMetrix 0810041CF	5201	14.1 $TCID_{50}$/mL	19/20
Sapovirus	Genogroup I, genotype 1	QIAGEN Barcelona - Clinical sample GI-88	187506	N/A	20/20
	Genogroup V	Universitat de Barcelona 160523351	3007	N/A	20/20

Exclusivity (analytical specificity)

The analytical specificity study was carried out by in vitro testing and *in silico* analysis to assess the potential cross-reactivity and exclusivity of the QIAstat-Dx Gastrointestinal Panel 2. On-panel organisms were tested to assess the potential for intra-panel cross-reactivity, and Off-panel organisms were tested to evaluate cross-reactivity with organisms not covered by the panel content. The On-panel and Off-panel organisms tested are shown in Table 8 and Table 9, respectively.

Samples were prepared by single spiking organisms into negative stool resuspended in Cary-Blair at the highest concentration possible based on the organism stock, preferably at 10^5 $TCID_{50}$/mL for viral, 10^5 cells/mL for parasite targets, and 10^6 CFU/mL for bacterial targets. The pathogens were tested in 3 replicates. There was no intra-panel or Off-panel cross-reactivity for all pathogens tested in vitro, except for two non-targeted *Campylobacter* species

(*C. helveticus* and *C. lari*) that cross-reacted with the *Campylobacter* assay oligonucleotides included in the QIAstat-Dx Gastrointestinal Panel 2.

Table 8. List of Analytical Specificity on-panel pathogens tested.

Type	Pathogen	
Bacteria	*Campylobacter coli*	*Plesiomonas shigelloides*
	Campylobacter jejuni	*Salmonella enterica*
	Campylobacter upsaliensis	*Shigella sonnei*
	Clostridium difficile	*Vibrio cholerae*
	Escherichia coli (EAEC)	*Vibrio parahaemolyticus*
	Escherichia coli (EPEC)	*Vibrio vulnificus*
	Escherichia coli (ETEC)	*Yersinia enterocolitica*
	Escherichia coli (STEC)	
Parasites	*Cryptosporidium parvum*	*Entamoeba histolytica*
	Cyclospora cayetanensis	*Giardia lamblia*
Viruses	Adenovirus F41	Norovirus GII
	Astrovirus	Rotavirus A
	Norovirus GI	Sapovirus

Table 9. List of Analytical Specificity off-panel pathogens tested

Type	Pathogen (potential cross-reactant)	
Bacteria	*Abiotrophia defectiva*	*Enterobacter cloacae*
	Acinetobacter baumannii	*Enterococcus faecalis*
	Aeromonas hydrophila	*Enterococcus faecium*
	Arcobacter cryaerophilus	*Escherichia fergusonii*
	Bacillus subtilis	*Escherichia hermannii*
	Bifidobacterium bifidum	*Escherichia vulneris*
	Campylobacter fetus	*Faecalibacterium prausnitzii*
	Campylobacter gracilis	*Gardnerella vaginalis*
	Campylobacter helveticus	*Haemophilus influenzae*
	Campylobacter hominis	*Helicobacter pylori*
	Campylobacter lari	*Klebsiella pneumoniae*
	Campylobacter mucosalis	*Lactobacillus casei*
	Campylobacter rectus	*Listeria monocytogenes*
	Chamydia trachomatis	*Proteus mirabilis*
	Citrobacter freundii	*Proteus vulgaris*
	Clostridium difficile non-toxigenic	*Pseudomonas aeruginosa*
	Clostridium perfringens	*Staphylococcus aureus*
	Clostridium septicum	*Staphylococcus aureus* subsp. *Aureus*
	Clostridium tetani	*Staphylococcus epidermidis*
	Corynebacterium genitalium	*Streptococcus agalactiae*
	Enterobacter aerogenes	*Streptococcus pyogenes*
Fungi	*Aspergillus fumigatus*	*Saccharomyces boulardii*
	Candida albicans	*Saccharomyces cerevisiae*
Parasites	*Babesia microti*	*Toxoplasma gondii*
	Blastocystis hominis	*Trichomonas tenax*
	Giardia muris	

Table 9. List of Analytical Specificity off-panel pathogens tested (continued)

Type	Pathogen (potential cross-reactant)	
Viruses	Adenovirus C:2	Coronavirus 229E
	Adenovirus B:34	Coxsackievirus B3
	Adenovirus B3	Cytomegalovirus
	Adenovirus E:4a	Enterovirus 6 (*Echovirus*)
	Adenovirus serotype 1	Enterovirus 68
	Adenovirus serotype 5	Herpes Simplex Virus Type 2
	Adenovirus serotype 8	Rhinovirus 1A
	Bocavirus Type 1	

In silico predictions of potential cross-reactions showed that the following cross-reactions may occur when testing stool samples with the QIAstat-Dx Gastrointestinal Panel 2 (Table 10).

Table 10. Potential cross-reactions based on *in silico* analysis.

QIAstat-Dx Gastrointestinal Panel 2 Target	Potential cross-reactive organisms
Enteropathogenic *E. coli* (EPEC)*	*Shigella boydii** †‡ *Escherichia albertii* *†
Campylobacter spp.	*Campylobacter lari* § *Campylobacter helveticus* §
Shiga-like toxin-producing *E. coli* (STEC) stx1	*Shigella sonnei* *‡ *Shigella dysenteriae** *Enterobacter cloacae**
Shiga-like toxin-producing *E. coli* (STEC) stx2	*Acinetobacter haemolyticus**¶ *Citrobacter freundii**¶ *Enterobacter cloacae**¶ *Aeromonas caviae**¶ *Escherichia albertii* *¶
E. coli O157	Non-STEC *E.coli* O157 strains**

* Note that these potential cross-reactions affect designs with target genes responsible of the pathogenicity of the corresponding QIAstat-Dx Gastrointestinal Panel 2 target pathogens which can be acquired within species in a known biological process in bacteria called horizontal gene transfer (42,108).

† Rare or less common eae intimin carrier organisms (100).

‡ On-panel target.

§ In vitro testing of *Campylobacter lari* and *Campylobacter helveticus* strains at high concentration confirmed potential cross-reactivity of these *Campylobacter* species with the QIAstat-Dx Gastrointestinal Panel 2 assay.

¶ Rare or less common Stx toxins producers (103, 109, 110, 111, 112, 113).

** *E. coli* O157 will only be reported by the QIAstat-Dx Gastrointestinal Panel 2 when there is a positive amplification for the *E. coli* (STEC) design according to the calling algorithm. An infrequent case of an *E. coli* (STEC) and an *E. coli* O157 co-infection will not be differentiated from a single infection caused by an STEC O157:H7 strain.

Inclusivity (analytical reactivity)

Analytical Reactivity (Inclusivity) was evaluated with gastrointestinal pathogen isolates/strains that were selected based on clinical relevance and genetic, temporal and geographical diversity. Based on in vitro (wet) testing and in silico analysis, the QIAstat-Dx Gastrointestinal Panel 2 primers and probes are specific and inclusive for clinically prevalent and relevant strains for each pathogen tested.

In vitro (Wet) testing

QIAstat-Dx Gastrointestinal Panel 2 is inclusive for 100% (143 out of 143) of the pathogen strains tested in vitro. Most pathogen strains evaluated in wet testing (133/143) were detected at ≤ 3-fold of the corresponding LoD reference strain (Table 10).

Table 11. Inclusivity test results for all the pathogens tested with the QIAstat-Dx Gastrointestinal Panel 2 Assay. LoD reference strain for every pathogen is written in bold

Table 11a. Inclusivity test results for *Campylobacter* strains

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalog ID	Times LoD
Campylobacter	***Campylobacter coli***	**76-GA2 [LMG 21266]**	**ATCC**	**43478***	**1x LoD**
	Campylobacter coli	Z293	ZeptoMetrix	804272	1x LoD
	Campylobacter coli	CIP 7080 [1407, CIP 70.80]	ATCC	33559*	3x LoD
	Campylobacter jejuni	**Z086**	**ZeptoMetrix**	**0801650***	**1x LoD**
	Campylobacter jejuni	subsp. *jejuni* RM3193	ATCC	BAA-1234*	0.1x LoD
	Campylobacter jejuni subsp. jejuni	O:19 HL7; D3180	ATCC	BAA-218	0.1x LoD
	Campylobacter jejuni subsp. jejuni	AS-83-79	ATCC	33291	0.1x LoD
	Campylobacter jejuni subsp. doylei	NCTC 11951	ATCC	49349	0.1x LoD
	Campylobacter upsaliensis	**NCTC 11541**	**ZeptoMetrix**	**0801999***	**1x LoD**
	Campylobacter upsaliensis	RM 3195 (1994)	ATCC	BAA-1059*	0.3x LoD
	Campylobacter upsaliensis	NCTC 11541 [C231]	ATCC	43954	1x LoD

* Strain tested during LoD verification study.

Table 11b. Inclusivity test results for *Clostridium difficile* strains

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalog ID	Times LoD
Clostridium difficile toxin A/B	*Clostridium difficile*	(90556-M6S) Toxinotype 0 A+ B+	ATCC	9689*	1x LoD
	Clostridium difficile	NAP1, toxinotype IIIb A+B+	ATCC	BAA-1805	1x LoD
	Clostridium difficile	5325, toxinotype V A+B+	ATCC	BAA-1875	1x LoD
	Clostridium difficile	1470, toxinotype VIII A-B+	ATCC	43598	1x LoD
	Clostridium difficile	toxinotype XII A+B+	ATCC	BAA-1812	1x LoD
	Clostridium difficile	toxinotype XXII A+B (unknown)	ATCC	BAA-1814	1x LoD
	Clostridium difficile	NAP1A, toxinotype III A+B+	ATCC	0801619*	0.1x LoD
	Clostridium difficile	NAP1, toxinotype III A+B+	ZeptoMetrix	0801620	3x LoD

*Strain tested during LoD verification study.

Table 11c. Inclusivity test results for *Plesiomonas shigelloides* strains

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalog ID	Times LoD
Plesiomonas shigelloides	*Plesiomonas shigelloides*	Z130	ZeptoMetrix	0801899*	1x LoD
	Plesiomonas shigelloides	GNI 14	ATCC	51903	1x LoD
	Plesiomonas shigelloides	CDC 3085-55 [Bader M51, NCIB 9242, NCTC 10360, RH 798]	ATCC	14029*	0.3x LoD

*Strain tested during LoD verification study.

Table 11d. Inclusivity test results for *Salmonella* strains

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalog ID	Times LoD
Salmonella	*Salmonella enterica*	Serovar Typhimurium Z005	ZeptoMetrix	0801437*	1x LoD
	Salmonella enterica	Subsp. Enterica, serovar Bareilly	–	NC05745	1x LoD
	Salmonella enterica	Subsp. Enterica, serovar typhi, Z152	ZeptoMetrix	0801933	0.1x LoD
	Salmonella enterica	Subsp. Enterica, serovar Enteridis, CDC K-1891 [ATCC 25928]	ATCC	13076	0.1x LoD
	Salmonella enterica	Subsp. Enterica, serovar Infantis, MZ1479 [SARB27]	ATCC	BAA-1675	0.1x LoD
	Salmonella enterica	Subsp. Enterica, serovar Montevideo, G4639	ATCC	BAA-710	0.1x LoD
	Salmonella enterica	Subsp. Enterica, serovar Javiana	–	NC06495	0.1x LoD
	Salmonella enterica	Subsp. Enterica, serovar Thompson	–	NC08496	0.1x LoD
	Salmonella enterica	Subsp. Enterica, serovar Saintpaul	–	9712	0.1x LoD
	Salmonella enterica	Subsp. Enterica, serovar Berta	–	NC05770	0.1x LoD
	Salmonella enterica	Subsp. Salame, II NCTC 10310 [JT945, SS140/61]	ATCC	700151	0.1x LoD
	Salmonella enterica	Subsp. diarizonae IIIb, 62	ATCC	29934	0.1x LoD
	Salmonella enterica	Subsp. houtenae IV, CIP 82.32 [264.66]	ATCC	43974	0.1x LoD
	Salmonella enterica	Subsp. Indica VI, CIP 102501 [F. Kauffmann 1240]	ATCC	43976	0.1x LoD

Table 11d. Inclusivity test results for Salmonella strains (continued)

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalog ID	Times LoD
	Salmonella enterica	Subsp. Enterica, serovar Agona, CDC 873 [CDC 1111-61]	ATCC	51957	0.1x LoD
	Salmonella enterica	Subsp. Enterica, serovar Muenchen, 54	ATCC	8388	0.1x LoD
	Salmonella enterica	Subsp. Enterica, serovar Oranienburg, E1093	ATCC	9239	0.1x LoD
	Salmonella enterica	Subsp. Enterica, serovar Paratyphi B var. Java, CDC 5	ATCC	51962	0.1x LoD
	Salmonella enterica	CIP 82.33 [1224.72]	ATCC	43975	0.3x LoD
	Salmonella enterica	Subsp. Enterica, serovar Choleraesius, NCTC 5735 [1348, K.34]	ATCC	13312*	0.3x LoD
	Salmonella enterica	Subsp. Enterica, serovar Newport, C487-69	ATCC	27869	0.3x LoD
	Salmonella enterica	Subsp. Enterica, 4, 5, 12:7:-, serovar Typhimurium	–	NC13952	0.3x LoD
	Salmonella enterica	Subsp. Enterica, serovar Braenderup	–	700136	0.3x LoD
	Salmonella enterica	Subsp. Enterica, serovar Anatum	–	NC05779	0.3x LoD
	Salmonella enterica	Subps. arizonae IIIa, NCTC 7311 [CDAI 426]	ATCC	700156	0.3x LoD
	Salmonella enterica	Subsp. Enterica, serovar Heidelberg, [16]	ATCC	8326	0.3x LoD
	Salmonella enterica	Subsp. Enterica, serovar Mississippi, CDC 2012K-0487	ATCC	BAA-2739	0.3x LoD

* Strain tested during LoD verification study.

Table 11e. Inclusivity test results for *Vibrio cholerae* strains

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalog ID	Times LoD
Vibrio cholerae	*Vibrio cholerae*	Z133; non-toxigenic	ZeptoMetrix	801902*	1x LoD
	Vibrio cholerae	Pacini 1854; NCTC 8021, O:1 Ogawa	CECT	514	1x LoD
	Vibrio cholerae	Z132; toxigenic	ZeptoMetrix	0801901*	0.3x LoD

* Strain tested during LoD verification study.

Table 11f. Inclusivity test results for *Vibrio parahaemolyticus* strains

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalog ID	Times LoD
Vibrio parahaemolyticus	*Vibrio parahaemolyticus*	EB101 [P. Baumann 113] (Japan)	ATCC	17802*	1x LoD
	Vibrio parahaemolyticus	VP250,O1:KUT	ATCC	BAA-242	1x LoD
	Vibrio parahaemolyticus	205 [9302]	ATCC	33846	3x LoD
	Vibrio parahaemolyticus	Z134	ZeptoMetrix	0801903*	0.3x LoD

* Strain tested during LoD verification study.

Table 11g. Inclusivity test results for *Vibrio vulnificus* strains

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalog ID	Times LoD
Vibrio vulnificus	*Vibrio vulnificus*	324 [CDC B9629]	ATCC	27562	1x LoD
	Vibrio vulnificus	329 [CDC B3547],Biotype 2	ATCC	33817*	1x LoD
	Vibrio vulnificus	Z473	ZeptoMetrix	804349	3x LoD

* Strain tested during LoD verification study.

Table 11h. Inclusivity test results for *Yersinia enterocolitica* strains

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalog ID	Times LoD
Yersinia enterocolitica	*Yersinia enterocolitica*	Z036	ZeptoMetrix	0801734*	1x LoD
	Yersinia enterocolitica	NTCC 11175, Biotype 4, serotype 3 (O:3)	ATCC	700822*	1x LoD
	Yersinia enterocolitica	33114 [CCUG 11291, CCUG 12369, CIP 80.27, DSM 4780, LMG 7899, NCTC 12982], Biovar 1, O:8	ATCC	9610	1x LoD
	Yersinia enterocolitica	0:9	ATCC	55075	3x LoD

* Strain tested during LoD verification study.

Table 11i. Inclusivity test results for Enteroaggreative *E. coli* (EAEC) strains

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalog ID	Times LoD
Enteroaggreative *E. coli* (EAEC)	Enteroaggreative *E. coli* (EAEC)	92.0147	ZeptoMetrix	0801919*	1x LoD
	Enteroaggreative *E. coli* (EAEC)	CDC3250-76, O111a, 111b: K58:H21, CVD432+, aggR+, stx1-, stx2-, eae-	ATCC	29552*	1x LoD
	Enteroaggreative *E. coli* (EAEC)	–	Vall d'Hebrón	Clinical sample; VH 529140369015	3x LoD

* Strain tested during LoD verification study.

Table 11j. Inclusivity test results for Enteropathogenic *E. coli* (EPEC) strains

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalog ID	Times LoD
Enteropathogenic *E. coli* (EPEC)	Enteropathogenic *E. coli* (EPEC)	O111:NM	ZeptoMetrix	0801747*	1x LoD
	Enteropathogenic *E. coli* (EPEC)	7.1493,O84:H28	ZeptoMetrix	0801938*	1x LoD
	Enteropathogenic *E. coli* (EPEC)	Stoke W,O111:K58 (B4):H-	ATCC	33780	1x LoD

* Strain tested during LoD verification study.

Table 11k. Inclusivity test results for Enterotoxigenic *E. coli* (ETEC) strains

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalog ID	Times LoD
Enterotoxigenic *E. coli* (ETEC) lt/st	Enterotoxigenic *E. coli* (ETEC) lt/st	ST+, LT+	ZeptoMetrix	0801624*	1x LoD
	Enterotoxigenic *E. coli* (ETEC) lt/st	H10407,O78:H11,LT(+)/ctx A11(+)	ATCC	35401*	0.3x LoD
	Enterotoxigenic *E. coli* (ETEC) lt/st	O27:H7,ST (+)/ LT (-)	SSI Diagnostica	82173	0.1x LoD
	Enterotoxigenic *E. coli* (ETEC) lt/st	O115:H15,ST (+)/ LT (-)	SSI Diagnostica	82174	3x LoD
	Enterotoxigenic *E. coli* (ETEC) lt/st	O169:H-,ST (-)/LT (+)	SSI Diagnostica	82172	10x LoD†

* Strain tested during LoD verification study.

Table 11l. Inclusivity test results for Enteroinvasive *E. coli* (EIEC)/ *Shigella* strains.

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalog ID	Times LoD
Enteroinvasive *E. coli* (EIEC)/ *Shigella*	**Enteroinvasive *E. coli* (EIEC)**	**CDC EDL 1282, O29:NM**	**ATCC**	**43892***	**1x LoD**
	Enteroinvasive *E. coli* (EIEC)	O172:H-	SSI Diagnostica	82171	3x LoD
	Shigella sonnei	**NCDC 1120-66**	**ATCC**	**25931***	**1x LoD**
	Shigella boydii (Serogroup C)	Z131	ZeptoMetrix	0801900	1x LoD
	Shigella flexneri (Serogroup B)	AMC 43-G-68 [EVL 82, M134]	ATCC	9199	1x LoD
	Shigella flexneri (Serogroup B)	Z046	ZeptoMetrix	0801757	1x LoD
	Shigella sonnei (Serogroup D)	WRAIR I virulent	ATCC	29930	1x LoD
	Shigella sonnei (Serogroup D)	Z004	ZeptoMetrix	0801627	3x LoD
	Shigella boydii (Serogroup C)	AMC 43-G-58 [M44 (Type 170)]	ATCC	9207	10x LoD

* Strain tested during LoD verification study.

Table 11m. Inclusivity test results for Shiga-like toxin-producing *E. coli* (STEC)(stx1-carrier strains)

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalog ID	Times LoD
Shiga-like toxin producing *E. coli* (STEC) - *stx1*	Shiga-like toxin producing *E. coli* (STEC) - *stx1*	O157:H7; EDL933	ZeptoMetrix	0801622*	1x LoD
	Shiga-like toxin producing *E. coli* (STEC) - *stx1*	O26:H4,stx1 (+)	ZeptoMetrix	0801748*	1x LoD
	Shiga-like toxin producing *E. coli* (STEC) - *stx1*	O22:H8,stx1c (+), stx2b (+)	SSI Diagnostica	91350	1x LoD
	Shiga-like toxin producing *E. coli* (STEC) - *stx1*	O8 ,stx1d (+)	SSI Diagnostica	91349	1x LoD
	Shiga-like toxin producing *E. coli* (STEC) - *stx1*	Reference ATCC 35150 (EDL 931),O157:H7,stx1 (+), stx2 (+)	Microbiologics	617	1x LoD
	Shiga-like toxin producing *E. coli* (STEC) - *stx1*	Reference CDC 00-3039,O45:H2,unknown	Microbiologics	1098	1x LoD
	Shiga-like toxin producing *E. coli* (STEC) - *stx1*	O103:H2,stx1 (+)	SSI Diagnostica	82170	3x LoD
	Shiga-like toxin producing *E. coli* (STEC) - *stx1*	O128ac:H-,stx2f (+)	SSI Diagnostica	91355	10x LoD

* Strain tested during LoD verification study.

Table 11n. Inclusivity test results for Shiga-like toxin-producing *E. coli* (STEC)(stx2-carrier strains)

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalog ID	Times LoD
Shiga-like toxin producing *E. coli* (STEC) - *stx2*	Shiga-like toxin producing *E. coli* (STEC) - *stx2*	O157:H7; EDL933	ZeptoMetrix	0801622*	1x LoD
	Shiga-like toxin producing *E. coli* (STEC) - *stx2*	O22:H8,stx1c (+), stx2b (+)	SSI Diagnostica	91350	1x LoD
	Shiga-like toxin producing *E. coli* (STEC) - *stx2*	O26:H11,stx2a (+)	SSI Diagnostica	95211	1x LoD
	Shiga-like toxin producing *E. coli* (STEC) - *stx2*	O101:K32:H-,stx2e (+)	SSI Diagnostica	91354	0.3x LoD
	Shiga-like toxin producing *E. coli* (STEC) - *stx2*	Reference ATCC 35150 (EDL 931),O157:H7,stx1 (+), stx2 (+)	Microbiologics	617	3x LoD
	Shiga-like toxin producing *E. coli* (STEC) - *stx2*	O92,O107:K+:H48, stx2d (+)	SSI Diagnostica	91352	10x LoD
	Shiga-like toxin producing *E. coli* (STEC) - *stx2*	O128ac:H-,stx2f (+)	SSI Diagnostica	91355	10x LoD

* Strain tested during LoD verification study.

Table 11o. Inclusivity test results for Shiga-like toxin producing *E. coli* (STEC) stx1/stx2 O157 strains

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalogue ID	Times LoD
Shiga-like toxin producing *E. coli* (STEC) O157	Shiga-like toxin producing *E. coli* (STEC) - O157	O157:H7; EDL933	ZeptoMetrix	0801622*	1x LoD
	Shiga-like toxin producing *E. coli* (STEC) O157	O128ac:H-,stx2f (+)	SSI Diagnostica	91355†	1x LoD
	Shiga-like toxin producing *E. coli* (STEC) O157	Reference ATCC 35150 (EDL 931), O157:H7, stx1 (+), stx2 (+)	Microbiologics	617	1x LoD

* Strain tested during LoD verification study.

†The *E. coli* strain 91355 from SSI Diagnostica is reported as following in its catalog: vtx2f+, eae+. However, it was found to amplify for *E. coli* O157 in both QIAstat-Dx and FilmArray devices.

Table 11p. Inclusivity test results for *Cryptosporidium* strains

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalog ID	Times LoD
Cryptosporidium	*Cryptosporidium parvum*	Iowa isolate	Waterborne	P102C*	1x LoD
	Cryptosporidium hominis	n/a	Public Health Wales	Clinical sample; UKM 84*	0.01x LoD
	Cryptosporidium parvum	–	ATCC	PRA-67DQ (isolated genomic DNA)	<0.01 LoD
	Cryptosporidium meleagridis	–	Public Health Wales	Clinical sample; UKMEL 14	<0.01 LoD

* Strain tested during LoD verification study.

Table 11q. Inclusivity test results for *Cyclospora cayetanensis* strains.

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalogue ID	Times LoD
Cyclospora cayetanensis	*Cyclospora cayetanensis*	n/a	Clinical sample	LAC2825*	1x LoD
	Cyclospora cayetanensis	n/a	Clinical sample	LAC2827*	1x LoD
	Cyclospora cayetanensis	–	ATCC	PRA-3000SD	1x LoD

* Strain tested during LoD verification study.

Table 11r. Inclusivity test results for *Entamoeba histolytica* strains

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalogue ID	Times LoD
Entamoeba histolytica	*Entamoeba histolytica*	HM-1:IMSS (Mexico City 1967)	ATCC	30459*	1x LoD
	Entamoeba histolytica	HK-9 (Korea)	ATCC	30015*	1x LoD
	Entamoeba histolytica	–	Vall d'Hebrón	Clinical sample; 1	1x LoD

* Strain tested during LoD verification study.

Table 11s. Inclusivity test results for *Giardia lamblia* strains

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalogue ID	Times LoD
Giardia lamblia	*Giardia lamblia*	Portland -1 (Portland, OR, 1971)	ATCC	30888*	1x LoD
	Giardia lamblia	WB (Bethesda, MD, 1979)	ATCC	30957*	1x LoD
	Giardia intestinalis	H3 isolate	Waterborne	P101	1x LoD

* Strain tested during LoD verification study.

Table 11t. Inclusivity test results for Adenovirus F40/F41 targets

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalog ID	Times LoD
Adenovirus F40/F41	Human Adenovirus F41	Tak	ZeptoMetrix	0810085CF*	1x LoD
	Human Adenovirus F41	Tak (73-3544)	ATCC	VR-930	10x LoD
	Human Adenovirus F40	Dugan [79-18025]	ATCC	VR-931	10x LoD
	Human Adenovirus Type 40	Dugan	ZeptoMetrix	0810084CF*	3x LoD

* Strain tested during LoD verification study.

Table 11u. Inclusivity test results for Astrovirus strains

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalog ID	Times LoD
Astrovirus	Human Astrovirus	ERE IID 2371 (type 8)	ZeptoMetrix	0810277CF*	1x LoD
	Human Astrovirus	HAstV-1	Universitat de Barcelona	Clinical sample; 160521599	1x LoD
	Human Astrovirus	ERE IID 2868 (type 4)	ZeptoMetrix	0810276CF*	1x LoD
	Human Astrovirus	HAstV-3	Universitat de Barcelona	Clinical sample; 151601306	1x LoD

* Strain tested during LoD verification study.

Table 11v. Inclusivity test results for Norovirus GI/GII strains

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalog ID	Times LoD
Norovirus GI/GII	**Human Norovirus Genogroup 1**	**Recombinant GI.1**	**ZeptoMetrix**	**0810086CF***	**1x LoD**
	Human Norovirus Genogroup 1	–	Indiana University Health	Clinical sample; IU3156	1x LoD
	Human Norovirus Genogroup 1	–	Indiana University Health	Clinical sample; IU3220	1x LoD
	Human Norovirus Genogroup 1	–	TriCore Reference Laboratories	Clinical sample; TC4274	3x LoD
	Human Norovirus Genogroup 2	**Recombinant GII.4**	**ZeptoMetrix**	**0810087CF***	**1x LoD**
	Human Norovirus Genogroup 2	GII.2	Vall d'Hebrón	Clinical sample; 198058327	1x LoD
	Human Norovirus Genogroup 2	GII.4	Universitat de Barcelona	Clinical sample; N26.2TA	1x LoD
	Human Norovirus Genogroup 2	–	Lacny Hospital	Clinical sample; LAC2019	1x LoD
	Human Norovirus Genogroup 2	–	Nationwide Children's Hospital	Clinical sample; NWC6063	1x LoD
	Human Norovirus Genogroup 2	GII.6	QIAGEN Barcelona (STAT-Dx)	Clinical sample; GI 12	3x LoD
	Human Norovirus Genogroup 2	–	Lacny Hospital	Clinical sample; LAC2133	10x LoD
	Human Norovirus Genogroup 2	–	Lacny Hospital	Clinical sample; LAC2074	10x LoD

* Strain tested during LoD verification study.

Table 11w. Inclusivity test results for Rotavirus A strains

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalog ID	Times LoD
Rotavirus A	Human Rotavirus A	69M	ZeptoMetrix	0810280CF*	1x LoD
	Human Rotavirus A	Wa, G1P1A[8]	ZeptoMetrix	0810041CF*	1x LoD
	Human Rotavirus A	DS-1, G2P1B[4]	ATCC	VR-2550	1x LoD
	Human Rotavirus A	Va70	ZeptoMetrix	0810281CF	1x LoD
	Human Rotavirus A	RRV	ZeptoMetrix	0810530CF	10x LoD

* Strain tested during LoD verification study.

Table 11x. Inclusivity test results for Sapovirus strains

QIAstat-Dx target	Pathogen	Strain	Supplier	Catalog ID	Times LoD
Sapovirus	Human Sapovirus Genogroup I	–	QIAGEN Barcelona	Clinical sample; GI-88*	1x LoD
	Human Sapovirus Genogroup V	n/a	Universitat Barcelona	Clinical sample; 160523351*	1x LoD
	Human Sapovirus Genogroup I	GI.1	Universitat Barcelona	Clinical sample; 171016324	1x LoD
	Human Sapovirus Genogroup II	GII.3	Universitat Barcelona	Clinical sample; 215512	1x LoD

* Strain tested during LoD verification study.

In silico analysis

In silico analysis of potential reactivity showed that the following organisms (including species, subspecies, subtypes, serotypes or serovars) are predicted to be detected with the QIAstat-Dx Gastrointestinal Panel 2 (Table 12).

Table 12. Organisms with predicted reactivity based on *in silico* analysis

QIAstat-Dx GI Panel 2	Organisms with predicted reactivity (species, subspecies, subtypes, serotypes, or serovars)
Bacteria	
Campylobacter	*Campylobacter coli**, *Campylobacter jejuni*, *Campylobacter jejuni* subsp. *jejuni*, *Campylobacter jejuni* subsp. doylei, *Campylobacter upsaliensis*
Clostridium difficile	Clostridium *difficile* (including ribotypes 01 and 17 and strains BI1, BI9, NAP1, SD1, SD2, M68, M120)
Salmonella	*Salmonella bongori**, *Salmonella enterica* subsp. salamae II (e.g. serovar 55:k:z39), *Salmonella enterica* subsp. arizonae IIIa (e.g. serovar 63:g:z51), *Salmonella enterica* subsp. diarizonae IIIb (e.g. serovar 47:l,v:z), *Salmonella enterica* subsp. houtenae IV (e.g. serovar 43:z4), *Salmonella enterica* subsp. indica VI. *Salmonella enterica* subsp. enterica (up to 92 different serovars including Agona, Anatum, Bareilly, Choleraesuis, Enteritidis, Heidelberg, Infantis, Kentucky, Montevideo, Newport, Paratyphi A*, Senftenberg, Tennessee, Thompson, Typhi, Typhimurium, Weltevreden*)
Plesiomonas shigelloides	*Plesiomonas shigelloides* (e.g. strains NCTC10360, ATCC 14029T, R4605035)
Vibrio cholerae	*Vibrio cholerae* (including biovars El Tor and Bengal)
Vibrio parahaemolyticus	*Vibrio parahaemolyticus*
Vibrio vulnificus	*Vibrio vulnificus*
Yersinia enterocolitica	*Yersinia enterocolitica*, *Yersinia enterocolitica* subsp. palearctica, *Yersinia enterocolitica* subsp. *enterocolitica*
Enteroaggregative *E. coli* (EAEC)	Enteroaggregative *E. coli* (EAEC) (including serotypes O104:H4, O111:HND, O126:HND, O25:H4, O86:H2, O86:HND, OUT:H4, OUT:HND)

Table 12. Organisms with predicted reactivity based on in silico analysis (continued)

QIAstat-Dx GI Panel 2	Organisms with predicted reactivity (species, subspecies, subtypes, serotypes, or serovars)
Enteroinvasive *E. coli* (EIEC)/*Shigella*	Enteroinvasive *E. coli* (EIEC), *Escherichia coli* sp., *Shigella flexneri*, *Shigella dysenteriae*, *Shigella boydii*, *Shigella sonnei*.
Enteropathogenic *E. coli* (EPEC)	Enteropathogenic *E. coli* (EPEC) (e.g. including serotypes OUT: HND, OUT:H6, OUT:H34, OUT:H21, O55:H7, O119:HNM, O117) Other eae-carriers bacteria: some Shiga-like toxin-producing *E. coli* (STEC), STEC O157:H7 and few *Shigella boydii* strains
Enterotoxigenic *E. coli* (ETEC)†	Enterotoxigenic *E. coli* (ETEC) (including H10407 and E24377A strains and serotypes O169:H41, O25:H42, O148:H28, O6:H16) carrier of: Heat-labile enterotoxin gene subtype LT-I and Heat-stable enterotoxin gene variant Sta, subtypes STp and STh
Shiga-like toxin-producing *E. coli* (STEC) - stx1	Shiga-like toxin-producing *E. coli* (STEC) (including non-O157 serotypes O111:NM, O111:H-, O26:H11, O145:NM, O145:H28, O45:H2, O26:H11, ONT:NM, and including STEC O157 serotypes O157:H7) Stx1 toxin subtypes predicted to be detected include stx1a, stx1c and stx1d Other stx-carriers bacteria: *Shigella sonnei*, *Shigella dysenteriae*
Shiga-like toxin-producing *E. coli* (STEC) - stx2	Shiga-like toxin-producing *E. coli* (STEC) (including non-O157 serotypes O111:NM, O104:H4, O111:H-, O26:H11, O121:H19, O145:H34, O113:H21, ONT:H-, O128:H2, OUT:HNM, O124:HNM and including STEC O157 serotypes O157:H7, O157:NM) Stx2 toxin subtypes predicted to be detected include stx2a, stx2b, stx2c, stx2d, stx2e, stx2f, stx2g, stx2h*, stx2i, stx2j, stx2k and stx2l
Shiga-like toxin-producing *E. coli* (STEC) O157	*Escherichia coli* O157 including: STEC O157:H7 strains (e.g. EDL933) and *E. coli* O157: non-H7 groups including Non-Shiga-toxigenic *E. coli* O157 bacteria (e.g. serotype O157:H45) Other bacteria with O157 O-antigen: *Escherichia fergusonii* O157

Table 12. Organisms with predicted reactivity based on in silico analysis (continued)

QIAstat-Dx GI Panel 2	Organisms with predicted reactivity (species, subspecies, subtypes, serotypes, or serovars)
Parasites	
Cryptosporidium‡	Common *Cryptosporidium* species involved in human disease: *C. parvum*, *C. hominis*. Less common *Cryptosporidium* species involved in human infections: *C. meleagridis*, *C. felis* , *C. bovis*, *C. viatorum*, *C. ubiquitum*, *C. tyzzeri*, *C. cuniculus*, *Cryptosporidium sp. Chipmunk genotype I*, *C. canis**. Rare or non-human species: *Cryptosporidium wrairi*
Cyclospora cayetanensis	*Cyclospora cayetanensis* (including strains LG, CY9, NP20, and NP21) *
Entamoeba histolytica	*Entamoeba histolytica* (e.g. strains HM-1: IMSS, EHMfas1, and HK-9)*
Giardia lamblia	*Giardia lamblia* (a.k.a. *Giardia duodenalis*, *Giardia intestinalis*)*
Viruses	
Adenovirus	Human Adenovirus F40/41
Astrovirus§	Human Astrovirus (including types 1, 2, 3, 4, 5, 6, 7, 8)
Norovirus GI/GII	Norovirus genogroup II genotypes: GII.1, GII.2, GII.3*, GII.4*, GII.5, GII.6, GII.7, GII.8, GII.9, GII.10, GII.12, GII.13, GII.14, GII.16, GII.17, GII.20, GII.21, GII.22, GII.23, GII.24*, GII.25, GII.26, GII.27, GII.NA1, and GII.NA2* Norovirus genogroup I genotypes: GI.1, GI2, GI.3*, GI.4*, GI.5, GI.6*, GI.7*, GI.8, and GI.9
Rotavirus	Rotavirus A including genotypes: G1P[8]*, G2P[4]*, G3P[8]*, G4P[8]*, G9P[6], G9P[8]*, G12P[6]* and G12P[8]*

Table 12. Organisms with predicted reactivity based on in silico analysis (continued)

QIAstat-Dx GI Panel 2	Organisms with predicted reactivity (species, subspecies, subtypes, serotypes, or serovars)
Sapovirus	Genogroups: GI (including genotypes GI.1*, GI.2*, GI.3*, GI.4, GI.5, GI.6* and GI.7), GII (including genotypes GII.1*, GII.2, GII.3, GII.4*, GII.5, GII.6, GII7, GII.8*), GIV (including genotype GIV.1), and GV (including genotypes GV.1* and GV.2*)

*Certain sequences are predicted to be detected with reduced sensitivity due to the presence of a reduced number of mismatches at critical positions of the primer-probe design.

†The assay is not predicted to detect bacteria carrier of Heat-labile enterotoxin gene subtype LT-II and/or of Heat-stable enterotoxin gene variant Stb.

‡The assay is not predicted to detect other *Cryptosporidium spp.* less involved in human disease: *C. andersoni* and *C. muris* (114).

§The assay is not predicted to detect Human Astrovirus types MLB1-3 and VA1-5.

Interfering substances

The effect of potentially interfering substances on the detectability of the QIAstat-Dx Gastrointestinal Panel 2 organisms was evaluated. Forty-three (43) potentially interfering substances were spiked into the sample mixes at a level predicted to be above the concentration of the substance likely to be found in stool specimens. Each organism was tested at 3x LoD and testing was performed in triplicates. Endogenous substances such as human whole blood, human genomic DNA and several pathogens were tested alongside exogenous substances like antibiotics, other gastrointestinal-related medications and different technique-specific substances.

For the vast majority of substances tested, no inhibition was observed, with the exceptions of mucin from bovine submaxillary, bisacodyl, calcium carbonate, nonoxynol-9, and Rotavirus reassortants, that may cause inhibition at high concentration.

Mucin from bovine submaxillary was found to interfere with the detection of EAEC at concentrations above 25.0 mg/mL.

Bisacodyl was found to interfere with the detection of EAEC at concentrations above 1.5 mg/mL.

Calcium carbonate was found to interfere with the detection of all the QIAstat-Dx Gastrointestinal Panel 2 targets at concentrations above 10.7 mg/mL.

Nonoxynol-9 was found to interfere with the detection of Entamoeba at concentrations above 0.2 µL/mL.

Rotavirus reassortants WC3:2-5, R574(9), and WI79-4,9 used in Rotavirus A vaccines were predicted to be reactive with Rotavirus A in the QIAstat-Dx Gastrointestinal Panel 2. Final concentrations without observable interfering effects on the detection of targets at 3x LoD

concentration for WC3:2-5, R574(9) and WI79-4,9 were $8.89x10^{-5}$ $TCID_{50}$/mL and 1.10 PFU/mL, respectively (see Table 13) for other concentrations tested.

Competitive interference was tested in a subset of pathogens. No interference was observed when evaluating competitive interference by target pathogens when two QIAstat-Dx Gastrointestinal Panel target pathogens were tested by spiking samples with one pathogen target at 3x LoD and one at 50x LoD. Results from the pathogen targets tested are provided in Table 14.

Results from the 43 interfering substances that could be present or introduced in a stool specimen are provided in Table 13.

Table 13. Final highest concentration without observable inhibitory effect

Substance tested	Concentration tested	Result
Endogenous substances		
Bovine and ovine bile	120.0 mg/mL	No Interference
Cholesterol	15.0 mg/mL	No Interference
Fatty acids (palmitic acid)	2.0 mg/mL	No Interference
Fatty acids (stearic acid)	4.0 mg/mL	No Interference
Human genomic DNA	20 µg/mL	No Interference
Human stool (overfill of Cary Blair vial)	300 mg/mL	No Interference
Human urine	0.5 mg/mL	No Interference
Human whole blood with Na Citrate	0.4 mg/mL	No Interference
Mucin from bovine submaxillary	50.0 mg/mL 25.0 mg/mL	Interference No Interference
Triglycerides	50 mg/mL	No Interference
Non-target microorganisms		
Aeromonas hydrophila	1 x 10^6 units/mL	No Interference
Bacteroides vulgatus	1 x 10^6 units/mL	No Interference
Bifidobacterium bifidum	1 x 10^6 units/mL	No Interference
Enterovirus Species D, Serotype EV-D68	1 x 10^5 units/mL	No Interference
Non-pathogenic *E. coli*	1 x 10^6 units/mL	No Interference
Helicobacter pylori	1 x 10^6 units/mL	No Interference
Saccharomyces cerevisiae (deposited as *S. boulardii*)	1 x 10^5 units/mL	No Interference
Exogenous substances		
Bacitracin	250.0 U/mL	No Interference

Table 13. Final highest concentration without observable inhibitory effect (continued)

Substance tested	Concentration tested	Result
Bisacodyl	3.0 mg/mL 1.5 mg/mL	Interference No Interference
Bismuth subsalicylate	3.5 mg/mL	No Interference
Calcium carbonate (TUMS® Extra Strength 750)	100 mg/mL 10 mg/mL	Interference No Interference
Docusate sodium	25 mg/mL	No Interference
Doxycycline hydrochloride	0.50 mg/mL	No Interference
Glycerin	0.50 mL	No Interference
Hydrocortisone	5.0 mg/mL	No Interference
Loperamide hydrochloride	0.78 mg/mL	No Interference
Magnesium hydroxide	1.0 mg/mL	No Interference
Metronidazole	15.0 mg/mL	No Interference
Mineral oil	0.50 mL	No Interference
Naproxen sodium	7 mg/mL	No Interference
Nonoxynol-9	12.0 µL/mL 6.0 µL/mL 3.0 µL/mL 1.5 µL/mL 0.75 µL/mL 0.20 µL/mL	Interference Interference Interference Interference Interference No Interference
Nystatin	10,000.0 USP units/mL	No Interference
Phenylephrine hydrochloride	0.75 mg/mL	No Interference
Sodium phosphate	50.0 mg/mL	No Interference

Table 13. Final highest concentration without observable inhibitory effect (continued)

Substance tested	Concentration tested	Result
Vaccine components		
Rotavirus reassortant WC3:2-5, R574(9) - VR 2195	8.89 x 10−3 $TCID_{50}$/mL 8.89 x 10−4 $TCID_{50}$/mL 8.89 x 10−5 $TCID_{50}$/mL	Interference Interference No Interference
Rotavirus reassortant WI79-4,9 - VR 2415	1.10 x 102 pfu/mL 1.10 x 10 pfu/mL 1.10 pfu/mL	Interference Interference No Interference
Technique-specific Substances		
Bleach	5.0 µL/mL	No Interference
Ethanol	2.0 µL/mL	No Interference
Fecal swab Cary-Blair Medium	100%	No Interference
Fecal Opti-Swab Cary-Blair Medium	100%	No Interference
PurSafe® DNA/RNA Preservative	100%	No Interference
Para-Pak C&S spoon	1 swab/2mL Cary Blair	No Interference
Sigma transwab	1 swab/2mL Cary Blair	No Interference

Table 14. QIAstat-Dx Gastrointestinal Panel 2 results for competitive interference

Sample Mix	Target	Final concentration tested x LoD	Co-infection detected
Norovirus 50x - Rotavirus 3x	Norovirus GI/GII	50x	Yes
	Rotavirus A	3x	
Norovirus 3x - Rotavirus 50x	Norovirus GI/GII	3x	Yes
	Rotavirus A	50x	

Table 14. QIAstat-Dx Gastrointestinal Panel 2 results for competitive interference (continued)

Sample Mix	Target	Final concentration tested x LoD	Co-infection detected
Giardia 50x - Adenovirus 3x	*Giardia lamblia*	50x	Yes
	Adenovirus F40/F41	3x	
Adenovirus 50x - *Giardia* 3x	*Giardia lamblia*	3x	Yes
	Adenovirus F40/F41	50x	
Norovirus 50x - *C.diff* 3x	Norovirus GII	50x	Yes
	Clostridium difficile toxin A/B	3x	
Norovirus 3x - *C.diff* 50x	Norovirus GII	3x	Yes
	Clostridium difficile toxin A/B	50x	
EPEC 50x - EAEC 3x	EPEC	50x	Yes
	EAEC	3x	
EPEC 3x - EAEC 50x	EPEC	3x	Yes
	EAEC	50x	
EPEC 50x - *C.diff* 3x	EPEC	50x	Yes
	Clostridium difficile toxin A/B	3x	
EPEC 3x - *C.diff* 50x	EPEC	3x	Yes
	Clostridium difficile toxin A/B	50x	
EPEC 50x - ETEC 3x	EPEC	50x	Yes
	ETEC	3x	
EPEC 3x - ETEC 50x	EPEC	3x	Yes
	ETEC	50x	
ETEC 50x - EIEC 3x	ETEC	50x	Yes
	EIEC/ *Shigella*	3x	

Table 14. QIAstat-Dx Gastrointestinal Panel 2 results for competitive interference (continued)

Sample Mix	Target	Final concentration tested x LoD	Co-infection detected
ETEC 3x - EIEC 50x	ETEC	3x	Yes
	EIEC/ *Shigella*	50x	

Carryover

A carryover study was performed to evaluate the potential occurrence of cross-contamination between consecutive runs when using the QIAstat-Dx Gastrointestinal Panel 2 on the QIAstat-Dx Analyzer 1.0.

Pathogen samples of stool sample matrix, with alternating high- positive (10^5– 10^6 organism/mL) and negative samples, were conducted on two QIAstat-Dx Analyzer 1.0 instruments.

No carryover between samples was observed in the QIAstat-Dx Gastrointestinal Panel 2, demonstrating that the system design and recommended sample handling and testing practices are effective in preventing false- positive results due to carryover or cross-contamination between samples.

Reproducibility

Reproducibility testing of contrived samples was performed at three test sites including one internal site (Site A) and two external sites (Site B and Site C). The study incorporated a range of potential variation introduced by sites, days, replicates, cartridge lots, operators, and QIAstat-Dx analyzers. For each site, testing was performed across 5 non-consecutive days with 6 replicates per day (leading to a total of 30 replicates per target, concentration, and site), 4 QIAstat-Dx Analyzers (2 analyzers per operator and per site), and at least 2 operators on each testing day. A total of 5 sample mixes (two combined samples at 1x LoD and 3x LoD

plus one negative sample) were prepared. For each mix, 6 replicates were tested and evaluated.

Table 15 shows the detection rate per target and concentration for each site of the Reproducibility study. In addition, data obtained at all three sites have been compiled to calculate the exact 2-sided 95% Confidence Interval by target and concentration. During the reproducibility study, potential variation introduced by sites, days, replicates, cartridge lots, operators, and QIAstat-Dx analyzers were analyzed showing no significant contribution to variability (Standard Deviation and Coefficient of Variation values below 1 and 5%, respectively) caused by any of the assessed variables.

Table 15. Detection rate per target and concentration for each site of the Reproducibility study and exact 2-sided 95% Confidence Interval by target and concentration

			% Agreement with Expected Result			
Pathogen Tested	**Concentration Tested**	**Expected Result**	**Site A**	**Site B**	**Site C**	**All Sites (95% Confidence Interval)**
Adenovirus F41 ZeptoMetrix 0810085CF	3x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	1x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	None	Not Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)

Table 15. Detection rate per target and concentration for each site of the Reproducibility study and exact 2-sided 95% Confidence Interval by target and concentration (continued)

			% Agreement with Expected Result			
Pathogen Tested	**Concentration Tested**	**Expected Result**	**Site A**	**Site B**	**Site C**	**All Sites (95% Confidence Interval)**
Clostridium difficile ZeptoMetrix 0801619	3x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	1x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	None	Not Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
Campylobacter ZeptoMetrix 801650	3x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	1x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	None	Not Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)

Table 15. Detection rate per target and concentration for each site of the Reproducibility study and exact 2-sided 95% Confidence Interval by target and concentration (continued)

			% Agreement with Expected Result			
Pathogen Tested	**Concentration Tested**	**Expected Result**	**Site A**	**Site B**	**Site C**	**All Sites (95% Confidence Interval)**
Escherichia coli **(EPEC)** ZeptoMetrix 801747	3x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	1x LoD	Detected	30/30 100%	29/30 96.67%	30/30 100%	89/90 98.89% (93.96 – 99.97%)
	None	Not Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98– 100.00%)
Entamoeba histolytica ATCC 30459	3x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	1x LoD	Detected	30/30 100%	30/30 100%	29/30 96.67%	89/90 98.89% (93.96 – 99.97%)
	None	Not Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)

Table 15. Detection rate per target and concentration for each site of the Reproducibility study and exact 2-sided 95% Confidence Interval by target and concentration (continued)

			% Agreement with Expected Result			
Pathogen Tested	**Concentration Tested**	**Expected Result**	**Site A**	**Site B**	**Site C**	**All Sites (95% Confidence Interval)**
Giardia lamblia ATCC 30888	3x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	1x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	None	Not Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
Norovirus GII ZeptoMetrix 0810087CF	3x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	1x LoD	Detected	29/30 96.67%	30/30 100%	30/30 100%	89/90 98.89% (93.96 – 99.97%)
	None	Not Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)

Table 15. Detection rate per target and concentration for each site of the Reproducibility study and exact 2-sided 95% Confidence Interval by target and concentration (continued)

			% Agreement with Expected Result			
Pathogen Tested	**Concentration Tested**	**Expected Result**	**Site A**	**Site B**	**Site C**	**All Sites (95% Confidence Interval)**
Rotavirus A ZeptoMetrix 0810280CF	3x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	1x LoD	Detected	30/30 100%	29/30 96.67%	30/30 100%	89/90 98.89% (93.96 – 99.97%)
	None	Not Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
***Escherichia coli* (STEC) O157:H7** ZeptoMetrix 0801622	3x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	1x LoD	Detected	30/30 100%	30/30 100%	29/30 96.67%	89/90 98.89% (93.96 – 99.97%)
	None	Not Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)

Table 15. Detection rate per target and concentration for each site of the Reproducibility study and exact 2-sided 95% Confidence Interval by target and concentration (continued)

			% Agreement with Expected Result			
Pathogen Tested	**Concentration Tested**	**Expected Result**	**Site A**	**Site B**	**Site C**	**All Sites (95% Confidence Interval)**
Escherichia coli* (STEC) *stx1 ZeptoMetrix 0801622	3x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	1x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	None	Not Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
Escherichia coli* (STEC) *stx2 ZeptoMetrix 0801622	3x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	1x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	None	Not Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)

Table 15. Detection rate per target and concentration for each site of the Reproducibility study and exact 2-sided 95% Confidence Interval by target and concentration (continued)

			% Agreement with Expected Result			
Pathogen Tested	**Concentration Tested**	**Expected Result**	**Site A**	**Site B**	**Site C**	**All Sites (95% Confidence Interval)**
Salmonella enterica ZeptoMetrix 0801437	3x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	1x LoD	Detected	30/30 100%	29/30 96.67%	29/30 96.67%	88/90 97.78% (92.20 – 99.73%)
	None	Not Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
Vibrio parahaemolyticus ATCC 17802	3x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	1x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	None	Not Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)

Table 15. Detection rate per target and concentration for each site of the Reproducibility study and exact 2-sided 95% Confidence Interval by target and concentration (continued)

			% Agreement with Expected Result			
Pathogen Tested	**Concentration Tested**	**Expected Result**	**Site A**	**Site B**	**Site C**	**All Sites (95% Confidence Interval)**
Yersinia enterocolitica Zeptometrix 0801734	3x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	1x LoD	Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)
	None	Not Detected	30/30 100%	30/30 100%	30/30 100%	90/90 100% (95.98 – 100.00%)

Repeatability

A repeatability study was conducted on the QIAstat-Dx Analyzer 1.0 instrument using a set of samples composed of low-concentrated analytes spiked into stool matrix (3x LoD and 1x LoD) and negative stool samples. Pathogens included in the positive samples were Adenovirus, *Clostridium difficile*, *Campylobacter*, Enteropathogenic *E. coli* (EPEC), *Entamoeba histolytica*, *Giardia lamblia*, Norovirus GII, Rotavirus, *E. coli* O157, STEC stx1, STEC stx2, *Salmonella enterica*, *Vibrio parahaemolyticus*, and *Yersinia enterocolitica*. Each sample was tested with the same instrument over 12 days. In total, 60 replicates of 1x LoD and 60 replicates of 3x LoD per each of the tested targets and 60 replicates of negative samples were run. Overall results showed a 93.33–100.00% and 95.00–100.00% detection rate for 1x LoD and 3x

LoD samples, respectively. Negative samples showed 100% of negative calls for all panel analytes.

Repeatability in the QIAstat-Dx Rise instrument was also evaluated in comparison with QIAstat-Dx Analyzers. A study was conducted on two QIAstat-Dx Rise instruments using a representative set of samples composed of low-concentrated analytes (3x LoD and 1x LoD) spiked into stool matrix and negative stool samples. Pathogens included in the positive samples were Norovirus GII, *Entamoeba histolytica*, *Clostridium difficile*, *Yersinia enterocolitica*, *Salmonella enterica*, Adenovirus F 40, and Rotavirus A. Samples were tested in replicates using two lots of cartridges. In total, 128 replicates of 1x LoD positive samples, 128 replicates of 3x LoD positive samples, and 64 replicates of negative samples were run on the QIAstat-Dx Rise instrument. Overall results showed a 99.22–100.00% detection rate for both 1x LoD and 3x LoD samples. Negative samples showed 100% of negative calls for all panel analytes. Testing with two QIAstat-Dx Analyzers (each with four Analytical Modules) was included in the study for results comparison. QIAstat-Dx Rise performance was shown to be equivalent to QIAstat-Dx Analyzer 1.0.

Clinical performance

The clinical performance shown below was demonstrated using QIAstat-Dx Analyzer 1.0. The QIAstat-Dx Analyzer 2.0 and the QIAstat-Dx Rise use the same Analytical Module as the QIAstat-Dx Analyzer 1.0; therefore, the performance is not impacted by using the QIAstat-Dx Analyzer 2.0 or the QIAstat-Dx Rise. The equivalency on performance between QIAstat-Dx Rise and QIAstat-Dx Analyzer 1.0 was confirmed through a repeatability study (see details on page 133).

Prevalence of Detected Analytes with QIAstat-Dx Gastrointestinal Panel 2

The number and percentage of positive results as determined by the QIAstat- Dx Gastrointestinal Panel 2 in the prospective clinical evaluation, stratified by age group, are presented in Table 16. Overall, the QIAstat-Dx Gastrointestinal Panel 2 detected at least 1 organism in 34.3% (665/1939) of the prospectively collected specimens.

Table 16. Prevalence Summary by Age Group for the Prospective Clinical study as determined by the QIAstat-Dx Gastrointestinal Panel 2

Analyte	Overall	0-6 years	6-21 years	22-49 years	50+ years	Not Reported
Viruses						
Adenovirus F40/F41	7 (0.4%)	4 (1.9%)	2 (1.3%)	0 (0.0%)	1 (0.1%)	0 (0.0%)
Astrovirus	9 (0.5%)	5 (2.3%)	0 (0.0%)	3 (0.6%)	1 (0.1%)	0 (0.0%)
Norovirus GI/GII	59 (3.1%)	25 (11.7%)	2 (1.3%)	17 (3.4%)	15 (1.4%)	0 (0.0%)
Rotavirus A	27 (1.4%)	15 (7.0%)	2 (1.3%)	7 (1.4%)	3 (0.3%)	0 (0.0%)
Sapovirus	15 (0.8%)	9 (4.2%)	3 (1.9%)	3 (0.6%)	0 (0.0%)	0 (0.0%)
Bacteria						
Campylobacter	101 (5.2%)	27 (12.7%)	7 (4.5%)	27 (5.3%)	40 (3.8%)	0 (0.0%)

Table 16. Prevalence Summary by Age Group for the Prospective Clinical study as determined by the QIAstat-Dx Gastrointestinal Panel 2 (continued)

Analyte	Overall	0-6 years	6-21 years	22-49 years	50+ years	Not Reported
Clostridium difficile	200 (10.3%)	20 (9.4%)	14 (8.9%)	44 (8.7%)	119 (11.3%)	3 (42.9%)
Plesiomonas shigelloides	9 (0.5%)	1 (0.5%)	0 (0.0%)	6 (1.2%)	2 (0.2%)	0 (0.0%)
Salmonella	33 (1.7%)	9 (4.2%)	6 (3.8%)	6 (1.2%)	12 (1.1%)	0 (0.0%)
Vibrio cholerae	2 (0.1%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	1 (0.1%)	0 (0.0%)
Vibrio parahaemolyticus	3 (0.3%)	0 (0.0%)	0 (0.0%)	2 (0.7%)	1 (0.2%)	0 (0.0%)
Vibrio vulnificus	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Yersinia enterocolitica	30 (1.6%)	3 (1.4%)	2 (1.3%)	13 (2.6%)	12 (1.1%)	0 (0.0%)
Diarrheagenic *E. coli*/*Shigella*						
Enteroaggregative *E. coli* (EAEC)	53 (2.7%)	11 (5.2%)	1 (0.6%)	24 (4.8%)	17 (1.6%)	0 (0.0%)
Enteropathogenic *E. coli* (EPEC)	192 (9.9%)	57 (26.6%)	14 (8.9%)	52 (10.3%)	69 (6.6%)	0 (0.0%)
Enterotoxigenic *E. coli* (ETEC) *lt/st*	36 (1.9%)	4 (1.9%)	2 (1.3%)	18 (3.6%)	12 (1.1%)	0 (0.0%)
Shiga-like toxin *E. coli* (STEC) *stx1/stx2*	24 (1.2%)	9 (4.2%)	1 (0.6%)	8 (1.6%)	6 (0.6%)	0 (0.0%)
E. coli O157	3 (0.2%)	3 (1.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Shigella/ Enteroinvasive *E. coli* (EIEC)	13 (0.7%)	1 (0.5%)	0 (0.0%)	7 (1.4%)	5 (0.5%)	0 (0.0%)
Parasites						
Cryptosporidium	9 (0.5%)	0 (0.0%)	2 (1.3%)	5 (1.0%)	2 (0.2%)	0 (0.0%)
Cyclospora cayetanensis	21 (1.1%)	0 (0.0%)	1 (0.6%)	8 (1.6%)	12 (1.1%)	0 (0.0%)
Giardia lamblia	16 (0.8%)	4 (1.9%)	1 (0.6%)	7 (1.4%)	4 (0.4%)	0 (0.0%)

The clinical performance of QIAstat-Dx Gastrointestinal Panel 2 was established during a multi- center international prospective study conducted at thirteen clinical settings representatives of different geographical areas within USA and Europe (9 sites in USA and 4 sites in Europe) between May and July 2021. All study sites were hospital-associated or independent clinical diagnostics laboratories that perform routine diagnostics of gastrointestinal infections. A total of 1939 prospectively collected stool specimens (stool in Cary-Blair transport medium using Para-Pak® C&S (Meridian Bioscience) or FecalSwab (COPAN) were obtained from patients with clinical indications of diarrhea caused by gastrointestinal infection. Table 17 provides a summary of the specimen's distribution across all study sites.

Table 17. Prospective Specimens Distribution Across the study sites

Site/Country	Prospective (Fresh)
Germany	339
Denmark	293
Spain	247
France	63
USA site 1	186
USA site 2	43
USA site 3	282
USA site 4	177
USA site 5	44
USA site 6	39
USA site 7	0*
USA site 8	131
USA site 9	95
Total	**1939**

* The specimens from this site were excluded from the analysis because they were collected with another device different to Para-Pak C&S or FecalSwab.

The demographic information for the 1939 specimens evaluated in the prospective study is summarized in Table 18.

Table 18. Demographic data for prospective evaluated specimens

Demographic data	N	%
Gender		
Female	1070	55.2
Male	869	44.8

Table 18. Demographic data for prospective evaluated specimens (continued)

Demographic data	N	%
Age Group		
0–5 years	213	11.0
6–21 years	159	8.2
22–49 years	505	26.0
50+ years	1055	54.4
Not Reported	7	0.4
Patient population		
Emergency room	75	3.9
Hospitalized	485	25.0
Immunocompromised	3	0.2
Outpatient	816	42.1
No information available	560	28.9
Number of Days between Symptom Onset and QIAstat-Dx Testing		
> 7 days	89	4.6
≤ 7 days	162	8.3
Not Reported	1688	87.1

The performance of the QIAstat-Dx Gastrointestinal Panel 2 was evaluated for each panel test result using one FDA-cleared/CE-marked test as comparator or using a composite comparator of three independent FDA-cleared/CE-marked test methods or two independent FDA-cleared/CE-marked tests methods and validated PCR assays followed by bi-directional sequencing (Table 19). The composite comparator method result was determined as the majority of the three individual test results.

Table 19. Comparator Methods for the Clinical Evaluation of QIAstat-Dx Gastrointestinal Panel 2

QIAstat-Dx GI Panel 2 Test Result	Comparator Method
Astrovirus	One FDA-cleared/CE-marked test method
Rotavirus A	
Sapovirus	
Campylobacter	
Clostridium difficile	
Plesiomonas shigelloides	
Salmonella	
Yersinia enterocolitica	
Shigella/Enteroinvasive *E. Coli* (EIEC)	
Enteroaggregative *Escherichia coli* (EAEC)	
Enteropathogenic *E. coli* (EPEC)	
E. coli O157	
Cryptosporidium	
Cyclospora cayetanensis	
Entamoeba histolytica	
Vibrio parahaemolyticus	One FDA-cleared/CE-marked test method and one validated PCR test followed by bidirectional sequencing*†
Vibrio vulnificus	
Adenovirus F40/F41	Composite of three FDA-cleared/CE-marked test methods *‡
Norovirus GI/GII	
Vibrio cholerae	
Enterotoxigenic *E. coli* (ETEC) *lt/st*	
Shiga-like toxin- *E. coli* (STEC) *stx1/stx2*	

Table 19. Comparator Methods for the Clinical Evaluation of QIAstat-Dx Gastrointestinal Panel 2 (continued)

QIAstat-Dx GI Panel 2 Test Result	Comparator Method
Giardia lamblia	Composite of two FDA-cleared/CE-marked test methods and two validated PCR tests followed by bi-directional sequencing*

*Each PCR assay used was a well-characterized and validated nucleic acid amplification tests (NAAT) followed by bi-directional sequencing analysis. Each assay was designed to amplify different sequences than those targeted by the QIAstat-Dx Gastrointestinal Panel 2. Positive results required to generate sequences from bi-directional sequencing with at least 200 bases of adequate quality that by BLAST analyses matched a sequence of the expected organism or gene from NCBI GenBank database with at least 95% query coverage and at least 95% identity compared to the reference.

†The FDA-cleared/CE-marked test method used did not differentiate between *V. parahaemolyticus* and *V. vulnificus* species, therefore additional testing was conducted on the positive specimens using validated PCR assays followed by bidirectional sequencing to identify the corresponding *Vibrio* species.

‡One of the FDA-cleared/CE-marked test methods used in the composite comparator did not differentiate *V. cholerae* species, additional testing was conducted on the positive specimens using a validated PCR test followed by bidirectional sequencing for *V. cholerae* identification.

In addition, to supplement the results of the prospective clinical study, a total of 750 preselected archived frozen specimens known to be positive for at least one of the QIAstat-Dx Gastrointestinal Panel 2 targets were also evaluated (retrospective study). These specimens served to increase the sample size for analytes that showed lower prevalence in the clinical prospective study or that were less represented in a particular sample type (Para-Pak C&S or FecalSwab). The same Comparator Methods detailed in Table 19 was used as confirmatory testing for the presence of the nucleic acids from the expected analytes.

In total, 2689 specimens (1939 prospectively collected and 750 preselected archived specimens) were evaluated in the clinical study. These specimens were collected using Para-Pak C&S (1150) or FecalSwab (1539).

The positive percentage agreement (PPA) and the negative percentage agreement (NPA) were calculated for the prospective and retrospective clinical studies combined.

The PPA was calculated as 100% x (TP / (TP + FN)). True positive (TP) indicates that both the QIAstat-Dx Gastrointestinal Panel 2 and comparator method showed a positive result for this specific target, and false negative (FN) indicates that the QIAstat-Dx Gastrointestinal Panel 2 result was negative while the comparator method result was positive. The NPA was calculated as 100% x (TN / (TN + FP)). True negative (TN) indicates that both the QIAstat-Dx Gastrointestinal Panel 2 and the comparator method showed negative results, and a false positive (FP) indicates that the QIAstat-Dx Gastrointestinal Panel 2 result was positive, but the comparator method result was negative. The PPA and NPA exact binomial two-sided 95% confidence interval was calculated.

Additionally, since several analytes, such as *Entamoeba histolytica* or *Vibrio* species are so rare that both prospective and retrospective testing efforts were insufficient to demonstrate system performance. To supplement the prospective and archived specimens' test results, an evaluation of contrived specimens was performed for several pathogens (Adenovirus F40/F41, Astrovirus, Rotavirus, Sapovirus, *Campylobacter*, ETEC, EIEC/*Shigella*, STEC *stx1*/*stx2*, *E. coli* O157, *Plesiomonas shigelloides*, *Salmonella*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificus*, *Yersinia enterocolitica*, *Cryptosporidium*, *Cyclospora cayetanensis*, *Entamoeba histolytica* , and *Giardia lamblia*). Contrived specimens were prepared using negative residual specimens that had previously tested negative by QIAstat-Dx Gastrointestinal Panel 2 and comparator methods. At least, 50% of these specimens were spiked at concentrations slightly above the Limit of Detection (2x LoD) and the rest at 5x and 10x LoD, using quantified strains for each pathogen. A minimum of 50 contrived specimens were tested for each evaluated analyte. The analyte status of each contrived specimen was blinded to the users analyzing the specimens. The PPA was established for the mentioned targets on contrived specimens as well.

The clinical performance results are summarized in individual performance tables for each target that include clinical specimens (prospective and archived) and contrived specimens test results (Table 20 to Table 42).

Discrepancies between the QIAstat-Dx Gastrointestinal Panel 2 and the comparator methods were investigated for the analytes that the QIAstat-Dx Gastrointestinal Panel 2 test result was compared to one FDA-cleared/CE-marked method. Discrepancies analyses are footnoted on each individual clinical performance Table below and data is presented before and after discordances analysis resolution, except for the 6 targets where a composite of three separate methods was used as comparator (Adenovirus F40/41, Norovirus GI/GII, *V. cholerae*, ETEC, STEC, and *Giardia lamblia*) and for the two *Vibrio* species (*V. parahaemolyticus* and *V. vulnificus*) where the comparator method included one FDA-cleared/CE-marked method and PCR assays followed bidirectional sequencing for specific *Vibrio* species identification.

Viruses

Table 20. Adenovirus F40/41

	Positive Percent Agreement			Negative Percent Agreement		
Sample group	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	51 / 52	98.1	89.7–100.0	1049 / 1050	99.9	99.5–100.0
Contrived	68 / 70	97.1	90.1–99.7	N/A	N/A	N/A

Table 21. Astrovirus

		Positive Percent Agreement			Negative Percent Agreement		
Sample group	**Analyses**	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	Pre-discordant	11 / 12	91.7	61.5–99.8	2124 / 2124	100.0	99.8–100.0
	Post-discordant	11/12*	91.7	61.5–99.8	2124 / 2124	100.0	99.8–100.0
Contrived	N/A	67 / 68	98.5	92.1–100.0	N/A	N/A	N/A

*Astrovirus was detected in the single false negative specimen (1/1) using a different FDA-cleared/CE-marked test method.

Table 22. Norovirus GI/GII

	Positive Percent Agreement			Negative Percent Agreement		
Sample group	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	100 / 111	90.1	83.0–95.0	1052 / 1055	99.7	99.2–99.9

Table 23. Rotavirus A

		Positive Percent Agreement			Negative Percent Agreement		
Sample group	**Analyses**	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	Pre-discordant	34 / 37	91.9	78.1–98.3	2096 / 2099	99.9	99.6–100.0
	Post-discordant	34 / 36*	94.4	81.3–99.3	2097 / 2100*	99.9	99.6–100.0
Contrived	N/A	69 / 70	98.6	92.3–100.0	N/A	N/A	N/A

*Rotavirus A was detected in two of three false negative specimens (2/3) and was not detected in the three false positive specimens (0/3) using a different FDA-cleared/CE-marked test method.

Table 24. Sapovirus

		Positive Percent Agreement			Negative Percent Agreement		
Sample group	**Analyses**	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	Pre-discordant	56 / 67	83.6	72.5–91.5	2213 / 2216	99.9	99.6–100.0
	Post-discordant	53 / 54*	98.2	90.1–100.0	2223 / 2229*	99.7	99.4–99.9
Contrived	N/A	69/ 69	100.0	94.8–100.0	N/A	N/A	N/A

*Sapovirus was detected in one of the eleven false negative specimens (1/11) and was detected in one of the three false positive specimens (1/3) using a different FDA-cleared/CE-marked test method.

Bacteria

Table 25. *Campylobacter*

		Positive Percent Agreement			Negative Percent Agreement		
Sample group	**Analyses**	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	Pre-discordant	129 / 132	97.7	93.5–99.5	1998 / 2006	99.6	99.2–99.8
	Post-discordant	134 / 134*	100.0	97.3–100.0	2001 / 2004*	99.9	99.6–100.0
Contrived	N/A	45/ 46†	97.8	88.5–99.9	N/A	N/A	N/A

**Campylobacter* was not detected in the three false negative specimens (0/3) and was detected in five of the eight false positive specimens (5/8) using a different FDA-cleared/CE-marked test method.

† Less than 50 contrived were tested for *Campylobacter* because the testing was discontinued due to the higher prevalence observed during clinical prospective and retrospective studies.

Table 26. *Clostridium difficile* toxin A/B

		Positive Percent Agreement			Negative Percent Agreement		
Sample group	**Analyses**	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	Pre-discordant	213 / 239	89.1	84.5–92.8	1899 / 1902	99.8	99.5–100.0
	Post-discordant	213 / 224*	95.1	91.4–97.5	1914 / 1917*	99.8	99.5–100.0

**Clostridium difficile* toxin A/B was detected on eleven of the twenty-seven false negative (11/27) and was not detected in any of the three false positive specimens (0/3) using PCR followed by bi-directional sequence analysis.

Table 27. *Plesiomonas shigelloides*

		Positive Percent Agreement			Negative Percent Agreement		
Sample group	**Analyses**	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	Pre-discordant	40 / 44	90.9	78.3–97.5	2227 / 2231	99.8	99.5–100.0
	Post-discordant	40/41*	97.6	87.1–99.9	2230 / 2234*	99.8	99.5–100.0
Contrived	N/A	67 / 68	98.5	92.1–100.0	N/A	N/A	N/A

**Plesiomonas shigelloides* was detected in one of the four false negative specimens (1/4) and was not detected in the four false positive specimens using a different FDA-cleared/CE-marked test method.

Table 28. *Salmonella*

		Positive Percent Agreement			Negative Percent Agreement		
Sample group	**Analyses**	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	Pre-discordant	64 / 68	94.1	85.6–98.4	2068 / 2070	99.9	99.7–100.0
	Post-discordant	64 / 64*	100.0	94.4–100.0	2072 / 2074*	99.9	99.7–100.0
Contrived	N/A	33 / 33†	100.0	89.4–100.0	N/A	N/A	N/A

**Salmonella* was not detected in the four false negative specimen (0/4) and was not detected in the two false positive specimens (0/2) using a different FDA-cleared/CE-marked test method.

†Less than 50 contrived were tested for *Salmonella* because the testing was discontinued due to the higher prevalence observed during clinical prospective and retrospective studies.

Table 29. *Vibrio cholerae*

	Positive Percent Agreement			Negative Percent Agreement		
Sample group	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	1 /1	100.0	2.5–100.0	987 / 989	99.8	99.3–100.0
Contrived	67 / 70	95.7	88.0–99.1	N/A	N/A	N/A

Table 30. *Vibrio parahaemolyticus*

	Positive Percent Agreement			Negative Percent Agreement		
Sample group	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	1 /2*	50.0	9.5–90.6	2133 / 2134*	99.9	99.7–100.0
Contrived	70 / 70	100.0	94.9–100.0	N/A	N/A	N/A

**Vibrio parahaemolyticus* was detected in one additional sample with the QIAstat-Dx Gastrointestinal Panel 2 which was also detected with the FDA-cleared/CE-marked comparator method as *Vibrio* but the specific *Vibrio* species could not be determined with the PCR assays followed by bidirectional sequencing, and therefore was not considered as true positive on the data analyses.

Table 31. *Vibrio vulnificus*

	Positive Percent Agreement			Negative Percent Agreement		
Sample group	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	0 / 0	N/A	N/A	2136 / 2136	100.0	99.8–100.0
Contrived	69 / 69	100.0	94.8–100.0	N/A	N/A	N/A

Table 32. *Yersinia enterocolitica*

		Positive Percent Agreement			Negative Percent Agreement		
Sample group	**Analyses**	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	Pre-discordant	51 / 54	94.4	84.6–98.8	2071 / 2083	99.4	99.0–99.7
	Post-discordant	51 / 51*	100.0	93.0–100.0	2074 / 2086*	99.4	99.0–99.7
Contrived	N/A	68 / 69	98.6	92.2–100.0	N/A	N/A	N/A

**Yersinia enterocolitica* was not detected in the three false negative specimens (0/3) and was not detected in the twelve false positive specimens (0/12) using a different FDA-cleared/CE-marked test method.

Diarrheagenic E. coli/Shigella

Table 33. Enteroaggregative *E. coli* (EAEC)

		Positive Percent Agreement			Negative Percent Agreement		
Sample group	**Analyses**	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	Pre-discordant	82 / 97	84.5	75.8–91.1	2035 / 2040	99.8	99.4–99.9
	Post-discordant	82 / 93*	88.2	79.8–94.0	2039 / 2044*	99.8	99.4–99.9

*Enteroaggregative *E. coli* (EAEC) was detected on thirteen of the seventeen false negatives (13/17) and none of the five false positive specimens were detected (0/5) using PCR followed by bi-directional sequence analysis.

Table 34. Enteropathogenic *E. coli* (EPEC)

		Positive Percent Agreement			Negative Percent Agreement		
Sample group	**Analyses**	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	Pre-discordant	289 / 318	90.9	87.2–93.8	1897 / 1901	99.8	99.5–99.9
	Post-discordant	295 / 316*	93.4	90.0–95.8	1914 / 1917*	99.8	99.5–100.0

*Enteropathogenic *E. coli* (EPEC) was detected in thirteen out of twenty-one false negative specimens (13/21) and was detected in one of the two false positive specimens (1/2) using PCR followed by bi-directional sequence analysis. There were eight (8) other false negative specimens and two (2) false positive specimens that were not further investigated by discrepant analysis.

Table 35. Enterotoxigenic *E.coli lt/st*

	Positive Percent Agreement			Negative Percent Agreement		
Sample group	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	63 / 67	94.0	85.4–98.4	963 / 975	98.8	97.9–99.4
Contrived	43 / 43	100.0	91.8–100.0	N/A	N/A	N/A

Table 36. Shiga-like toxin *E. coli* (STEC) *stx1/stx2*

	Positive Percent Agreement			Negative Percent Agreement		
Sample group	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	70 / 75	93.3	85.1–97.8	937 / 945	99.2	98.3–99.6
Contrived	200 / 200*	100.0	98.2–100.0	N/A	N/A	N/A

*A higher number of test results are shown for STEC *stx1/stx2* target on contrived specimens because they come from non-O157 STEC strains as well as STEC strains with serogroup O157.

Table 37. *E.coli* O157

		Positive Percent Agreement			Negative Percent Agreement		
Sample group	**Analyses**	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	Pre-discordant	39 / 41	95.1	83.5–99.4	26 / 26	100.0	86.8–100.0
	Post-discordant	39 / 39*	100.0	91.0–100.0	28 / 28	100.0	87.7–100.0
Contrived	N/A	67 / 69	97.1	89.9–99.7	N/A	N/A	N/A

**E. coli* O157 was not detected in the two false negative specimens (0/2) using a different FDA-cleared/CE-marked test method.

Table 38. *Shigella*/Enteroinvasive *E. coli* (EIEC)

		Positive Percent Agreement			Negative Percent Agreement		
Sample group	**Analyses**	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	Pre-discordant	34 / 36	94.4	81.3–99.3	2099 / 2100	99.9	99.7–100.0
	Post-discordant	36 / 37*	97.3	85.8–99.9	2100 / 2100*	100.0	99.8–100.0
Contrived	N/A	69 / 69	100.0	94.8–100.0	N/A	N/A	N/A

**Shigella*/Enteroinvasive *E. coli* (EIEC) was detected in one of the two false negative specimens (1/2) and was detected in the single false positive specimen (1/1) using an FDA-cleared/CE-marked test.

Parasites

Table 39. *Cryptosporidium*

		Positive Percent Agreement			Negative Percent Agreement		
Sample group	**Analyses**	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	Pre-discordant	40 / 42	95.2	83.8–99.4	2220 / 2223	99.9	99.6–100.0
	Post-discordant	40 / 40*	100.0	91.2–100.0	2223 / 2226*	99.9	99.6–100.0
Contrived	N/A	58 / 58	100.0	93.8–100.0	N/A	N/A	N/A

**Cryptosporidium* was not detected in the two false negative specimens (0/2) and was not detected in the three false positive specimens using PCR followed by bi-directional sequence analysis.

Table 40. *Cyclospora cayetanensis*

		Positive Percent Agreement			Negative Percent Agreement		
Sample group	**Analyses**	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	Pre-discordant	23 / 24	95.8	78.9–99.9	2112 / 2112	100.0	99.8–100.0
	Post-discordant	23 / 24*	95.8	78.9–99.9	2112 / 2112	100.0	99.8–100.0
Contrived	N/A	56 / 56	100.0	93.6–100.0	N/A	N/A	N/A

**Cyclospora cayetanensis*, there was one (1) false negative specimen that was not further investigated by discrepant analyses.

Table 41. *Entamoeba histolytica*

		Positive Percent Agreement			Negative Percent Agreement		
Sample group	**Analyses**	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	Pre-discordant	0 / 0	N/A	N/A	2136 / 2136	100.0	99.8–100.0
	Post-discordant	0 / 0	N/A	N/A	2136 / 2136	100.0	99.8–100.0
Contrived	N/A	69 / 70	98.6	92.3–100.0	N/A	N/A	N/A

Table 42. *Giardia lamblia*

	Positive Percent Agreement			Negative Percent Agreement		
Sample group	**TP/TP+FN**	**%**	**95% CI**	**TN/TN+FP**	**%**	**95% CI**
Clinical	63 / 63	100.0	94.3–100.0	983 / 993	99.0	98.2–99.5
Contrived	56 / 56	100.0	93.6–100.0	N/A	N/A	N/A

Clinical Performance Summary

The results for all target pathogens obtained during clinical specimens testing in the prospective and retrospective studies is summarized in Table 43. For the targets that discordances were analyzed, the data is presented after resolution.

Table 43. Clinical Performance Summary in the Prospective and Retrospective studies

Analyte	Positive Percent Agreement			Negative Percent Agreement		
	TP/TP+FN	%	95% CI	TN/TN+FP	%	95% CI
Viruses						
Adenovirus F40/F41	51 / 52	98.1	89.7–100.0	1049 / 1050 *	99.9	99.5–100.0
Astrovirus	11 / 12	91.7	61.5–99.8	2124 / 2124	100.0	99.8–100.0
Norovirus GI/GII	100 / 111	90.1	83.0–94.9	1052 / 1055 *	99.7	99.2–99.9
Rotavirus A	34 / 36	94.4	81.3–99.3	2097 / 2100	99.9	99.6–100.0
Sapovirus	53 / 54	98.2	90.1–100.0	2223 / 2229	99.7	99.4–99.9
Bacteria						
Campylobacter	134 / 134	100.0	97.3–100.0	2001 / 2004	99.9	99.6–100.0
Clostridium difficile	213 / 224	95.1	91.4–97.5	1914 / 1917	99.8	99.5–100.0
Plesiomonas shigelloides	40 / 41	97.6	87.1–99.9	2230 / 2234	99.8	99.5–100.0
Salmonella	64 / 64	100.0	94.4–100.0	2072 / 2074	99.9	99.7–100.0
Vibrio cholerae	1 / 1	100.0	2.5–100.0	987 / 989 *	99.8	99.3–100.0
Vibrio parahaemolyticus	1 / 2	50.0	9.5–90.6	2133 / 2134	99.9	99.7–100.0
Vibrio vulnificus	0 / 0	N/A	N/A	2136 / 2136	100.0	99.8–100.0
Yersinia enterocolitica	51 / 51	100.0	93.0–100.0	2074 / 2086	99.4	99.0–99.7

Table 43. Clinical Performance Summary in the Prospective and Retrospective studies (continued)

Analyte	Positive Percent Agreement			Negative Percent Agreement		
	TP/TP+FN	%	95% CI	TN/TN+FP	%	95% CI
Diarrheagenic *E. coli*/*Shigella*						
Enteroaggregative *E. coli* (EAEC)	82 / 93	88.2	79.8–94.0	2039 / 2044	99.8	99.4–99.9
Enteropathogenic *E. coli* (EPEC)	295 / 316	93.4	90.0–95.8	1914 / 1917	99.8	99.5–100.0
Enterotoxigenic *E. coli* (ETEC) *lt/st*	63 / 67	94.0	85.4–98.4	963 / 975*	98.8	97.9–99.4
Shiga-like toxin *E. coli* (STEC) *stx1/stx2*	70 / 75	93.3	85.1–97.8	937 / 945*	99.2	98.3–99.6
E. coli O157	39 / 39	100.0	91.0–100.0	28 / 28	100.0	87.7–100.0
Shigella/ Enteroinvasive *E. coli* (EIEC)	36 / 37	97.3	85.8–99.9	2100 / 2100	100.0	99.8–100.0
Parasites						
Cryptosporidium	40 / 40	100.0	91.2–100.0	2223 / 2226	99.9	99.6–100.0
Cyclospora cayetanensis	23 / 24	95.8	78.9–99.9	2112 / 2112	100.0	99.8–100.0
Entamoeba histolytica	0 / 0	N/A	N/A	2136 / 2136	100.0	99.8–100.0
Giardia lamblia	63 / 63	100.0	94.3– 100.0	983 / 993*	99.0	98.2–99.5
Overall Panel Performance						
All Analytes	**1464 / 1536**	**95.3**	**94.1–96.3**	**39527/ 39608**	**99.8**	**99.8–99.8**

*The sample size for clinical specificity (NPA) is smaller for the pathogens evaluated with a composite reference (Adenovirus F40/41, Norovirus GI/GII, *Vibrio cholerae*, ETEC, STEC, *Giardia lamblia*) due to a portion of all true negative samples (> 33%) being tested with the full composite comparator method (39.03–43.59 %).

Co-infections

The QIAstat-Dx Gastrointestinal Panel 2 reported multiple organism detections (i.e., mixed infections) for a total of 142 prospectively collected specimens. This represents 21.3% of positive specimens (142/665). Most multiple detections contained two organisms (107/142; 75.4%), while 17.6% (25/142) contained three organisms, 4.2% (6/142) contained four organisms, and 2.8% (4/142) contained five organisms. The most common multiple infections are shown in Table 44 below.

Table 44. Most Prevalent Multiple Detection Combinations (≥5 instances) as Determined by the QIAstat-Dx Gastrointestinal Panel 2

Multiple Detection Combination	Number of Specimens
Enteropathogenic *E. coli* (EPEC) + Enterotoxigenic *E. coli* (ETEC) *lt/st*	5
Enteroaggregative *E. coli* (EAEC) + Enterotoxigenic *E. coli* (ETEC) *lt/st*	6
Enteroaggregative *E. coli* (EAEC) + Enteropathogenic *E. coli* (EPEC)	7
Enteropathogenic *E. coli* (EPEC) + Norovirus GI/GII	10
Campylobacter + Enteropathogenic *E. coli* (EPEC)	13
Clostridium difficile toxin A/B + Enteropathogenic *E. coli* (EPEC)	16

As shown in Table 45, the analytes most commonly found (≥10 instances) in mixed infections were EPEC (88), *Clostridium difficile* toxin A/B (44), *Campylobacter* (34), EAEC (33), Norovirus GI/GII (30), ETEC (23), and STEC (12).

Table 45. Prevalence of Analytes in Mixed Infections as determined by the QIAstat-Dx Gastrointestinal Panel 2

Analyte	N	%
Adenovirus F40/F41	5	1.5
Astrovirus	3	0.9
Campylobacter	34	10.2
Clostridium difficile toxin A/B	44	13.2
Cryptosporidium	2	0.6
Cyclospora cayetanensis	4	1.2
E. coli O157	3	0.9
Enteroaggregative *E. coli* (EAEC)	33	9.9
Enteropathogenic *E. coli* (EPEC)	88	26.4
Enterotoxigenic *E. coli* (ETEC) lt/st	23	6.9
Giardia lamblia	6	1.8
Norovirus GI/GII	30	9.0
Plesiomonas shigelloides	8	2.4
Rotavirus A	8	2.4
Salmonella	7	2.1
Sapovirus	8	2.4
Shiga-like toxin *E. coli* (STEC) *stx1/stx2*	12	3.6
Shigella/Enteroinvasive *E. coli* (EIEC)	6	1.8
Vibrio cholerae	2	0.6
Vibrio parahaemolyticus	1	0.3
Yersinia enterocolitica	6	1.8

Summary of Safety and Performance

The summary of safety and performance section can be downloaded from the Eudamed website at the following location: **https://ec.europa.eu/tools/eudamed/#/screen/search-device**

Disposal

- Disposal of hazardous waste in compliance with local and national regulations. This also applies to unused products.
- Follow recommendations in the Safety Data Sheet (SDS).

Troubleshooting Guide

This troubleshooting guide may be helpful in solving any problems that may arise. For more information, see also the Frequently Asked Questions page at our Technical Support Center: **www.qiagen.com/FAQ/FAQList.aspx** (for contact information, visit **www.qiagen.com**).

Additional information about specific QIAstat-Dx Gastrointestinal Panel 2 error codes and messages can be found in Table 46:

Table 46. Information about specific QIAstat-Dx Gastrointestinal Panel 2 error codes and messages

Error Code	Error message displayed
0x02C9	
0x032D	
0x0459	
0x045A	Cartridge execution failure: Sample concentration too high. Please repeat by loading 100 microliters of the sample in a new cartridge (per IFU explanation).
0x04BF	
0x0524	
0x058B	
0x05E9	
0x0778	
0x077D	
0x14023	

When the sample concentration is too high and the test must be repeated by loading 100 µL, follow the workflow detailed in "Appendix C: Additional instructions for use" on page 168.

Symbols

The following symbols appear in the instructions for use or on the packaging and labeling:

Symbol	Symbol definition
	Contains reagents sufficient for <N> reactions
	Use by
	This product fulfills the requirements of the European Regulation 2017/746 for in vitro diagnostic medical devices.
	In vitro diagnostic medical device
	Catalog number
	Lot number
	Material number (i.e., component labeling)
	Global Trade Item Number
	Unique Device Identifier
	Contains

Symbol	Symbol definition
	Component
	Number
	Gastrointestinal application
Rn	R is for revision of the Instructions for Use and n is the revision number
	Temperature limitation
	Manufacturer
	Consult instructions for use downloadable from **resources.qiagen.com/674623**
	Protect from light
	Do not reuse
	Caution, consult accompanying documents

Symbol	Symbol definition
	Do not use if package is damaged
	Flammable, risk of fire
	Corrosive, risk of chemical burn
	Health Hazard, risk of sensitization, carcinogenicity
	Risk of harm
EC REP	Authorized representative in the European Community

Appendices

Appendix A: Installing the Assay Definition File

The Assay Definition File (ADF) of the QIAstat-Dx Gastrointestinal Panel 2 must be installed on the QIAstat-Dx Analyzer 1.0, QIAstat-Dx Analyzer 2.0, or QIAstat-Dx Rise prior to testing with QIAstat-Dx Gastrointestinal Panel 2 Cartridges.

Note: For QIAstat-Dx Rise, please contact Technical Service or your sales representative to upload new assay definition files.

Note: Whenever a new version of the QIAstat-Dx Gastrointestinal Panel 2 assay is released, the new QIAstat-Dx Gastrointestinal Panel 2 Assay Definition File must be installed prior to testing.

The Assay Definition File (.asy file type) is available at **www.qiagen.com**

The Assay Definition file (.asy file type) must be saved onto a USB Drive prior to installation on the QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0. This USB Drive must be formatted with a FAT32 file system.

To import an ADF from the USB to the QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0, proceed with the following steps:

1. Insert the USB stick containing the Assay Definition File into one of the USB ports on the QIAstat-Dx Analyzer 1.0 or QIAstat-Dx Analyzer 2.0.
2. Press **Options**, then **Assay Management**. The Assay Management screen will appear in the Content area of the display (Figure 55).

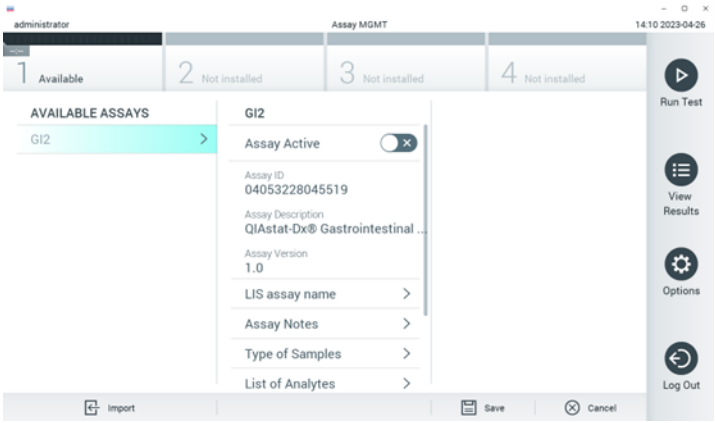


Figure 55. Assay Management screen.

3. Press **Import** in the bottom left of the screen (Figure 55).
4. Select the file corresponding to the assay to be imported from the USB drive.

   A dialog box will appear to confirm upload of the file.

   Note: In case a previous version is available, a dialog box will appear to override the current version by a new one. Press **Yes** to override.
5. To activate the assay, enable the **Assay Active** option (Figure 56).

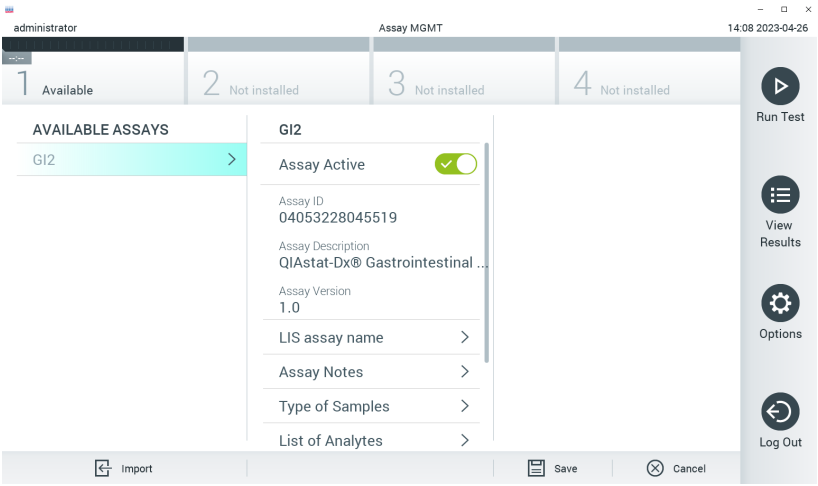


Figure 56. Activating the assay.

6. To assign the active assay to a user, perform these steps:
   a. Go to **Options** > **User Management**.
   b. Select the user who should be allowed to run the assay.

      Note: If needed, this step can be repeated for every user created in the system.
   c. Select **Assign Assays** from the User Options tab.
   d. Enable the assay, then press **Save** (Figure 57).

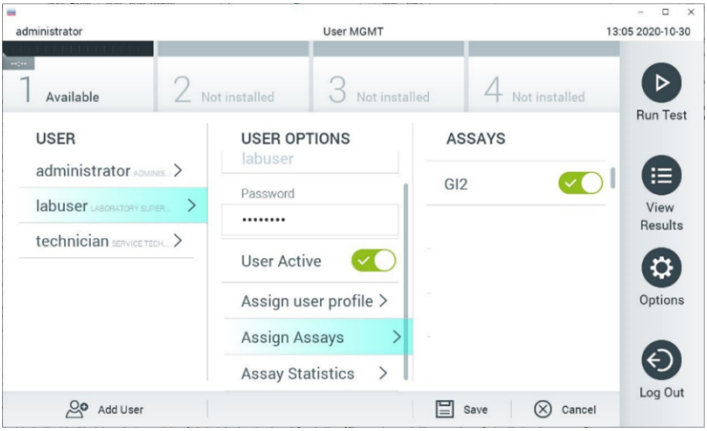


Figure 57. Assigning the active assay.

Appendix B: Glossary

Amplification curve: Graphical representation of the multiplex real-time RT-PCR amplification data.

Analytical Module (AM): The main QIAstat-Dx Analyzer 1.0 hardware module, in charge of executing tests on QIAstat-Dx Gastrointestinal Panel 2 Cartridges. It is controlled by the Operational Module. Several Analytical Modules can be connected to one Operational Module.

IUO: For investigational use only.

IFU: Instructions For Use.

Main port: In the QIAstat-Dx Gastrointestinal Panel 2 Cartridge, inlet for transport medium liquid samples.

Nucleic acids: Biopolymers, or small biomolecules composed of nucleotides, which are monomers made of three components: a 5-carbon sugar, a phosphate group, and a nitrogenous base.

Operational Module (OM): The dedicated QIAstat-Dx Analyzer 1.0 hardware that provides the user interface for 1–4 Analytical Modules (AM).

Operational Module PRO (OM PRO): The dedicated QIAstat-Dx Analyzer 2.0 hardware that provides the user interface for 1–4 Analytical Modules (AM).

PCR: Polymerase Chain Reaction.

QIAstat-Dx Analyzer 1.0: The QIAstat-Dx Analyzer 1.0 consists of an Operational Module and an Analytical Module. The Operational Module includes elements that provide

connectivity to the Analytical Module and enables user interaction with the QIAstat-Dx Analyzer 1.0. The Analytical Module contains the hardware and software for sample testing and analysis.

QIAstat-Dx Analyzer 2.0: The QIAstat-Dx Analyzer 2.0 consists of an Operational Module PRO and an Analytical Module. The Operational Module PRO includes elements that provide connectivity to the Analytical Module and enables user interaction with the QIAstat-Dx Analyzer 2.0. The Analytical Module contains the hardware and software for sample testing and analysis.

QIAstat-Dx Gastrointestinal Panel 2 Cartridge: A self-contained disposable plastic device with all pre-loaded reagents required for the complete execution of fully automated molecular assays for the detection of gastrointestinal pathogens.

QIAstat-Dx Rise: The QIAstat-Dx Rise Base is an in vitro diagnostic device for use with the QIAstat-Dx assays and QIAstat-Dx Analytical Modules, which provides full automation from sample preparation to real-time PCR detection for molecular applications. The system can be operated either in random access or batch testing, and the system throughput can be escalated up to 160 test/day by including up to 8 Analytical Modules. The system also includes a multi-test front drawer that can accomodate up to 16 tests at the same time, and a waste drawer to automatically discard the performed tests, enhancing the walk-away efficiency of the system.

RT: Reverse Transcription.

Swab port: In the QIAstat-Dx Gastrointestinal Panel 2 Cartridge, inlet for dry swabs. The swab port is not used for the QIAstat-Dx Gastrointestinal Panel 2 assay.

User: A person who operates the QIAstat-Dx Analyzer 1.0 / QIAstat-Dx Analyzer 2.0 / QIAstat-Dx Rise / QIAstat-Dx Gastrointestinal Panel 2 Cartridge in the intended way.

Appendix C: Additional instructions for use

In case cartridge execution failures corresponding to error codes (0x02C9, 0x032D, 0x0459, 0x045A, 0x04BF, 0x0524, 0x058B, 0x05E9, 0x0778, 0x077D, 0x14023) occur during the testing, the following error message will be displayed in the QIAstat-Dx Analyzer 1.0 or the QIAstat-Dx Analyzer 2.0 screen after the run has finalized.

> "Cartridge execution failure: Sample concentration too high. Please repeat by loading 100 microliters of the sample in a new cartridge (as per IFU explanation)."

In this case the test should be repeated using 100 µL of the same sample following equivalent testing procedures detailed in the "Procedure" Section in the IFU adapted to 100 µL sample input volume:

1. Open the package of a new QIAstat-Dx Gastrointestinal Panel 2 Cartridge using the tear notches on the sides of the packaging.
2. Remove the QIAstat-Dx Gastrointestinal Panel 2 Cartridge from the packaging.
3. Manually write the sample information, or place a sample information label, on the top of the QIAstat-Dx Gastrointestinal Panel 2 Cartridge. Make sure that the label is properly positioned and does not block the lid opening.
4. Place the QIAstat-Dx Gastrointestinal Panel 2 Cartridge flat on the clean work surface so that the bar code on the label faces upwards. Open the sample lid of the main port on the front of the QIAstat-Dx Gastrointestinal Panel 2 Cartridge.
5. Thoroughly mix the stool in the Cary-Blair transport medium, for example, by vigorously agitating the tube 3 times.
6. Open the tube with the sample to be tested. Use the supplied transfer pipette to draw up fluid. Draw the sample to the first fill line on the pipette (i.e., 100 µL).

Important: Do not draw air, mucus, or particles into the pipette. If air, mucus, or particles are drawn into the pipette, carefully expel the sample fluid in the pipette back into the sample tube and draw up fluid again.

7. Carefully transfer the sample into the main port of the QIAstat-Dx Gastrointestinal Panel 2 Cartridge using the supplied single-use transfer pipette.
8. Firmly close the lid of the main port until it clicks.
9. From this point, proceed following the instructions described in the IFU.

Ordering Information

Product	Contents	Cat. no.
QIAstat-Dx Gastrointestinal Panel 2	For 6 tests: 6 individually packaged QIAstat-Dx Gastrointestinal Panel 2 Cartridges and 6 individually packaged transfer pipettes.	691413
Related Products		
QIAstat-Dx Analyzer 1.0	1 QIAstat-Dx Analytical Module, 1 QIAstat-Dx Operational Module and related hardware and software to run molecular diagnostic QIAstat-Dx assay cartridges.	9002824
QIAstat-Dx Analyzer 2.0	1 QIAstat-Dx Analytical Module, 1 QIAstat-Dx Operational Module PRO and related hardware and software to run molecular diagnostic QIAstat-Dx assay cartridges.	9002828
QIAstat-Dx Rise	1 QIAstat-Dx Rise Base Module and related hardware and software to run molecular diagnostics on QIAstat-Dx assay cartridges.	9003163

For up-to-date licensing information and product-specific disclaimers, see the respective QIAGEN kit Instructions for Use. QIAGEN kit Instructions for Use are available at **www.qiagen.com** or can be requested from QIAGEN Technical Services or your local distributor.

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Document Revision History

Revision	Description
R1, October 2024	Initial release.
R1, November 2024	Inclusion of QIAstat-Dx Analyzer 2.0.

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